

Study Information - WRAIR #2007 (MAL071)

WRAIR #2007: Phase IIA, open-label, controlled, single-center, single-country study, to evaluate efficacy, safety, reactogenicity and immunogenicity of GSK Biologicals' candidate malaria vaccine RTS,S/AS01_B administered as standard doses at 0 and 1 months and 1/5th standard dose at 7 months (delayed fractional dose group) and administered as three standard doses one month apart (0, 1, 2-month group) in healthy malaria-naive volunteers aged 18-50 years.

Study Objective: This study is being conducted to evaluate the safety and effectiveness of an experimental malaria vaccine. Specifically, this study will be comparing different dosing regimens. One regimen will be standard dose vaccine at 0,1,2 months and the other regimen will be full dose vaccine at 0 and 1 month, then a reduced dose at 7 months.

- 1.** This vaccine is called RTS,S/AS01_B. RTS,S/AS01_B contains a protein that resembles one produced by the *P. falciparum* malaria parasite. This protein is not the malaria germ itself and cannot cause the disease malaria.
- 2. Has this vaccine been tested in humans before?** This vaccine has been tested in approximately 150 adults, and the pediatric (child) formulation, which is half the adult dose, has been tested in more than 11,000 babies and children 6 weeks to 4 years of age.
- 3. Study Duration:** You will be in the study for approximately 15 months if you are in the group receiving 2 standard vaccine doses 1 month apart and the reduced third dose of vaccine at Month 7, and approximately 10 months if you are in the group receiving 3 standard doses 1 month apart. You will be in the study about 7 months if you are in the group that does not receive the study vaccine.
- 4. Number of People in the Study:** Sixty-five volunteers will be enrolled in this study. Of these 65 volunteers, 51 will be vaccinated and will be invited to participate in the challenge phase of the study. In addition, 14 volunteers ("infectivity controls") will be enrolled who will not be vaccinated but will have the "malaria challenge" to prove that the mosquitoes are carrying the malaria parasite (described below). Two of these infectivity control volunteers will act as alternates and only have the "malaria challenge" if all 12 infectivity controls are not available at time of challenge.
- 5. Study Background:** Malaria is a parasitic disease transmitted by mosquitoes. It is a significant cause of death and disability in tropical areas of Africa, Asia, Oceania (Pacific islands) and Latin America. Humans become infected when they are bitten by infected mosquitoes. People don't feel well with this disease – its effects are similar to the flu, with symptoms such as fever, headache, body aches, upset stomach and diarrhea. Therefore, this disease impacts people and communities due to lost time in the home, at work and school.

A vaccine against the parasite would be a major contribution to public health. The U.S. Army is at the forefront of malaria vaccine research and development because soldiers are deployed to areas with malaria. In the current proposed study, we want to evaluate the safety of a new anti-malarial vaccine.

Study Information - WRAIR #2007 (MAL071)

6. Brief review of inclusion / Exclusion criteria (Full criteria in protocol)

Inclusion:

- Men and non-pregnant, non-lactating women, civilian or military
- ages 18-50 (inclusive)
- in good health
- no plans to travel to a country with malaria throughout the study
- low cardiac risk

Exclusion:

- History of malaria or receipt of an investigational malaria vaccine
- History of malaria chemoprophylaxis within the past 60 days
- Heart, lung, liver, or kidney disease (high blood pressure, diabetes)
- Neurologic disease
- Splenectomy
- History of sickle cell disease or other blood diseases
- Positive for HIV or viral hepatitis
- Use of investigational drug or non-registered vaccine within 30 days before the first immunization
- Use of any vaccine within 7 days before the first immunization
- Allergic reaction to a vaccine
- Pregnancy or planned pregnancy during the study time period
- Use of certain prescription medications
- Inability to make all follow-up appointments
- Active duty military volunteers will require approval from their supervisory chain
- Alcohol or drug abuse
- Any other significant finding that in the opinion of the clinical investigators would make participation in the study unsafe

7. Study Plan:

Screening

A person who wants to enroll in the study will be screened to ensure they are eligible to participate. Screening includes:

- A detailed explanation of the study
- Completion of the informed consent documents
- Brief medical history and physical exam
- Urine pregnancy test and blood tests
- EKG (electrocardiogram which measures the “electrical activity” of the heart)

Vaccination

- There are 3 vaccinations given at 0, 4, and 8 weeks for one group and 0, 4, and 28 weeks for the other group.
- The vaccine is given through a needle into a muscle in the volunteer’s upper arm.
- Volunteers will be required to come in for several follow-up visits after each vaccination.
- Study staff will see the volunteer at each visit. Volunteers will have blood drawn at most visits. Volunteers in the control group will not receive vaccinations.
- A urine pregnancy test will be performed for all women before each vaccination

Study Information - WRAIR #2007 (MAL071)

Challenge

- Volunteers will consent to participate in a malaria challenge to find out if the vaccine was effective. The challenge involves being bitten by mosquitoes infected with the malaria parasite. The mosquitoes are contained in a small cup with a screen on top. This procedure doesn't hurt, but the volunteer's arm may itch later, as with any mosquito bite. Volunteers may develop malaria from the mosquito bite.
- A urine pregnancy test will be performed for all women before the challenge

Post-challenge and Hotel Phase

- Volunteers will need to return to the Clinical Trials Center one and five days after the challenge to provide blood for testing. They will then return every day on days 6-9.
- Starting the night of the 9th day after the initiation of malaria challenges, volunteers will need to check in to a specific hotel each night to stay for a maximum of 10 days to allow for rapid assessment and treatment by study staff. The reason is that this is the period of time volunteers are most likely to become sick with malaria.
 - Each morning, volunteers will be seen by a study physician and have a small amount of blood drawn to test for malaria.
 - Each afternoon, a study staff member will call to see how each volunteer feels and relay the test results.
 - Volunteers will only have to sleep at the hotel, but can come and go for work and outside activities as long as they return for clinical visits.
- The symptoms of malaria include fever, chills, headache, fatigue, vomiting, diarrhea, muscle aches, and stomachache.
- If malaria does develop, volunteers will be treated with a medication taken by mouth; Chloroquine, which is taken 4 times within 48 hours. This drug is FDA approved and has been used safely for many years. The medication is expected to completely cure the malaria.

Post-Hotel Phase

- Volunteers will also be required to return to the Clinical Trials Center for follow-up visits for approximately 6 months after the challenge.
- Each volunteer will have a unique schedule, based on whether or not they develop malaria.
- Blood will be drawn at these visits.

8. Risks to the Volunteers may include:

- Note: study staff have methods to decrease or limit most, if not all, side effects
- From vaccinations: typical side effects from this vaccine are redness, swelling, and soreness at the site of injection. Although there is much experience with this vaccine in humans, there may be other unknown side effects.
- From challenge: local reaction at the site where mosquitoes bite, side effects from the FDA- approved anti-malaria medication (such as upset stomach, nausea, diarrhea, tiredness, ringing in ears)
- From malaria: fever, chills, headache, fatigue, vomiting, diarrhea, muscle aches, and stomachache
- From blood draws: bruising at the site
- Loss of confidentiality: For each volunteer that participates in this study, there is a chance that limited, volunteer information may be disclosed to persons outside of this

Study Information - WRAIR #2007 (MAL071)

study to include: representatives of GSK, the USAMRMC, the Food and Drug Administration (FDA), the Western Institutional Review Board (WIRB) and the WRAIR Institutional Review Board (IRB). These representatives may have access to review research records as part of their responsibility to protect humans in research but they must also maintain confidentiality of volunteer records within the limits of the law.

9. Payment:

- Payments will be made for blood drawn during the study (\$50 per blood draw plus \$25 for screening) but not for transportation or other expenses.
- Payments will also be made for participation in study activities (\$50 per visit).
- Vaccination plus challenge: compensation may range up to approximately **\$4,425** for volunteers who participate in both the vaccination and challenge portions, depending on whether they become positive for malaria and when, or remain negative for malaria.
- Control (Unvaccinated) volunteers: approximately **\$2,975**, depending on when they become positive for malaria.
- Active duty personnel and Federal employees will only be paid \$50 per blood draw, unless the visits occur during off duty hours or they are on leave. In that case, they will be paid \$50 for participating in the study activities, the same as non-military/non-Federal personnel.

10. Study Setting: Outpatient