OREGON HEALTH & SCIENCE UNIVERSITY

IRB#: 25307

MED. REC. NO. _____
NAME _____
BIRTHDATE _____

CLINICAL RESEARCH CONSENT AND AUTHORIZATION SUMMARY OF KEY INFORMATION ABOUT THIS STUDY

TITLE: A Phase I/II Study of the Immunogenicity of the Yellow Fever Vaccine 17D (YFVax®**)** in Adults With Prior 17D Vaccination.

PRINCIPAL INVESTIGATOR: William Messer, MD PhD *(503) 494-2185*

You are being asked to join a research study. This consent form contains important information to help you decide if you want to join the study or not.

PURPOSE:
The purpose of the study is to learn more about the how the yellow fever vaccine YFVax®, also known as 17D, protects against yellow fever virus infection. Because you have received 17D once already, your immune system will respond to re-vaccination with 17D in a manner that is similar to the immune response to a true yellow fever virus infection. We will study your immune responses before and after vaccination to better understand how your immune system recognizes and controls yellow fever virus infection.

DURATION:
Your participation in the study will consist of 10 visits over up to 60 days. Visits will last up to 1 hour. We may ask to follow your health through the use of medical record review and follow up phone calls for up to 60 days.

PROCEDURES:
If you decide to take part in this study, you will receive the Yellow Fever Vaccine 17D. You will be asked to have a number of tests and procedures including:

- A blood draw at all visits.
- Review and collection of information from you and your medical record.
- Travel History Questionnaire completed at screening and symptoms diaries completed at all follow up visits.
- Examination by study physician.

RISKS:
Risks associated with the blood draws include some pain when the needle is inserted and a small risk of bruising and/or infection at the place where the needle enters the arm. Some people may experience lightheadedness, nausea, and/or fainting.

CO1450

Some of the most common side effects after vaccination that the investigator knows about are:

- Pain, redness, swelling or hardness at the injection site
- You might also feel light-headed, tired or sick, have fever, flu-like symptoms, swollen tonsils, headache, or aching muscle or joints

There is a rare risk of injury to the liver or brain.

There is also a minimal risk of loss of confidentiality.

BENEFITS:
You will not directly benefit from taking part in this research.

ALTERNATIVES:
You may choose not to participate in this study or participate in another study if one is available.

This is a voluntary research study. You do not have to join the study. Even if you decide to join now, you can change your mind later. Please ask the Investigator if you have any questions about the study or about this consent form.

END OF CONSENT SUMMARY

OREGON HEALTH & SCIENCE UNIVERSITY

MED. REC. NO. _____
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IRB#: 25307

Clinical Research Consent and Authorization Form

TITLE: A Phase I/II Study of the Immunogenicity of the Yellow Fever Vaccine 17D (FYVax®) In Adults With Prior 17D Vaccination.

PRINCIPAL INVESTIGATOR: William Messer, MD, MPH (503) 494-2185

WHO IS PAYING FOR THE STUDY?: This study is paid for by the National Institutes of Health (NIH).

WHY IS THIS STUDY BEING DONE?:
YFV-17D, also known as YFVax®, is an FDA-approved vaccine against yellow fever disease caused by the mosquito transmitted yellow fever virus (YFV). This vaccine been administered to more than 500 million people worldwide. Historically, the vaccine was administered every 10 years to maintain immunity, but in 2016 the Centers for Disease Control and Prevention (CDC) changed this recommendation to a once in a lifetime vaccination. This recommendation was based on the vaccine's history of preventing disease and evidence that the majority of people who are vaccinated have vaccine generated antibodies in their blood more than 10 years after vaccination. However, we still do not fully understand how this vaccine protects against YFV infection. A key part of the vaccine immune response is the generation of antibodies in the blood that can neutralize the virus if a person is infected with YFV, preventing illness. These so-called "neutralizing antibodies" are thought to be necessary and sufficient to protect against infection, but we do not know how many, or how strong, these neutralizing antibodies need to be in order to completely protect against infection. We also do not know if there is a level of neutralizing antibodies below which protection may be incomplete or even absent. This study will begin to answer these questions about the role that neutralizing antibodies, or other parts of the immune system, play in protecting a person from infection.

CO1450

17D is a "live-attenuated virus" or LAV, meaning that the vaccine virus has been weakened but not killed. When given, the vaccine virus replicates in the blood of a vaccinated person, but does not typically cause disease. Other LAV vaccines you may be familiar with are the measles, mumps and rubella vaccines. Because 17D imitates a natural viral infection, it can also be used to "challenge" the immunity of a previously vaccinated person. If the previously vaccinated person has very potent neutralizing antibodies, the 17D virus will be killed immediately by those antibodies, and cannot be detected in blood. but if the antibodies are not potent, or at very low levels, the vaccine virus may be able to spread again, and be detected in the vaccinee's blood. It is also possible that there are other parts of the immune system that can control the vaccine virus without antibodies.

Research by several investigators have shown that within 10 years after vaccination, about 4 in 5 people will still have high levels of antibodies, but that about 1 in 5 will have low levels of antibodies. We are interested in whether these differing levels of antibodies will protect against "challenge" with the 17D vaccine.

You have been invited to be in this research study because you have previously received the Yellow Fever 17D vaccine between 8 and 10 years ago. If you choose to participate in this study, you will receive a “challenge” booster vaccination of the Yellow Fever 17D vaccine. The purpose of this study is to improve our understanding of how the yellow fever vaccine works within your immune system following vaccination.

This study requires 10 visits to the clinic and will take 60 days to complete.

We expect to enroll 34 participants over the course of two years. This study is only being conducted at OHSU.

WHAT EXAMS, TESTS AND PROCEDURES ARE INVOLVED IN THIS STUDY?

If you choose to participate in the study, you will be asked to provide:

- medical history, including current and past medical conditions,
- medications,
- vaccination history,
- allergies,
- Country of birth,
- a life-time travel history to countries where yellow fever and/or other related mosquito-borne viruses are transmitted.

This information will be collected prior to your yellow fever vaccination. If you consent to participate in the study you will provide 1 tablespoon (15.0 mL) blood sample before you are vaccinated. This blood will be used to test your blood for yellow fever vaccine antibodies and do a complete blood count and tests of your kidney and liver functions. If your complete blood count or kidney or liver function tests are abnormal, you will not be able to continue to participate in the study.

After the results of your CBC and liver and kidney function have been evaluated, you will be scheduled for the booster vaccine. Following vaccination, you will be asked to return to the research clinic eight times, roughly every other day until 14 days after vaccination. Each follow up visit after your initial screening visit you will provide a blood sample that ranges from 1/6 of a tablespoon (2.5 mL) to 1 3/4 tablespoon (26.0 mL) in volume, depending on what is scheduled for the visit. The visit schedule is in the table below. At the first two visits and final visit, the study doctor will perform a physical examination. Blood tests of your liver function will be performed at the time you enroll in the study and at days 6, 14, and 28 after vaccination. You may have an examination at the study doctor’s discretion at the other study visits.

There are ten total visits, the pre-vaccination visit, the vaccination visit, and eight visits in the 28 days following vaccination.

You will be asked to complete an at home “diary card” for the first 28 days after you are vaccinated to track any reactions you may have to the vaccine. The diary card will be reviewed with you at each study visit.

The First study visit is expected to take up to 60 minutes, each visit thereafter is expected to take up to 45 minutes.

Visit	Screening visit	Baseline V1	V2	V3	V4	V5	V6	V7	V8	V9
Visit window (days post vaccination)	**Up to 30 days pre-vaccination**	**0**	**2 (±1)**	**4 (±1)**	**6 (±1)**	**8 (±1)**	**10 (±1)**	**12 (±1)**	**14 (±1)**	**28 (±7)**
Informed consent	X									
Assessment of eligibility criteria	X									
Demographics, medical history, and prior medication/ vaccination	X									
Concomitant medications/vaccinations	X									
Travel History Questionnaire	X									
Urine Pregnancy Test (if applicable)	X									
Blood sample for plasma and peripheral blood mononuclear cells[1]		20 mL			10 mL				10 mL	10 mL
Blood sample for serum viremia and/or innate immune response as specified in the protocol		3 mL	3 mL	3 mL	3 mL	3 mL	3 mL	3 mL	3 mL	
Blood sample for serology (screening and post-vaccination antibodies)	3 mL									5.0 mL
Blood sample for complete blood count	5.0 mL									
Blood sample for kidney and liver function tests	5.0 mL				5.0 mL				5.0 mL	5.0 mL
Blood sample for Paxgene*		2.5 mL								
Total Blood Volume	13.0 mL	25.5 mL	3 mL	3 mL	18 mL	3 mL	3 mL	3 mL	18 mL	20 mL
Study Diary		X	X	X	X	X	X	X	X	X
YFV Vaccination		X								
Full Investigator examination	X	X								X
Focused investigator examination as needed			X	X	X	X	X	X	X	

*Paxgene is used to preserve cells that contain your genetic information.

In the future, your blood samples and information will not be given to researchers for other research studies.

WILL I RECEIVE RESULTS FROM THE [TESTING] IN THIS STUDY?
The results of the research tests will not be made available to you because the research is still in an early phase and the reliability of the results is unknown.

WHAT RISKS CAN I EXPECT FROM TAKING PART IN THIS STUDY?:

Vaccine Risks:
Between 10% and 30% people report the following vaccine reactions:

- mild headaches
- muscle pain
- fatigue

Less than 5% of people report:

- fever
- injection site reactions, including:
  - pain

  - redness
  - swelling
  - hardness
- light-headedness
- feeling tired or sick
- flu-like symptoms
- swollen tonsils
- moderate headache
- aching muscle or joints

Rare but severe and/or life-threatening allergic reactions (including anaphylaxis) are estimated to occur at a rate of ≤ 17 cases per ten-million vaccinations in booster vaccination. Rare but severe and potentially life-threatening neurological disease (YFV-AND) requiring hospitalization is estimated to occur at a rate of approximately 15 cases per ten-million vaccinations in subjects aged 19 to 49. Booster doses, such as administered in this study account for ~3% of all cases. Rare but severe and life-threatening viscerotropic disease (YEL-AVD) requiring hospitalization is estimated to occur in 7 to 24 cases per ten-million vaccinations in subjects aged 19 to 49. Booster doses such as in this study account for ~3% of all cases.

Blood Draws: We will draw blood from your arm. You may feel some pain when your blood is drawn. There is a small chance the needle will cause bleeding, a bruise, an infection, or fainting.

Diary Card: Some of these questions may seem very personal or embarrassing. They may upset you. You may refuse to answer any of the questions that you do not wish to answer.

For pregnancy/risk to fetus: If you are nursing an infant or you are pregnant now, you must not be in the study. This study may involve risks to an embryo, fetus, or nursing infant that are currently unknown. If you are sexually active and could become pregnant, you and your male partner(s) must use birth control that works well or you must not have sex. The investigator will talk to you about the types of birth control that are acceptable. You will have to do this the whole time you are in this study. If you become pregnant during the research study, please tell the investigator and your doctor immediately. If you become pregnant, the study drug will be stopped immediately and we will request to monitor your pregnancy until the baby is born.

If you have been surgically sterilized or have been through menopause (discuss this with the investigator), you do not need to meet any contraception requirements to take part in this trial. If you are sexually active with a male partner who has not been sterilized and you could get pregnant, you must be willing to use an acceptable method of contraception.

Acceptable methods of contraception are:

- Hormonal contraceptives such as oral, injection, transdermal patch, implant, cervical ring.
- Condom with spermicide or diaphragm with spermicide.
- Intrauterine device
- Abstinence

Be aware that you can still become pregnant even if you use an acceptable birth control method. In order to enter the study, you must have a pregnancy test to confirm that you are not pregnant.

For pregnancy/risk to fetus (For Men): The drugs in this study may damage sperm or be present in seminal fluid. You should not father a child or donate sperm while you are in this

study. If you are a sexually active male and could cause a pregnancy, you must be sure that your female partner(s) are using birth control that works well or you must not have sex. This study may involve risks to an embryo or fetus that are currently unknown. The investigator will talk to you about the types of birth control that are acceptable. If a sexual partner becomes pregnant during the research study, please tell the investigator and ask your partner to tell her doctor immediately. If your partner becomes pregnant, we will request to monitor your partner's pregnancy until the baby is born.

Risks of Questionnaires. Some of these questions may seem very personal or embarrassing. They may upset you. You may refuse to answer any of the questions that you do not wish to answer. If the questions make you very upset, we will help you to find a counselor.

Risks of loss of confidentiality. Although we have made efforts to protect your identity, there is a small risk of loss of confidentiality. If the results of these studies of your genetic makeup were to be accidentally released, it might be possible that the information we will gather about you as part of this study could become available to an insurer or an employer, or a relative, or someone else outside the study. Even though there are certain genetic discrimination and confidentiality protections in both Oregon law and federal law, there is still a small chance that you could be harmed if a release occurred.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination if you have already been diagnosed with the genetic disease being tested.

WHAT ARE MY CHOICES IF I DECIDE NOT TO TAKE PART IN THIS STUDY?

You may choose not to be in this study.

WHO WILL SEE MY PERSONAL INFORMATION?

We will take steps to keep your personal information confidential, but we cannot guarantee total privacy. We will create and collect health information about you as described in the WHY IS THIS STUDY BEING DONE? and the WHAT EXAMS, TESTS AND PROCEDURES ARE INVOLVED IN THIS STUDY? sections of this form. Health information is private and is protected under federal law and Oregon law. By agreeing to be in this study, you are giving permission (also called authorization) for us to use and disclose your health information as described in this form.

Giving access to your health information is voluntary. You get to choose. No matter what you decide, now or in the future, it will not affect your medical care. You can change your mind at any time in the future. However, if you choose not to give us access to your health information now, we will not be able to enroll you in the research study.

We will be able to see all the information in your electronic health record (EHR), but we will only collect the information we need for the research study.

How will my health information be used and disclosed (released)?

The investigators and study staff at OHSU may use the information we collect and create about you in order to conduct and oversee this research study.

We may release this information to others outside of OHSU who are involved in conducting or overseeing research, including:

- The Food and Drug Administration
- Oregon Health And Science University (OHSU)
- The Office for Human Research Protections, a federal agency that oversees research involving humans

Those listed above may also be permitted to review and copy your records, including your medical records.

OHSU complies with Oregon state requirements for reporting certain diseases and conditions to local health departments. In certain situations, we would not be able to keep your information confidential. State law requires us to report cases of child abuse, elder abuse, and certain diseases. We may also disclose your information in response to serious threats of harm to you or others.

We will not release information about you to others not listed above, unless required or permitted by law. We will not use your name or your identity for publication or publicity purposes, unless we have your special permission.

When we send specimens or information outside of OHSU, they may no longer be protected under federal or Oregon law. In this case, your specimens or information could be used and re-released without your permission.

We may continue to use and disclose your information as described above indefinitely.

Some of the information collected and created in this study may be placed in your OHSU medical record. While the research is in progress, you may or may not have access to this information. After the study is complete, you will be able to access any study information that was added to your OHSU medical record. If you have questions about what study information you will be able to access, and when, ask the investigator.

WILL MY SENSITIVE INFORMATION RECEIVE ANY ADDITIONAL PROTECTIONS?

State and federal privacy laws protect your health information. We will do our best to protect your confidentiality by using standard security measures as required by law. We will also remove or separate information that identifies you (such as your name or address) from the rest of your health information whenever possible. A code number will be assigned to you, your cells and genetic information if applicable, as well as to information about you. Only the investigators and people involved in the conduct of the study will be authorized to link the code number to you.

Everyone with access to your information has received training in the protection of sensitive information. Still, there is a small chance your information could be released accidentally. There are also certain situations where we may be required by law to release your information. Once your information has been given to others, it may no longer be protected by state or federal privacy laws. It will be protected by other rules and agreements with the recipients. However, there is still a risk that a recipient could share your information without your permission. We will not release information about you to others not listed above, unless required or permitted by law. We will not use your name or your identity for publication or publicity purposes, unless we have your special permission.

WILL ANY OF MY INFORMATION OR SAMPLES FROM THIS STUDY BE USED FOR ANY COMMERCIAL PROFIT?

Blood samples obtained from you in this research may be used for commercial purposes, such as making a discovery that could, in the future, be patented or licensed to a company, which could result in a possible financial benefit to that company, OHSU, and its researchers. There are no plans to pay you if this happens. You will not have any property rights or ownership or financial interest in or arising from products or data that may result from your participation in this study. Further, you will have no responsibility or liability for any use that may be made of your samples or information.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

There will be no cost to you or your insurance company to participate in this study.

You will receive $50 for each visit to the clinic during your participation in the study. This amount will be loaded onto a reloadable gift card at the end of each visit. There may be fees (for example, if the card is inactive for more than six months), which will be deducted from the balance on your card. Details on how to use the card and any fees are included in the separate card member agreement and FAQ sheet. We may request your social security number in order to process any payments for participation.

Payment received as compensation for participation in research is considered taxable income for a research subject. If payments are more than $600 in any one calendar year, OHSU is required to report this information to the Internal Revenue Service (IRS). Research subject payments exceeding $600 during any calendar year will result in a 1099 (Miscellaneous Income) form being issued to the research subject and a copy will be sent to the IRS.

WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?:

If you believe you have been injured or harmed as a result of participating in this research and require treatment, contact study investigator William Messer, MD PhD at (503) 494- 2185.

If you are injured or harmed by the study drug or study procedures, OHSU will provide necessary medical treatment as covered by your usual health benefits. OHSU and the sponsor do not offer any other financial compensation if you are injured or harmed as a result of participating in this research. OHSU and National Institute of Infectious Diseases do not offer any financial compensation or payment for the cost of treatment if you are injured or harmed as a result of participating in this research. Therefore, any medical treatment you need may be billed to you or your insurance. However, you are not prevented from seeking to collect compensation for injury related to negligence on the part of those involved in the research. Oregon law (Oregon Tort Claims Act (ORS 30.260 through 30.300)) may limit the dollar amount that you may recover from OHSU or its caregivers and researchers for a claim relating to care or research at OHSU, and the time you have to bring a claim.

If you have questions on this subject, please call the OHSU Research Integrity Office at (503) 494-7887.

This federally funded study also does not have the ability to provide compensation for research-related injury. If you are injured or become ill from taking part in this study, it is important to tell your study doctor. Emergency treatment may be available but you or your insurance company will be charged for this treatment.

WHERE CAN I GET MORE INFORMATION?

If you have any questions, concerns, or complaints regarding this study now or in the future, contact the study coordinator, Matt Strnad, at 503-494-2136. The study coordinator may route your question to the OHSU Principal Investigator William Messer, MD PhD, as needed.

This research has been approved and is overseen by an Institutional Review Board ("IRB"), a committee that protects the rights and welfare of research subjects. You may talk to the IRB at (503) 494-7887 or irb@ohsu.edu if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get more information or provide input about this research.

You may also submit a report to the OHSU Integrity Hotline online at https://secure.ethicspoint.com/domain/media/en/gui/18915/index.html or by calling toll-free (877) 733-8313 (anonymous and available 24 hours a day, 7 days a week).

WHAT ARE MY RESPONSIBILITIES IN THIS STUDY?

- Attend all scheduled study visits
- Answer questions on enrollment questionnaire.
- Complete the study diary daily as instructed.

DO I HAVE TO TAKE PART IN THIS STUDY?

Your participation in this study is voluntary. You do not have to join this or any research study. You do not have to allow the use and disclosure of your health information in the study, but if you do not, you cannot be in the study.

IF I DECIDE TO TAKE PART IN THIS STUDY, CAN I STOP LATER?

If you do join the study and later change your mind, you have the right to quit at any time. This includes the right to withdraw your authorization to use and disclose your health information. If you choose not to join any or all parts of this study, or if you withdraw early from any or all parts of the study, there will be no penalty or loss of benefits to which you are otherwise entitled, including being able to receive health care services or insurance coverage for services. Talk to the investigator if you want to withdraw from the study.

If you no longer want your health information to be used and disclosed as described in this form, you must send a written request or email stating that you are revoking your authorization to:

Dr. William Messer
Oregon Health and Science University
L220
6588 Richard Jones Hall
3181 SW Sam Jackson Park Rd.
Portland, OR 97239
messer@ohsu.edu

Your request will be effective as of the date we receive it. However, health information collected before your request is received may continue to be used and disclosed to the extent that we have already acted based on your authorization.

If you choose to withdraw, you will be asked to provide a reason for withdrawal for our study records. If you choose not to provide a reason, then "no reason provided" will be entered into our study records. You will not be asked to attend any follow up visits.

If in the future you decide you no longer want to participate in this research, we will remove your name and any other identifiers from your samples and information but the material will not be destroyed and we will continue to use it for research.

You may be removed from the study if you do not or are unable to follow study instructions.

We will give you any new information during the course of this research study that might change the way you feel about being in the study.

SIGNATURES:

Your signature below indicates that you have read this entire form and that you agree to be in this study.

We will give you a copy of this signed form.

Participant Printed Name	Participant Signature	Date

Person Obtaining Consent Printed Name	Person Obtaining Consent Signature	Date

Complete if the participant is not fluent in English and an interpreter was used to obtain consent. Participants who do not read or understand English must not sign this full consent form, but instead sign the short form translated into their native language. This form should be signed by the investigator and interpreter only.

Print name of interpreter: _____

Signature of interpreter:_____Date: _____

An oral translation of this document was administered to the subject in _____ (state language) by an individual proficient in English and_____(state language).

See the attached short form for documentation.