INFORMED CONSENT FORM
AND
AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

Sponsor / Study Title:	**National Institutes of Health (NIH)/Division of Microbiology and Infectious Diseases (DMID) / A Phase 2b, Double-Blind, Placebo Controlled Trial to Evaluate the Efficacy of Intramuscularly Administered CssBA+dmLT against Moderate-severe Diarrhea in a Controlled Human Infection Model with Enterotoxigenic *Escherichia coli* (ETEC) Strain B7A in Healthy Adults**
Protocol Number:	**23-0006**
Principal Investigator: (Study Doctor)	**«PiFullName»**
Telephone:	**«IcfPhoneNumber»**
Address:	**«PiLocations»**

KEY INFORMATION

You expressed interest in this research study. This study will look at an experimental (not yet approved or available to the public) vaccine to see if it helps prevent infection from a germ called Enterotoxigenic *Escherichia coli* (ETEC). ETEC is a leading cause of bacterial diarrheal illness. To be in this study, you must be healthy, must not be pregnant, and must be between the ages of 18 and 49 (not yet have had your 50th birthday).

This form gives you information to help you decide whether to be in the study. Being in the study is voluntary. Please read this form carefully. Take your time to ask the study staff your questions. The investigator or study staff will explain words or information you do not understand. If you decide to take part in this study, you must sign your name at the end of this form and date it. You will be given a copy of this form.

The study is sponsored by the National Institutes of Health (NIH) and the Infectious Diseases Clinical Research Consortium (IDCRC). Study products will be provided by PATH Vaccine Solutions, the U.S. Army, and the U.S. Navy.

Your participation, if eligible and enrolled in this study, will last for about 10 months, which includes up to 2 months for screening and 8 months for the study. The study includes the

vaccination period, the ETEC challenge period (inpatient stay and given an ETEC "germ" that may cause illness), and follow-up visits for up to 6 months after your last vaccination.

- You will have up to 10 outpatient clinic visits (2 screening visits, 6 visits for the vaccination period, and 2 visits for follow-up after the challenge period), approximately a 10-day inpatient stay, and 2 telemedicine (over the phone) visits.
- You will receive 3 shots of either the investigational (study) vaccine or placebo in your arm on Days 1, 22, and 43. A placebo is an inactive substance which, in this case, will be salt water. You will not know whether you receive the study vaccine or placebo.
- If you qualify and are selected at 4 weeks after 3rd vaccination, you will be admitted to the inpatient unit and given ETEC strain B7A (also called the ETEC challenge agent, which is a drink with the infectious germ).
- You will receive antibiotics during your inpatient stay to treat ETEC germs.
- You will have physical exams, blood draws, stool collection (bowel movements), and health assessments.
- You will be asked to complete a daily Memory aid (like a diary log) at home to record any side effects that you may have for 7 days after each shot and 5 days after your inpatient stay.
- You will also be asked to avoid people who may be at risk and avoid certain medications and vaccines. This information is described under the "Lifestyle Considerations" section below.
- There are risks to participating:
    - The most common risks from the shots are site redness, pain, discoloration of skin at injection site and hardness. You may have other symptoms, including diarrhea, headache, and body aches.
    - One serious possible risk is anaphylaxis or a severe allergic reaction to the study vaccine. See this consent form's "Risks of Participation" section for more information. You should discuss these risks in detail with the study staff.
    - If not protected against infection with ETEC (such as if you got the placebo or the study vaccine does not work), we expect that following the challenge, approximately 70-90% of people will develop diarrhea which may be moderate to severe. Diarrhea may start as soon as 12 hours after inpatient ETEC challenge dosing, but in some people, symptoms do not start for 4 days after challenge.
    - There is a risk of loss of confidentiality of your health information. Practices to protect your privacy per site policies will be followed
- You will not benefit from being in this study.

When you take part in this study, you are asked to consent to **secondary research** (research not planned yet). We will use your coded information, (not your name or any personally identifiable information), leftover samples, and extra samples collected for secondary research. The secondary research may include **genetic** testing. If you do not want your samples and data used for secondary research, you should not enroll in this study.

Background: WHAT IS ETEC?

ETEC is a bacteria that is one of the most common causes of "travelers' diarrhea" as well as diarrhea among children living in low- and middle-income countries. The diarrhea caused by ETEC can lead to dehydration, which, if untreated, can result in death, particularly in children under the age of five. People usually get ETEC infection by eating or drinking food or liquids containing ETEC related bacteria. The World Health Organization (WHO) has made it a priority to find ways to decrease the risk of being infected with ETEC, including developing effective vaccines.

PURPOSE OF THE STUDY

The purpose of the study is to evaluate the safety, immune response (body's ability to protect), and if this investigational vaccine protects against developing ETEC infection. An investigational vaccine is one that has not yet been approved by the United States Food and Drug Administration (FDA) but has been approved for research. The study vaccine to be studied is called CssBA+dmLT.

This study will compare the CssBA+dmLT vaccine to a placebo.

LIFESTYLE CONSIDERATIONS

- Avoid food or drink with poppy seeds for 72 hours before the screening visit, as this could cause a false positive urine drug screen result.
- ALL participants of child-bearing potential MUST use an effective method of birth control at least 30 days prior to screening and first study vaccination. You must keep using birth control for at least 60 days following the ETEC challenge agent, or last vaccination if you do not receive the challenge agent.
- During the inpatient stay, avoid caffeine on the days you take antibiotics.
- For 7 days after leaving the inpatient unit, avoid interactions with people who may be immunocompromised (elderly persons aged 70 years or more, diapered individuals, persons with disabilities, pregnant/breastfeeding people, children under 2 years of age, or anyone with low/diminished immune system).
- For 7 days after leaving the inpatient unit, do not work or plan to work in either a patient care setting, day care center, or as a food handler.
- Do not receive a licensed, live vaccine within 30 days before first vaccination or after each vaccination and after receipt of the challenge agent.
- Do not receive an inactivated vaccine within 2 weeks before first vaccination until 2 weeks after receipt of challenge agent (an exception is a COVID an/or influenza vaccine which may be received within 7 days of vaccination).
- All participants must not take prescription or over-the-counter medication for weight reduction 3 months prior to screening through the completion of the challenge phase.

- Do not participate in another study evaluating an investigational product (i.e. vaccine, drug, medical device, treatments made from human blood, or medication) within 30 days prior to receipt of study vaccination, and through 60 days after receipt of your last dose for study vaccine or ETEC challenge agent.
- Do not donate blood or plasma (outside of this trial) within 30 days of receipt of study vaccine or for 30 days after discharge from the inpatient unit.

WHAT WILL HAPPEN DURING THE STUDY?

If you take part in this study, it is important for you to understand that you will be asked to keep appointments for outpatient visits (where you leave the same day) and be willing to complete an inpatient stay. If you are selected for the challenge phase of the study, you will be admitted to an inpatient unit and remain there until discharge. You will be asked to have about 9 outpatient clinic visits, a 10-day inpatient stay, and 2 phone calls. You may be asked to complete extra visits if it is in your best medical interest.

SCREENING

Volunteers will be screened for enrollment into the study.

During screening, the following will occur:

- Study staff will explain the purpose of the study and go over the consent form with you.
- You will be asked to sign the consent form.
- Study staff will ask about your medical history and medications, vaccines, and birth control.
- A physical examination, including height and weight will be performed.
- Your heart rate, blood pressure, and temperature will be checked.
- Approximately 6 tablespoons of blood will be collected from an arm or hand vein to:
    - Check your liver, kidney, and blood counts
    - Test for hepatitis B and C (viruses that infect the liver) and HIV (the virus that causes AIDS). If you are positive for these, you will not be allowed in this study. The investigator may be required by law to report the result of these tests to the local health authority.
    - See if you have evidence of having had ETEC infection in the past
    - Store blood for secondary research
- Urine will be collected to check for:
    - Protein (if present in large amount could indicate kidney disease)
    - Opioids (addictive substances)
- If you are capable of becoming pregnant, a urine pregnancy test will be performed.
- A stool (poop) sample will be collected to check your baseline protection to ETEC infection.

A member of the study staff will provide you with the results of your clinical lab tests. If you have results that exclude you from eligibility and are sensitive in nature, you will be asked to return to the clinic to receive test results and counseling regarding follow-up care.

Screening will continue until about 72 participants have been found eligible for further study participation. These participants will be randomly assigned (like the flip of a coin) to receive either the investigational vaccine (CssBA+dmLT) or placebo. You will have a 50% chance of receiving CssBA+dmLT or placebo. This is a double-blind study, which means neither you nor the study staff, investigator, or the sponsor will know which of these study drug groups you will be assigned to. However, in an emergency, the blind can be broken to determine whether you received the study vaccine or placebo.

STUDY VACCINATION PHASE

Based on your randomization assignment (if you got the study vaccine or the placebo), about 3-weeks apart, you will receive a shot of either CssBA+dmLT or placebo in an arm muscle. You will receive a total of 3 doses of either study vaccine or placebo.

At each of the vaccination visits, the following will be done:

- Review your medical history and medications to make sure you are eligible for the study vaccine.
- Based on answers on your medical history, a physical exam may be performed.
- Check your blood pressure, heart rate, and temperature.
- If you are capable of becoming pregnant, a urine pregnancy test will be performed before each study dose.
- Approximately 1 tablespoon of blood will be collected to check your health and also to see how your body is responding to the study vaccine.

You will stay in the clinic for at least 30 minutes after each study vaccine/placebo study dose. The study staff will do a post-vaccination check for any side effects or reactions before you are released from the clinic.

Before leaving the clinic after each study dose of study vaccine/placebo, you will be given a thermometer to check for any fever, a web-based Memory aid (to record how you feel or any changes you may notice), instructions for usage, and site contact information for asking questions or reporting problems. You may receive emails or text messages to remind you to complete the Memory Aid if you fail to do so. The Memory Aid will include reminders for you to report if you have had other symptoms or changes to your health or medications. As needed, study staff will contact you to discuss reported symptoms and changes to your medication. If it is noted that you have not entered data into your Memory Aid, you will be sent an automated email to remind you to enter your information. You will be asked to complete an e-Memory aid and given a backup paper Memory aid that you will bring to clinic visits for review with study staff if you are unable to complete the e-Memory aid.

About 1 week after you receive each dose of study vaccine/placebo, you will be asked to come to the clinic for a follow-up visit.

During the 3 follow up vaccination visits, the following will be done:

- Review your Memory Aid
- Review your medical history, medications, and any changes to your health to confirm that you remain eligible for continued participation
- Based on answers to your medical history review, a physical exam may be performed
- Have blood collected, approximately 3 to 5 tablespoons, to check your health, to see how your body is responding to the study vaccine/placebo, and for secondary research
- Temperature will be checked
- Blood pressure and heart rate may be checked
- A stool kit will be provided to you to collect a sample that will check your health, see how your body is responding to the study vaccine/placebo, and for secondary research

STUDY CONTACT VISIT #1

About 2 weeks after your last study vaccination clinic visit, you will be contacted by a member of the study staff.

During this study contact visit the following will be collected:

- Updates to medications
- Review your medical history and collect any changes to your health

CHALLENGE PHASE (INPATIENT)

About a month after receiving your third dose of study vaccine/placebo, if you are selected, you will be admitted to an inpatient unit for about 10 days. You will be instructed by study staff on items that you are and are NOT allowed to bring with you for the inpatient stay. You also will receive an overview of what will happen during the inpatient stay and what you will be asked to do. After you have checked into the inpatient unit, visitors will not be permitted, and you will not be allowed to leave until you are eligible for discharge.

Upon arrival to the inpatient unit, the following will be done:

- Review your medical history and medications to ensure you are still eligible for continued participation.
- A physical exam will be performed.
- If you can become pregnant, a pregnancy test will be performed prior to the challenge.
- If you have any disease or medical condition, that in the opinion of the study staff prevents your participation in the challenge study, you will be discharged to home and the ETEC challenge agent will not be administered.
- Your blood pressure, heart rate and temperature will be checked, and you will be weighed.

- Your blood will be collected, about 5 tablespoons, to check your health prior to the challenge dose, to see how your body is responding to the study vaccine/placebo, and for secondary research.
- Stool will be collected for secondary research.

As part of the inpatient stay, you will be asked to drink a dose of the ETEC challenge (this drink will contain infectious ETEC bacteria). For at least 90 minutes prior to and after taking the ETEC challenge, you must **not** eat or drink anything.

At the time of the challenge, you first will drink about half a cup of bicarbonate (like baking soda). Five minutes later, you will drink about 1 ounce of bicarbonate solution with the ETEC challenge.

Following the challenge, you will be monitored for at least 90 minutes, during which time your temperature will be taken, and you will be watched for any problems.

If you do not have protection against infection with ETEC, we expect that about 70-90% of people in this study will get diarrhea which may be moderate to severe. Diarrhea may start as soon as 12 hours after the challenge, but in some people, symptoms may not start for up to 4 days after the challenge.

At least daily while in the inpatient unit:
- Your temperature will be taken and any medications you take will be recorded.
- An interim medical history will be obtained.
- You will be evaluated for signs/symptoms of ETEC infection.
- Study staff will collect and measure ALL of your stools. If you are unable to produce at least 1 stool per day, we will ask you to self-collect a rectal swab. Study staff will explain how to do this.
- Study staff will measure vomit to know the amount of fluid you have lost and ask you to drink enough fluids to prevent dehydration.
- On Day 8 of the inpatient admission, we will collect approximately 2 tablespoons of blood, to see how your body is responding to the ETEC challenge.

During your stay in the inpatient unit the following additional procedures may be performed:
- Physical examination based on how you are feeling
- Blood pressure, heart rate, and weight
- Repeat blood collection to check your health

To get rid of the ETEC bacteria from your body, approximately 5 days after drinking the challenge, you will be treated with an antibiotic (either ciprofloxacin or trimethoprim/sulfamethoxazole [Bactrim]) for 3 days. If the investigator thinks it is needed, you may be treated with antibiotics before Day 5.

During the challenge period, oral fluid replacements (drinks given to replace the salts and sugars lost through diarrhea and/or vomiting) and additional medications for comfort may be given if the investigator approves. If illness is severe, you may be given intravenous (I.V.) fluids through a needle to prevent or treat dehydration.

We plan to discharge you to home around the 8th day of your inpatient stay.

If at any time during the inpatient stay you become sick and need medical care that is not able to be provided in the inpatient unit, you will be moved to a hospital that is able to give you the level of care you need.

All the following criteria must be met to be discharged:

- Feel back to your usual baseline and can eat and drink normally
- Have completed 3 days of antibiotic therapy

At the end of your inpatient stay, you will be given a stool collection kit and instructions. You will be asked to bring a stool sample and your back up memory aid with you to the next clinic visit.

FOLLOW UP VISITS

After going home from the inpatient unit, you will be asked to complete 2 follow up clinic visits.

During your follow up clinic visits, the following may be performed:

- Blood pressure, heart rate, and temperature will be measured, if needed
- Review of your medical history
- Review of your current medications
- Physical exam, if needed
- Have blood collected, up to 5 tablespoons, to check your health, see how your body is responding to the ETEC challenge, and for secondary research
- Information about signs and symptoms of ETEC will be collected
- Review of your Memory aid
- Collect a stool sample

STUDY CONTACT VISIT #2

About 5 months after the ETEC challenge part of the study, someone from the study staff will contact you.

During this study contact visit the following will be performed:

- Review your medical history and changes to your health
- Review physical symptoms after vaccination or challenge

EXPECTATIONS

If you participate in this study, you will be expected to:

- Follow the instructions you are given
- Complete all your study visits and study procedures as planned
- Remain on the inpatient unit, until you can be discharged safely (no longer have ETEC bacteria in your stool and have completed your antibiotics)
- Tell us about any changes in your health or the way you feel including any need to go to the emergency room, hospitalizations, or becoming pregnant.

RISKS, SIDE EFFECTS, AND/OR DISCOMFORTS

The risks associated with the study procedures and products are listed below.

For study vaccine/placebo:

- Redness of skin at vaccination site
- Pain at vaccination site
- Swelling at vaccination site
- Discoloration at vaccination site
- Diarrhea
- Headache
- Muscle pains

ETEC Challenge Strain (B7A):

This is an infectious strain of ETEC that causes illness ranging from mild (watery diarrhea being the main symptom) to severe.

- Moderate to severe diarrhea which may lead to dehydration. Dehydration may be manifested by a number of symptoms including:
    - Lightheadedness
    - Decreased urine output
    - Dry mouth
    - Severe cases of dehydration could result in very low blood pressure
- Other symptoms associated with an ETEC infection including:
    - Nausea
    - Vomiting
    - Loss of appetite
    - Lightheadedness
    - Feverish
    - Chills
    - Abdominal cramping
    - Gas
    - Dehydration
    - Increased heart rate (>100 beats per minute)

- Not feeling well
- Feeling tired
- Headache
- Body aches
- Fever

RISKS OF STUDY PROCEDURES

- Blood samples: Possible side effects from blood drawing include brief discomfort, faintness, inflammation of the vein, pain, bruising, or bleeding at the site of puncture. These are common and do not last long. Infection or blood clot at the site of blood collection are rare but possible.
- Rectal swabs: Rectal swabs may cause discomfort for participants and in case of special conditions (e.g., hemorrhoids, and rectal polyps) you might have some bleeding. A rectal swab is only collected when it is not possible to get a study required bulk stool sample. Study staff will instruct you on how to self-collect the rectal swab sample.
- Bicarbonate buffer drink: Mild stomach distress may occur due to consumption of the bicarbonate solution.
- Antibiotic therapy:
    - The most frequently reported drug related events for ciprofloxacin therapy have been:
        - Nausea
        - Diarrhea
        - Abnormal liver function tests
        - Vomiting
        - Rash
        - Increased risk of tendonitis (an inflamed tendon)
        - Increased risk of tendon rupture
        - In high-risk participants:
            - Increased risk of tears or ruptures in the main artery
            - QT prolongation (when the heart muscle takes longer to contract and relax than usual).
    - Other symptoms rarely seen include:
        - Exaggerated or inappropriate immune responses
        - Dizziness
        - Inflammation of the colon
        - Damage to the nerves outside the brain and spinal cord.

  If you are allergic to ciprofloxacin, trimethoprim-sulfamethoxazole (Bactrim) will be the alternate antibiotic administered. The most common adverse effects (side effects) of Bactrim are:
        - Nausea
        - Vomiting

- Anorexia
- Rash
- Hives

RISK OF SPREADING ETEC

This is unlikely since you will be in the inpatient unit when you are contagious. Everyone will be instructed on handwashing and how to avoid the spread of infection. You may not leave the inpatient unit until you have taken every dose of the antibiotic given to treat any remaining ETEC bacteria.

LOSS OF CONFIDENTIALITY

There is a risk of loss of participant confidentiality. To decrease this risk, investigators and study staff will make every effort to maintain the confidentiality of participant medical and research information.

GENETIC INFORMATION NONDISCRIMINATION ACT

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.

This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that the sponsor will get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that the sponsor will get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

All health insurance companies and group health plans and all employers with 15 or more people must follow this law.

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.

UNFORESEEN RISKS

Since the study vaccine is investigational, there may be other risks that are unknown. Taking the study vaccine may involve risks to a pregnant person, an embryo, fetus, or nursing infant if you or your partner becomes pregnant. No one knows what all these risks are right now, or if

this study vaccine could cause a pregnant person to have the baby prematurely (early) or to have a baby with birth defects.

You will be made aware of any safety risks or updates about the study vaccine, placebo, and the challenge.

BIRTH CONTROL RESTRICTIONS

Participants assigned female at birth (AFAB):

If you are AFAB or intersex at birth, you cannot be enrolled in this study if you are:

- Pregnant
- Planning to become pregnant during the study
- Breast-feeding a child

Participants AFAB:

If you can become pregnant, you must use an acceptable method of birth control from 1 month before your first study vaccination through 2 months after receipt of the ETEC challenge agent or last dose of study product if not challenged. This criterion does not apply to participants in a same sex relationship. Acceptable forms of primary contraception include monogamous relationship with a vasectomized partner who has been vasectomized for 180 days or more prior to the participant's first vaccination, intrauterine devices, birth control pills, injectable/implantable/insertable hormonal birth control products, and barrier methods such as condoms or diaphragms with spermicide. True abstinence is also acceptable. You should not participate in this study if you can become pregnant but cannot use one of these birth control methods. Some methods of birth control will not work when you are taking certain drugs. Be aware that individuals AFAB can still become pregnant even if using an acceptable birth control method. You must have a negative urine pregnancy test before each study vaccination. You cannot participate in this study if you are breastfeeding.

If you become pregnant while you are in this study, you should report this immediately to the investigator or study staff. Pregnancy will be followed to outcome. This follow-up will include pregnancy and newborn outcomes. The investigator may share this information with the study sponsor and with the Advarra Institutional Review Board (IRB), a group of people who review research studies to protect the rights and welfare of research participants.

ALTERNATIVES TO PARTICIPATION

Your participation in this study is entirely optional, and you are not required to be a participant. Your access to healthcare at your study site won't be impacted if you decide not to participate.

NEW FINDINGS

Any new important information that is discovered during the study and which may influence your willingness to continue participation in the study will be provided to you.

BENEFITS

Being a participant in this study will not directly benefit you in any way. The knowledge gained from this study will help us better understand ETEC infections, how the immune system defends the body against them, and whether vaccinations of CssBA+dmLT can be used against ETEC infections.

COMPENSATION FOR PARTICIPATION

«Compensation»

You will be paid up to a total of $xx.xx if you complete this study. You will be paid for the visits you complete according to the following schedule:

- $Xx.xx for Vaccination Visit.
- $xx.xx for Participant Compensation.
- $xx.xx for Televisit.

If you do not complete the study, for any reason, you will be paid for each study visit you do complete.

You will be paid _____ ***["following each completed visit", "monthly", "quarterly", "at the end of your participation in the research study", "following each completed visit or at the end of your participation in the research study, whichever you prefer"]***.

If you have any questions regarding your compensation for participation, please contact the study staff.

CERTIFICATE OF CONFIDENTIALITY

To help us protect your privacy, we have a Certificate of Confidentiality (Certificate) from the NIH. Study staff cannot provide to any person not connected with the research your name, or any materials that contain identifiable, sensitive information about you, unless permitted by a legal exception, such as state laws that require reporting of some contagious diseases. The most important protection provided by the Certificate is that the study staff cannot be forced to provide any of your identifiable, sensitive information, in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding, such as if there is a court subpoena, without your permission. The researchers will use the Certificate to resist any demands for information that would identify you, except for reporting of communicable diseases to State and local health departments.

The study staff will use the Certificate to resist any demands for information that would identify you.

CONFIDENTIALITY

Records of your participation in this study will be held confidential except when sharing the information is required by law or as described in this informed consent. The Investigator, the sponsor or persons working on behalf of the sponsor, and under certain circumstances, the United States Food and Drug Administration (FDA) and the Institutional Review Board (IRB) will be able to inspect and copy confidential study-related records which identify you by name. This means that absolute confidentiality cannot be guaranteed. If the results of this study are published or presented at meetings, you will not be identified.

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

COMPENSATION FOR INJURY

If you become ill or are injured while you are in the study, get the medical care that you need right away. You should inform the healthcare professional treating you that you are participating in this study. If you tell the study staff that you think you have been injured, then they will help you get the care you need.

The study site will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH or the Federal Government. By signing and dating this document, you will not lose any of your legal rights or release anyone involved in the research from responsibility for mistakes.

To pay medical expenses, the study staff will need to know some information about you like your name, date of birth, and Medicare Beneficiary Identifier (MBI). This is because the study staff has to check to see if you receive Medicare and if you do, report the payment it makes to Medicare.

COSTS

There will be no charge to you for your participation in this study. The study drug, study-related procedures, and study visits will be provided at no charge to you or your insurance company.

While you are in the study, you still need to get regular medical care. You (and/or your health care payer) will still have to pay for the costs of your regular medical care that are not a part of this study.

USE OF DATA OR SAMPLES IN OTHER STUDIES

We may remove the codes from your information or samples (so that we cannot identify you) and use these in secondary research. These may be shared with other researchers without your additional consent. We may also wish to retain samples with the codes for secondary research; this is explained in the next section.

STORAGE OF DATA AND SAMPLES FOR SECONDARY RESEARCH

As part of the study, at some of the study visits, we will be collecting extra blood and stool samples which will be stored for possible secondary research. Also, any samples of blood or stool that remain after we do the testing for this study will be stored for possible secondary research. Secondary research is research that is not part of this study and is not planned yet.

Your data and extra/leftover samples will be stored indefinitely (time does not expire) once this study is completed. This is a requirement for enrollment in the study. **You should not join the study if you do not want your data and samples stored indefinitely.**

These samples (blood and stool) may be used for secondary research to learn more about the ETEC infection and the body's immune response (defense) to it. Your samples may also be studied, tested, and used for research related to infectious diseases. This may include **genetic** research to study immune responses.

Stored samples and your information may be shared with other investigators, institutions, or drug companies. The samples will not be sold or used directly for production of any commercial product. You will not receive compensation for this research. You will not share in the commercial profit if your specimens provided for this study lead to a licensed product.

Samples will be coded so that your name cannot be readily identified with a sample. Each sample will be labeled with a barcode and a unique tracking number (ID codes). Personnel at the storage facility and testing lab will not know your identity. However, the researchers who enrolled you will keep in a secure area a list with your name and the ID code (called a code key) that matches the samples to identify you, if needed.

Samples may be stored indefinitely at a site determined by the NIH. These leftover and extra samples will be stored with the same confidentiality measures used for the study's samples. You will not be contacted about the types of secondary research. The risks include a potential loss of confidentiality if someone can identify you, however, the risk is low because information is maintained with limited access by the study staff. There are no benefits to you for storing and using your samples or data in secondary research, however society may benefit from new knowledge.

Reports about research done with your samples will not be put in your health record. Results from secondary research using your samples may be presented in publications and meetings, but your name will not be identified. There are no plans to contact you if we perform this secondary research on your samples.

GENETIC TESTING WITH EXTRA AND LEFTOVER SAMPLES

Leftover and extra samples for secondary research may include genetic testing. Genetic testing looks at the material in your cells that tells each cell in your body how to work. The genetic testing is for research purposes only and it will not be able to tell you about relatives, paternity, or country of origin nor will it tell you about diseases that you may get in the future. We will not give you the results from the genetic research testing.

Researchers can look closely at large amounts of your genetic information by sequencing, or "reading", every letter in your DNA (your genome). Reading a person's entire genetic code is called whole genome sequencing. The research **might include** whole genome sequencing (for example, sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

Open access database: A summary of the genetic results from all participants in this study can be placed in a public, unrestricted open access database that anyone can freely use. No individual genetic testing information or results will be placed in an open access database. The risk of anyone identifying you with this information is very unlikely.

Restricted access database: We may share your genetic information (data) through a "closed" database, also called a restricted data repository. NIH gives permission to other researchers to use your genetic information for research. To qualify, researchers must receive approval from NIH to access and use the research information. Types of secondary research using your data may be related to the research in this study or other types of research. Your individual data will not contain information that can easily identify you. It may be possible to identify you with your DNA; however, the researchers must follow rules specifically to not identify you. If you change your mind and want to remove your data from the database, you should contact the research site that collected your information and specimens. If possible, your information can be removed for secondary research. Your data cannot be removed if it has already been used.

If you enroll in this study, you are providing consent to store and use samples for secondary research which may include genetic research. You should not join the study if you do not want your data and samples stored and used for this purpose. You may change your mind and withdraw consent for the storage and use of your coded samples or information at any time. Please contact the investigator at the telephone number listed on the first page of this consent document. We will destroy your samples that are in storage if you withdraw consent. Research that has already begun using your specimens cannot be withdrawn. For example, if some research with your specimens and data has already been completed, the information from that

research may still be used. Also, if the specimens and data have been shared already with other researchers, it might not be possible to withdraw the specimens and data.

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

WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns, or complaints about the study such as:

- Whom to contact in the case of a research-related injury or illness.
- Payment or compensation for being in the study, if any.
- Your responsibilities as a research participant
- Eligibility to participate in the study.
- The Investigator's or study site's decision to withdraw you from participation.
- Results of tests and/or procedures.

Please contact the Investigator at the telephone number listed on the first page of this consent document.

If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, contact:

- By **mail**:
  Study Participant Adviser
  Advarra IRB
  6100 Merriweather Dr., Suite 600
  Columbia, MD 21044
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00081748.

VOLUNTARY PARTICIPATION / WITHDRAWAL

Your decision to participate in this study is voluntary. You may choose to not participate, or you may withdraw from the study for any reason without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care. However, please

note that the FDA requires that any information collected up to the point of your withdrawal cannot be removed from the study.

Furthermore, the investigator or sponsor may remove you from the study without your consent if this research is not in your best interests for the following reason(s):

- You fail to attend research visits or fail to follow research guidelines or instructions, such as using an effective birth control method.
- You experience a severe or unexpected response.
- Reasons related to you (for example, if you move to another city or if you do not agree to receive your study vaccination).
- Because the entire study is stopped (the sponsor may stop the study at any time).
- If you become pregnant.
- Any other reason.

If you decide to leave the study before it is finished, an early termination appointment will be planned. During this clinic visit, the following procedures may be performed:

- Targeted physical examination based on study staff assessment, response to study vaccine/placebo, or medical history review, including weight, may be performed if needed.
- Review of medical history.
- Review of current medications.
- Review of adverse events and serious adverse events.

If you choose to withdraw from the study after being admitted to the inpatient unit and receiving the ETEC challenge, you will be advised about the risk of spreading ETEC to close contacts. You will be directly observed by the study staff swallowing the first dosage of antibiotic before leaving the facility. The remaining antibiotics will be sent home with you to finish the 3-day course of treatment at home.

Regardless of when or if you wish to withdraw consent, you are encouraged to return for safety assessments prior to withdrawal until any adverse event or laboratory abnormality is considered resolved or stable.

When you or the investigator decide to end the consent process for the research, we will cease collecting your data and samples. However, this study may continue to use any data and samples gathered before withdrawal.

The sponsor (NIH), the FDA, other regulatory bodies, or the Advarra Institutional Review Board (IRB), which oversees the conduct of this study, may halt it at any moment due to safety concerns or other problems.

PRIMARY HEALTH CARE PROVIDER NOTIFICATION OPTION

I consent to having my family doctor or primary health care provider notified by the study site of my participation in this study and/or any significant findings related to my health (please check yes or no).

☐ **YES** (If yes, please complete the information below)
☐ **NO**

Name and address of family doctor or primary health care provider:	Name: Address:
Telephone and Fax Number:	Tel: Fax:

CONSENT

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to participate in this study until I decide otherwise. I do not give up any of my legal rights by signing and dating this consent document. I will receive a copy of this signed and dated consent document.

_____
Participant ’s Printed Name

_____ _____
Participant ’s Signature Time Date

_____
Printed Name of the Person Conducting the Consent Discussion

_____ _____
Signature of the Person Conducting the Consent Discussion Time Date

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

If you decide to be in this study, the investigator and study staff will use and share health data about you to conduct the study. Health data may include:

- Your name.
- Address.
- Phone number.
- Date of birth.
- Medical history.
- Information from your study visits, including all test results.

Health data may come from your study records or from existing records kept by your doctor or other health care workers.

For this study, the study staff may share health data about you with authorized users. Authorized users may include:

- Representatives of Infectious Diseases Clinical Research Consortium (IDCRC),
- Division of Microbiology and Infectious Diseases (DMID), National Institute of Allergy and Infectious Diseases (NIAID).
- Representatives of FHI 360
- Representatives of Advarra IRB (an Institutional Review Board that reviews this study).
- The Food and Drug Administration (FDA) and other US federal and state agencies.
- Government agencies to whom certain diseases (like HIV, hepatitis, and STDs) must be reported.
- Outside individuals and companies, such as laboratories and data storage companies, that work with the researchers and sponsor and need to access your information to conduct this study.
- Other research doctors and medical centers participating in this study, if applicable.
- A safety monitoring committee which oversees this study, if applicable.

Your health data will be used to conduct and oversee the research, including for instance:

- To see if the study vaccine works and is safe.
- To compare the study vaccine to other vaccines.
- For other research activities related to the study vaccine.

Once your health data has been shared with authorized users, it may no longer be protected by federal privacy law and could possibly be used or disclosed in ways other than those listed here.

Your permission to use and share health data about you will end in 50 years unless you revoke it (take it back) sooner.

You may revoke (take back) your permission to use and share health data about you at any time by writing to the investigator at the address listed on the first page of this form. If you do this, you will not be able to stay in this study. No new health data that identifies you will be gathered after your written request is received. However, health data about you that has already been gathered may still be used and given to others as described in this form.

Your right to access your health data in the study records will be suspended during the study to keep from changing the study results. When the study is over, you can access your study health data.

If you decide not to sign and date this form, you will not be able to take part in the study.

STATEMENT OF AUTHORIZATION

I have read this form and its contents were explained. My questions have been answered. I voluntarily agree to allow study staff to collect, use and share my health data as specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing and dating this form.

_____
Printed Name of Participant

_____ _____
Signature of Participant Time Date

_____
Printed Name of Person Explaining Authorization

_____ _____
Signature of Person Explaining Authorization Time Date