



WRAIR study #1692, Principal Investigator Dr. Bennett:

Purpose: The purpose of this study is to test the safety and effectiveness of a new malaria vaccine, called VMP001. The study is specifically looking at a vaccine against *Plasmodium vivax*, the most common form of malaria in Asia. This is the first time the VMP001 vaccine will be given to humans.

Background: Malaria is a parasitic disease transmitted by mosquitoes. Approximately 40% of the world's population is at risk for malaria caused by *Plasmodium vivax*. This parasite causes 132 - 391 million infections around the world each year. 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. In some parts of the world, *P. vivax* has become resistant to drugs used in the past, and a vaccine against this disease would therefore help people living in, or traveling to areas where it is commonly found. The U.S. Army is at the forefront of malaria vaccine research and development because soldiers are deployed to areas with malaria.

Vaccine Information: This new vaccine is made up of two parts. The first part is called VMP001 and it is designed to look like a part of the malaria parasite. The second part is called AS01B, and is the component to boost the body's immune response to VMP001.

Has this vaccine been tested in humans before? The VMP001 portion of the vaccine has not been tested in humans before; however, the AS01B portion has been tested in humans and has not been found to cause serious side effects.

Number of People in the Study: There are two groups: 30 who will receive three vaccinations and 6-12 controls, who will not receive vaccinations, for a total of 36-42.

Study Duration: Up to 12 months for vaccinated subjects and approximately 9 months for non-immunized controls

Brief review of inclusion / Exclusion criteria

Inclusion:

- Men and non-pregnant, non-lactating women
- ages 18-55 (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
- Recent travel to *P. vivax* endemic area within the past three months
- 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 hepatitis C
- Use of investigational drug or non-registered vaccine within 30 days before the first immunization
- Use of any licensed 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
- Alcohol or drug abuse

1. 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 to 12 weeks.
- The vaccine is given through a needle into a muscle in your upper arm.
- You will be required to come in for several follow-up visits after each vaccination.
- A study physician will see you at each visit, and you will have blood drawn at several visits. Volunteers in the control group will not receive vaccinations.
- A urine pregnancy test will be performed for all women before each vaccination

Challenge

- All volunteers will participate in a malaria challenge to find out if the vaccine was effective. The challenge involves being bitten by five 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 your arm may itch later, as with any mosquito bite. You 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 every other day in the first 5 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 challenge, 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.



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- Each morning, you 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 you feel and relay the test results to you.
 - You will only have to sleep at the hotel, but you can come and go for work and outside activities as long as you return for your clinical visits.
 - The symptoms of malaria include fever, chills, headache, fatigue, vomiting, diarrhea, muscle aches, and stomachache.
 - If you do develop malaria, you will be treated for two weeks with medications you take by mouth; Chloroquine, which is taken for three days, and Primaquine, taken daily for two full weeks. These drugs are FDA approved and have been used safely for many years. The medications are expected to completely cure the malaria.
 - A urine pregnancy test will be performed for all women before starting anti-malaria medication.

Post Hotel Phase

- Volunteers will also be required to return to the Clinical Trials Center for follow-up visits.
- Each volunteer will have a unique schedule, based on whether or not you develop malaria.
- Blood will be drawn at some of these visits.

Risks to the Volunteers may include *(Note: study staff have methods to decrease or limit most, if not all, side effects)*

- From vaccinations: this vaccine has not been administered to humans, however typical side effects from vaccines are redness, swelling, and soreness at the site of injection. 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

Payment: Payments will be made for blood drawn during the study (\$100 per blood draw plus \$25 for screening) but not for transportation or other expenses.

- Vaccination plus challenge: compensation may range up to \$3775 to \$4225 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 \$2075, depending on when they become positive for malaria.