Consent of an Adult to Be in a Research Study

In this form "you" means a person 18 years of age or older who is being asked to volunteer to participate in this study.

Participant's Name_____

What is the purpose of this form?

This form will provide you with information about this research study. You do not have to be in the study if you do not want to. You should have all your questions answered before you agree to be in this study.

Please read this form carefully. If you want to be in the study, you will need to sign this form. You will be given a signed copy of this form.

Who is funding this study?

This study is being funded by a grants from CSL Behring and the Jeffrey Modell Foundation. Additional funding may be provided by The University of Virginia Department of Medicine, Division of Asthma, Allergy and Immunology.

Key Information About This Research Study

Principal Investigator:	Larry Borish, M.D. 2955 Ivy Road, Suite 311 Charlottesville, VA 22903 434-924-2227
Sponsor:	1) CSL Behring 2) The Jeffrey Modell Foundation 3) University of Virginia Department of Medicine, Division of Asthma, Allergy and Immunology

You are being asked to take part in a research study. You do not have to take part in this study. You should only agree to take part in this study after reading this consent form and discussing it with the study team.

You may also discuss this with your family, friends, health care providers or others before you make a decision.

What problem is this study trying to solve?

IgE is the antibody thought to be responsible for developing allergies. Undetectable serum IgE (an IgE below the lower limit of detection) is found in about 3% of the general population. In the past, it has been thought that having an undetectable IgE does not have any health impact,

other than meaning that you are at low risk for having allergies. However, recent studies of patients with undetectable IgE have shown higher rates of infections, autoimmune disease and cancer.
Patients with an immune deficiency called common variable immunodeficiency (CVID) also have higher rates of infections, autoimmune disease and cancer. Recently, we have shown that most patients with CVID have a low/undetectable serum IgE.

This study is trying to find out if an undetectable serum IgE is a biomarker, or early sign of, the development of CVID or other antibody deficiencies. You are being asked to take part in this study because you had your IgE measured for another reason (for example, to look for allergic disease), and it was found to be undetectable.

We propose to first confirm that you have no history of recurrent infections and normal levels of the infection-fighting antibodies IgG, IgA and IgM, and therefore do not have CVID or any other form of known immune deficiency. We will then administer the *Salmonella typhi* polysaccharide vaccine, which is a traveler's vaccine that protects against typhoid fever. The response to this vaccine has recently been shown to be a useful tool in the diagnosis of antibody deficiency. We will measure if your response to the vaccine is normal or impaired. We will also measure the ability of your immune cells to make IgE.

Why would you want to take part in this study?

You may want to participate in this study because you find it rewarding to help advance our scientific knowledge of the significance of an undetectable IgE. Another benefit of participating in this study is the protection from infection you gain from receiving the *Salmonella typhi* vaccine**.** Aside from receiving the vaccine, you will not be helped by participating in this study; however, the information gained by doing this study may help others in the future.

Why would you NOT want to take part in this study?

Participation in this research study is completely voluntary. At this time, we are unsure of the significance of an undetectable serum IgE. This may be incidental finding and have no impact on your immune system, or it may serve as an early marker of an immune system defect. This is why we would like to study it.

You might not want to participate in this study because of the inconvenience of the study as it requires two blood draws, administration of a vaccine, and follow up (phone call and blood draws) at years 1, 3, and 5 post-study. You also may not want to participate in this study because there are possible side effects of the vaccine.

What will I have to do if I take part in this study?

Full details of all the procedures are found later in this form.
If you take part in this study you will:

- Undergo a blood draw to measure your serum antibody levels including IgE

- Complete a brief questionnaire regarding your history of infections and your family's history of infections
- Receive the Salmonella typhi vaccine (2nd blood draw)
- Have a repeat blood draw in 4-6 weeks (3 blood draws)
- Be contact via telephone at years 1, 3, and 5 post-study to see if you have developed recurrent infections or autoimmune conditions.
- Return to the clinic and have blood draws at years 1, 3, and 5 post-study (3 blood draws).
- It should take under 30 minutes for each blood draw

What is the difference between being in this study and getting usual care?

- As part of your usual care, you would not likely have the vaccine or have your blood tested three times for serum antibody levels including IgE .
- This vaccine is approved by the U.S. Food and Drug Administration (FDA) and recommended by the Centers for Disease Control (CDC) for administration to travelers to parts of the world where typhoid is common; people in close contact with a typhoid carrier; and laboratory workers who work with *Salmonella typhi* bacteria. It is approved in children ages 2 years and older and adults. This vaccine may be safely used in individuals with undetectable IgE; however, the use of this vaccine to look at the immune response is experimental and not typically how this vaccine is used.

You are being asked to take part in this study because based on prior labs you have an undetectable serum IgE.

Up to 45 people will be in this study at UVA.

How long will this study take?

Your participation in this study will require 3 study visits over a 4-6 week period of time. Each visit will last 15-30 minutes. There will also be follow ups at years 1, 3, and 5 post-study.

What will happen if you are in the study?

SCREENING (30 minutes)

If you agree to participate, you will sign this consent form before any study related procedures take place. Before you can start in the study, there will be a screening period. You will have tests and procedures during this time to make sure you are eligible and it is safe for you to participate. These include the following:

- A brief study questionnaire regarding current immunosuppressant medication use, your personal history of infections and your immediate family's history of infections. This will take about 10 minutes to complete.
- A blood test to measure your serum antibody levels (1/3 tablespoon of blood or 5mL)

- All of this may be combined with information from your health record

If these tests show you are eligible, you will return to the clinic within 30 days to begin the study.

VISIT 1 (Week 1, 15 minutes)

You will receive the Salmonella typhi vaccine. You will have another blood draw (4 tablespoons of blood) for measurement of baseline levels of antibodies against *Salmonella typhi*. We will also use this blood to separate your B cells (a type of white blood cell that makes antibodies) to test their ability to make IgE antibodies. Your vaccine response will be compared to healthy controls for the data analysis.

VISIT 2 (Week 4-6, 15 minutes)

You will return in 4-6 weeks to the same laboratory for repeat blood draw to measure your antibody response to the vaccine (1/3 tablespoon of blood). This should take about 15 minutes. After completion of the second blood draw, you will have completed the study.

FOLLOW UP

- You will be contacted via telephone at 1, 3, and 5 years after study completion. We will ask you if you have developed a history of recurrent infections or autoimmune conditions
- You will asked to return to the clinic for a blood draw at 1, 3, and 5 years after study completion (about 1/3 tablespoon or 5 mL). The blood will be use to check for certain proteins called antibodies).

What are your responsibilities in the study?

You have certain responsibilities to help ensure your safety during the study.

These responsibilities are listed below:

- You must come to each study visit.
- You must be completely truthful about your health history.
- Follow all instructions given.
- You should tell the study doctor or study staff about any changes in your health or the way you feel.
- Answer all of the study-related questions completely.

Blood Testing

We will take up to 4 tablespoons of blood per blood draw; there are a total of 3 blood draws separated by 4-10 weeks**.** The total amount of blood we will take will not exceed 5 tablespoons during the study period. For follow up, the total amount of blood drawn will be 1/3 tablespoon per year.

The blood we take will be tested to measure your serum antibody levels as well as your vaccine response. Additionally, we will isolate your B cells (a type of white blood cell that makes antibodies) to test their ability to make IgE antibodies.

If you want to know about the results before the study is done:

During the study your study leader will let you know of any test results that may be important to your health. In addition, as the research moves forward, your study leader will keep you informed of any new findings that may be important for your health or may help you decide if you want to continue in the study. The final results of the research will not be known until all the information from everyone is combined and reviewed. At that time you can ask for more information about the study results.

Collection of Samples and Health Information for Specimen Banking

What Sort of Research Will Be Done On Your Sample(s)?

You are being asked to provide samples of your blood to be used for research. Along with specimens, researchers may need to collect some health information about you. Combining information from the specimen with information from your health records may be useful for this research. For this research, the following types of information could be included: your history of infections and your family history of infections.

In addition, if you agree, specimens collected for research will be added to a research specimen bank. The purpose of a specimen bank is to process, and store samples until researchers need them for future research. The long term goals of the samples collected in this bank will be mainly used for research on immunodeficiencies. It is not possible to list every research project that will include the samples because we cannot predict all of the research questions that will be important over the coming years. As we learn more, new research questions and new types of research may be done.

What will you have to do to give samples for research?

We will obtain blood samples from you for testing. This will be collected during Visit 1 and Visit 2. We will obtain blood at years 1, 3, and 5 during the post-study follow up. These samples will be saved for future research.

How Will Your Sample(s) Be Stored and Labeled for Specimen Banking?

Dr. Larry Borish will be responsible for storing your sample and for protecting your privacy.

Your sample(s) will not be labeled with your name or other information that would identify you directly. Instead, it will have a unique code that allows for it to be linked to some of your health information. This link means that your specimen can be identified but only indirectly. We can find out if we need to know which sample is yours in the event you wish the sample to be removed at a later date.

Which researchers can use your samples and what information about you can they have?
Your sample may be shared with researchers at the University of Virginia and at other institutions and the sponsor. Dr. Larry Borish will not give your name to other researchers who want to use your sample, but will only give them information like your age and what disease/condition you have. Those who would see the information would include researchers and the others listed under "Who will see your private information?" section of this consent document.

Some of the people who receive your information may not have to follow the privacy laws and may share or release your information because they do not have to follow the privacy laws.

What Are the Benefits To Donating Your Sample(s) For Specimen Banking?
The specimen banking that is done with your sample is not meant to help you. But, doctors hope that in the future it will help people who have other diseases or conditions.

It is very unlikely that any future research performed using your specimen(s) would benefit you directly, but it may provide important medical knowledge that could help other patients with your medical condition or other medical problems in the future.

What Are The Risks of Donating Your Sample(s) For This Study?
Risks to Privacy from Specimen Banking:
The main risk of allowing us to store and use your samples and certain limited health information for research is a potential loss of privacy. One of the risks to you is the release of information from your health records. The University of Virginia will do its best to protect your records so that facts about you and your health will be kept private. The chance that information identifying you will be given to someone else is very small. However, we cannot *guarantee* it will be safe. To further safeguard your privacy, information obtained from future research will not be placed in your medical record.

There are certain risks of having health information given to other people by mistake. In the unlikely event that this happens, it could cause discrimination or mental harm to you or your family members if others were to see this information. The results could be that you may not be able to get or keep certain kinds of insurance. It could also hurt family relationships.

Will You Find Out the Results of the Research on Your Sample(s) for Specimen Banking?
Neither you, your health care provider**,** nor anyone in your family, will receive the results of any research done on your sample(s). The results will not be put in your health records. Therefore, results from any research done on your sample(s) will not affect your medical care. This helps protect you and other members of your family from harm that might be caused by this information.

What If You Change Your Mind About Donating Your Sample(s) for Specimen Banking?

If you decide now that your sample(s) can be kept for specimen banking, and later change your mind, you can simply withdraw the sample(s) at that time. To withdraw you will need to write to the Principal Investigator listed on the first page of this form. We will then destroy any of your tissue that has not already been used. However, if your sample has been used in genetic research, the information that we have learned will remain in the study, even if you withdraw. Unless you withdraw from the study, permission for researchers to use your tissue and to use and share your private health information for this study will never end.

Will You Be Paid For Donating Your Sample(s) for Specimen Banking?
You will not be paid to donate your sample(s) for specimen banking.

Will Donating Your Sample(s) Cost You Any Money?
There is no cost to you to have your samples collected or used for specimen banking.

Specimen Banking Options:

You do not have to participate and agree for specimens to be collected for specimen banking in order to be in the main part of this study. No matter what you decide to do, your decision will not affect your medical care. You can tell us your choice by placing your initials in one of the options below:

SPECIMEN BANKING:
Please indicate your choice by placing your initials below (if applicable):

___ YES **Your sample(s) may be saved for future research and stored in a specimen bank.**

___ NO **Your sample(s) may not be saved for future research and stored in a specimen bank.**

What are the risks of being in this study?

Risks and side effects related to the vaccine:

Likely

- Pain from the vaccine
- Swelling at the site of the vaccine

Less Likely

- Flu like symptoms following the vaccine
- Large local reaction to the vaccine

Rare but serious

- Severe allergic reaction to the vaccine

- Neurologic conditions secondary to the vaccine such as Guillian-Barre syndrome (less than 1 in 1 million)

Risks from Completing Questionnaire:
You may feel uncomfortable answering some of the questions. If you do not wish to answer a question, you may skip it and to the next question.

Risks of having your blood drawn:
Having blood drawn may cause:
- ✓ pain (common),
- ✓ a bruise (sometimes),
- ✓ fainting or passing out (not very often), and
- ✓ infection (rare).

If the people doing the study are exposed to your blood or body fluids in a way that could give them a disease, your blood may be tested. The tests might check for:
- ✓ hepatitis,
- ✓ HIV (Human Immunodeficiency Virus), or
- ✓ other infections.

You and the person exposed would be told the test results. However, your name would be kept private. If your test is positive for hepatitis or HIV or any other infection that may affect your clinical care, we will tell you the results and help you understand what the results mean for you.

Other unexpected risks:
You may have side effects that we do not expect or know to watch for now. Call the study leader if you have any symptoms or problems.

Could you be helped by being in this study?
You may or may not benefit from being in this study. Possible benefits include: identification of poor vaccine response which could suggest that your immune system does not function normally**.** In addition, information researchers get from this study may help others in the future.

What are your other choices if you do not join this study?
The only choice is not to be in this study.

If you are a patient at UVa your usual care will not be affected if you decide not to participate in this study. If you are an employee of UVa your job will not be affected if you decide not to participate in this study.

Will you be paid for being in this study?

You will be paid $10 for completing screening. If you are eligible, you will be paid $20 for completing Visit 1 and $20 for completing Visit 2. You will be paid by gift card at the end of your screening visit and at the end of Visit 2. If you withdraw from the study for any reason you will be paid accordingly for the parts of the study which you completed. If the study leader says you cannot continue, you will be paid the full amount for the study. During the post-study follow up, you will be paid $50 with gift cards for each blood draw at years 1, 3, and 5.
The maximum total compensation is $200.

The income may be reported to the IRS as income. If you owe money to any Virginia state agency, the state can use the money you earn in this study to pay those debts. These state agencies include the UVa Medical Center, VCU Medical Center or a college or university. The money may be withheld to pay back debt for such things as unpaid medical bills, taxes, fines, child support. Even if this happens, the money you earn may be reported to the IRS as taxable income.

By agreeing to be in this study, you are donating blood samples for research, and giving up any property rights you may have in them. The results of this research using your donated materials may have commercial value. However, you will not receive any payments.

Will being in this study cost you any money?

All of the procedures in this study will be provided at no cost to you or your health insurance.

You and/or your insurance company must pay for any tests or care given beyond what is required in this study. In addition, you and/or your health insurance may also have to pay for other drugs or treatments that are given to help you control any side effects. You will have to pay for any costs not covered by your health plan. You may be responsible for any co-payments or deductibles. You may wish to ask your insurance company for an estimate of what these costs might be or if pre-approval is required.

You will be responsible for the cost of travel to come to any study visit and for any parking costs.

What if you are hurt in this study?

You do not give up any legal rights, such as seeking compensation for injury, by signing this form. If you feel you have been injured as a result of this study you may contact the Principal Investigator or the IRB (phone numbers are located near the end of this form). If you are hurt as a result of being in this study, there are no plans to pay you for medical expenses, lost wages, disability, or discomfort. The charges for any medical treatment you receive will be billed to your insurance. You will be responsible for any amount your insurance does not cover.

What happens if you leave the study early?

You can change your mind about being in the study any time. You can agree to be in the study now and change your mind later. If you decide to stop, please tell us right away. You do not have to be in this study to get services you can normally get at the University of Virginia.

Even if you do not change your mind, the study leader (Dr. Larry Borish) can take you out of the study. Some of the reasons for doing so may include

a) Your study physician is concerned about your health
b) You do not follow your doctor's instructions
c) The study sponsor closes the study for safety, administrative or other reasons

If you decide to stop being in the study, we will ask you to: please contact the study's leader as soon as possible**.**

Any data collected about you up until the time you leave the study must be kept in order to determine the results of the study.

How will your personal information be shared?

The UVa researchers are asking for your permission to gather, use and share information about you for this study. If you decide not to give your permission, you cannot be in this study, but you can continue to receive regular medical care at UVA.

If you sign this form, we may collect any or all of the following information about you:

- Personal information such as name, address and date of birth
- Social Security number ONLY IF you are being paid to be in this study
- Your health information if required for this study. This may include a review of your medical records and test results from before, during and after the study from any of your doctors or health care providers. This may include mental health care records, substance abuse records, and/or HIV/AIDS records.
- Tissue or blood samples if you agree to provide them for genetic testing for this study

Who will see your private information?

- The researchers to make sure they can conduct the study the right way, observe the effects of the study and understand its results
- People or groups that oversee the study to make sure it is done correctly
- The sponsor(s) of this study, and the people or groups it hires to help perform or review this research
- Insurance companies or other organizations that may need the information in order to pay your medical bills or other costs of your participation in the study
- Tax reporting offices (if you are paid for being in the study)
- People who evaluate study results, which can include sponsors and other companies that make the drug or device being studied, researchers at other sites conducting the same

study, and government agencies that provide oversight such as the Food and Drug Administration (FDA) if the study is regulated by the FDA.
- If you tell us that someone is hurting you, or that you might hurt yourself or someone else, the law may require us to let people in authority know so they can protect you and others.

Information about you and/or samples from you may be given to other researchers outside of the University of Virginia after all identifiers such as name, address, phone # have been removed. Some of the people outside of UVa who will see your information may not have to follow the same privacy laws that we follow. They may release your information to others, and it may no longer be protected by those laws.

The information collected from you might be published in a medical journal. This would be done in a way that protects your privacy. No one will be able to find out from the article that you were in the study.

Information and samples obtained from you during this study may be used in future research. Your information and samples may be shared with other researchers inside or outside of the University of Virginia. They will not be sent with information that could identify you such as name, address or phone number.

What if you sign the form but then decide you don't want your private information shared?

You can change your mind at any time. Your permission does not end unless you cancel it. To cancel it, please send a letter to the researchers listed on this form or complete the "Leaving the Study Early" part of this form and return it to the researchers. Then you will no longer be in the study. The researchers will still use information about you that was collected before you ended your participation.

Please contact the Principal Investigator listed earlier in this form to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator: Larry Borish, MD
2955 Ivy Road, Suite 311
Charlottesville, VA 22903 Telephone: 434-924-2227

What if you have a concern about this study?

You may also report a concern about this study or ask questions about your rights as a research subject by contacting the Institutional Review Board listed below.

University of Virginia Institutional Review Board for Health Sciences Research
PO Box 800483
Charlottesville, Virginia 22908 Telephone: 434-924-9634

When you call or write about a concern, please give as much information as you can. Include the name of the study leader, the IRB-HSR Number (at the top of this form), and details about the problem. This will help officials look into your concern. When reporting a concern, you do not have to give your name.

Signatures

What does your signature mean?

Before you sign this form, please ask questions about any part of this study that is not clear to you. Your signature below means that you have received this information and all your questions have been answered. If you sign the form it means that you agree to join the study. You will receive a copy of this signed document.

Consent From Adult

_____	_____	_____
PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

To be completed by participant if 18 years of age or older.

Person Obtaining Consent

By signing below you confirm that you have fully explained this study to the potential subject, allowed them time to read the consent or have the consent read to them, and have answered all their questions.

_____	_____	_____
PERSON OBTAINING CONSENT (SIGNATURE)	PERSON OBTAINING CONSENT (PRINT)	DATE

Notification of My Health Care Provider

Your health care provider will be notified of your participation in this study.

Leaving the Study Early

Signatures should be obtained in this section if the subject decides to leave the study early.

If you leave the study early the study leader will keep the data collected about you up until the time you leave the study to help determine the results of the study.

Check one option below:

____ I am withdrawing my consent from the intervention or treatment part of this study but agree to continue to have follow up information about me collected by the study team.
The follow up information will be collected by the study team:

- Obtaining information from my medical records

____ I am withdrawing my consent for this study. No additional information may be collected about me including follow up information from my medical records.

Consent From Adult

_____	_____	_____
PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

To be completed by participant if 18 years of age or older.

Person Obtaining Consent

By signing below you confirm that you have fully explained the implications of withdrawing from the study to the subject and have answered all their questions.

_____	_____	_____
PERSON OBTAINING CONSENT (SIGNATURE)	PERSON OBTAINING CONSENT (PRINT)	DATE