
PARTICIPANT INFORMATION AND CONSENT FORM

Protocol Title:	A Randomized, Placebo Controlled, Partially Blinded Phase II Study to Evaluate Safety, Immunogenicity, and Prevention of Infection with <i>Mycobacterium tuberculosis</i> of AERAS-404 and BCG Revaccination in Healthy Adolescents
Protocol Number:	C-040-404
Short Title:	Prevention of Infection with <i>Mycobacterium tuberculosis</i> of AERAS-404 and BCG Revaccination
Study Doctor and Telephone:	Dr Mark Hatherill (Principal Investigator) +27 21 404 7618
Research Site:	South African Tuberculosis Vaccine Initiative (SATVI) Brewelskloof Hospital, Haarlem Street, Worcester 6850 South Africa
Sponsor:	Aeras, Rockville, Maryland, United States

Introduction

You have been asked to join a research study of an experimental vaccine that may help prevent tuberculosis (TB). TB is an infection caused by a bacteria (germ) called *Mycobacterium tuberculosis*. TB is very common in South Africa. TB can spread from one person to another and can often cause death. A vaccine is different than medicine. It can prevent you from getting TB by helping your body fight the bacteria.

You probably received the BCG vaccine against TB as a baby. Previous studies have shown that the BCG vaccine works in babies, but does not work very well to prevent TB in teenagers or adults. Vaccine researchers are looking for better vaccines, or better ways to use the BCG vaccine. The vaccine used in this study (AERAS 404) is called “experimental” because it is still being tested and we do not know if it works. AERAS 404 vaccine is not approved for use or sold anywhere in the world. In this study we are looking at either vaccinating you with AERAS 404 or revaccinating you with the BCG vaccine. Some study participants will not get either the Aeras

404 vaccine or the BCG, but will get a dummy vaccine called a “placebo”. The placebo is a harmless injection of salt water. Some participants will get the placebo so that we can compare their reactions to participants who did receive one of the other 2 active vaccines. We are researching if AERAS 404 (experimental vaccine) or revaccination with BCG vaccine can prevent teenagers from getting infected with the TB germ.

Although all people who get sick from TB have been infected with the TB germ, only a few of the people who have been infected go on to become sick with TB. For this reason, and because infection with the TB germ is so common in South Africa, people who have been infected are only treated if they become sick with TB (unless they have an extra risk for TB, such as people with HIV infection and young babies).

It is your choice whether or not to join the study. You do not have to be in the study if you do not want to. Consent means agreeing to take part in a research study.

This consent form will tell you the purpose of this study, what you will be asked to do if you are in the study, and any possible harm to you from being in the study.

Please ask the study doctor or a member of the study team to explain any words or other things you do not understand about the study. Do not sign this consent form until you have answers to all of your questions. You will be given a signed copy of this consent form.

A summary of this study (in English) is on the website <http://www.ClinicalTrials.gov> or <http://www.sanctr.gov.za>. This website does not include information that could identify anyone participating in this study. You can search this website at any time.

Why is this study being done?

The main purpose of this study is to see if AERAS 404 (experimental vaccine) or revaccination with BCG vaccine can prevent adolescents from getting infected with the TB germ. Some people are infected with TB and do not get sick or show symptoms. We will test your blood to see if you are already infected with TB before you are enrolled in the study. We want to study if either vaccine can prevent infection in participants who are not already infected with the TB germ.

What are the experimental vaccines being tested in this study?

The study vaccine is called AERAS-404. AERAS-404 may prevent your body from getting TB. There is no danger of getting TB from an injection of AERAS-404. The other vaccine is BCG. It is approved to be used in babies, but in this study revaccination with BCG will be experimental.

How many participants will be in this study? How long will I be in this study?

About 1000 participants in one country will be in this study. You will be in the study for up to 30 months (2 ½ years), depending on the results of your blood tests during the study.

If I decide to join the study what happens first?

If you want to join this study and you sign this consent form, you will be asked some questions and some tests will be done to see if you can be in the study.

This will be done during a Screening Visit at the clinic.

The following things will happen during the Screening Visit:

- You will be asked to give the study staff a telephone number or a method to contact you during the study.
- You will be asked if you are willing to complete all scheduled study visits.
- You will be asked questions about your health and the medicines you take.
- Your height, weight, temperature, and pulse rate will be measured.
- You will have a physical exam.
- The study staff may contact your regular doctor (if you have one) to get your medical history, and to inform the doctor about this study.
- Females who are able to get pregnant will have a urine pregnancy test.
- Your urine will be tested for routine lab tests.
- You will be asked if you have /had TB or have been close to someone who has/had TB. If you have/had TB or have been exposed to someone who has TB, you cannot be in the study.
- Blood will be collected for a TB test. This test will tell us if you are infected with the TB germ. The TB test is not to see if you are sick and have symptoms of TB. If this test is positive, you cannot be in this study.
- The study staff will ask your permission to review your medical records and to check your HIV status. If you have ever had a positive HIV test you cannot be in this study.
- Blood will be collected from you for an HIV test. We will counsel you privately about HIV testing before the HIV test and we will counsel you about the meaning of the HIV test result afterwards. The results of the HIV test will be provided and explained to you after the counselling session in a confidential setting at the research clinic. If the result is

positive, you cannot be enrolled into the study, but we will refer you to your local clinic for HIV treatment. If the HIV test is negative you can be in the study, depending on the results of the other tests.

- The total amount of blood collected during these visits will be about 16 mls (1 tablespoon).

After the study staff reviews all this information they will decide if you can be in this study. If you cannot be in the study, the study doctor will tell you why.

How will this study be done?

If you are eligible to be in this study you will receive either BCG, or the study vaccine AERAS 404, or a placebo. A placebo looks like the vaccine but does not have any vaccine in it. Which group you will be in is decided by chance, like flipping a coin. You have a 1 in 3 chance of getting BCG, the AERAS 404 study vaccine, or placebo.

You will know if you are getting the BCG vaccine, but if it is decided by chance that you will get AERAS 404 or placebo, you will not know which one you receive. The study is done this way to compare the AERAS 404 vaccine to the placebo so that we know if any effects are caused by the vaccine.

If you receive BCG, you will receive one injection (with a needle) in the upper arm. If you receive AERAS 404, or placebo, you will receive an injection in the upper arm on 2 different days (Study Visits) about 56 days apart.

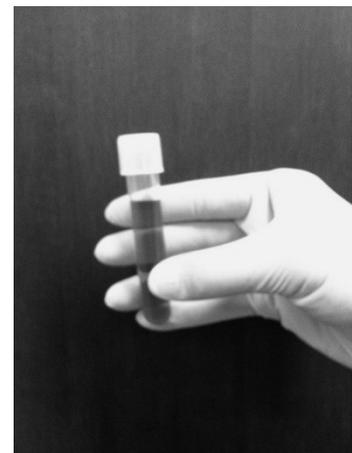
How long you stay in the study will depend on the results of your blood tests. You will have to visit the clinic/hospital up to 15 different days for tests and evaluations no matter which vaccine you receive.

What will happen at the study visits?

You will have to visit the clinic up to 15 times during the study. Each of these visits is called a Study Visit.

Blood will be collected from you on some of these Study Visits. This photograph shows you how much blood is in "1 tube" of blood. One tube collects about 10 mLs of blood.

At some visits one or more tubes of blood will be collected. Three months after the first vaccination, we will start testing your blood



to see if you have been infected with the TB germ. If the test at three months shows that you have been infected you will only need to come back for one more Study Visit. If your blood test shows that you have been infected with the TB germ after the three months Study Visit (at Months 6 to 24), we will ask you to come back to the clinic two more times over the next six months to recheck your blood. So you may participate up to 30 months. If you stay in the study for the whole 30 months, the total amount of blood collected from you during this study will be approximately 350 mls (23 tablespoons or 35 tubes).

If you start to show symptoms of TB at any time during the study, we will test you for TB. If the TB test results confirm that you have TB, the study doctor will advise you about your future medical care and treatment for TB disease.

The table's below shows what will happen at each Study Visit.

Study Group BCG Revaccination

Tests done on Study Days 0 to Month 24

Study Visit	Injection	Blood Collected*	Urine Collected	Blood pressure, temperature, pulse rate taken	Review Diary Card	TB symptom screen	HIV Test
Screen		16mls	Yes	Yes		Yes	Yes
Day 0	Yes	53mls	Yes	Yes			
Day 7		16mls	Yes		Yes		
Day 28						Yes	
Day 70		32.5mls				Yes	
Day 84		10mls				Yes	
Month 6		52.5mls				Yes	
Month 12		52.5mls				Yes	
Month 18		52.5mls				Yes	
Month 24		52.5mls				Yes	

*All blood volumes are approximate

Study Groups Aeras-404 and placebo

Tests done on Study Days 0 to Month 24

Study Visit	Injection	Blood Collected*	Urine Collected	Blood pressure, temperature, pulse rate taken	Review Diary Card	TB symptom screen	HIV Test
Screen		16mls	Yes	Yes		Yes	Yes
Day 0	Yes	53mls	Yes	Yes			
Day 3		6mls	Yes				
Day 7		10mls	Yes		Yes		
Day 28						Yes	
Day 56	Yes		Yes	Yes	Yes	Yes	
Day 63		10mls	Yes		Yes		
Day 70		32.5mls					
Day 84		10mls				Yes	
Month 6		52.5mls				Yes	
Month 12		52.5mls				Yes	
Month 18		52.5mls				Yes	
Month 24		52.5mls				Yes	

*All blood volumes are approximate

What else happens on the injection days?

The following things will happen **before the injection**:

- Females who are able to get pregnant will have another urine pregnancy test. If you are pregnant or nursing you cannot be in the study.
- You will be asked if you have recently been vaccinated with any other vaccines.
- Your blood pressure, temperature, and pulse rate will be measured.

The following things will happen **after the injection**:

- You must remain in the clinic for at least 30 minutes (half an hour) after receiving each injection to make sure you don't have any bad side effects. Your temperature and pulse rate will be taken and must be normal before you can leave the clinic.

What are your duties as a study participant?

Your duties as a study participant include the following:

- You sign the informed consent if you understand it and want to remain in the study. (You previously signed an assent form when you were under 18).

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- Come to all Study Visits when you are told to. You may have a total of up to 15 Study Visits.
 - Give complete and truthful information about your medical history and any signs of illness you may have during the study.
 - Give complete and truthful information about all medicines you take (or stop taking) during the study, including medicines from other doctors, herbal medicines, and medicine you buy yourself.
 - Give blood and urine samples to be tested for routine safety tests and responses to the vaccine.
 - Complete the daily diary and remember to bring it to the study clinic for review;
 - Tell the study doctor if you no longer want to be in the study.

What are the possible harms?

Expected side effects include those commonly seen with other vaccine injections, such as pain, redness, warmth, or swelling at the place where you get the injection. These side effects usually last less than one week. As with any new vaccine, unexpected and serious reactions, including allergic reactions to the vaccine, may occur. This could include an allergic reaction called anaphylaxis, which can be described as feeling dizzy, with difficulty in breathing, an itchy throat, or tingling arms. If you should experience any of these symptoms, you need to contact the study doctor or the nearest doctor immediately. This vaccine has been tested before in both humans and animals, and anaphylaxis did not occur in any of them.

As a result of the BCG vaccine, you may also experience a small sore that might grow into a circle and may become crusty, and which can take up to three months to go away. A small scar may also develop at the site of vaccination. The following are some of the possible other side effects of vaccination:

- Headache
- Fever
- Tiredness
- Enlargement of glands

Other less likely side effects from vaccines include diarrhea and nausea. Other side effects may also occur that are unknown at this time.

Very rarely, people who receive BCG can have bone infections or severe local infections called abscesses. These severe reactions usually happen in people who have other medical problems, like HIV infection. We do not expect to see these kinds of severe reactions in this study.

When blood is collected you might feel brief pain or burning where the needle enters the skin. Your skin might be bruised and you may feel dizzy. You might faint, but this rarely happens. During the study you will receive general check-ups and a study team member will be available to evaluate any side effects and answer your questions. We will teach you about the symptoms of TB, and will ask you if you have any of these symptoms. If we think you might have TB we will help you get medical care.

This is not the first study of Aeras-404 in humans. 196 persons in total have received Aeras-404. In other research studies with Aeras-404, some participants experienced redness at the place where the injection was given. Pain at the place where the injection was given is common. Aeras-404 has also been tested and shown to be safe in animals such as mice, rabbits, and guinea pigs.

For females

- Females who are pregnant or breastfeeding cannot be in the study because it is not known if the study vaccine is safe for pregnant women, fetuses, and breastfeeding children. You will not be given an injection if you have a positive pregnancy test at Screening or on an injection day.
- If you are able to become pregnant, it is very important that you do not become pregnant during the study. You must agree to the following acceptable methods of birth control starting 28 days prior to the first study vaccine injection and for the 24 months period during the study.
 - Acceptable methods of avoiding pregnancy include a sterile sexual partner, sexual abstinence (not engaging in sexual intercourse), hormonal contraceptives (oral, injection, transdermal patch, or implant), vaginal ring, intrauterine device (IUD), or the combination of a condom or diaphragm with spermicide
- If you think you have become pregnant while in the study, you must contact the study doctor immediately. The study doctor will advise you about your baby's future medical care.

What will happen to my samples?

All the samples collected in this study (like blood or urine) will be stored up 5 years after the study is finished. The samples will only be used for tests needed for this study. You will be asked later if we can use your samples for other tests. The samples will be stored at the SATVI laboratory at the University of Cape Town, at the Aeras South Africa Endpoint Assay lab in Cape

Town, or the Aeras laboratory in the USA. We may transfer some of the stored samples to other places too to do the tests.

Are there any benefits to me from being in the study?

There are no medical benefits to you for being in this study except you may receive medical tests that you do not usually get. The information learned from this study may lead to the development of a new vaccine to prevent TB that could benefit society.

Are there any alternative to being in this study?

Your alternative is not to be in this study.

How can I leave the study?

Being in this study is your choice. You may choose not to be in the study. You can also leave the study at any time. If you decide to leave the study, you should tell the study doctor immediately. If you do not want to join the study, or wish to stop being in the study before it is over, it will not affect the medical care you have already received. If you wish to leave the study early, we may ask you to come for one final study visit to do a final physical examination and to do some final blood tests. If new information about the study vaccine becomes available that might affect your decision to participate in the study, you will be told right away.

Could I be taken out of the study? Could the study be stopped?

You may be taken out of the study if the study doctor decides this would be best for you or if you do not follow the study rules. The study sponsor or a government health authority like the Medicines Control Council could also decide to stop the study at any time.

Who is paying for this study?

Aeras and Sanofi-Pasteur are paying for the study vaccine, placebo, tests, medical exams, and procedures in this study. Your insurance company will not have to pay anything for you to be in this study. The study doctor(s) and study staff do not have a direct financial interest in Aeras or the Aeras-404 vaccine.

Will I be paid for being in the study?

You will receive money as compensation for your time, inconvenience, and any additional costs for being in this study. You will receive R150 per visit during this study.

Samples (like blood or urine) collected from you during this study may be used to develop products that could be patented or sold in the future. You will not receive any money or other benefits from these products.

What if I am injured because of this study?

If you suffer a physical injury from this study, the South African TB Vaccine Initiative (SATVI) will give you immediate medical treatment. SATVI may also refer you to a doctor or clinic for further care.

Aeras has taken out insurance in the event of a study-related injury to you. This insurance follows the **Association of the British Pharmaceutical Industry Guidelines**. The guidelines recommend that the sponsor compensates you for any injury that is caused by the study vaccine or study procedures. You do not have to prove that the company is at fault.

Aeras will not pay to treat a medical condition or disease you had before joining this study or expenses for injury, treatment, or hospitalization you may require that are not the result of your participation in the study.

No other compensation, such as lost wages or other damages, will be available. You do not waive any of his/her legal rights by you signing this consent form.

You may make a claim from the sponsor's insurer. If successful, you may be asked to say that you won't make further claims. But even if you say so at that time, you still have the right to make a separate claim against the sponsor in a South African court.

How will my personal information and rights be protected?

Your samples (like blood and urine) will be stored and tested for this study. Your name will not appear on the samples.

Your study records will contain personal health information. Aeras (and their representatives) will visit the clinic/hospital from time to time to check that the study is being done correctly and will review your study records. You will not be identified by name in these study records. However, Aeras has the right to see your name, if they need to do so. Aeras will not share your study records or identity with other parties unless it is required by law. Aeras will do everything they can to ensure that your study records and samples are protected. However, we cannot promise that records and samples will be fully protected.

Your study records may also be reviewed by the Human Research Ethics Committee, University of Cape Town. The Ethics Committee will make every reasonable attempt to keep your identity confidential and will not share your study records with other parties unless it is required by law.

Your study records and medical records may also be reviewed by representatives from government agencies or other health authorities of South Africa. Your study records will be kept at the clinic/hospital for an undetermined amount of time following the completion of the study. After the study is completed (1) you may see your records, (2) you will be told whether you received the study vaccine or the placebo, and (3) you will be told the results of the study. If you decide to leave the study, information already collected from you may still be used for the study.

Aeras, the study doctor, or other doctors involved in the study may publish reports or articles on the study or present the study findings to scientific groups. Your study records may be provided to the people preparing the reports and may be included in the reports. However, your identity and name will not be revealed in any of those reports, articles, or presentations.

Who can I contact for information about the study?

If you have questions about the study you can contact the Investigator on site, **Dr Hennie Geldenhuys**, or other study team members by calling **076 692 1837**.

If you have any symptoms or injuries you think might be related to being in this study contact **Dr Hennie Geldenhuys** the 24-hour telephone number to call is **076 692 1837**

If you have any additional questions about your rights as a research participant, you should contact the University of Cape Town Human Research Ethics Committee, which is overseeing the conduct of this study at The South African TB Vaccine Initiative. An Ethics Committee is an independent committee established to help protect the rights of research participants. If your doctor or the Ethics Committee did not provide you or you with answers to your satisfaction, you should write to the South African Medicines Control Council (MCC).

Contact person	The Ethics Committee Chairperson	The Registrar
Address	University of Cape Town Faculty of Health Sciences, Human Research Ethics Committee Old Main Building, Groote Schuur Hospital, OBSERVATORY 7925	Medicines Control Council Private Bag X828, Pretoria, 0001
Telephone number	021 406 6338 or 021 406 6626	012 395 8000
Fax number	021 406 6411	012 395 8468

CONSENT TO PARTICIPATE IN A RESEARCH STUDY

AERAS C-040-404, A Randomized, Placebo Controlled, Partially Blinded Phase II Study to Evaluate Safety, Immunogenicity, and Prevention of Infection with Mycobacterium tuberculosis of AERAS-404 and BCG Revaccination in Healthy Adolescents

I have had the chance to read this consent form, discuss this study and ask questions. My questions have been answered to my satisfaction. I understand that by signing this consent form, I do not give up any of my legal rights.

I hereby consent to be in this study. I will receive a copy of this signed consent form.

Printed name of participant

Signature/mark or thumbprint of participant

Date (MM/DD/YY) & time

Printed name and designation of person conducting informed consent discussion

Signature of person conducting informed consent discussion

Date (MM/DD/YY) & time

*Printed name of impartial witness

*Signature of impartial witness

Date (MM/DD/YY) & time

*(Required only if participant or legally appointed representative is illiterate, an interpreter is used, or if required by another party.)

This original signed consent form will remain in the files of the doctor conducting the study. A copy of the signed consent form will be given to the study participant.

CONSENT TO USE SAMPLES FROM STUDY FOR FUTURE TB RESEARCH

Sample Storage

We are asking permission to store samples collected from you during this study (such as blood, urine, etc.) and use them for future TB research. This research would not be part of this study. As new tests become available for TB research, your samples would be used to help learn more about TB and how to prevent it and treat it.

Your decision whether or not to allow your samples to be stored and used for future TB research is separate from your choice to join this study. If you choose NOT to allow your samples to be used for future research you can still join this study.

Control of Samples and Privacy

If you give permission, your samples will be placed in a secure storage facility. Aeras will be responsible for managing the facility. Your name and any other information that could identify you will be removed from the samples before storage. The sample will be identified by a number or barcode and the information linking you to this number/barcode will be held under safe, secure conditions by SATVI. If as a result of the future research, Aeras becomes aware of information which is clinically relevant and could affect the health and wellbeing of the participant they will supply the information to the doctor at SATVI who will then link the number / barcode to the participant and contact the participant for an appointment where this information can be discussed.

Your samples will be stored for an undetermined amount of time.

If you agree to have your samples stored and then later change your mind you can contact Dr Geldenhuys on 023 346 5400 to ask that your samples not be used and be destroyed. The results of any tests done on your samples before the request is received will be kept by the researchers.

Risks

There is a risk that your samples (and any test results) could be linked to you. This could impact your job, insurance, or family relationships. The chance of this happening is very small. Aeras will do their best to protect your privacy and keep your identity secret.

Benefits

You will not receive any direct benefit by allowing your samples to be used for future TB research. It may benefit others if knowledge is gained through the research.

Tests done on your samples may help Aeras or other researchers develop a commercial product. You will not receive any financial profit if this occurs. Any publication resulting from this future research will not include any names or other identifiers of participants.

Participant agreement:

If any of the blood samples I have provided for this research project are unused or left over when the research is completed, (tick ONE choice from each of the following boxes):

I want my samples destroyed immediately

OR

I give permission for my samples to be stored indefinitely.

AND

if the sample is to be stored:

I give permission for my samples to be stored and used in future TB research

AND

I am willing to be re-contacted by the researcher about possible future use of more blood samples in future research.

OR

I do not want to be re-contacted to ask me to give more blood samples in the future or to take part in future studies.

I have read the information, or it has been read to me. I have been informed that my sample will be identified by a number / barcode and not my name. I have had the chance to ask questions about it and I am satisfied with the answers I was given. I consent voluntarily and understand that I have the right to withdraw my consent without this affecting the research I am currently taking part in or my medical care.

Printed name of participant

Signature/mark or thumbprint of participant

Date (MM/DD/YYYY) & time

Printed name and designation of staff member conducting informed consent discussion

Signature of person conducting informed consent discussion

Date (MM/DD/YYYY) & time

*Printed name of impartial witness

*Signature of impartial witness

Date (MM/DD/YYYY) & time

*(Required only if participant or legally appointed representative is illiterate, an interpreter is used, or if required by another party.)