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PATH and WRAIR announce largest-ever controlled malaria infection

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PATH's Malaria Vaccine Initiative (MVI) and the US Department of Defense's Walter Reed Army Institute of Research (WRAIR) announced today that vaccinations are under way in a clinical trial to evaluate modifications to the vaccine regimen of GSK's RTS,S/AS01 (RTS,S) malaria vaccine candidate. The partners seek to understand if these modifications will provide equal or increased protection compared to the standard pediatric regimen.

With 160 participants, this is the largest trial of its kind, in which adult US volunteers will be exposed to malaria-causing parasites via mosquito bites under controlled laboratory conditions. This critical step—called controlled human malaria infection, or CHMI—will take place at WRAIR three months after the last vaccine dose is administered.

CHMI allows researchers to evaluate a malaria vaccine candidate's safety and efficacy in a highly controlled laboratory setting and serves as a precursor to field studies in regions of the world where malaria is endemic. Those volunteers who become infected are treated with antimalarial drugs to clear their infections.

"A highly effective vaccine, used in combination with other malaria interventions, could help to eliminate and eventually eradicate malaria," said Lieutenant Colonel (LTC) James Moon at WRAIR, the study's principal investigator. "Such a vaccine would make a major contribution to global public health, and in turn, benefit national security."

Malaria is a devastating parasitic disease transmitted by mosquitoes. It causes approximately 200 million cases of illness and more than 400,000 deaths per year. Sub-Saharan Africa carries the greatest disease burden. Malaria also remains the number one threat to US military force health protection and readiness.

The CHMI study will evaluate the efficacy, immunogenicity, and safety of various regimens using two different formulations of RTS,S. In addition to testing the vaccine for its protective abilities, researchers also seek to understand better how the vaccine works. They will evaluate the immune mechanisms associated with vaccine efficacy as the study progresses.

"This study represents an important step in determining whether the RTS,S vaccine, originally developed to prevent clinical malaria in young African children, can be effectively adapted to prevent infection in all at-risk populations in endemic countries to accelerate parasite elimination," said Dr. Ashley Birkett, Director of MVI.

RTS,S is the malaria vaccine most advanced in development globally and will be administered in selected areas of three countries in Africa—Ghana, Kenya, and Malawi—starting in 2018 through a pilot implementation program coordinated by the World Health Organization (WHO). It will be administered in a four-dose regimen, with the first dose given as soon as possible after the age of five months.

Pilot implementation of RTS,S is an important step to help protect young children in sub-Saharan Africa, the population most at risk of developing malaria. Data from a large-scale phase 3 efficacy and safety trial showed that the recommended four-dose regimen of RTS,S prevented four in ten cases of malaria over four years of follow-up.

To help achieve malaria elimination and eradication goals, it is assumed

that a vaccine with significantly higher efficacy that could also be administered across an entire at-risk population, including adults, would be needed.

The CHMI trial currently under way builds on two earlier CHMI studies also conducted at WRAIR. Those studies showed that reducing and delaying administration of the third dose of RTS,S resulted in higher protection against malaria infection. Results of one of these studies, published in the Journal of Infectious Diseases, indicated that this alternative regimen protected 87 percent of participants from becoming infected, compared to 63 percent with the standard regimen.

The current 15-month trial at WRAIR will have five arms that assess several variables, including vaccine formulation and dosage. The healthy, malaria naïve adults enrolled in the trial have been randomly assigned to the various arms and will be closely monitored throughout the trial to assess the immunogenicity of the vaccine and to monitor for safety issues.

"We are grateful to the volunteers who are giving us their trust and their time to help develop a potential vaccine against malaria," said LTC Moon. "Increasing parasite resistance to current antimalarial drugs has made the quest for a vaccine more important than ever."

WRAIR designed and is implementing and conducting the trial at their facilities in Silver Spring, Maryland. This project is financially supported by MVI, which also provided input into the design of the trial and will oversee it. GSK is the trial sponsor and a collaborator on its design and conduct.

"WRAIR is at the forefront of malaria vaccine research and development," said MVI's Birkett. "They pioneered the malaria challenge approach, and their decades of experience make them an ideal

partner to conduct the largest CHMI study ever. The data from this study will answer important questions regarding the potential for RTS,S to serve as a supplemental tool to accelerate malaria parasite elimination and eventual eradication."

Provided by Burness