

You Are Being Asked to Be in a Research Study

What Is a Research Study?

The main purpose of research studies is to gain knowledge. This knowledge may be used to help others. Research studies are not intended to benefit you directly, though some might.

Do I Have to Do This?

No. Being in this study is entirely your choice. If you decide to join this study, you can change your mind later on and withdraw from the research study.

Taking part in a study is separate from medical care. The decision to join or not join the research study will not affect your status as a patient.

What Is This Document?

This form is an informed consent document. It will describe the study risks, procedures, and any costs to you.

This form is also a HIPAA Authorization document. It will describe how your health information will be used and by whom.

Signing this form indicates you are willing to take part in the study and allow your health information to be used.

What Should I Do Next?

1. Read this form, or have it read to you.
2. Make sure the study doctor or study staff explains the study to you.
3. Ask questions (e.g., time commitment, unfamiliar words, specific procedures, etc.)
4. If there will be medical treatment, know which parts are research and which are standard care.
5. Take time to consider this, and talk about it with your family and friends.

Emory University
Consent to be a Research Subject / HIPAA Authorization

Title: A Phase 1, Double-Blinded, Placebo Controlled, Clinical Trial to evaluate the Safety, Reactogenicity, and Immunogenicity of HEV-239 (Hecolin®) in a Healthy US Adult Population

Study Number: **DMID Protocol Number: 15-0108**

Principal Investigator: **Evan Anderson, MD**
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Sponsor: **Vaccine Treatment and Evaluation Units (VTEU)**
 Division of Microbiology and Infectious Diseases (DMID)
 National Institute of Allergy and Infectious Diseases (NIAID)
 National Institutes of Health (NIH)

Introduction

You are being asked to be in a medical research study because you are a person in good general health who is between 18 and 45 years of age. This form is designed to tell you everything you need to think about before you decide if you want to be a part of the study. **It is entirely your choice. If you decide to take part, you can change your mind later on and withdraw from the research study.** The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.

Before making your decision:

- Please carefully read this form or have it read to you
- Please listen to the study doctor or study staff explain the study to you
- Please ask questions about anything that is not clear

You can take a copy of this consent form, to keep. Feel free to take your time thinking about whether you would like to participate. You may wish to discuss your decision with family or friends. Do not sign this consent form unless you have had a chance to ask questions and get answers that make sense to you. By signing this form you will not give up any legal rights.

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 may search this Web site at any time.

What is the purpose of this study?

Hepatitis is inflammation or infection of the liver. Hepatitis can be due to viruses infecting the liver. Hepatitis E is the most common cause of viral hepatitis in the world. Some people that get hepatitis E infection do not develop symptoms. Other people can have mild symptoms of liver inflammation such as fever, vomiting and tiredness. Some people develop severe hepatitis symptoms that require hospitalization such as liver failure. It can progress to chronic liver failure (cirrhosis) particularly in those with weakened immune systems. Rarely infection with hepatitis E can lead to problems in other organs such as the pancreas or kidney, and has been associated with a rare neurological disease that results in weakness called Guillain-Barre syndrome. Adults and

pregnant women tend to have more severe infections. Most of the time, it will get better on its own. There are medicines or treatments that work against Hepatitis E.

Hepatitis E outbreaks have been reported worldwide although most cases are found in Asia, Africa, and Central America. The virus is primarily transmitted by contamination of food or water. Animals such as deer, rabbits, cows and pigs can carry hepatitis E virus and eating undercooked meat from an infected animal can lead to human infection.

No vaccines are available in the U.S. for prevention of hepatitis E. A vaccine has been studied and is currently approved for use only in China. This vaccine is called HEV-239 (Hecolin®). We are using HEV-239 (Hecolin®) in this study. This vaccine has been created from hepatitis E by using genetic material that creates a protein that sits on the surface of this virus. This protein will hopefully cause your immune system to respond to the vaccine by making antibodies. Antibodies could help protect against future Hepatitis E infection. The vaccine also contains buffered saline, thimerosal, and aluminum hydroxide as an adjuvant to help stimulate the immune response. The vaccine was tested in animal models and humans and was found to be well tolerated and safe. Individuals who received 3 doses of HEV-239 (Hecolin®) had protective antibodies that lasted for at least 4.5 years. This study will test Hecolin® outside of China. If this vaccine works and is safe, it would be helpful for travelers, medical personnel working in these areas, and possibly for preventing outbreaks from spreading to other areas of the world.

The purpose of this research study is to see whether HEV-239 (Hecolin®), a vaccine for Hepatitis E, is safe, tolerable and stimulates a good immune response.

How many people are in this study?

We will administer vaccine to about 25 healthy adults that are from 18 – 45 years old. To do this, we may need to screen as many as 50 people to see if they are eligible for this study.

How long will I be in this study?

If you qualify to take part in this study and agree to do so, you will be in the study for approximately 12 months. The screening period may take up to an additional 28 days.

Who May Participate In This Study?

To be in the study, you must be in general good health and between 18 and 45 years of age. You must not have previously been infected with Hepatitis E or have chronic liver disease. You must not have travelled to Asia, the Middle East, Africa, or Central America or to an area with an active Hepatitis E outbreak in the last 90 days or plan to travel to any of these countries during your participation in this study. You must not have health conditions that weaken your body's ability to fight infections. You should not be taking drugs that weaken the body's ability to fight infections, such as steroids. You also must not have infection with HIV, hepatitis B virus, or hepatitis C virus.

Women who are pregnant or breast-feeding cannot be in the study because there is no safety information available about these vaccines for pregnant or breast-feeding women. If you are female and able to have children, you will have a blood pregnancy test at the first (screening) visit. You will also have a urine pregnancy test before each vaccination. The result of the pregnancy test must be negative for you to be in the study.

If you are female and able to have children, you must agree to use an acceptable method of birth control from at least 28 days before the first vaccination until at least 3 months after the last study vaccination. You will be counseled about avoiding getting pregnant during the study.

If you are male and not surgically sterile (e.g., vasectomy), you must agree to use an acceptable method of birth control from the time of the first vaccine until 3 months after the last study vaccination. You will be counseled about not conceiving a child during the study.

You cannot participate in the study if you have or will receive a live vaccine (such as measles, mumps, rubella [MMR] vaccine) within 28 days before or after of any vaccine dose. You also cannot participate in the study if you have or will receive an inactivated vaccine (such as influenza vaccine) within 14 days before or after any vaccine dose. There may be other reasons why you cannot participate in the study such as allergies to aluminum, any component of the vaccine, or other vaccines or medicines. The study doctor or study staff will review these with you. You cannot be in the study if you do not have the ability to enter your symptoms and temperature daily over the internet.

It is possible that some of your health screening tests could be abnormal. If your tests for hepatitis, HIV or other health problems returned abnormal, this might be upsetting. We will discuss your test results with you. Positive tests will be reported to the Public Health Department. At your request, the results of the HIV or other pre-screening health testing can be forwarded to your own doctor. You or your medical insurance company would be responsible for any further costs medical care or counseling if any problems were found at the time of study screening.

What will I be asked to do?

If you will be assigned by chance, like flipping a coin, to receive either the HEV-239 (Hecolin®) vaccine or placebo. The placebo in this study is salt water without vaccine. If you receive placebo it is not expected to result in an immune response to hepatitis E. You have an 80% (4:5) chance of receiving vaccine and a 20% (1:5) chance of receiving placebo. Neither you nor the study doctor will know which group you are in until the study is over. You will receive 3 doses of either the vaccine or the placebo. The second dose will occur about 1 month after the initial dose and the third will occur about 6 months after the first dose.

While you are in the study, you must:

- Follow the instructions you are given.
- Come to the study center for all visits with the study doctor or study staff.
- Keep track of symptoms that you might have in the week after you receive each vaccine dose.
- Tell the study doctor or study staff immediately of any severe symptoms that prevent your daily activity or any other severe symptoms or health complaints. This is particularly important in the 4 weeks after each study vaccine. We will follow up with you promptly if this were to happen by telephone and/or in person.
- Tell the study doctor or study staff if you want to stop being in the study at any time.
- Tell the study doctor or study staff immediately if you have a life-threatening event or are hospitalized during the study.

The activities at each study visit are described below and summarized in a Table. None of these study tests are a part of your regular medical care. There are 13 scheduled blood draws during the study. The amount of blood that will be drawn at any visit is from just over 2 to just over 6 tablespoons. The total amount of blood that will be drawn over the study is up to 640 mL (less than 3 cups).

Screening visit(s) (Up to 28 days before you receive the first study vaccination)

Before you can receive any vaccines as part of the study, the study doctor or study staff (which we will refer to as “we” or “us” in this consent) will screen you to see if you are eligible for the study. At this screening visit, we will first talk with you about the study. If you decide to join this study, you will be asked to sign this consent form. To see if you are eligible to be in the study, the screening visit(s) will take place within 28 days before the first dose of vaccine. If more than 28 days passes before you can return for the first study vaccination (Visit Day 1), we will ask you to return to have some of your labs repeated. You will not need to go through the consenting process again for this visit.

We will discuss your health, medications and medical history. The study doctor or study staff will ask if you have an allergy to aluminum hydroxide, other vaccines, or medicines. You will undergo a physical examination, which will include measuring your height, weight, oral temperature, heart rate, and blood pressure.

We will test your blood to learn about your general health. These tests include measures of your complete blood counts and tests for kidney and liver function. The results of these tests must be normal for you to be in the study. Your blood will also be tested for HIV (the virus that causes AIDS), hepatitis B, hepatitis C and hepatitis E. We will discuss the risks and benefits of these tests. Your test results must be negative for you to be in the study. We will collect a sample of your urine for a drug screen for amphetamines (e.g., speed), cocaine, opiates (e.g., heroin), and phencyclidine (PCP). If your drug screen results are positive, you will not be able to join the study.

Women who are capable of bearing children will be asked about their birth control history and we will collect a sample of your blood for a pregnancy test. We will give you your results. Your pregnancy test results must be negative in order for you to be in the study. Men who are capable of conceiving children will be asked about their method of contraception. You will be counselled on ways to avoid conceiving a child.

If the evaluations done at the screening visit indicate that you are able to participate in this study, you will be scheduled to come back for the first study vaccination visit (see below).

Study Vaccination Visits (Days 1, 29, 180)

Before you receive study vaccine, you will be asked about any changes in your health history. This will include asking about any new symptoms or medications you have taken since the screening visit. We will check your heart rate, blood pressure, and temperature. The study doctor may perform a physical exam. The study vaccination may be delayed if you have been sick or had a temperature equal to or greater than 100.4°F (38°C) in the 3 days before this visit. We will ask about any symptoms that you have before administering the vaccine. We will also draw blood at these visits to test the immune response to the study vaccine and for future research studies. If you are female, we will review your birth control history and we will collect a urine sample to test for pregnancy.

Before receiving the first study vaccine, you will be randomly assigned to either the vaccine or placebo group. You will not know to which group you are assigned. You will receive your second dose of vaccine approximately 1 month after your first (Day 29) and your third dose of vaccine ~150 days after your second dose of vaccine (Day 180).

After receiving each study vaccine, you must wait in the study clinic for at least 30 minutes. We will check your vital signs, assess the vaccination site, and ask about any symptoms that you have after receiving the vaccine. If you have no unusual reactions to the study vaccine, you will then be allowed to leave.

You will be asked to record, on the electronic memory aid, any symptoms that you have each day starting on the evening of your study vaccination and for at least the 8 days after each vaccine dose. This will require logging into a website on a daily basis to enter your symptoms and temperature. It could take up to 20 minutes depending on the speed of your internet connection. The information you input into the system will be monitored regularly by the study staff, and will be discussed with you at your follow-up visits. To help protect your privacy, this information will be entered into a different database than the rest of the study information. After this data is complete, it will be added to the primary study database. We will also give you a back-up paper memory aid in case there are any internet or computer problems. You will be given a thermometer to measure your temperature and a ruler to measure injection site reactions to record on the memory aid. You should also call the study team if you have severe symptoms that prevent you from performing your daily activities even if they are not listed on the electronic memory aid. The study team will counsel you to use adequate birth control methods to avoid pregnancy.

You will not be able to receive the second vaccination (Day 29) or the third vaccination (Day 180) for certain reasons, such as if you have a bad reaction to the first (or second) vaccination; if you have severely abnormal laboratory test as determined by the study team, if you are planning to travel to an area of the world with a Hepatitis E outbreak, or if you have had other changes in your health since the last vaccination.

At the Day 180 visit, we will retest your blood to ensure that your complete blood counts and tests for kidney and liver function have not changed.

Follow-up Telephone Call (Days 4, 32, 120, 184, 270)

On study days 4, 32, and 184, the study staff will call you to review the memory aid data you have been recording. On all telephone calls they will ask you about any new symptoms, serious adverse events you may have had, and any new medications you have taken since your last visit. During the Day 120 telephone call, the study team will counsel you to use adequate birth control methods to avoid pregnancy.

Follow-up Visits (Day 8, 15, and 29 after each boost vaccination- Days 8, 15, 36, 43, 57, 187, 194, 208)

On study days 8, 36, and 187, the study staff will review the memory aid data you have recorded. We will check your heart rate, blood pressure, temperature, and your arm where the vaccine was given. At these visits, the study doctor or study staff will talk with you about any new symptoms or medications you have taken since your last visit. The study doctor may perform a brief physical exam, if needed, due to symptoms. We will draw blood on Day 8 after each vaccination (Days 8, 36 and 187) to run tests about your general health. These tests include measures of your complete blood counts and tests for kidney and liver function. At these visits, we will also draw blood to test the immune response to the study vaccine and for future research studies. The study team will counsel you to use adequate birth control methods to avoid pregnancy.

Follow-up Visits (Day 15, after each vaccination – Days 15, 43, and 194)

On study days 15, 43, and 194, the study staff may need to review the memory aid data you have been recording. We will check your heart rate, blood pressure, temperature, and may check the site where the vaccine was given. At these visits, the study doctor or study staff will talk with you about any new symptoms or medications you have taken since your last visit. The study doctor may perform a brief physical exam if needed due to symptoms. We may need to draw blood on Day 15 after each vaccination (Days 15, 43, and 194) to run tests about your general health if they were abnormal Day 8 after each vaccine dose. We will also draw blood at these study visits to test the immune response to the study vaccine and for future research studies. The study team will counsel you to use adequate birth control methods to avoid pregnancy.

Follow-up Visits (Day 29 after each boost vaccination – Days 57 and 208)

On study days 57 and 208, the study staff will talk with you about any new symptoms or medications you have taken since your last visit. The study doctor may perform a brief physical exam if needed due to symptoms. We will also draw blood at these study visits to test the immune response to the study vaccine and for future research studies. The study team will counsel you to use adequate birth control methods to avoid pregnancy.

Final Follow-up Visit (Day 360)

At this visit, the study doctor or study staff will talk with you about any new symptoms or medications you have taken since your last visit. The study doctor may perform a brief physical exam. We will also take a blood sample to test the immune response to the study vaccine and for future use assays at this visit.

The information about the study visits is summarized in the following Visit Summary Table:

Visit Summary Table	Screening	Vaccine (Days 1, 29, 180)	Follow-up (Days 8, 15, 29 after each vaccine)	Follow-up telephone call (Days 4, 32, 120, 184, 270)	Final Study Visit (Day 360)
Consent	X				
Randomized into Vaccine or Placebo Group		X			
Vaccine		X			
Review adverse reactions		X	X	X	X
Review medical history	X	X			
Review medications	X	X	X	X	X
Vital signs/Physical Exam	X	X/Maybe	X/Maybe		No/Maybe
Blood for safety labs	X	Only on Day 180	Day 8 after each vaccine, Day 15 after each vaccine only if abnormal at Day 8		
Blood to test for prior hepatitis E exposure	X				
Urine drug screen	X				
Pregnancy test	X	X			
Blood draw for vaccine responses and future use		X	X		X

Unscheduled Visits

You may be asked to come back to the study clinic at other times if the study staff feels there is a need to do so. The study staff would review with you your symptoms and determine what additional activities or testing would be necessary.

Early Withdrawal from the Study

If you decide to withdraw from the study prior to the final visit, we will ask you if needed to allow us to obtain a blood sample to evaluate immune response to the study vaccine. If needed, we would like to check your heart rate, blood pressure, temperature, and perform a brief physical examination. The study doctor or study staff will talk with you about any changes in your health history, including any adverse reactions that you may have had and may ask about medications you have taken since your last visit. If you have recently received vaccine, we may ask you to continue filling in the memory aid or to keep track of any symptoms until they are resolved. If needed, we will draw blood to run tests about your general health (measures of your complete blood counts

and tests for kidney and liver function). If it is within 14 days after a study vaccination, the study staff will look at the study vaccination site. For women of childbearing potential: a urine sample may be collected to check for pregnancy and you will be reminded to avoid pregnancy for 3 months after the last vaccination you received.

If you are no longer able to continue to receive study vaccinations, you may be able to continue in the study. If this is the case, you will follow the study schedule outlined above as long as it does not affect your safety.

Who owns my study information and samples?

If you join this study, you will be donating your samples and study information. You will not receive any compensation if your samples or information are used to make a new product.

CONSENT FOR STORAGE AND USE OF SAMPLES IN FUTURE RESEARCH – ALL SUBJECTS

Residual samples are those that are left over after the study has been completed. After tests are done on your blood as part of this study, we will keep any leftover blood for future research studies. Future use samples are extra tubes of blood collected and stored for possible use in future research studies. We will be collecting blood specifically for future research studies at every visit when you have your blood obtained except for the screening visit. Retention of residual and future use samples and the potential for use in future research studies will be a condition of study participation. If you join this study, you agree to allow future research studies to be conducted on any residual samples and the extra blood collected specifically for future use.

These studies would most likely test parts of the immune response to hepatitis E virus. Stored blood samples might be used in new or different laboratory tests, to develop new laboratory tests, to give information for the development of new vaccines, for genetic testing, or for studies of hepatitis E or other infections. After this study is over, stored blood samples may be shared with other researchers at other institutions.

The risks of storing your samples for use in possible future research studies or having them used in future research studies are those associated with possible loss of confidentiality. The future use samples and any leftover blood samples will be stored indefinitely at a site determined by the sponsor, NIH. Stored blood samples will be labeled only with a barcode and a unique tracking number. Stored blood samples will not be labeled with your name or initials, or any other information that could readily identify you, and will be kept confidential to the best of the sponsor's ability, and as required by law. These coded samples may be stored and shared with other investigators at other institutions. Electronic files associated with these samples will be password protected. Only people who are involved in the conduct, oversight, or auditing of this study will be allowed access to uncoded information that could identify you.

Residual and future use samples will not be sold or used directly for production of any commercial product. There are no benefits to you from the collection, storage and subsequent use of your blood for future research.

If these stored samples are tested in the future, the results may be published. You will not be identified in such publication. None of your identifying information will be used in the reporting or publication of any results. In other words, the publication will not contain any information about you that would enable someone to determine your identity. Results from this future research would not be reported to you or your own regular doctor or placed in your medical record.

Although the results from this future research, including your donated samples, may be patentable or have commercial value, you will have no legal or financial interest in any commercial development resulting from the research.

To join this study, you must agree to storage and future use of your blood (any residual samples that are left over and the blood specifically drawn for future use). By signing this consent form, you are agreeing to the collection of your samples during this trial for future research, your samples will be used for future research. You may withdraw consent for study participation at any time by notifying the study doctors or nurses in writing. However, any data from sample(s) collected prior to the withdrawing consent will not be removed including genomic data. There will be no further use of residual samples or collection and use of future use samples after consent has been withdrawn.

Ask us if you have questions about how your blood samples may be used.

_____ (Initials) I understand, if I take part in this study, then my blood samples will be stored for an indefinite period and may be used for future research.

Risks and Discomforts

General Risks and Discomforts

While in the study, you are at risk for some side effects. You should discuss these with the research team and/or your regular doctor. There also may be other side effects that we cannot predict. The potential risks due to your participation in the study are those related to drawing your blood with a needle, vaccine administration, and possible reactions to the vaccine.

Some people may feel lightheaded or faint during, or just after, a vaccination. In the days after vaccination there may be pain, soreness, redness, swelling, itching, warmth, or firmness at the vaccination site. Bruising or bleeding can also occur at the vaccination site. Some people who receive the vaccine develop a nodule (small rounded lump) at the site of the vaccination. This almost always disappears over time. The skin at the vaccination site may become discolored which could be permanent.

After vaccination, you may experience fever, chills, rash, itching, aches and pains, nausea, headache, and fatigue. Other mild or moderate symptoms may also occur, such as generally not feeling well, dizziness, swelling of glands in the neck, head and underarms, and hot flashes. Occasionally, people might miss work or school.

Very rarely people have allergic reactions to vaccines. A very bad allergic reaction is called “anaphylaxis” (also known as allergic shock). It is the same thing that can happen to people who are allergic to bees are stung. Some things that happen during this type of an allergic reaction are a rash (hives); having a hard time breathing; wheezing when you breathe; loss of consciousness; sudden drop in blood pressure; swelling around the mouth, throat, or eyes; fast pulse; and/or sweating. This type of allergic reaction requires immediate medical attention. If this reaction occurs, the study staff will have emergency medications available. Most people who experience anaphylaxis recover completely, but very rarely people can die. You will be monitored for 30 minutes after each vaccine dose to watch for this type of allergic reaction.

HEV-239 (Hecolin®) Risks and Discomforts

HEV-239 is not currently licensed for use in the U.S. It has been given to over 93,000 people in China since it was licensed in 2012 and shown to be generally well-tolerated and safe. The vaccine was given to people who had already been infected with Hepatitis E and to people vaccinated against Hepatitis B and was well-tolerated and safe in both groups. The main risk associated with HEV-239 has been reactions at the vaccine site. These were primarily pain and swelling but also included redness, firmness and itching. Some people experienced more general symptoms such as fever, fatigue, and headaches. Most of these symptoms were mild and resolved on their own. Post-marketing safety data is limited but one individual did develop a whole body rash that got better about 3 weeks after vaccination.

Safety information regarding aluminum hydroxide and thimerosal which are ingredients in HEV-239 (Hecolin®) are included in the overall vaccine safety profile. Aluminum hydroxide is used as an adjuvant in other approved vaccines such as Hepatitis A, Hepatitis B, Diphtheria-tetanus-pertussis (DTaP, Tdap), Haemophilus influenza type b (Hib), human papillomavirus (HPV) and pneumococcal vaccines. Thimerosal has been suggested to increase the risk of autism in children although multiple studies have not proved that there is an association.

It is possible that the researchers will learn something new during the study about the risks of the vaccine. If this happens, they will tell you about it. Then you can decide if you want to continue to be in this study, or not. You may be asked to sign a new consent form that includes the new information if you decide to stay in the study.

Side effects of having blood taken

Having your blood taken can cause discomfort. This discomfort is temporary but may cause lightheadedness or fainting. Taking blood can cause bruising. Bruising can be prevented or reduced by putting pressure on the site for a few minutes after the blood is taken. Rarely, some people get an infection where the needle was put in their arm to draw the blood. To reduce the risk of infection, we will wipe the area clean with alcohol and use sterile equipment. You will not be able to donate blood until Day 270, and possibly longer depending on local blood donation requirements.

Reproductive Risks

If you are a woman: to protect against possible side effects of the study drug, women who are pregnant or nursing a child may not take part in this study. If you become pregnant, there may be risks to you, the embryo, or fetus. These risks are not yet known. If you are a woman of childbearing ability, you and the study doctor must agree on a method of birth control to use throughout the study. If you think that you have gotten pregnant during the study, you must tell the study doctor immediately. Pregnant women will be taken out of the study.

All women who are able of bearing children must have a blood pregnancy test before starting the study and urine pregnancy test done before each following dose of study vaccine. This test must be negative for you to receive vaccine. If you are female and able to bear children, you must agree to use an acceptable method of birth control for at least 28 days before your first study vaccine, and to continue using it until at least 3 months after the final study vaccine.

Acceptable birth control methods include abstinence (no sexual intercourse with men), monogamy with a vasectomized partner, an intrauterine device (IUD), a barrier method plus spermicide, or approved hormonal methods (such as NuvaRing®, birth control pills or shots). If you become pregnant or think you are pregnant while you are in the study you should report this to the study staff immediately.

If you become pregnant, you will not receive any further study vaccines. With your permission, the researchers will still obtain all study blood samples continue to monitor your health and the outcome of your pregnancy. The study staff may ask for information about the pregnancy and the birth of the baby. The study staff will share this information with the sponsors and its designees.

If you are a man: the effect of the study drug on sperm is not known. To protect against possible side effects, if you are a man you should not get a sexual partner pregnant after receiving the study vaccine for 3 months after the last dose. You and the study doctor should agree on a method of birth control to use throughout the study.

Will I benefit directly from the study?

This study is experimental research and there is no guarantee that you will get any benefit from it. Vaccination with HEV-239 (Hecolin®) may or may not provide you with protection against Hepatitis E virus should you ever be exposed. However, we hope that in the future, other people might benefit from this study as knowledge of the safety and effectiveness of the HEV-239 (Hecolin®) vaccine will lead to better prevention of Hepatitis E.

Will I be compensated for my time and effort?

You will be compensated while you are in this clinical trial for your time, travel, and inconvenience as follows:

- \$75 for screening
- \$75 for each vaccination clinic visit (up to 3 total)
- \$50 for each follow-up clinic visit
- \$20 for each scheduled phone call
- \$20 for unscheduled visits, if needed

You will have 1 screening visit, 3 total vaccination visits, 9 follow-up clinic visits, and 5 phone calls. You will get \$850 if you complete all study visits. If you do not finish the study, we will compensate you for the visits you have completed.

Our preferred method of compensation will be the use of Clincards. All payments are made using a personal payment card. We issue this to you for free. The payment card is a prepaid debit card. It can be used exactly like a MasterCard.

We load money onto your card electronically every time you need to be paid. The card scheme is run by Greenphire, an independent company specializing in payments for research studies and clinical trials. To issue your card, we need to give Greenphire some of your personal information. Banks and other financial institutions can access this information if they need to verify your identity when you use your card.

Emory University is required by law to report any payments we make to the IRS. To do this, Emory University Department of Finance needs to keep your Social Security Number on file. We are asking you to allow us to communicate your name, address, date of birth, research study name and Social Security Number to Greenphire and

Emory University Department of Finance. If you want to receive e-mail or text alerts when payments are made to you, we will ask you to provide your e-mail or phone number as well. All of this information will be stored on computers owned by Greenphire. Greenphire will not have access to any other information collected during this study. Full instructions about using your card are included when we issue it. Please ask if you have any questions or concerns about the card scheme.

We would also like the option of compensating you in the form of cash, check or gift card if ClinCard accessibility is not available. You will be asked to fill out a tax form, including your Social Security or Taxpayer Identification Number, in order to be reimbursed, depending on the amount and method of payment. Some payment methods involve mail coming to your house, which may be seen by others in your household. You can decline payment if you are concerned about confidentiality, or you can talk to the study team to see if there are other payment options. You will need to fill out a W-9 form.

What are my other options?

You do not have to take part in this study. Instead of being in this study you may choose not to take part. At this time, there is no licensed (approved) vaccine in the US that offers protection against hepatitis E virus.

Taking part in this study, however, may make you unable to participate in some other research studies. You should discuss this with the researchers if you have concerns. You may wish to research other study options at websites like clinicaltrials.gov and ResearchMatch.org.

Confidentiality

Certain offices and people other than the researchers may look at your medical charts and study records. Government agencies and Emory employees overseeing proper study conduct may look at your study records. These offices include:

- Food and Drug Administration (FDA)
- The Office for Human Research Protections
- The Sponsors and their designees: including the Division of Microbiology and Infectious Diseases (DMID), Vaccine and Treatment Evaluation Unit (VTEU) and National Institutes of Health (NIH)
- Emory University: Institutional Review Board (IRB), Office of Research Compliance, Office for Clinical Research and the Environmental Health & Safety Office.

The authority to collect this information is under 42 USC 285f.

Emory will keep any research records we create private to the extent we are required to do so by law. A study number rather than your name will be used on study records wherever possible. Your name and other facts that might point to you will not appear when we present or publish the results of this study.

Certificate of Confidentiality

There is a Certificate of Confidentiality from the National Institutes of Health for this Study. The Certificate of Confidentiality helps us to keep others from learning that you participated in this study. Emory will rely on the Certificate of Confidentiality to refuse to give out study information that identifies you. For example, if Emory received a subpoena for study records, it would not give out information that identifies you.

The Certificate of Confidentiality does not stop you or someone else, like a member of your family, from giving out information about your participation in this study. For example, if you let your insurance company know that you are in this study, and you agree to give the insurance company research information, then the investigator cannot use the Certificate to withhold this information. This means you and your family also need to protect your own privacy.

The Certificate does not stop Emory from making the following disclosures about you:

- Giving state public health officials information about certain infectious diseases,
- Giving law officials information about abuse of a child, elderly person or disabled person.

- Giving out information to prevent harm to you or others.

Giving the study sponsor or funders information about the study, including information for an audit or evaluation.

Research Information Will Go Into the Medical Record:

If you are or have been an Emory Healthcare patient, you have an Emory Healthcare medical record. If you are not and have never been an Emory Healthcare patient, you do not have one. Please note that an Emory Healthcare medical record **will** be created if you have any services or procedures done by an Emory provider or facility for this study.

If you agree to be in this study, a copy of the consent form and HIPAA patient form that you sign will be placed in your Emory Healthcare medical record. Emory Healthcare may create study information about you that can help Emory Healthcare take care of you. Some tests obtained specifically for the study (e.g., HIV, Hepatitis B, and Hepatitis C tests) will be available in your Emory Healthcare medical record. Anyone who has access to your medical record will be able to have access to all the study information placed there. The confidentiality of the study information in your medical record will be protected by laws like the HIPAA Privacy Rule. On the other hand, some state and federal laws and rules may not protect the research information from disclosure.

Emory does not control results from tests and procedures done at other places. So these results would not be placed in your Emory Healthcare medical record. They will not likely be available to Emory Healthcare to help take care of you. Emory also does not have control over any other medical records that you may have with other healthcare providers. Emory will not send any test or procedure results from the study to these providers. So if you decide to be in this study, it is up to you to let them know.

The researchers will review the results of certain study tests and procedures only for the research. The researchers **will not** be looking at the results of these tests and procedures to make decisions about your personal health or treatment. For this study, those things include:

- Vital Signs, Height and Weight
- Physical Examination
- Pregnancy Test (if a woman of child bearing potential)
- Laboratory test results
- HIV, Hepatitis B and Hepatitis C test results
- Memory Aids
- Adverse Event or Serious Adverse Event assessments

If medical attention is needed to address these results, the study team may ask you to follow-up with your regular healthcare provider (or the study team can refer you to a healthcare provider if you don't have a regular provider).

A Safety Monitoring Committee, an independent group of experts, will be reviewing the data from this research throughout the study. The investigator will tell you about new information from this or other studies that may affect your health, welfare, or willingness to stay in this study.

The information from the research study may be published. You will not be identified in such publication. The publication will not contain information about you that would enable someone to determine your identity as a research participant without your authorization.

In Case of Injury:

If you get ill or injured from being in the study, Emory would help you to get medical treatment. If you suffer physical injury from this study, the study doctor will provide immediate medical treatment. The study doctor will also provide referrals to appropriate health care facilities. Your insurer will be billed for your treatment costs. If you do not have insurance, or if your insurer does not pay, then you will have to pay these costs. No financial compensation by the doctors that gave you the vaccine will be made for any discomfort suffered because of participation in this study. The only exception is if it is proven that your injury or illness is directly caused by the negligence of an Emory or sponsor employee. “Negligence” is the failure to follow a standard duty of care. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH or the Federal Government.

If you do not have insurance, or if your insurer does not pay, then you will have to pay these costs.

If you believe you have become ill or injured from this research, you should contact Dr. Evan Anderson at telephone number (404) 727-1746. You should also let any health care provider who treats you know that you are in a research study.

By signing this consent form you do not give up any of the legal rights you have as a participant in a research study.

Costs

Other than basic expenses like transportation, there will be no costs to you for participating in this study. You will not be charged for any of the research activities. However, if any non-study related health concerns are discovered that require further medical care or counseling, you or your health insurance company will be responsible for these costs.

You will have to pay for the items or services for which the study sponsor does not pay. The sponsor will not pay for your regular medical care. If you have insurance, Emory will submit claims to your insurance for items and services that the sponsor does not cover. Emory will send in only those claims for items and services that it reasonably believes your insurance will pay and that the sponsor has not paid.

The actual amount that you have to pay depends on whether or not you have health insurance and whether or not that insurance will pay for any research study costs. Generally, insurance companies will not pay for items and services that are required just for a research study. Some insurance companies will not pay for regular medical treatment or treatment for complications if you are in a study. How much you will have to pay for any co-payments, deductibles or co-insurance depends on your plan. Emory and the sponsor will not pay for these costs.

It is a good idea to contact your insurance provider and tell them you want to be in this research study. Ask them what they will pay for and what they will not pay for. You can also ask the study team for help in figuring out what you will have to pay.

If you do not have insurance, Emory will review your case as part of its program for low-income patient care. The standard policies of that program will apply. The program will figure out if you have to pay any costs for taking part in the study and what those costs will be.

Withdrawal from the Study

You have the right to leave a study at any time without penalty. If you leave the study before the final planned study visit, the researchers may ask you to have some of the final testing done for your safety. No further information will be collected for the purposes of the study, but we will keep the information collected prior to the withdrawal for the integrity of the study.

The researchers and sponsor also have the right to stop your participation in this study without your consent if:

- They believe it is in your best interest.
- You could be removed from the study for reasons related only to you (for example, if you move to another city, you have a serious reaction to the vaccine, you planned to travel to an epidemic Hepatitis E area, you no longer used adequate birth control, or you refuse to receive your study vaccine).
- You were to object to any future changes that may be made in the study plan.
- The FDA, sponsor, the study doctor or Institutional Review Board may stop the study at any time.

Authorization to Use and Disclose Protected Health Information

The privacy of your health information is important to us. We call your health information that identifies you, your “protected health information” or “PHI.” To protect your PHI, we will follow federal and state privacy laws, including the Health Insurance Portability and Accountability Act and regulations (HIPAA). We refer to all of these laws as the “Privacy Rules.” Here we let you know how we will use and disclose your PHI.

PHI that Will be Used/Disclosed:

The PHI that we will use or share for the main research study includes:

- Medical information about you including your medical history and present/past medications.
- Results of exams, procedures and tests you have before and during the study.
- Laboratory test results.

Purposes for Which Your PHI Will be Used/Disclosed:

We will use and share your PHI for the conduct and oversight of the research study. We will use and share your PHI to provide you with study related treatment and for payment for such treatment. We will also use and share your PHI to conduct normal business operations. We may share your PHI with other people and places that help us conduct or carry out the study, such as laboratories, data management centers, data monitors, contract research organizations, Institutional Review Boards (IRBs) and other study sites. If you leave the study, we may use your PHI to determine your health, vital status or contact information.

Use and Disclosure of Your Information That is Required by Law:

We will use and disclose your PHI when we are required to do so by law. This includes laws that require us to report child abuse or abuse of elderly or disabled adults.

Authorization to Use PHI is Required to Participate:

By signing this form, you give us permission to use and share your PHI as described in this document. You do not have to sign this form to authorize the use and disclosure of your PHI. If you do not sign this form, then you may not participate in the research study.

People Who will Use/Disclose Your PHI:

The following people and groups will use and disclose your PHI in connection with the research study:

- The Principal Investigator and research staff will share your PHI with other people and groups to help conduct the study or to provide oversight for the study.

- NIH is the Sponsor of the study. The Sponsor may use and disclose your PHI to make sure the research is done correctly and to collect and analyze the results of the research. The Sponsor may disclose your PHI to other people and groups like study monitors to help conduct the study or to provide oversight for the study.
- The following people and groups will use your PHI to make sure the research is done correctly and safely:
 - Emory offices that are part of the Human Research Participant Protection Program and those that are involved in study administration and billing. These include the Emory IRB, the Emory Research and Healthcare Compliance Offices, and the Emory Office for Clinical Research.
 - Government agencies that regulate the research including: Office for Human Research Protections; Food and Drug Administration.
 - Public health agencies.
 - Research monitors and reviewer.
 - Accreditation agencies.
 - The National Institutes of Health
- Sometimes a Principal Investigator or other researcher moves to a different institution. If this happens, your PHI may be shared with that new institution and their oversight offices. PHI will be shared securely and under a legal agreement to ensure it continues to be used under the terms of this consent and HIPAA authorization.

Expiration of Your Authorization

Your PHI will be used until this research study ends.

Revoking Your Authorization

If you sign this form, at any time later you may revoke (take back) your permission to use your information. If you want to do this, you must contact the study team at:

Evan Anderson, MD
2015 Uppergate Drive
Atlanta, GA 30322

At that point, the researchers would not collect any more of your PHI. But they may use or disclose the information you already gave them so they can follow the law, protect your safety, or make sure that the study was done properly and the data is correct. If you revoke your authorization you will not be able to stay in the study.

Other Items You Should Know about Your Privacy

Not all people and entities are covered by the Privacy Rules. HIPAA only applies to health care providers, health care payers, and health care clearinghouses. If we disclose your information to people who are not covered by the Privacy Rules, including HIPAA, then your information won't be protected by the Privacy Rules. People who do not have to follow the Privacy rules can use or disclose your information with others without your permission if they are allowed to do so by the laws that cover them.

To maintain the integrity of this research study, you generally will not have access to your PHI related to this research until the study is complete. When the study ends, and at your request, you generally will have access to your PHI that we maintain in a designated record set. A designated record set is data that includes medical information or billing records that your health care providers use to make decisions about you. If it is necessary for your health care, your health information will be provided to your doctor.

We may remove identifying information from your PHI. Once we do this, the remaining information will not be subject to the Privacy Rules. Information without identifiers may be used or disclosed with other people or organizations for purposes besides this study.

Contact for Future Studies

We may want to contact you in the future to see if you would be interested in participating in future studies. If and when you are contacted, you can decide if you want to participate in any of the other studies and you will sign another consent form to participate in those studies. Your decision regarding future contacts will not affect your participation in this study. Agreeing to be contacted does not obligate you to participate in any future studies.

Please initial your decision about permission for possible participation in future research studies (select only ONE option):

_____ YES, you may contact me about future studies.

_____ NO, you may not contact me about future studies.

Contact Information

Contact Dr. Evan Anderson at 404-727-1746. After hours, please call the emergency phone number at 678-825-5428.

- if you have any questions about this study or your part in it,
- if you feel you have had a research-related injury or a bad reaction to the study drug, or
- if you have questions, concerns or complaints about the research

Contact the Emory Institutional Review Board at 404-712-0720 or 877-503-9797 or irb@emory.edu:

- if you have questions about your rights as a research participant.
- if you have questions, concerns or complaints about the research.
- You may also let the IRB know about your experience as a research participant through our Research Participant Survey at <http://www.surveymonkey.com/s/6ZDMW75>.

Consent and Authorization

TO BE FILLED OUT BY SUBJECT ONLY

Please **print** your name, **sign**, and **date** below if you agree to be in the main study. By signing this consent and authorization form, you will not give up any of your legal rights. We will give you a copy of the signed form to keep.

Name of Subject

Signature of Subject (18 or older and able to consent)

Date

Time

TO BE FILLED OUT BY STUDY TEAM ONLY

Name of Person Conducting Informed Consent Discussion

Signature of Person Conducting Informed Consent Discussion

Date

Time