Study Title Phase 1 Pharmacokinetic Trial of Sofosbuvir/Velpatasvir in Pregnant Women with Chronic Hepatitis C Virus Infection

Consent Version V5.0, 02Dec2020 **Protocol Version** V5.0, 02Dec2020

NCT Number: NCT04382404

Document Date: 19Apr2022

CONSENT TO ACT AS A PARTICIPANT IN A RESEARCH STUDY

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Consent Version	V5.0, 02Dec2020	**Protocol Version**	V5.0, 02Dec2020
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Funding agencies	Gilead Sciences; National Institutes of Health; PA Department of Health		

********************************KEY INFORMATION************************************

You are being asked to take part in a research study. Participation is voluntary.

This research study involves evaluating a study medication for hepatitis C in pregnant women. The medication is a pill taken by mouth daily for 12 weeks; the pill contains two medications, Sofosbuvir and Velpatasvir (SOF/VEL for short). Although this medication is approved by the US Food and Drug Administration (FDA), it has not been studied in pregnant women.

Approximately 10 participants (and their infants once born) will take part in this study. All of the women (and infants) will be enrolled at UPMC Magee-Womens Hospital in Pittsburgh, PA.

If you are a pregnant woman with chronic hepatitis C and you join the study, you are consenting to enroll yourself and your baby after he/she is born. You will be in this study for approximately 7 months. Your infant will be in the study (once born) until he/she is about one year old.

There are a total of 7 scheduled maternal study visits. The Screen visit will help researchers determine if you are eligible. The Enroll visit is when study medication is started. The Follow-up visits include blood draws for safety testing and/or to see how much study medication is present in your blood. Some of the visits are longer in length (up to 13 hours) and will require you to stay at Magee all day.

Even if you decide to screen for the study, you are under no obligation to enroll even if you are eligible. You may also withdraw from the study at any time, for any reason.

There are risks associated with participation in any research study. There may be risks that are unknown and possibly life threatening. The table below outlines the most common risks.

Study procedure	Risk
Use of study medication (SOF/VEL)	• No studies in pregnant women

Study procedure	Risk
	• Dose may not be adequate in pregnancy and may lead to drug resistance to SOF/VEL, limiting the choice of effective treatments after pregnancy • Generally well tolerated in non-pregnant patients with the most common adverse reactions being headache, fatigue, nausea, muscle weakness, difficulty sleeping, rash and depression • If you previously had hepatitis B virus, it may become active again • Risk of taking with amiodarone (exclusion to participate) • Blood test abnormalities • Unknown if excreted in human breast milk
Blood draw and starting an IV	Bleeding, discomfort, dizziness, fainting, bruising, swelling, infection
HIV testing/positive results	Worry, sadness, depression
Participation in research	Inconvenient; breach of confidentiality
Use of PittBox® app and/or other electronic transmission of information	Breach of confidentiality from sending texts/videos; text and data rates may apply based on carrier
Risk to fetus	There is no data on use of SOF/VEL during pregnancy so the effects on a fetus/unborn child are not known. The drug may cross the placenta and get to the fetus/unborn infant.
Infant blood draw	In addition to above maternal risks, infant may cry and the procedure may be stressful to the mother

There may be no direct benefit to you for participating, but others may benefit in the future from information learned from this study.

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INTRODUCTION

Participating in a research study is not the same as getting regular medical care. The purpose of regular medical care is to improve your health. The purpose of a research study is to gather information. Being in this study does not replace your regular medical or prenatal care. Before deciding to participate in this study, we recommend that you talk with your regular, non-study physician or others to discuss taking SOF/VEL during pregnancy before you decide if you want to participate.

REASON FOR STUDY

Chronic hepatitis C is the most common cause of liver disease in the US and can cause problems in pregnancy with the possibility of passing hepatitis C to the infant, leading to health problems in the infant. The study drug, SOF/VEL, has been used to treat non-pregnant patients with hepatitis C with cure rates over 95% when taken for 12 weeks. SOF/VEL is approved by the Food and Drug Administration (FDA) for use in non-pregnant patients but is not FDA approved for use in pregnant women. The study medication is sofosbuvir/velpatasvir which is a pill containing both of these medications. It is taken by mouth, once a day for 12 weeks. This study will look at the drug levels of

a 12 week course of SOF/VEL when used in pregnant women diagnosed with chronic hepatitis C. The study will also look at the safety of the medication for both mom and infant.

PARTICIPATION

You have been asked to join this study because you are a pregnant woman, 18 to 39 years old, who has been diagnosed with chronic hepatitis C. To participate, you must be willing to give informed consent for you and your infant and follow the study procedures listed in this consent form. Your participation is voluntary. The study team members will explain the study to you and will answer any questions you might have. Your regular doctor may be part of this study team. You should take your time to make your decision and discuss with others if needed.

You cannot take part in this study if you have received another experimental drug/device within 60 days prior to this study or plan to receive any other experimental medicine during your participation in this study. You may not qualify if you have had a positive urine drug screen, you have already been treated for hepatitis C with similar medication, or you have certain health conditions. There may be other reasons why you cannot participate in the study. Study staff will review these with you.

As part of the study, you allow researchers to access, review and print your medical/prenatal records and associated testing, including urine drug screening, for study purposes throughout the study.

STUDY DETAILS FOR MATERNAL VISITS: The specific procedures for each visit are summarized in the table and provided in more detail following the table.

	Screen	Enroll	Follow-up Visits						
	V1	V2	V3	V3a	V4	V5	V5a	V6	V7
Timing (GA = weeks of gestation)	GA: 14+0 to 22+6	GA: 23+0 to 25+6	3 wks after first dose	24 hrs after V3 dose	6 wks after first dose	9 wks after first dose	24 hrs after V5 dose	Within 7 d of completion	12 wks after completion
Length of Visit	2 hrs	1 hr	13 hrs	0.5 hrs	1 hr	13 hrs	0.5 hrs	0.75 hrs	0.75 hrs
Informed consent	x								
Med record release	x								
Med record review	x	x	x		x	x		x	x
Contact information	x	x	x		x	x		x	x
Visit questionnaire	x	x	x	x	x	x	x	x	x
Medical history	x	x	x		x	x		x	x
Medication review	x	x	x		x	x		x	x
Blood sample(s)	x	x	x		x	x		x	x
Safety labs*	x		x		x				x
HIV,Hep B & C*	x								
Hep C viral load*	x	x	x		x	x		x	x
Study med levels			x	x	x	x	x		
Study med use		x	x		x	x			
Study med log		x	x		x	x			
PittBox® app		x	x		x	x			
Physical exam	x	x	x		x	x		x	x
Fetal heart tones	x	x	x		x	x		^	^
Visit payment	$50	$50	$250	$100	$50	$250	$100	$20	$50

x Required procedure ^ As necessary procedure *The results of these tests will be given to you

In addition to the above visits, you will also be seen during delivery admission to collect your blood and cord blood. A questionnaire will be completed and your medical records will be reviewed. You will receive $50 for notifying the staff you are being admitted and $50 for maternal visit procedures.

V1: SCREENING VISIT (an opportunity for you to decide if you want to join the study and for researchers to make sure you are eligible)

- Collect your information (i.e. age, race, ethnicity), where you live and how to best get in contact with you (i.e. phone number, email, alternate contacts).
- Visit questionnaire, including your medical and social history, sexual history, pregnancy history, medication use including prescribed and over-the- counter medication.
- HIV testing including pre- and post-test counseling.
- Physical exam (i.e. height, weight, listen to your heart and lungs, measure and feel your belly, listen to fetal heart tones) including your vital signs (heart rate, blood pressure, respirations, temperature).
- Confirm gestational age by reviewing your prenatal records, including ultrasound reports.
- Blood draw, approx. 7 teaspoons to test blood count, liver and kidney functions, clotting test, HIV, hepatitis C viral load (amount of virus in your blood), hepatitis C type, and Hepatitis B. In the event that you had a HCV genotype test performed within the past 3 months and that result is available to the study staff at the time of screening, approximately 1 less teaspoon of blood will need to be drawn.
- At this visit or any time before V2, a trained interviewer from the Qual EASE team (CHRC Data Center, University of Pittsburgh) will conduct an in depth interview/questionnaire with you to ask questions about Hepatitis C infection including risks of transmission, treatment and participation in research. This interview may be conducted virtually over an approved platform (i.e. Zoom, Microsoft Teams, Google) and may be recorded until the answers are transcribed into written form. The recording will be destroyed once the written copy is complete.
- Screening tests may be repeated. For instance, if the value is out of range or low normal and physician investigators feel it is reasonable to repeat for eligibility, you may be asked to return to have the test(s) repeated.

V2: ENROLLMENT VISIT (if you are found eligible)

- Confirm that you would still like to participate.
- Review and update contact information.
    - You will be asked your preference for being contacted throughout your participation. The study staff may contact you for things such as study medication reminders, appointment reminders, etc. You will be able to discuss which options for communication you prefer and how often you prefer to receive the notifications.
- Visit questionnaire, including review of medical and social history, sexual history, prenatal care and medication use since the last visit.
    - If you take anti-acids, you will be instructed when to take your anti-acid medication to prevent it from interacting with the study medication.
- Remind you of importance of following study procedures.
- Blood draw (approximately 1 teaspoon) for hepatitis C viral load (amount of virus in blood).
- Repeat a physical exam (same as at the Screening Visit).
- Provide study medication to last through the next study visit.

- Review study medication instructions and provide paper study medication log.
- You will be asked to return any unused medication and the log at your next visit.
- If you agree, you will be asked to download the PittBox® app on your smartphone to track the day/time you take your study medication at home. This app basically takes a video of you taking your medication and records the date and time. Texting and data rates may apply.

- Schedule your next study visit.
- Provide you with researcher's contact information.

V3, V4, V5: VISITS TO COLLECT BLOOD SAMPLES FOR STUDY DRUG LEVELS

These three visits will be scheduled from your first dose of study medication.

- **At V3 and V5, you will be instructed NOT take your home dose of study medication on the morning of each of these visits**. These visits will each be approximately 13 hours in duration. You should plan to stay at Magee in the Clinical Translational Research Center (CTRC) all day. You will not be permitted to leave, unless you have a scheduled appointment at Magee.
- V4 will be approximately one hour in duration.
  - You will have a single blood sample collected for study medication levels.
- Contact information will be reviewed/updated as necessary.
- Visit questionnaire, to include review/update of medical history, medication use, sexual history, prenatal visits, medication use and documentation of any new issues/concerns.
- You will have approximately 1 teaspoon of blood collected at each visit for viral load.
- You will be asked to return your study medication bottle and completed study medication log so that staff can review and collect them. PittBox® videos will be reviewed, as applicable
- You will be asked questions about study medication compliance and will be counseled regarding the importance of following study medication instructions.
- You will be instructed to call study staff when you are in labor/being admitted to labor and delivery so study staff can see you during your stay.
- Brief physical exam (i.e. heart, lungs, and targeted assessment based on any symptoms you may be having), including vital signs, weight and fetal heart tones.
- V3 and V5
  - You will have an IV (catheter inserted into a vein) placed so that the blood samples throughout the day can be collected from the IV. A small amount of fluid (i.e. saline solution) will drip through the IV to attempt to keep the IV open during the study visit. It is possible that the IV may fail. A new IV may need to be placed or individual blood draws/sticks may be needed to collect the remaining samples.
  - A blood sample will be collected prior to taking the study medication to check the amount of study medication in your blood (less than one teaspoon).
  - You will be asked not to eat for 10 hours prior to your visit. You may drink water.
  - Breakfast will be provided to you in the clinic that has a certain calorie and fat content. You will take your dose of study medication during this breakfast or within 5 minutes of finishing it. You will be asked to drink water with your study medication.
  - The time you take your dose will be documented.
  - Blood samples (less than 1 teaspoon) will be collected throughout the day at the following times: ½ hour, 1, 2, 3, 4, 5, 8 and 12 hours after taking study medication.
  - Additional blood will be collected at the 2 hour collection (for a total of 2 teaspoons) to check the amount of protein in your blood.

- Because of the length of these visits, two additional meals will be provided to you during the visit.
- You will be asked to return to the study office 24 hours after the dose of medication was administered to you during V3 and V5. These will be considered V3a and V5a. A short questionnaire will be asked and approximately 1 teaspoon of blood will be collected.

- V3 and V4
  - You will have additional blood tubes (approximately 3 teaspoons) collected to check the health of your blood (including blood clotting tests), liver and kidney functions. If there are significant changes in your laboratory results and the study doctor thinks it is unsafe to continue, the study doctor may repeat the blood test and/or decide that you have to stop taking the study medication. If you have significant amount of hepatitis C virus present in your blood at V3, you will be asked to return for an additional blood sample for hepatitis C resistance testing (testing to see if the hepatitis virus has become resistant or non-responsive to the study medication).
- You will be provided with more study medication to last you through your next scheduled visit (or through a 12 week course of study medication) and a new study medication log will be given to you to document the date/time of your doses along with a reminder to use PittBox® if you agree. You will be asked to return any unused study medication and your completed log at your next visit.
- You will be reminded about the importance of study procedures, how to take your study medication and to call staff when you are in labor.

V6: END OF TREATMENT VISIT

This visit will be approximately 45 minutes and will include the following:

- You will be asked to return to the clinic within a week of completing 12 weeks of study drug. This visit may occur before or after delivery.
- You will be asked to return any unused study medication and your study medication log.
- Study staff will review and update your contact information
- Visit questionnaire to update medical history, medication use and any new issues/concerns.
- Brief physical exam (i.e. heart, lungs, and targeted assessment based on any symptoms you may be having), including vital signs, weight and fetal heart tones, if applicable.
- Blood draw for hepatitis C viral load (about 1 teaspoon).
- You will be counseled about the importance of following all study procedures.
- At this visit or any time before V7, a trained interviewer from the Qual EASE team (CHRC Data Center, University of Pittsburgh) will conduct an additional in depth interview/questionnaire with you to ask questions about Hepatitis C infection including risks of transmission, treatment and participation in research. This interview may be conducted virtually over an approved platform (i.e. Zoom, Microsoft Teams, Google) and may be recorded until the answers are transcribed into written form. The recording will be destroyed once the written copy is complete.

DELIVERY VISIT

You will be reminded throughout your study visits to call the study staff when you are in labor or are being admitted to labor and delivery so that study staff can arrange the following:

- A maternal blood sample for hepatitis C viral load (about 1 teaspoon)
- Collect blood (for hepatitis C viral load) from the umbilical cord after the cord has been cut.
- Review and update your contact information
- Visit questionnaire, including changes in medical history, medication use or new issues/concerns. If available, this information may be taken from your medical record.
- Brief physical exam, including vital signs and weight. Alternately, this information can be taken from your labor and delivery records.
- Review your medical records and your infant's medical records from delivery to obtain information needed for the study (type of delivery, medications, weight, length, head measurements, etc.). A copy of your (and your infant's) delivery records may be printed and filed in your research record.
- Remind you about the importance of following all study procedures.
- Remind you to take the rest of the study medication if you are still taking it.
- Dispense study medication (as applicable) to complete the 12 week course of study medication.
- If you are still on study medication at the time of delivery, study staff will collect a blood sample from you and an additional sample of cord blood to test the amount of study medicine and protein present.
- If you plan to breastfeed and you are still on study medication, you will be asked to stop taking study medication and will have blood collected for hepatitis C resistance testing (about ½ teaspoon).

* If you deliver outside of UPMC Magee-Womens Hospital the blood samples and cord blood will not be collected, however, you will still be instructed to call the study office when you are admitted to the hospital and you will be asked to sign a medical release, as necessary, to obtain your delivery information.

V7: POST-PARTUM VISIT

This study visit could occur/be scheduled at the same time as the 1st infant follow-up visit listed below (iV1) as long as it has been 12 weeks from the time you took your last dose of study medication.

This visit includes:

- Review and update contact information.
- Visit questionnaire including review of medical history, medication use and any new issues/concerns.
- Reminder of importance of infant study visits/procedures.
- Brief physical exam, including vital signs and weight.
- Blood draw to check health of your blood, liver and kidney function, clotting test and hepatitis C viral load testing (for a total of 3 teaspoons).
- This will be the last scheduled visit for you unless you have any ongoing side effects that the study staff need to follow.

Early Withdrawal Visit

If you (or your infant if applicable) leave the study early, you will be asked to come back for an early withdrawal visit. At that visit, the following will be done:

- You will be asked about your (and your infant's) current health, including any reactions or illnesses you may have had.
- Any unused study medication and your study drug log will be collected from you.
- You will be asked about any medicines you have taken since your last visit.
- You may have a brief physical examination, if indicated.
- You may have your vital signs taken.
- You will have a blood sample collected for drug levels, resistance testing since you did not complete 12 weeks of LDV/SOF, and possibly hepatitis C viral load (about 2 ½ teaspoons). You may also have blood tests drawn to check the health of your blood (less than 1 teaspoon).

You will be asked to continue the remaining scheduled maternal and infant visits for safety.

HIV Testing

- As part of the screening process for this study your blood will be tested for infectious diseases including HIV (the virus that causes AIDS). All information will be handled in compliance with the Pennsylvania law on HIV-related confidential information. You do not have to take part in this testing, however if you refuse you will not be able to participate in this study. Counseling is available to you before you make the decision to participate in this testing. Once you have the test performed it is a requirement that you be informed of the results if they are positive. If you test positive for HIV you will be referred by the study team for appropriate medical care and you will be excluded from this study. Pennsylvania state regulations require study staff to report the names of people who test positive for HIV and other infections passed during sex to the Allegheny County Health Department (ACHD). Outreach workers from ACHD may then contact you about informing your partners, since they also should be tested. If you do not want to inform your partners yourself, the outreach workers will contact them, according to the confidentiality guidelines of ACHD.
- A positive HIV test means that your blood sample tested positive for HIV and that repeat testing will be performed to confirm (prove) this finding. If your sample is proven to be positive for HIV, it means that you are a carrier of HIV. It also means that you can pass the virus to others by intimate sexual contact, by sharing needles, and through donating blood and organs. A negative HIV test means that at this time, no antibody to HIV was found in your blood sample based on the result of the initial screening test, repeat screening tests, or a confirmatory test.
- There can be individuals who have HIV test results that are called "false positive," that is, for some reason, the test indicates that HIV antibodies are present in the blood when they are not. There can also be false negative results which can have two possible meanings; the person has been infected with HIV, but that person's body has not yet made antibodies to the virus, or HIV antibody is present in the person's blood, but for some reason the test failed to detect it.
- You may ask the study physician for more information on HIV testing prior to having this test performed.
- You may have repeat HIV testing done as indicated throughout the study (i.e. based on risk factors, concerns of exposure, symptoms).

STUDY DETAILS FOR INFANT VISITS

Your infant will be seen 4 times over the course of a year: at delivery (if delivered at UPMC Magee-Womens Hospital), approximately 8 weeks, 6 months and one year. The table below includes the procedures performed at each visit, with more details following the table.

Scheduled infant study visits

	iV1	iV2	iV3
Infant age at visit	Approx. 8 wks	Approx. 6 mos	Approx. 12 mos
Contact info	x	x	x
Demographic info	x		
Medical release	x	^	^
Medical history	x	x	x
Medication use	x	x	x
Physical exam	x	x	x
Development exam		x	x
Collect blood (Hep C)*	x	x	^
Visit payment	$50	$50	$50

x Required procedure ^ As necessary procedure *The results of these tests will be given to you

In addition to the above scheduled infant study visits, your infant will also be seen during delivery admission (if at UPMC Magee-Womens Hospital) to perform a physical exam by a study pediatrician or delegate and to review your infant's medical records. The infant delivery visit payment is $50.

At each study visit, the following will occur:

- Contact information will be reviewed and updated
- Your infant's demographic information (i.e. sex, date of birth, race, ethnicity) will be collected
- You will be asked to sign a medical record release so that researchers can get records from your infant's pediatrician and other healthcare providers as necessary. Records will be reviewed and information needed will be abstracted (i.e. medications, illnesses). Copies of the records will be placed in the research record.
- Your infant's medical history and medication use will be reviewed/collected from the medical record, including review and documentation of any new issues or concerns since the last visit
- Growth will be assessed/collected from the medical record (i.e. weight, length, head circumference)
- An age appropriate physical exam, including vital signs, will be performed or the information will be collected from the medical record (i.e. delivery record)
- At 6 months and 1 year, a developmental examination will be performed by a qualified examiner to test how your baby is developing. The findings of this examination will be shared with you and if there are any concerns regarding the examination, the examiner may talk to your pediatrician and/or refer your infant for additional evaluation/intervention as needed.
- A blood sample of approximately 1 teaspoon will be collected for hepatitis C testing at each visit. After two negative hepatitis C results, no further blood draws will be needed from the infant for this study (for example, if the 8 week blood sample and 6 month blood sample are negative, no blood will need to be drawn at the infant's 12 month visit). If at any time the infant's hepatitis C test is positive, an additional ½ teaspoon will be collected for resistance testing. At the delivery visit, the sample will be collected from the umbilical cord as described above. If the cord blood cannot be obtained, a blood sample may be collected from your infant. A trained professional will draw blood from an accessible vein at each study visit

required. In the event that a sample cannot be obtained from your infant at any visit, researchers may request results from routine/standard testing performed by your infant's pediatrician.

Unscheduled Visits

Unscheduled visits for you/your infant may occur at any time during the study, for instance if you are having side effects, you have concerns, or to follow up on an abnormal test result. At those visits, study procedures may be repeated as clinically indicated. For example:

- You may be asked about current health, including any reactions or illnesses.
- You may be asked about any drugs or medicines taken since last visit.
- A brief physical examination may be performed, if indicated, including vital signs.
- Additional testing (i.e. blood tests for low hemoglobin or other out of range laboratory tests that may have significance to your care) may be done as determined by the investigators.

At any time during the study you have an increase in viral load (the amount of hepatitis C virus in your blood) or if you do not complete the 12 week course of study medication or if deemed clinically indicated by a physician investigator, you may have an additional blood sample collected for hepatitis C resistance testing (less than 1 teaspoon).

WITHDRAWING FROM THE STUDY

You (or your child if applicable) may stop taking part in this study at any time, for any reason; you can also withdraw your authorization for us to use your identifiable medical information for the purposes described above. This means that you will also be withdrawn from further participation in this research study. Any identifiable research or medical information obtained as part of this study prior to the date that you withdrew your consent will continue to be used and disclosed by the investigators for the purposes described above. Your decision to withdraw from this study will have no effect on your current or future relationship with the University of Pittsburgh or UPMC.

If you decide to stop participating in the study, we encourage you to talk with the study doctor and your regular doctor first and continue with any safety follow-up, including resistance testing if you did not complete 12 full weeks of study medication.

The study doctor or sponsor may decide to stop you (or your child if applicable) from taking part in this study at any time. You (or your child if applicable) could be removed from the study for reasons related only to you (for example, if you move to another city or if you have a bad reaction to the study medication) or because the entire study is stopped. The sponsor, the study doctor or Institutional Review Board may stop the study at any time.

LAB TESTING OF SAMPLES

Some of the blood collected from you will be used for research tests to determine the amount of study drug in these samples. The results of these blood tests are useful only for research purposes and will not be available to you or your health care provider. These specimens will be sent to an outside testing laboratory. The specimens will not be labeled by your name or other identifying information but rather by a unique study identifier. Personnel at the testing laboratory will not know your identity.

Blood samples to test the health of your blood, liver and kidney function, HIV, HCV testing, etc. will be sent to the clinical lab associated with Magee. They will also be sent by your study number,however the results of these tests will be given to you. At screening, abnormal test results, including hepatitis B and HIV tests, could prevent you from participating. If abnormal labs are identified during the course of the study, they may be repeated as clinically appropriate and/or you may be referred to your own doctor for additional evaluations.

If you test positive for hepatitis B virus or HIV, the Commonwealth of Pennsylvania requires that your name be given to the Allegheny County Health Department.

PROTECTION OF CONFIDENTIALITY AND PERSONAL HEALTH INFORMATION

We are requesting your authorization or permission to review your medical records to determine whether you meet the conditions for participation in this study, to compare your earlier test results to the findings from this study, and if possible, to use your previous exam/test results in place of, or in addition to, some of the exams/tests needed for this study. We will obtain information such as confirmation of your diagnosis, age, past medical history, diagnostic procedures (i.e. scans or liver biopsies), and results of any blood tests and urine drug screens done throughout your prenatal care. In addition, if you join the study and you have a test/procedure done for routine care on the same day as a study appointment, the results of the test/procedure may be used instead of repeating the same test/procedure at the study appointment (i.e. fetal heart tones, vital signs, blood work). Researchers would review the results of tests done as part of your prenatal care, including urine drug screens and may print a copy of prenatal visits and tests for your research record.

This identifiable medical record information will be made available to members of the research team for an indefinite period of time. Your and your infant's medical information, as well as information obtained during this research study, may be shared with other groups, possibly including authorized officials from the Food and Drug Administration, Gilead Sciences, the National Institutes of Health, and the University of Pittsburgh Office of Research Protections, for the purpose of monitoring the study. Authorized representatives of UPMC or affiliated health care providers may also have access to this information to provide services and address billing and operational issues. Results from this research may also be shared with other investigators, however this information will be de-identified.

As part of this research study, some information that we obtain from you may be placed into your or your infant's medical records held at UPMC, including a note indicating that you are involved in this study.

To protect your and your infant's confidentiality we will use a number instead of your or your infant's name on all the forms for the study, and we will store your and your infant's data in password protected files located on secure computers. If information from this study is shown publicly or published in a journal, we will not mention your or your infant's name, or anything else that could identify you or your infant.

We will make every attempt to protect the privacy and the confidentiality of your and your infant's records, as described in this document, but cannot guarantee the confidentiality of your or your infant's research records, including information obtained from your and your infant's medical records once your and your infant's personal information is disclosed to others outside UPMC or the University. This authorization is valid for an indefinite period of time. However, you can always

withdraw your authorization to allow the research team to review your or your infant's medical records by contacting the investigator listed on the first page and making the request in writing. If you do so, you or your infant will no longer be permitted to participate in this study. Any information obtained from you or your infant up to that point will continue to be used by the research team.

By signing this form, you consent to participate in this research study and provide your authorization to share your medical records/your infant's medical records with the research team.

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

Your data or specimens used in this research study may contribute to a new discovery or treatment. In some instances, these discoveries or treatments may be of commercial value and may be sold, patented, or licensed by the investigators and the University of Pittsburgh for use in other research or the development of new products. You will not retain any property rights, nor will you share in any money that the investigators, the University of Pittsburgh, or outside agencies may receive.

Per University of Pittsburgh policy all research records must be maintained for at least 7 years following final reporting or publication of a project. For projects involving children, records must be maintained for 5 years past age of majority (age 23 per PA State law) after study participation ends. In unusual cases, the investigators may be required to release your identifiable research information (which may include your identifiable medical record information) in response to an order from a court of law. If the investigators learn that you or someone with whom you are involved is in serious danger or potential harm, they will need to inform the appropriate agencies, as required by Pennsylvania law.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings;) if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

RISKS AND DISCOMFORTS FROM TAKING PART IN THIS STUDY

As with any research study, there may be adverse events or side effects for you and/or your fetus/infant that are currently unknown and certain of these unknown risks could be permanent, severe or life-threatening.

There are no studies of SOF/VEL in pregnant women. There have been animal studies of SOF/VEL in pregnant rats and rabbits. [VEL studies in animals: no effects on fetal development have been observed in rats and rabbits at the highest doses tested. SOF studies in animals: no effects on fetal development have been observed in rats and rabbits at the highest doses tested]. In our previous study where 9 pregnant women were successfully treated with ledipasvir (a medicine that is similar to VEL) and SOF, there were no problems with the baby after in utero exposure. However, animal reproduction studies do not always predict how humans will respond to the medications.

It is also not known whether SOF/VEL is present in human breast milk, so if you deliver your infant and you have not completed 12 weeks of study medication, you will be asked to stop the study medication and have hepatitis C resistance testing done.

There is a risk that the hepatitis virus may become resistant to SOF/VEL because the dose used in this study may not be adequate for treating pregnant women with hepatitis C or if a woman does not complete the entire 12 weeks of study medication. If resistance occurs, this may limit the choices for effective therapy after pregnancy for you and possibly your infant. It is not known whether this study medication will be effective in treating hepatitis C. Since hepatitis C can be passed through sex, you should use protection (i.e. condoms) every time you have sex to avoid passing hepatitis C to your sexual partner(s).

MATERNAL RISKS:
The following side effects have been associated with the use of oral SOF/VEL used daily for 12 weeks of duration in 1035 men and non-pregnant women participating in other clinical studies.

	Percentage of Participants N = 1035
Headache	22%
Fatigue	15%
Nausea	9%
Asthenia (decreased muscle strength)	5%
Insomnia (difficulty sleeping)	5%
Rash	2%
Depression	1%

Changes (increases) in kidney, liver and pancreas function tests have been seen with use of SOF/VEL in other clinical studies. Baseline laboratory blood tests will be done as part of screening for this study to be sure the results are acceptable prior to starting study medication. The lab tests will be repeated during the study to be sure there are no unsafe changes with use of the study medication. Increases in any of these tests could result in repeat testing or stopping the study medication if the study doctors feel continuing the study medication would be unsafe for you or your fetus/infant.

There are known drug interactions with SOF/VEL and other prescription and non-prescription medications, so it is important you tell the study team about all medications you are taking, even over-the-counter and herbal medications (i.e. carbamazepine, St. John's wort). This information will

help investigators determine if you are eligible to participate and/or will allow investigators to provide you with specific instructions about timing of your medication.

There is a risk of Hepatitis B virus (HBV) reactivation (coming back) while receiving treatment for HCV in patients who are co-infected with HBV and HCV. HBV reactivation has been reported, in some cases resulting in fulminant hepatitis (severe and sudden start of disease), hepatic failure and death. You will be tested during your screening visit to determine your HBV status.

Drawing blood or starting an IV may lead to excessive bleeding, discomfort, feelings of dizziness or faintness, and/or bruising, swelling and/or infection.

Disclosure of HIV or HCV status may cause worry, sadness or depression. Disclosure of HIV or HCV-positive status has been associated with depression, suicidal ideation, and denial as well as social isolation. Trained counselors will be available to help participants deal with these feelings.

Participation in clinical research includes the risks of confidentiality loss.

INFANT RISKS:
Risk to the fetus/infant: There is not data on use in pregnant women with this medication, so the effects on a fetus/unborn child are not known. The study medication may cross your placenta and get to your fetus/unborn infant exposing your fetus to the study medication. Since there are no studies with this medication in pregnancy, it is not known whether the study drug is safe for unborn human babies. Therefore, it is not known whether unborn babies whose mothers take SOF/VEL will develop normally or will have side effects of the drug.

Infant blood draws: Obtaining blood samples from your infant may cause your infant to cry, may cause bleeding, bruising or a clot. It may be distressful to you to watch your baby have his/her blood drawn.

GENERAL RISKS:
You will be asked to provide personal/protected health information (PHI). All attempts will be made to keep your and your infant's PHI confidential within the limits of the law. However, there is a chance that unauthorized persons will see your or your infant's PHI. All paper records will be kept in a locked file cabinet or maintained in a locked room at Magee. Electronic files will be password protected. Only people who are involved in the conduct, oversight, monitoring, or auditing of this study will be allowed access to the PHI that is collected. Any publications from this study will not use information that will identify participants by name. Organizations that may inspect and/or copy research records maintained at the participating sites for quality assurance and data analysis include groups such as the National Institute of Health (NIH) or its designee and the US Food and Drug Administration (FDA).

If at any time during the study the staff learns of possible child abuse and/or neglect or a risk of harm to you or others, they will be required to tell the proper authorities.

BENEFITS TO TAKING PART IN THIS STUDY

This study is a safety study of use of SOF/VEL in pregnancy and as such the study medication may not treat HCV in pregnancy as it may not be the correct dose. You may find some benefit in the generalizable knowledge of this study in pregnant women with chronic hepatitis C or in the follow up of your child (i.e. developmental exams). Participants and others may benefit in the future from information learned from this study. Specifically, information learned in this study may lead to evidence based guidance for the treatment of chronic hepatitis C infection in pregnancy and prevention of perinatal hepatitis C transmission.

ALTERNATE CHOICES TO PARTICIPATION

You do not have to take part in this study. You may choose to use this same medication (SOF/VEL) outside of a study after your pregnancy to treat hepatitis C as this medication is marketed for use outside of pregnancy and may be obtainable without participating in this study. However, there may be risks to mothers who have chronic Hepatitis C and their unborn baby if pregnant women are not treated for hepatitis C. If you choose to take part in this study, it is recommended that you discuss participation with your regular doctor to see if you should receive treatment for hepatitis C during pregnancy or wait to receive treatment after you are no longer pregnant.

COST

There will be no costs to you for being in this study and there are no anticipated expenses related to your participation. You will not have to pay to receive the study medication in this study. There are no costs for the physical examinations, laboratory testing, or clinic visits. They will be included as part of the study. During the study, should you test positive for HIV or HBV, you would be responsible for the cost of your evaluation and treatment.

STUDY PAYMENT FOR PARTICIPATION

There is no cost to you to participate. You will receive the payments as listed in the tables above for each visit/procedure that is completed.
In addition to the payments listed in the table, you will receive an additional $50 for each In-depth interview (IDI) completed. These are scheduled to be performed at two time points in the study: Screening (prior to V2) and V6 (prior to V7).

You will also be reimbursed an additional $200 at the completion of the one year infant visit if all your and your infant visits have been completed within the specified window period. Transportation assistance may be provided as needed (estimated $5 value). If necessary, the study staff may make arrangements for a paid overnight stay in order to attend certain study visits (i.e. V3a and V5a).

You will also be reimbursed (up to four times) for using the PittBox app to collect/send videos of yourself taking the study medication. The following payment schedule will be used:
Completion of:
100% of videos: $20
75-99% of videos: $15
50-74% of videos: $10
1-49% of videos: $5

Since you are being compensated for your participation in this study, your name, address, and social security number will be released to the Accounting Office. Your study payments will be loaded onto a UPMC cash card at the completion of each visit. If the total reimbursement for your participation in

research is greater than $600 in a year, this will be reported to the Internal Revenue Service (IRS) as income.

RIGHT TO WITHDRAW

Your and your infant's participation in this study is voluntary. You and your infant do not have to take part in this research. You are free to withdraw your and your infant's consent at any time. Refusal to take part or to stop taking part in the study will involve no penalty or loss of benefits to which you or your infant are otherwise entitled. If you decide to stop taking part, or if you have questions, concerns, or complaints, or if you need to report a medical injury related to the research, please contact the investigator (study doctor), Dr. Catherine Chappell, and/or research staff at 412-641-4242 during the day or 412-463-1337 during the day and after hours.

If you withdraw yourself or your infant from this study, already collected data may not be removed from the study database. You will be asked whether the investigator can collect data from your or your infant's routine medical care. If you agree, this data will be handled the same as research data.

You will be told of any significant new findings which develop during the study which may affect your willingness for you or your infant to participate in the study. You may be asked to sign a revised consent form if this occurs.

REMOVAL FROM THE STUDY

Investigators (study doctors), the Institutional Review Board (a committee at the University of Pittsburgh charged with protecting the safety and rights of people taking part in research studies), Gilead Sciences or the NIH (National Institutes of Health) can remove you or your infant from the research study without your approval. You or your infant could be removed from the study/study medication for any of the following reasons:

- Reasons related only to you (for example, if you move to another city, if you do not agree to take your study medication as instructed, if you fail to follow instructions of the research staff, or if you have a serious reaction to your study medication).
- Because the entire study is stopped (the sponsor, FDA, or Institutional Review Board [IRB] may stop the study at any time),
- You have significant abnormal laboratory findings including liver function tests and hepatitis viral load tests
- You deliver your baby while on study medication and intend to breastfeed
- If you do not later consent to any future changes that may be made in the study plan
- If the investigators or the IRB decides that the research study is no longer in your best interest.

If you decide to stop participating in the study, or if your participation is ended, the study doctor or study staff may ask you some questions about being in the study. Any time a participant is permanently discontinued from study medication you will be asked to complete the procedures listed under the Early Termination visit described above.

RESEARCH-RELATED INJURY

If you believe that participating in this study has resulted in an injury to you, immediately contact the Principal Investigator who is listed on the first page of this form. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you

by the hospitals of UPMC. Your insurance provider may be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care. At this time, there is no plan for any additional financial compensation.

PROBLEMS OR QUESTIONS
If you have any questions about your rights as a research subject or wish to talk to someone other the research team, please call the University of Pittsburgh Human Subjects Protection Advocate toll-free at 866-212-2668.

VOLUNTARY PARTICIPATION
Your participation in this research study is entirely voluntary. You may want to discuss this study with your family and friends and your personal physician before agreeing to participate. If there are any words you do not understand, feel free to ask us. The investigators will be available to answer your current and future questions.

Whether or not you provide your or your infant's consent for participation in this research study will have no effect on your or your infant's current or future relationship with the University of Pittsburgh. Whether or not you provide your consent for your or your infant's participation in this research study will have no effect on your or your infant's current or future medical care at a UPMC hospital or affiliated health care provider or your or your infant's current or future relationship with a health care insurance provider.

BLOOD SAMPLES AFTER THE END OF THE STUDY
After the study tests are done, we would like your permission to keep any remaining samples from you or your infant to use in possible future research studies. These future studies may test for reasons that the drug concentrations are different in pregnancy or the way that hepatitis C or hepatitis C treatment affects pregnancy. No human genetic tests will be performed on your or your infant's samples. Your and your infant's samples will be labeled only by a unique study code and will not be labeled with your or your infant's name or initials. These coded samples may be shared with other investigators at other institutions.

If these stored samples are tested in the future, no identifying information will be used in the reporting or publication of any results. The results of any future testing will be kept confidential in the same way as the results of testing done for this study. Results from this future research will not be reported to you or your or your infant's doctor.

Your or your infant's samples might be used in new or different laboratory tests, to provide information for the development of treatment of hepatitis C in pregnancy. All samples will be used only for research purposes. Samples obtained in this study may result in the development of a product that could be patented or licensed. There are no plans to provide financial compensation to you or your infant should this occur. No samples will be used to generate a cell line for genetic testing.

There are no benefits to you or your infant in the collection, storage, and future research use of specimens. You do not have to agree to this storage and future testing in order to be in the study. You will be able to decide whether or not you agree to the storage and future testing for your and

your infant's specimens below. If you choose for them to be stored, they can either remain with your or your infant's code number or with that number removed. You may change your mind at any time by writing to the study doctor. If some of your or your infant's samples have already been tested, the information from this research will still be used.

If you decide not to allow part of your or your infant's samples to be stored and tested in the future, your or your infant's samples will be destroyed at the end of this study. Your decision about your or your infant's samples will not affect your or your infant's participation in this study or other studies or your or your infant's medical care.

MATERNAL SAMPLE (BLOOD) STORAGE AND FUTURE TESTING **Please initial next to your choice:**

_____ Yes, I agree to allow my *coded* samples to be stored and tested in the future. My blood may be used in new or different laboratory tests, to provide information for understanding hepatitis C infection and use of SOF/VEL during pregnancy. If I decide later to cancel my consent to storage and future testing, I will write a letter to the study doctor at the address listed on page 1 of this form.

_____ No, I DO NOT agree to allow my samples to be stored and tested in the future. My decision will not affect my ability to participate in the study. Leftover samples collected for this study will be destroyed at the end of this study.

INFANT SAMPLE (BLOOD) STORAGE AND FUTURE TESTING **Please initial next to your choice:**

_____ Yes, I agree to allow my infant's *coded* samples to be stored and tested in the future. My infant's blood may be used in new or different laboratory tests, to provide information for understanding hepatitis C infection and use of SOF/VEL during pregnancy. If I decide later to cancel my consent to storage and future testing of my infant's specimens, I will write a letter to the study doctor at the address listed on page 1 of this form.

_____ No, I DO NOT agree to allow my infant's samples to be stored and tested in the future. My decision will not affect my or my infant's ability to participate in the study. Leftover infant samples collected for this study will be destroyed at the end of this study.

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VOLUNTARY CONSENT FOR PARTICIPANTS

The above information has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions, voice concerns or complaints about any aspect of this research study during the course of this study, and that such future questions, concerns or complaints will be answered by a qualified member of the research team or by the Principal Investigator listed on the first page. I understand that I may always request that my questions, concerns or complaints be addressed by the Principal Investigator. At any time, I may also contact the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns and questions; obtain information; offer input; or discuss situations in the event that the research team is unavailable. By signing this form, I agree to participate in this research study for the purposes described above and I provide my authorization for the research team to obtain (from UPMC, R3, and/or outside facilities) my applicable medical records/my infant's medical records once born. A copy of this consent form will be offered to me.

I understand that, as a minor (less than 18 years), the infant named below is not permitted to participate in this research without my consent. Therefore, by signing this form, I give my consent for my infant to participate in this study after he/she is born.

_____

Printed Name of (Maternal) Participant

_____

Printed Infant Participant's Name (if infant name unknown, document as « BABY » and last name)

_____ _____ _____

(Maternal) Participant Signature Date Time (am/pm)

CERTIFICATION OF INFORMED CONSENT

I certify that I have explained the nature and purpose of this research to the above individual and I have discussed the potential benefits and possible risks of study participation. Any questions the individual has about the study have been answered, and we will always be available to address future questions as they arise. I further certify that no research component of this protocol was begun until after this consent form was signed.

_____ _____

Printed name of Person Obtaining Consent Role in Research Study

_____ _____ _____

Signature of Person Obtaining Consent Date Time (am/pm)