SUBJECT INFORMATION/INFORMED CONSENT FORM and AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

Sponsor / Study Title:	**Henry M. Jackson Foundation (HJF) for the Advancement of Military Medicine, Inc. / A Proof-of Concept, Randomized, Controlled Study of Tuberculosis Immunization with BCG to Prevent Infection in Healthy Adults (TIPI trial)**
Protocol Number:	**2019-01**
Project Principal Investigator/Protocol Chair:	**Naomi Aronson MD, Uniformed Services University of the Health Sciences (USUHS), Bethesda, MD**
Site Principal Investigator: (Study Doctor)	**«PiFullName»**
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CONCISE SUMMARY OF KEY INFORMATION (to consider in determining why/why not one might participate in this research study):

The purpose of this research is to find out if a single dose of pre-travel vaccination with BCG (a living organism preparation) can lessen Tuberculosis (TB) infection by producing an immune response (development of TB fighter cells within the body) when given to adults traveling to countries with a high burden of TB. BCG will be compared with a placebo (an inactive vaccine). BCG (Japan) is used globally but is not approved for use in the United States, therefore it is considered experimental.

If you choose to take part in this research study, you will be randomly assigned (this is like a coin flip) to receive BCG vaccine or placebo.

You will be in this research study for about 4 months to 2.5 years depending on how long you travel. There will be typically 4 but up to 6 study visits, dependent upon results of blood sampling. Each clinic visit, on average, will require a time commitment of approximately 1-2 hours to complete.

While you are in the study you will have different evaluations, tests and/or procedures that are a part of your standard care and for study purposes. The major research requirements of the study consists of: interviews, physical examinations, blood draws (two - up to 4 total depending on what previous blood test results reveal), completion of questionnaires, and keeping a record for 14 days of any side effects after receiving study vaccine (if any should occur).

There are risks to the BCG study vaccine that are described later in this consent form. Some risks and side effects include those which are:

Likely: A small local reaction at the injection site consisting of pain, itching, redness, swelling, blistering, ulcer, or scarring.
Less likely: Flu-like symptoms such as fever, nausea, muscle aches and joint pain, fatigue
Rare, but serious (usually only seen in people with weakened immune systems): Bone infection or generalized infection causing sepsis (the body's over-whelming and life-threatening response to infection)

You may not personally benefit from taking part in this research. However, it is hoped that information learned will help other travelers in the future and/or prevent against TB infection.

The alternative to being in this study is to not take part.

The information presented in this section is discussed in greater detail in the rest of this document.

If you are interested in learning more about this study, please continue to read below.

About this consent form

This is a consent form for research participation. It contains important information about this research study and what to expect if you decide to participate. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

This consent form describes the purpose of this research study, and the risks and possible benefits of participating. If there is anything in this form you do not understand or is unclear, please ask a member of the study team to further explain. You may take an unsigned copy of this consent form with you to think about or discuss with colleagues, family or friends before making your decision.

Please read this form carefully. Take your time to ask the study doctor or study staff as many questions about the study as you would like. The study doctor or study staff can explain words or information that you do not understand. Taking part in this research is **voluntary**. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your benefits to which you are otherwise entitled. If you decide to take part in this study, you will be asked to sign this consent form. We will give you a signed and dated copy of this form.

If significant new findings develop during the course of this study that may relate to your decision to continue participation, you will be informed.

This is a multi-site study (involving up to 10 participating sites) led by Dr. Naomi Aronson of the Uniformed Services University of the Health Sciences (USUHS) (the coordinating center responsible for overseeing the research-related activities at each research site) located in Bethesda, MD.

This research is sponsored by the HJF in Bethesda, MD with funding by a component of the United States Government Defense Health Program (DHP)) through a Cooperative Agreement between USUHS and HJF.

Introduction
Tuberculosis (TB) is a contagious infection caused by bacteria called the *Mycobacterium tuberculosis* complex. It is a serious, world-wide health problem with approximately 10 million new cases and 1.6 million deaths from TB worldwide every year.

There are medicines to effectively treat TB infection, but these medicines can take a long time to work, can produce side effects, and can be ineffective if TB has associated drug resistance (lowered effectiveness of a medication).

Bacillus Calmette-Guérin (BCG) is an effective vaccine that is used to protect people from getting TB. BCG is a weakened (attenuated) version of a live bacteria strain called *Mycobacterium bovis*. In many countries outside of the U.S., BCG is given to infants right after they are born to protect them from developing TB disease. BCG has been used for over 90 years in billions of infants and is generally well tolerated.

Why is this research study being done?
This research study is being conducted to find out if a single dose of pre-travel BCG vaccination (a living organism preparation) can prevent TB infection by producing an immune response (development of TB fighter cells within the body) when given to adults traveling to countries with a high burden of TB. BCG will be compared with a placebo (an inactive vaccine).

In this study, you will get BCG or placebo study vaccine; you will not get both. We will assess your TB exposure using a blood test known as IGRA (interferon gamma release assay). This test will change from a negative (absent) to a positive (present) result when TB infection is present.

The primary goal of this research study is to find out if BCG prevents participants from getting TB infection. Additionally, we would like to collect information regarding exposure to and infection with TB, risk factors for TB infection during travel, and any respiratory illness during travel.

There are many strains of BCG. For this study, BCG Tokyo-172 strain will be used. Although used in several countries, accounting for over 50% of the global BCG use, BCG Tokyo-172 has not been approved for use by the United States Food and Drug Administration (FDA), therefore it is considered experimental. However, the FDA has allowed its use to study its effectiveness under an Investigational New Drug (IND) application # 19065. There is a similar licensed, FDA approved BCG vaccine in the United States, but the manufacturer is unable to provide it for research purposes at this time due to limited production availability.

How many people will take part in this study and who can participate?
We anticipate enrolling a total of 2,000 healthy male/female, adult travelers, age 18-65 years, who are planning to travel to countries with a high rate of TB infection. Individuals from different medical facilities and travel clinics will take part in this study, and approximately xxxx people will take part at (insert site location)

You are being asked to take part in this research study because you are either a health care worker or long-term traveler who will be working for an extended period of time (at least 4 weeks and up to 2.5 years), in a country that has a high incidence of TB infection. Working closely with people who could be infected with TB puts you at higher risk for exposure to TB. TB is spread through breathing in infectious airborne droplets.

What are the study procedures?
Some of the procedures in this study will be repeated several times. Tests that are part of your regular, routine medical care will continue to be performed. In this study, the following procedures and/or information will be collected for research purposes:

- Interviews: A study team member will take your medical history, along with a listing of any medications you are currently taking. Throughout the study you will be asked to report to the study team if you think that anything new has happened to you as a result of the study.
- Physical Examination: Exams will be conducted before and during the study including measurements of temperature, blood pressure, heart rate and respiratory rate.
- Blood Draw(s): Blood sample(s) will be obtained:
    - To determine if you qualify for study participation (one sample, approximately one tablespoon, will be drawn for baseline TB IGRA and HIV testing). The study doctor may be required by law to report the result of tests to the local health authority.
    - To measure your IGRA level after you return from travel to find out if you were infected with TB bacteria while away (up to 3 separate samples could be collected at different time points, depending on what the previous blood test result reveals. Approximately 1/2 tablespoon of blood will be collected each time)
- Questionnaires: Pre-travel and Post-Travel information will be collected regarding your travel experience. Additionally, information will be collected to assess for development of respiratory symptoms during traveling abroad
- Administration of a single dose of study vaccine (either BCG or placebo)
- Collection of side effects that you may experience after receiving the study vaccine. We will provide you with a memory aid card to assist with this recall.
- Pregnancy Test: If you are a female and of childbearing potential we will collect a urine pregnancy sample at two time points in this study
- Birth Control: *For female subjects*: You will need to take safety measures to prevent pregnancy (such as not having sexual intercourse, or using a reliable method of contraception) for a minimum of 30 days prior to BCG/placebo vaccination and 6 weeks following BCG/ placebo vaccination. If you have questions about how to avoid pregnancy, talk to your study doctor and they will provide you with information on contraceptive choices.

How long will I take part in this research study?
It will take you approximately 4 months to 2.5 years to complete this study, depending on your length of travel. During this time, you will be asked to make up to 6 study visits to the research clinic site.

What will happen in this research study?
This research study will compare BCG study vaccine (test article) to a placebo (control substance that has no therapeutic effect) vaccine. The placebo will look like the BCG study vaccine but contains no active ingredient of BCG. During this study, you will be randomized (like flipping a coin) to receive either BCG or placebo. A placebo is inactive medicine that looks like real medicine, but it is not. It has no effect on a person because it has no real medicine in it.

You will have an equal chance of receiving BCG or placebo. You will not know whether you receive BCG or placebo, but your study team will know**.**

If you choose to take part in this study, the study team will discuss the study and review this combined consent and Health Insurance Portability and Accountability Act (HIPAA) Authorization document, and if you still would like to participate in this study, you will be asked to sign and date this consent form,

prior to performing any research study procedures. You will receive a copy of this combined informed consent and HIPAA authorization form.

Once you sign and date the consent form, you will be assigned a unique 6-digit identification number that will be used throughout the study. This will be known as your study ID number and used to code all of your protected health information so that your identity remains anonymous.

This study will consist of up to 6 study visits:

Visit	Purpose	Main Procedures	Duration
Visit 1, Day 0	Screening Visit	Blood tests (urine test if female), Interview and physical to determine if eligible to participate, Pre-travel Questionnaire	1.5 to 2 hours
Visit 2, less than or equal to 30 Days of Visit 1	Study Vaccination (BCG/placebo)	Verification of study participation eligibility, vital signs, administration of study vaccine based on randomization assignment, safety monitoring for 30 minutes after receiving study vaccine, review of memory aid card to be used to capture any side effect you may experience, counseling about TB prevention during travel	1.5 to 2 hours
Visit 3, 4 weeks after Visit 2	Post-Study Vaccination Follow-Up	Interview and assessment of injection site, collection of possible injection site reactions, targeted physical if necessary, review of memory aid card **For long-term travelers only:** Instructions for completing an online respiratory infection questionnaire every 2 months during travel	1 hour
Visit 4, 8-10 weeks (if travel is 6 months or less) **or** within 1 month after return from travel (if travel is more than 6 months)	Post-Travel Follow-Up/End of Study*	TB IGRA blood test, Post-Travel Questionnaires (in paper format), Interview, targeted physical & vital signs if necessary	1.5 hours
*Visit 5, greater than or equal to 4-6 weeks after Visit 4, only if applicable	Repeat TB IGRA blood test and/or arranging referral for TB care	TB IGRA blood test, possible referral for TB treatment, interview, targeted physical & vital signs if necessary	1 hour
*Visit 6, 4-6 months from return post-travel, only if applicable	Re-Test IGRA to evaluate for sustained (positive) conversion	TB IGRA blood test	30 minutes

*Below is a description of each.

Screening- Study Visit 1
The Screening Visit will take about 2 hours. The study staff will ask you questions and run tests that will help determine if you are eligible to participate in this study. This screening process and eligibility determination will be completed prior to your ability to receive the study vaccine (BCG or placebo).

At this visit, a member of the research team will perform some tests and procedures to see if you are eligible to take part in this research study. The study doctor will review the results of these tests and procedures. If you are not eligible to participate in the study, the study doctor/designated study staff will tell you why.

At this visit, the study team will:

- Ask you about your medical history, and about any medicines you are currently taking or have taken recently.
    - In order to qualify for this study you must also not be taking any steroids or other immune- modulating medicines (medicines that modify the immune response or the functioning of the immune system) by mouth (within the last 30 days) or intravenously ("IV") (within the last 90 days), or not have received radiation or chemotherapy within the last 180 days.
    - You will not be permitted to participate in this study if you have experienced a probable exposure to someone with lung TB within 8-10 weeks of Visit 1 (screening).
- Ask you about your past exposure to TB
- Ask you about your vaccination history. You will not be eligible to participate in this study if you have previously received BCG.
    - You will not be permitted to participate in this study if you have recently received 2 or more live vaccinations (within 30 days of planned administration of BCG/placebo vaccine), and you will be asked to forego any periodic tuberculin skin test screening procedures for 6 months after receiving BCG/placebo vaccine as this can cause a false positive IGRA result temporarily.
- Perform a physical exam, including obtaining your temperature and vital signs (heart rate, respiratory rate and blood pressure).
- Draw a sample of blood (a total of approximately 1 tablespoon).
    - Some of your blood will be tested for HIV
    - Some of your blood will be tested for TB (IGRA test)

  If the results of your blood tests are positive/ indeterminate for HIV or positive/borderline for TB IGRA, you will be informed, but will not be able to participate in the study. You will be provided with information about arranging follow-up care.
- Ask you to complete a questionnaire about your upcoming travel plans.
- If you are a female and able to become pregnant, you will be required to provide a urine sample that must be negative for pregnancy in order to be eligible for study participation. Females who are pregnant cannot take part in this research study.

During screening, you will be required to provide the study staff with an e-mail address and/or telephone number of where you can be contacted during the study.

Randomization and Study Vaccination (BCG/placebo) Study Visit 2
You will be asked to return to the clinic within 30 days of the screening visit. Visit 2 will take about 1.5 to 2 hours. At this visit, the study team will:

- Ask you how you are feeling and obtain your temperature and vital signs (heart rate, respiratory rate and blood pressure)
- Ask you if there have been any changes in your health, and if you have taken any new medications since your last visit
- If you are a female and able to become pregnant, you will undergo another urine pregnancy test that must be negative in order to participate (even if the pregnancy testing conducted at the screening visit was negative).
- Administer the BCG/placebo study vaccine intradermally (an injection given shallowly in the dermis/second layer of skin) over the outer lower area of the deltoid (upper arm) region. You will need to keep the injection site dry and loosely covered for the first 24 hours.
  You will be "blinded" meaning you will not be told which study vaccine you receive. Your study team will know whether you received BCG or placebo study vaccine. The facility where the blood test will be analyzed will also be blinded (not know which study vaccine was given).
- Check your vital signs after the injection and also inspect your injection site for any adverse reactions.
- Provide you with a memory aid card and instructions for completing it. This is to track any reactions you may have to the vaccine. You will be asked to complete the memory aid card for the first 14 days after receiving the study vaccine then return it to the clinic at your next research visit. To supplement, you may also take pictures of the injection site which can be downloaded at your next visit.
- Counsel you about things to do to protect yourself from exposure to TB during travel.

You will need to stay in the clinic for at least 30 minutes after your injection to make sure you do not have an allergic reaction to the study vaccine. The study staff will have medicines available to treat you if an allergic reaction occurs.

During the 30 minutes after receiving the study vaccine (BCG or placebo), the study team will show you a video which discusses TB risk reduction activities and prevention methods. They may also give you printed materials on this topic.

Post-Study Vaccination Follow-Up - Study Visit 3
You will be asked to return to the clinic within 2-6 weeks after your study vaccination visit. This visit will take approximately 1 hour. During this visit:

- You will be asked how you are feeling
- You will be asked if there have been any changes to your health and if you have taken any new medicines since the last study visit.
- Your symptom memory aid card will be reviewed and collected. Any pictures you took of the injection site will be downloaded and kept with your study file.
- Your arm where you received the injection will be examined as well as your lymph nodes in your armpit and neck

- If in the event your study doctor has any concerns or feels your condition warrants it, you will also have a brief physical examination focusing on the areas of concern
- Give you a copy of the questions you will be asked at your post travel visit pertaining to your travel exposures relevant to TB and all-cause respiratory symptoms/infection to keep notes on
- If you will be a long-term traveler, you will receive brief instructions for completing an 'on-line'questionnaire pertaining to any occurrences of respiratory infections. You will be required to complete these every 2 months during your travel
- Exchange of contact information

Post-Travel (return from travel) - Study Visit 4
After you return from travel, you will be asked to come for a study visit. This visit will occur eight (8) to ten (10) weeks after your return (if your travel was 6 months or less),but may be done immediately (within one month) upon return if your travel length was more than 6 months. This visit will take approximately 1.5 hours. During this visit:

- You will be asked to fill out a questionnaire regarding your potential exposure to TB during your travel/time working in a high-risk location.
- You will be asked to complete a questionnaire related to whether you experienced any of the listed respiratory symptoms during travel and if you sought medical care or treatment for your illness
- You will be asked to confirm the areas and actual dates of where you traveled.
- You will be asked if there have been any changes in your health status.
- Your arm where you received the injection will be examined as well as your lymph nodes in your armpit and neck.
- If in the event your study doctor has any concerns or feels your condition warrants it, you will also have a brief physical examination focusing on the areas of concern.
- A blood sample will be drawn for an IGRA test (approximately 1/2 tablespoon) to determine if you have a TB infection.
- You may be asked for permission to obtain copies of your medical records for any care overseas or upon return.

If you are unable to physically return to the clinic for Study Visit 4, a member of the study team will conduct this follow-up visit by phone or by email (to obtain the needed information). Additionally, arrangements will be made by the study team to have your blood test (to determine if TB infection is present), performed by a local U.S. medical facility.

Based on the results of your Visit 4 post-travel IGRA test, the following action will take place:

- If your Visit 4 post-travel IGRA test result is negative, no further follow-up visits will be required of you.
- If your Visit 4 post-travel IGRA test result is borderline**:** You will be asked to return to the clinic to be seen within 4-6 weeks for a Study Visit 5 for the purpose of having a repeat IGRA blood test performed (to determine if TB infection is present).
- If your Visit 4 post-travel IGRA test is positive: You will be asked to return to the clinic to be seen within 4-6 weeks for a Study Visit 5 for the purpose of arranging clinical management of your TB infection.

If applicable, within 3 working days of the site receiving your Study Visit 4 post-travel IGRA test results, a member of the study team will notify you by email or phone to schedule an appointment for a follow-up Study Visit 5.

Study Visit 5 (if applicable)
Only those subjects who were found to have a borderline or positive TB IGRA test result at Visit 4 or an on-going study vaccine associated reaction that in the opinion of the study doctor, requires follow-up will be seen at this visit. This visit will take approximately 1 hour. During this visit:

- If your post-travel blood test result at Visit 4 was borderline, you will have a repeat IGRA blood draw (approximately 1/2 tablespoon). If this repeat blood test result is positive, arrangements will be made for management of your TB infection and to establish follow-up medical care as needed. You will be provided with a copy of the IGRA laboratory report.
- If your post-travel blood test result at Visit 4 was positive, you will receive consultation with the study doctor to establish referral plans for management of your TB infection. You will be provided with a copy of the IGRA laboratory report.

Study Visit 6 (if applicable)
Only those subjects who were found to have post-travel IGRA conversion results (positive) at Visit 4/ Visit 5 will be required to have an additional repeat TB IGRA blood test scheduled 4-6 months from return post-travel for the purpose of determining sustained conversion. This visit will take approximately 30 minutes. During this visit:

- You will have a repeat IGRA blood draw (approximately 1/2 tablespoon).
- If willing, you will be asked to postpone treatment of your TB infection until this follow-up IGRA testing occurs.

Stopping the Study Early – How can I leave the study?

- Your decision to be in this study is voluntary. You may choose not to be in this study. There will be no penalty or loss of your benefits if you decide not to participate in this study.
- If you do join this study, you can stop at any time (without having to give a reason) by contacting the study doctor or a study team member. Leaving the study will not affect any other benefits that you may have.
- You will be told about any new findings learned during this study that may affect your decision to stay in this study.
- If the study doctor is concerned about your health, he (she) may end your participation in the study at any time without your consent.
- Failure to follow the study procedures may result in ending your participation without your consent.
- The sponsor of the study, HJF, may end the study early without your consent.

If you received the study vaccine (BCG or placebo) and you wish to withdraw from the study, or if the study doctor withdraws you from the study, for safety reasons, you will be asked to return to the clinic to be seen by the research team to have a final study evaluation performed. If agreeable, and depending on the time frame in which you are withdrawn from the study, you will have a blood sample obtained for the purposes of determining if you have TB and safety assessments will be conducted.

Study Information Included in Your Electronic Medical Record

A notation that you are taking part in this research study may be made in your electronic medical record. Information from the research that relates to your general medical care may be included in the record (for example: list of allergies, results of standard blood tests done at the hospital labs).

Please ask your study doctor if you have any questions about what information will be included in your electronic medical record.

What are the risks and possible discomforts from being in this research study?
Risks of Receiving BCG Vaccine
Receiving BCG study vaccine may cause you to have one or more of the side effects listed below.
Common side effects (defined as occurring 95 % of the time):

- Injection site pain and/or itching
- Redness and/or swelling
- Blistering (vesicle)
- Ulcer
- Scarring

A small local reaction consisting of tender redness/swelling, blistering (vesicle), and then an ulcer at the injection site is usual after receiving BCG. When these reactions occur, they may last for weeks to several months, and in some cases may last even longer, before healing and scar formation takes place. The study team will show you how to keep the site clean and covered with gauze to help avoid infection.

Less common side effects (defined as occurring 70-75% of the time):

- Flu-like symptoms including fever and headache
- Muscle aches
- Joint pain
- Skin rash
- Dizziness
- Fatigue (tiredness)
- Nausea
- Gastrointestinal problems

These symptoms may occur within hours after receiving the study vaccine but are usually self-limiting and resolve within a few days without treatment.

Occasional side effect (defined as occurring 1-2% of the time):

- Swelling of the gland in the armpit, above the collarbone, or neck, on the side where the injection was given

Enlargement of the gland in the arm pit may appear later, 2-4 months following immunization; seldom does this condition go on to form pus or discharge.

Rare side effects (usually only seen in people with weakened immune systems):

- Bone infections may occur in 1 to 700 per million persons
- Generalized infection causing BCG sepsis (the body's over-whelming and life-threatening response to infection) which could result in death may occur in 2-3 per million persons, usually those with an immune defect

If BCG is inadvertently given into the subcutaneous (fat) layer just beneath the skin, this may produce abscess formation (a confined pocket of pus that collects in tissues) and may lead to scarring or keloids

(thickened scar tissue) at the injection site. Rarely an adverse effect may occur later; after termination from study participation (6 months to 3 years). If this happens, you should seek medical care with your primary physician as well as reporting it to the study sponsor using one of the methods provided at the end of this document.

BCG can also cause your tuberculin skin test (TST) to become positive. This does not mean that you are infected with TB. The TB IGRA test result will not be affected.

All vaccines can cause allergic reactions soon after they are administered. There is a small chance that you may have a serious allergic reaction (anaphylaxis) to the study vaccine. Serious allergic reactions may cause a drop in blood pressure, difficulty breathing, or hives. Some people have died from serious allergic reactions. If a serious allergic reaction occurs, you will need immediate medical attention. This is part of the reason why you will be required to stay at the study site for at least 30 minutes after receiving the study vaccine.

There is a potential risk that tiny glass fragments (microscopic particles) could be caused during the snap opening for the glass vial (ampule) that the study vaccine comes in. These could be picked up in the syringe when taking the liquid study vaccine out of the vial, possibly resulting in injection into your skin when the study vaccine is given. We will use a very thin small needle in this study to decrease the chances of this occurring as well as using an alcohol swab or gauze around the ampule when snapping.

There may be other risks of BCG that are currently unknown.

Risks to an Embryo or Fetus, or to a Breastfeeding Infant
The effect of BCG on an embryo or fetus (developing baby still in the womb), or on a breastfeeding infant, is unknown and may be harmful. Because of these unknown risks, women cannot take part in this study if they are:

- Pregnant
- Trying to become pregnant
- Breastfeeding

If you are female and menopausal (defined as not having had a menstrual period for the past 12 months or more), you will not be required to have a pregnancy testing. Also, if your medical history contains a documented method of surgical sterilization, you will not need to have to undergo pregnancy testing. Methods of surgical sterilization include having had a hysterectomy (removal of the uterus), bilateral oophorectomy (removal of both ovaries), a tubal ligation (having your tubes tied), and transvaginal occlusion (plugging the opening of the tubes with a coil). All other female subjects must have a negative pregnancy test before receiving the study vaccine, and agree to use adequate birth control and refrain from breast-feeding for at least 6 weeks after receiving the study vaccine.

If you are sexually active and able to become pregnant, you must agree to use one of the birth control methods listed below. You must use birth control for at least 30 days before and for at least 6 weeks after your dose of study vaccine.

Acceptable birth control methods for use in this study are:

- Hormonal methods, such as birth control pills, patches, injections, vaginal rings, or implants
- Barrier methods (such as a condom or diaphragm) used with a spermicide (a foam, cream, or gel that kills sperm)
- Intrauterine device (IUD)
- Abstinence (no sex)

If you miss a period, or think you might be pregnant during the study, you must tell the study doctor immediately. If you have already received the study vaccine and become pregnant, the study doctor may ask for your permission to collect information about the outcome of your pregnancy and the condition of your newborn.

Medications Not Allowed while Participating in the Study
You must be willing not to take certain medications before or after receiving BCG study vaccine as listed below. These medications may cause side effects or interfere with the results of the study:

- Antibiotics that have a TB effect for example, rifampin, quinolones, linezolid, imipenem, amoxicillin-clavulanate etc. These should not be taken for the first 3 weeks after receiving the study vaccine.
- You should not receive 2 or more live vaccinations within 30 days before receiving the study vaccine. After receiving the study vaccine (at Visit 2), you may receive 1 live vaccine (if needed), provided it is administered in the opposite arm.
- You will be asked to forego any periodic tuberculin skin test screening procedures for 6 months after receiving study vaccine as this can cause a false positive TB IGRA result temporarily.
- If you have taken any medications that may compromise your immune system within the last month, you may not be allowed on the study
- If you have received a COVID-19 vaccine within 7 days prior to time it is anticipated that you will receive the study vaccine, you may not be allowed on the study until 7 days have passed.
- You will be asked to not receive a COVID-19 vaccine for at least 7 days after receiving the study vaccine
- If you have received radiation or chemotherapy within the last 6 months, you may not be allowed on the study.

If you have any questions about your medications, please ask your study doctor/study team.

Risk of Blood Draws
You may have a bruise (a black and blue mark) or pain where we take the blood samples. There is also a small risk of infection, lightheadedness, and/or fainting.

Risk Related to Completing Questionnaires
You will be asked to complete questionnaires pre-travel and post-travel that will take approximately 10-15 minutes to complete. Some of the questions may be upsetting or make you feel uncomfortable. You can skip any of the questions you do not want to answer and you can stop at any time.

Risk of Invasion of Privacy/Breach in Confidentiality
As part of this study we may collect some information from your medical record, if applicable. This will include information such as, but not limited to your age, sex, race, medical history, physical exam findings, medication/vaccine use and the results of any laboratory or diagnostic tests.

Because this study involves collecting personal, identifiable information about you, there is a potential for invasion of privacy or breach in confidentiality. To minimize this risk, we will assign you a unique 6-digit study number instead of labeling the information we collect from you with your name [or medical record number, if applicable]. Questionnaires that require on-line completion (e.g. for long-term travelers) will be through a secure website. However, labeling of the blood samples obtained for this research study will be handled in the same manner consistent with standard practices; the blood tubes will be labeled with your name and date of birth and your lab result reports will contain your name and other relevant

identifiers. All of the information we collect, including information that identifies you will be stored in a secure manner and with restricted access.

What measures will be taken for my safety?
For safety reasons, the study team will ask you to stay at the clinic for at least 30 minutes after the study vaccine injection and will have medications available to treat a serious allergic reaction if one occurs. People trained to treat allergic reactions will be nearby. During each study visit, a study team member will be available to evaluate any side effects and to answer your questions while you are in the study.

What are the possible benefits from being in this research study?
There are no medical, financial, or other benefits to you as an individual resulting from being in this study. If you receive BCG study vaccine, it is possible that you will have some prevention against TB infection, although this is not known in adult travelers. You will have TB IGRA testing at no cost to you to see if you were infected during travel. Other travelers in the future may benefit from what is learned in this study.

What other alternatives are there to being in this study?
You may choose not to participate in this study. If you were to develop latent TB infection or TB disease during your travel, your healthcare provider can give you drugs that are available to treat TB.

Can I still get medical care at this facility if I don't take part in this research study, or if I stop taking part?
Yes. Your decision to participate or not to participate in the study will not result in loss of benefits to which you are otherwise entitled.

Taking part in this research study is up to you and strictly voluntary. You can decide not to take part. If you decide to take part now, you can change your mind and drop out later. We will tell you if we learn new information that could make you change your mind about taking part in this research study.

Will I be paid for taking part in this research study?
We will pay you XXX (*insert per site*) if you complete all study visits (or up to XXX (*insert per site*) if you have to come back to repeat the post travel IGRA). If you do not complete the study, then we will pay you XXX (*insert per site*) for each visit that you complete.

The information learned in this study and the results obtained from testing performed on specimens collected from you as part of this study may be used to develop commercial products and processes that could be patented or licensed. You will not receive any financial compensation or other benefit for the use of this information or your specimens collected for these purposes.

What will I have to pay for if I take part in this research study?
There will be no cost to you for being in this study. The HJF is the sponsor of this study; however, the U.S. Government (USG) through USUHS, is paying most of the costs to conduct this study. HJF, USG, and the study doctors and other study team members do not have a direct financial interest in the BCG study vaccine.

Study funds will pay for certain study-related items and services. We may bill your health insurer for, among other things, routine items and services you would have received even if you did not take part in the research (standard of care). You will be responsible for payment of any deductibles and co-payments required by your insurer for this routine care or other billed care. If you have any questions about costs to you that may result from taking part in the research, please speak with the study doctors and study staff. If necessary, we will arrange for you to speak with someone about these costs.

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. We will share only the minimum necessary information in order to conduct the research. 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.

What happens if I am injured because I took part in this research study?
If you suffer an injury from participating in this study, you should notify the study doctor or a member of the research study team immediately to determine if you should obtain medical treatment at the study site. The study team will offer you the care needed to treat injury that directly results from taking part in this research study. The Sponsor (HJF) reserves the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer. It is possible that this could result in an increase in your insurance costs.

If you suffer physical injury from the study, the clinical research center will provide immediate medical treatment. The clinical research center will refer you to appropriate healthcare facilities for further care.

The Sponsor (HJF) of this study may pay for reasonable costs not covered by your insurance for reasonable and medically necessary treatment of adverse (bad or harmful) reactions to the BCG study vaccine (not placebo) that you experience while enrolled in the study. HJF will not cover costs incurred for any long term adverse effects that may occur later after your participation in the study has ended. In addition, HJF will not pay for expenses or for a part of expenses for injury, treatment, or hospitalization you may require that are not a result of your participation in the study. HJF will not pay any expenses for injury, treatment, or hospitalization if the clinical research center conducting this study has not followed the study plan, has acted negligently, or has engaged in willful misconduct. Transportation to and from hospitals or clinics will not be provided or paid for by HJF. No other compensation, such as lost wages or other damages, will be available. You do not waive your legal rights by signing and dating this consent form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, contact the study team or the study doctor of the study as soon as possible.

What will happen to the blood specimens obtained for this research?
The blood samples obtained to determine if you qualify for study participation (HIV and TB IGRA) and for assessment pertaining to TB infection (TB IGRA) will not be saved once the analysis has been performed; any leftover blood will be destroyed per individual laboratory policies performing the test. Therefore, blood specimens collected as a part of this research will not be used or distributed for future research studies nor be used for any sort of commercial profit.

Additional Information Regarding Genome Sequencing: 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 being conducted will not 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).

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, 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.

If you have questions or concerns about the study or questions regarding your rights as a research participant and wish to speak with someone not directly involved in this research study, please contact the office of the Institutional Review Board (IRB),

- By mail:
  Study Subject Adviser
  Advarra IRB
  6100 Merriweather Drive, 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: Pro00036693.

Should you experience an adverse effect you feel is research-related after completing your study participation, please contact the Office of Medical Regulatory Affairs at HJF (study sponsor) to report its occurrence using the following information below:

- By **email**: regulatoryaffairs@hjf.com
- or **call**: The Office of Medical Regulatory Affairs @ 240) 694-2067

HEALTH INSURANCE PORTABILITY AND ACCOUNTABILITY ACT (HIPAA) AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

If I take part in the research study, how will my privacy be protected?
Procedures to protect the confidentiality of the data in this study include but are not limited to: coded data, removal of personal information, computer password protection, creation of firewalls around the data, locking of drawers and offices. A firewall is a protection or barrier within a computer to protect the information from being viewed by unauthorized people. Researchers will make every effort to protect your privacy and confidentiality: however, there are risks of breach of information security and information loss.

Before researchers use or share any health information about you as part of this study, the study site is required to obtain your authorization. This section helps explain to you how this information will be used or shared with others involved in the study.

In the context of the research study, identifiable medical data, including information on your sex, age, race, address and phone numbers/email addresses,

- Will be documented in an anonymous form (your name will not be attached to any data; your unique 6-digit subject number will be used instead)
- Any information that is obtained in connection with this study and that can be identified with you will remain confidential.
- Your responses to the questionnaires will be anonymous. Please do not write any identifying information on the questionnaires.
- The data will be kept on a password-protected computer using special software
- Your subject study file will be kept in a secured area with limited access
- Your IGRA blood specimen(s) sent for processing to the outside laboratory are required to contain your name and date of birth, but will be kept confidential to the greatest extent possible provided by law. Once test results are identified and completed, specimens (or any leftover sample) will be disposed of by the laboratory performing the test.

Data collected during this study may be shared with HJF, USUHS, the Department of Defense (DoD) representatives who are responsible for human research protection, and the FDA. Additionally, coded data collected will be shared with the study statistician contracted to assist with analysis of the study results.

A master list will be created linking your name and personally identifying information to a unique study ID number. This will be stored in a secure location with limited access to the study team. Your data collected for this study will be coded with this study ID and that does not contain any information that could identify you. The master list linking personal information to the unique study ID number will be maintained for 6 years after study completion and then destroyed, rendering all study data as coded. Coded study data will be maintained indefinitely.

Coded data collected will be stored on a HIPAA compliant system with limited access and password protected. These data will be made available to the sponsor of the study and to persons and companies working with the sponsor for the purposes of scientific evaluation, use in future research in the development of drugs and diagnostics, and for publication purposes. The study doctor and research staff will be the only people who will be able to connect your personal information to the anonymous study data, and they will only reveal your identity if required by law or a medical emergency.

In order to verify that the study is being conducted correctly, certain people/agencies will be able to inspect your personal records held by the study doctor. These authorized representatives are obligated to observe the rules of professional medical confidentiality.

In this study, we may collect health information about you from:

- Past, present, and future medical records
- Research procedures, including research office visits, tests, interviews, and questionnaires

Who may see, use, and share your identifiable health information and why they may need to do so:

There are some reasons why people other than the researchers may need to see information you provided as part of the study. This includes organizations responsible for making sure the research is done safely and properly. The principal investigator will keep your research records in a secure area with limited access. These records may be looked at by:

- Research staff involved in this study
- The sponsor of this study, and the people or groups it hires to help perform this research
- Other researchers and medical centers that are part of this study and their human research protections personnel

- Those who oversee the safety, data and conduct of this research project
- Non-research staff within the facility who need this information to do their jobs (such as for treatment, payment (billing), or health care operations)
- The IRB and the DoD Human Research Protections Program Official who oversees research
- People from organizations that provide independent accreditation and oversight of hospitals and research
- People or groups that we hire to do work for us, such as data storage companies, insurers, and lawyers
- The vaccine manufacturer, Japan BCG Laboratories
- Federal and state agencies (such as the FDA, DoD, and other US or foreign government bodies that oversee or review research as directed by state and federal law)
- Public health and safety authorities (for example, if we learn information that could mean harm to you or others, we may need to report this, as required by law)

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

Authorization Period

Because research is an ongoing process, this authorization will not expire unless you change your mind and revoke it in writing. There is no set date at which your information will be destroyed or no longer used. This is because the information used and created during the study may be analyzed for many years, and it is not possible to know when this will be completed. In California and any other state that requires an expiration date, the Authorization will expire 50 years after you sign and date this authorization document.

Your Privacy Rights

You have the right **not** to sign and date this form that allows us to use or share your health information for research; however, if you don't sign and date it, you can't take part in this research study.

You have the right to withdraw your permission for us to use or share your health information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing. Once permission is withdrawn, you cannot continue to take part in this study.

If you withdraw your consent, any information that was collected up until the time of your withdrawal will be utilized for this research project; data collected about you up to the time of your withdrawal will remain in the study database and be included in the data analysis (evaluation). We will not be able to take back information that has already been used or shared with others.

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.

You have the right to see and get a copy of your health information that is used or shared for treatment or for payment. However, you will not be able to see or copy your study-related information until the study is completed. This includes any portion of your medical records that may describe study treatment.

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 Subject

Signature of Subject Date Time

Informed Consent Statement of Person Giving Informed Consent

- I have read this consent form.
- This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions.
- I understand the information given to me.
- I understand that I will be given a copy of this signed and dated consent form
- I prefer to be contacted by (initial any that apply) ___email ___ text ____telephone call

Signature of Subject:

I voluntarily agree to take part in this research study.

_____
Printed Name of Subject

_____ _____ _____
Subject Signature Date Time

Signature of Study Team Member Obtaining Consent

- I have explained the research to the study subject.
- I have answered all questions to the best of my ability.

_____
Printed Name of Individual Obtaining Consent

_____ _____ _____
Signature of Individual Obtaining Consent Date Time