Document Coversheet

Study Title: Increasing Access to Hepatitis C Treatment in Opioid Endemic Rural Areas: The Kentucky Viral Hepatitis Treatment (KeY Treat) Study

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INFORMATION FOR KeY TREAT

You are being invited to take part in a research study to treat your hepatitis C infection with a drug called Epclusa because you passed the screening test.

WHAT IS THE PURPOSE, PROCEDURES, AND DURATION OF THIS STUDY?

The purpose of this study is to learn about how to treat hepatitis C infection in rural areas. We want to know why people may or may not start treatment, finish treatment, get cured, and/or get re-infected with the hepatitis C virus. You will be asked to take the study medication once per day for 12-weeks, and if you are cured, we will contact you to see if you are still hepatitis C-free 12 weeks, 6 months and 1 year after cure.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

If you are infected with the hepatitis C virus, or suspect you may be infected, you might volunteer. We will screen everyone who suspects they may have been exposed to the hepatitis C virus to determine whether they may take part in the study. There are other reasons as well. Right now in Kentucky, you may not qualify to be treated for your hepatitis C with drugs like Epclusa. Insurance may not cover the treatment if you are using illicit drugs or were recently using illicit drugs or if your liver does not yet have enough damage. Also, most insurances make it so a special doctor has to treat the disease, and there are not many of those doctors in rural areas. If you do not have insurance, you may not be able to afford the drug. This study will screen and treat anyone who has chronic hepatitis C as long as you are at least 18 years old, whether or not you meet the insurance criteria or are uninsured, whether you are injecting drugs, using drugs, or were recently using drugs, and whether or not you have liver damage at no cost to you. We will also provide treatment for opioid use disorder if you are interested in receiving treatment, at no cost to you. The information we gather from this study will be used to design a rural hepatitis C treatment program for other parts of rural Kentucky and the U.S.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

You may not want to volunteer for this study if you are not at least 18 years old, do not have chronic hepatitis C, are pregnant or intend to become pregnant in the next six months, or do not live in Perry County. If you choose not to participate in this study, we are not offering any alternatives.

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits or rights you would normally have if you choose not to volunteer. You can stop at any time during the study; however, we will encourage participants to complete the 12-weeks of medication so that they increase the chances of curing their hepatitis C.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

The person in charge of the study is Jennifer Havens of the University of Kentucky, Department of Behavioral Science. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study her contact information is: Jennifer.havens@uky.edu or 859-323-6553.

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact staff in the University of Kentucky (UK) Office of Research Integrity (ORI) between the business hours of 8am and 5pm EST, Monday-Friday at 859-257-9428 or toll free at 1-866-400-9428.

DETAILED CONSENT

ARE THERE REASONS WHY YOU WOULD NOT QUALIFY FOR THIS STUDY?

You will not qualify for this study if you meet any of the following criteria: 1) you do not have chronic hepatitis C (which will be determined by testing for what we call “viral RNA”); 2) you are currently pregnant, or have a positive pregnancy test during the study screening, or intend to become pregnant before completing the study medications; 3) you have a serious mental illness that will not allow you to consent to participate. Other criteria for entering the study are that you are at least 18 years of age and are currently living in Perry County. If you have been exposed to hepatitis C (meaning you have a positive *antibody test*) but do not have a positive test for chronic hepatitis C (*RNA test*), you may return every six months for RNA testing.

WHERE IS THE STUDY GOING TO TAKE PLACE AND HOW LONG WILL IT LAST?

Once enrolled in KeY Treat, all research activities will be conducted at the study office in Hazard. We may also screen for KeY Treat at the Syringe Services Program at the Perry County Health Department. If you choose to receive treatment for an opioid use disorder, those services will take place at Behavioral Health Group (BHG) in Hazard. Your participation in the study will involve a medical screening, up to seven (7) interviews and seven (7) blood draws over a four-year period. The follow-up interviews will take place approximately 2, 6, 12, 24, 36 weeks from when you start the study. We will also follow-up with you six months and one-year after you complete treatment, if you are cured. The first medical screening, interview and blood draw will take approximately 3 hours to complete, and the follow-up interviews will take approximately 15 minutes to complete. Blood draws will take up to 15 minutes to complete. The total amount of time you will be asked to volunteer for data collection for this study is approximately 15 hours over the next two years.

WHAT WILL YOU BE ASKED TO DO?

We will do a full blood draw to confirm you hepatitis C RNA result, determine the specific type of hepatitis C you are infected with (genotype), and whether you have been exposed to hepatitis A and B. We will also determine through a blood test (Fibrosure) whether you have had any damage to your liver as a result of the hepatitis C infection. Finally, we will do a basic blood panel to assess overall health (complete blood count [CBC] and complete metabolic panel [CMP]).

You will also be asked questions in an interview with a research assistant from the University of Kentucky. The interview asks about illicit drug use, medical history and people you may interact with. We will also do an interview to determine how ready you are for hepatitis C treatment. However, your answers to the hepatitis readiness interview will not impact whether you qualify for the study. Your interview responses will be kept completely confidential. The nurse practitioner will do a physical, and will ask you questions about your health, and any medications you take.

We will also ask you to complete a Locator Form so that we will have the necessary information to locate you for the follow-up interviews and medication refills. The Locator Form includes questions about things like your address and phone number, people who live with you, contact information for relatives and friends who will know where to find you, and places where you meet with friends. In gathering this information for locating you, we will only say we are trying to locate you for a “Health Study.” We will not disclose the nature of the study or give any study-based information to anyone we speak with that is not you.

If you would like, we will send you a daily text message reminder to take your medication at a time of your choosing. At this first visit, you will receive the first two weeks of the medicine. You will come back after two weeks for a finger-stick or blood draw, and then you will receive four weeks of medication. Finally, you will return at six weeks for another blood draw, and if you are taking the medication once per day as prescribed, you will receive the last 6 weeks of medication. We will ask you to return once you finish the medication and 12-weeks after that to determine whether you are cured. It is very important to know this information. If you are not cured, we will look into re-treating you with Epclusa, or using another drug called Vosevi. We would also like to talk to you six months and one year after you complete the treatment, and will contact you at that time to set up the visits.

If you choose to enroll in treatment through this study for an opioid use disorder, we may ask that you sign a separate form so that we may access the records from your treatment program. If you choose not to sign this form, your participation in this study is not affected. If you do sign the form, the information we get from the treatment program will not affect your participation in the study and will not be given to your study nurse or doctor. This information will be used for research purposes only.

Once you start taking the medicine, it is very important that you take it once per day, every day, for 12 weeks. You will receive a medication delivery device that allows you to access one pill every day, using a scan of your finger. Once you start the medication, if you are unable to follow-up at this location to receive your study medication, if is very important that you contact the project staff and we will work out a way to get you the medication (606-487-1182), or respond to the text we send you every day with any concerns.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

The primary risks for taking part in this research are those related to the study drug, Epclusa (sofosbuvir/velpatasvir). Epclusa is a new type of drug called a direct acting antiviral (DAA for short) that has very few side effects. Common side effects are fatigue (tiredness) and headache. There is also a potentially serious side effect if you have ever had hepatitis B and were not treated. If you do have hepatitis B and are treated with the study drug for your hepatitis C, your hepatitis B infection may get worse. For that reason, we will test for hepatitis B, and if you are positive, we will work with the study nurses and doctors to decide if it is safe for you to take Epclusa. There are also certain medications and/or supplements that you might be taking that may make it so Epclusa does not work as well to treat your hepatitis C. For this reason it is important that you let your study nurse know all medications and/or supplements that you are taking. The study clinicians may suggest changing medications and/or supplements, and if this is the case, it will be important for you to discuss this with your own physician before starting Epclusa.

In the rare event that you take the medication as prescribed and are not cured, we may treat you with Vosevi (sofosbuvir/velpatasvir/voxilprevir), which is similar to Epclusa, but with an additional drug. Vosevi and Epclusa also have similar side effects, but people have also reported diarrhea and nausea with Vosevi. There is also a potentially serious side effect if you have ever had hepatitis B and were not treated. If you do have hepatitis B and are treated with Vosevi for your hepatitis C, your hepatitis B infection may get worse. For that reason, we will test for hepatitis B, and if you are positive, we will work with the study nurses and doctors to decide if it is safe for you to take Vosevi. There are also certain medications and/or supplements that you might be taking that may make it so Vosevi does not work as well to treat your hepatitis C. For this reason it is important that you let your study nurse know all medications and/or supplements that you are taking. The study clinicians may suggest changing medications and/or supplements, and if this is the case, it will be important for you to discuss this with your own physician before starting Vosevi.

Talking about your past and present experiences may make you feel uncomfortable. Some of the interview questions are sensitive and personal, especially those where we ask about activities that your friends or family may be participating in. You do not have to answer any questions that you do not want to answer, and you can stop answering questions or quit at any time. The study staff are taking every precaution so that the information you provide is not available to anyone except specific study personnel. There may also be social risks such as impact on employment, insurance, and freedom to travel to other countries if you learn you have HIV, hepatitis B or C. Also, you may experience physical or psychological/emotional problems such as anxiety and depression should you learn that you have HIV, hepatitis B or C. A member of the research staff will provide post-test counseling and will be able to make appropriate referrals for community services. The research treatments/procedures in this study are no different. In addition to the risks described in this consent, you may experience a previously unknown risk or side effect.

WILL YOU BENEFIT FROM TAKING PART IN THIS STUDY?

While there is no guarantee that you will get any benefit from participating, if you take the medication as prescribed, you may be cured of your hepatitis C. You will have the opportunity for HIV, hepatitis B and C testing, as well as referrals for psychosocial and medical services (medication assisted treatment for opioid use disorder), where necessary. There are also potential benefits to society because the study will provide important information related to the treatment of hepatitis C in rural areas. Your willingness to take part may help doctors better understand and/or treat others for hepatitis C.

WHAT WILL IT COST YOU TO PARTICIPATE?

There is no charge to you for participating in the study, as all of the study assessments, hepatitis C medication and substance abuse treatment (if you have opioid use disorder and choose to use it), are provided free of charge. If there are other costs to you for any health concerns, you and/or your insurance company, Medicare or Medicaid will be responsible for the costs of all care and treatment that you would normally receive. There are costs that are considered medically necessary and will be part of the care you receive even if you do not take part in the study.

WHO WILL SEE THE INFORMATION THAT YOU GIVE?

We will make every effort to keep confidential all research records that identify you to the extent allowed by law. Your information will be combined with information from other people taking part in the study. When we write about the study to share it with other researchers, we will write about the combined information we have gathered. You will not be personally identified in these written materials. We may publish the results of this study; however, we will keep your name and other identifying information private.

We will make every effort to prevent anyone who is not on the research team from knowing that you gave us information, or what that information is. Your name will be kept separate from the information you give, and these two things will be stored in different places under lock and key. Also, all electronic data will be password protected and accessible only be the researchers on this study. In addition, your clinical information and research information will be kept separate. That is, information you give to the research assistant about your behaviors will not be shared with the nursing staff, and clinical information you give to the nursing staff will not be given to the research assistants.

Your name, social security number, and address will be requested for your payment form, but will not be placed on your research records. You may choose not to give us your social security number and it will not affect your participation in the study. Only a research number will be placed on your records, including blood sent to the laboratory. Your name, address, social security number and research number will be placed in one location that will be locked at all times except when they are being used by selected research staff. If your screening test for HIV, hepatitis B or C is positive, your results will be reported to the Kentucky Department for Public Health in Frankfort. This reporting is confidential, meaning once the state receives the report, they will not share it with anyone, including the health department in your county. Thus, none of this information will be made known to anyone but select research staff.

We have obtained a Certificate of Confidentiality from the Department of Health and Human Services (DHHS). This Certificate protects investigators from being forced to release any identifying research data in which you are identified, even under a court order or a subpoena. This protection, however, is not absolute. It does not, for instance, apply to any state requirement to report certain communicable diseases (HIV, hepatitis B and C). In addition, if you reveal any information about a child being abused, exploited, or neglected, the researchers may make a report to the Kentucky Department of Community Based Services. Should a report have to be made, the child's name, address, and parents' names will have to be given to the interviewer who will then report this information to the Department of Community Based Services. Researchers may also provide information to appropriate individuals and organizations if intent to harm others is revealed during the course of the study. Also, because this research is sponsored by the National Institute on Drug Abuse (NIDA) and the National Cancer Institute (NCI), staff from this and other DHHS agencies such as the Food and Drug Administration may review records that identify you. In addition, officials from the University of Kentucky may also look at or copy portion of records that identify you to ensure your protection in this research project. However, it is the policy of these agencies and these investigators that every attempt will be made to resist demands to release information that identifies you. If you choose to have KeY Treat pay for substance abuse treatment at BHG while you are enrolled in the study, we will have to provide your name when you are referred. However, BHG will not provide any information to KeY Treat on whether you enroll or remain in treatment. When results of this study are published, your name will not be used.

CAN YOU CHOOSE TO WITHDRAW FROM THE STUDY EARLY?

If you decide to take part in the study you still have the right to decide at any time that you no longer want to continue. You will not be treated differently if you decide to stop taking part in the study. However, there is a chance that if you discontinue the study before completing the medication that you may not be cured of your hepatitis C infection.

The individuals conducting the study may also need to withdraw you from the study. This may occur if you experience unexpected side effects from the medication, are not able to follow the directions they give you for the taking the medication regularly, if they find that your being in the study is more risk than benefit to you, or if the agency funding the study decides to stop the study early for a variety of scientific reasons.

ARE YOU PARTICIPATING OR CAN YOU PARTICIPATE IN ANOTHER RESEARCH STUDY AT THE SAME TIME AS PARTICIPATING IN THIS ONE?

You cannot take part in this study if you are enrolled in another study involving taking a medication for your hepatitis C. You may take part in this study if you are currently involved in another research study that does not involve taking medicines for hepatitis. It is important to let your doctor know if you are in this research study and that you are taking a medication to treat your hepatitis C. You should also discuss with the investigator before you agree to participate in another research study while you are enrolled in this study.

WHAT HAPPENS IF YOU GET HURT OR SICK DURING THE STUDY?

If you believe you are hurt or if you get sick because of something that is due to the study, you should call Jennifer Havens, Ph.D. at (859) 323-6553, one of the study nurses (606-487-1182) or the study physician, Takako Schaninger, M.D. (859)-323-5544 immediately. If you agree to participate in this study sponsored by the University of Kentucky and experience any subsequent problems, you will receive names of health, mental health, and substance abuse treatment providers who can treat you.

It is important for you to understand that the University of Kentucky does not have funds set aside to pay for the cost of any care or treatment that might be necessary because you get hurt or sick while taking part in this study. Also, the University of Kentucky will not pay for any wages you may lose if you are harmed by this study.

The medical costs related to your care and treatment because of research related harm will be your responsibility. No form of compensation (i.e., payment) is available from the University of Kentucky or the Federal Government. Treatment may be provided at your own expense or at the expense of your health care insurer (e.g., Medicare/Medicaid [if you have any questions regarding Medicare/Medicaid coverage you should contact Medicare by calling 1-800-Medicare/1-800-633-4227 or Medicaid 1-800-635-2570], or Blue Cross/Blue Shield), which may or may not provide coverage.

If you have questions, you should contact your insurer. You do not give up your legal rights by signing this form.

IF YOU DON'T WANT TO TAKE PART IN THE STUDY, ARE THERE OTHER CHOICES?

If you don't want to take part in the study to receive treatment for your hepatitis C, there are other choices such as going a local physician or hospital. However, study medications and treatment outside of this study are subject to payment using either medical insurance or cash (out-of-pocket). In addition, there are drugs other than Epclusa that can be used to treat chronic hepatitis C.

WILL YOU RECEIVE ANY REWARDS FOR TAKING PART IN THIS STUDY?

You will receive $50 for completing the baseline interview, $25 for each of the follow-up research interviews. You will also receive $10 for each eligible participant you refer (for a total of up to $60). You will also receive $1 per day for each text reminder that you respond to. If you get a new phone, please contact us immediately so that you continue to receive the texts and the daily reward. Since the treatment is 12 weeks long, you may receive up to $84 if you respond every day that you received the text. Therefore, if you complete all of the interviews, testing, referrals, and text responses, you are eligible to receive $344 over a one and a half year period. If you should decide to withdraw early from the study, your rewards will be pro-rated based on the parts you complete.

WHAT IF NEW INFORMATION IS LEARNED DURING THE STUDY THAT MIGHT AFFECT YOUR DECISION TO PARTICIPATE?

If the researcher learns of new information in regards to this study, and it might change your willingness to stay in this study, the information will be provided to you. You may be asked to sign a new informed consent form if the information is provided to you after you have joined the study.

WILL YOU BE GIVEN INDIVIDUAL RESULTS FROM THE RESEARCH TESTS?

Do you give permission for us to contact you about research results or incidental findings that are determined to be important to you/your family's health? (Incidental findings are unforeseen findings discovered during the course of the research that may affect you or your family's health).

☐ **Yes** ☐ **No** **Initials**_____

You may also withdraw your consent to be contacted with information about research results or incidental findings by sending a written request to Jennifer Havens, PhD, 845 Angliana Avenue, Lexington, KY 40508.

WILL WE CONTACT YOU WITH INFORMATION ABOUT PARTICIPATING IN FUTURE STUDIES?

The research staff would like to contact you in the future with information about participating in additional studies. If so, it will be limited to 1-2 times per year.

Do you give your permission to be contacted in the future by Jennifer Havens or other UK Health Study staff regarding your willingness to participate in future research studies?

☐ **Yes** ☐ **No** **Initials**_____

WHAT ELSE DO YOU NEED TO KNOW?

If you volunteer to take part in the study, you will be one of about 900 people to do so through the University of Kentucky. The National Institutes of Health (National Institute on Drug Abuse and National Cancer Institute) are providing financial support and/or materials for this study. In addition, Gilead Sciences, Inc. has donated the medications that are being used for the study. However, no information about you or your study participation will be shared with Gilead. A description of this clinical trial will be available on ClinicalTrials.gov as required by U.S. Law. 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.

If you become jailed/incarcerated during the study, you have the option of allowing the research team to contact you to conduct study-related visits in the jail. If you agree to be followed in jail, we may ask you to answer questionnaires and complete a blood draw with a certified phlebotomist. In addition, if you are incarcerated during the 12-weeks that you are taking the study medication, we will bring the medication to the jail so that you can continue to take it.

Do you give your permission to be followed-up in jail/prison?

☐ **Yes** ☐ **No** **Initials**_____

STORING AND SHARING YOUR INFORMATION OR SPECIMEN SAMPLES FOR FUTURE USE:

We would like to store, use, and share blood samples for future research. Having these samples from many people helps researchers identify trends and discover better ways to diagnose, prevent, and treat many conditions. Researchers can use the stored samples to learn more about hepatitis, drug abuse and cancer or research additional scientific questions.

We may use the genetic material (genes, DNA, RNA) in your sample to learn about the role genes play in heath and disease. Genetic studies help explain why traits or diseases are passed down in families. Results of genetic studies may also reveal information about your family members.

WHERE WILL INFORMATION OR SPECIMEN SAMPLES BE STORED AND FOR HOW LONG?

The information will be stored at the Center on Drug and Alcohol Research in their Hazard office during the study period, and will then be transported to the Center's Lexington office to be stored indefinitely.

ARE THERE RISKS FROM ALLOWING YOUR INFORMATION OR SPECIMEN SAMPLES TO BE STORED FOR FUTURE RESEARCH?

There is no additional physical risk from collecting leftover tissue from a procedure that is being done as part of your clinical care. Risks associated with blood sampling and finger-stick are generally slight, but may include soreness, bruising, pain, infection, possible fainting, bleeding.

There is a risk that someone could get access to the stored information or samples. In spite of the security measures and safeguards we will use, we cannot guarantee that your identity will never become known. Even without your name or identifiers, genetic information is unique to you making it possible for someone to trace it back to you. The results of genetic research apply to both you and your family members. Genetic information used improperly to discriminate or support negative stereotypes could cause you or your family distress.

There is a federal law called the Genetic Information Nondiscrimination Act (GINA). Generally, GINA makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. Be aware that GINA does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. It also does not prohibit discrimination on the basis of an already known genetic disease. Finally, there may be risks that at this time are unknown. As technology advances, there may be new ways of linking information back to you that we cannot foresee now.

We will take careful steps to keep your information confidential. We will remove your name or other direct identifiers from your information or samples. We will label your information or samples with a code and will store the key separately from the master code list. Only select staff will have access to the list that links the code to you. This list and any other identifiable information is kept on a server at the University of Kentucky that requires two separate passwords. We will store samples in a -70 freezer with a door that locks.

The staff follow procedures to keep your identity a secret to the extent allowed by law. In very unusual cases,

staff may be required to release your identifiable research information in response to an order from a court of law. Officials of the Food and Drug Administration, the National Institute on Drug Abuse, the National Cancer Institute, and the University of Kentucky, may look at or copy pertinent portions of records that identify you.

HOW WILL WE SHARE YOUR INFORMATION OR SPECIMEN SAMPLES WITH OTHER RESEARCHERS?

The researchers requesting access to blood samples must send an application to the Principal Investigator. If this research is approved, the researchers must sign an agreement to use the data responsibly before they will receive the samples.

Before sharing your blood samples, we will remove identifiers such as (e.g., your name, medical record number, or date of birth). Your de-identified information or samples may be shared with other University of Kentucky (UK) researchers and researchers outside of UK, without your additional informed consent. We will use spreadsheets to track what information is shared without releasing your identity.

What if you change your mind and want to withdraw your information or specimen samples?

You may withdraw your permission to allow your information or samples to be used for future research. To do so, you must send a written withdraw request to Dr. Jennifer Havens, 845 Angliana Avenue, Lexington, KY 40508.

We will destroy any remaining information and samples that have been stored. In addition, it may be possible to destroy the code that links you with your information and specimen samples. However, we cannot withdraw the information and samples that have already been used.

Will you receive any commercial profit from future research discoveries?

The information and samples that you provide will no longer belong to you. The research may lead to new medical knowledge, tests, treatments, or products. These products could have some financial value. There are no plans to provide financial payment to you or your relatives should this occur.

Will you be given individual results from the future research tests?

Tests done for research purposes are not meant to provide clinical information or help care for you. The results are only important for research. Therefore, the results of tests done with your information and samples will not be provided to you. In the rare event that a finding might affect the health of you or your family, we will contact you and you can choose whether to receive or refuse the information.

Do you give permission for Dr. Jennifer Havens to store your blood samples for future research?

☐ **Yes** ☐ **No** **Initials**_____

Remember, you can still be in the main study even if you even if you do not wish to allow your information and/or specimens stored for this investigator's future research.

INFORMED CONSENT SIGNATURES

This consent includes the following:

- **Key Information Page**
- **Detailed Consent**

You will receive a copy of this consent form after it has been signed.

_____ _____

Signature of research subject **Date**

_____

Printed name of research subject

_____ _____

Printed name of [authorized] person obtaining informed consent and HIPAA authorization Date

_____

Signature of Principal Investigator or Sub/Co-Investigator