

Summary of the “Malaria Vaccine: WHO Position Paper- January 2016”

This is the first WHO position paper on a malaria vaccine. It focuses primarily on the available evidence concerning the only malaria vaccine to have received a positive regulatory assessment, which was issued by the European Medicines Agency (EMA) in July 2015.

Background

Malaria is a vector-borne disease transmitted through the bites of *Anopheles* mosquitoes. Several species of the *Plasmodium* protozoan parasite can infect humans (*P. falciparum*, *P. vivax*, *P. ovale*, *P. malariae* and *P. knowlesi*).

According to the latest WHO data, an estimated 438,000 people died of malaria in 2015, with over 90% of these deaths occurring in sub-Saharan Africa. Most of these deaths occur in African children younger than 5 years of age. Almost all malaria deaths are caused by *P. falciparum*. Morbidity due to infection with *P. falciparum* can range from mild febrile illness, which is difficult to distinguish clinically from other similar illnesses, to life-threatening disease with coma, respiratory distress, severe anaemia or circulatory shock. In most African countries, substantial malaria control activities have been implemented, including the widespread deployment of long-lasting insecticidal nets, the use of indoor residual spraying of insecticides in some settings, prompt diagnosis using quality-assured rapid diagnostic tests and treatment with highly effective artemisinin-combination therapies. These interventions are associated with substantial reduction of incidence rates of malaria and malaria deaths.

More than 30 *P. falciparum* malaria vaccine candidates are at either advanced preclinical or clinical stages of evaluation, but only the RTS,S/AS01 vaccine has completed Phase 3 evaluation and received a positive regulatory assessment. Among trial participants given a 4-dose schedule starting at 5-17 months of age, vaccine efficacy against severe malaria was 31.5% (95%CI 9.3, 48.3) over approximately 4 years of follow up. Vaccine efficacy against severe malaria was lower when immunization was initiated at an age of 6-12 weeks. There was one identified risk (febrile seizures) for RTS,S/AS01 and three safety signals (meningitis, cerebral malaria and all-cause mortality in girls) that emerged from the Phase 3 trial that will require further exploration in post-licensure studies.

WHO Position

WHO recognizes the importance of malaria due to *P. falciparum* as a major cause of morbidity and mortality, particularly in sub-Saharan Africa, and the essential role of existing malaria control measures in significantly reducing the burden of disease in recent years. Nevertheless, malaria transmission, morbidity and mortality remain high in many endemic settings. Prevention still needs to be strengthened further and new tools are needed.

A number of uncertainties related to programmatic aspects, vaccine impact, and vaccine safety still need to be resolved in order to assess the advisability of introducing the RTS,S/AS01 vaccine for routine use. WHO therefore recommends further evaluation of RTS,S/AS01 in a series of pilot implementations, addressing several gaps in knowledge, before considering wider country level introduction.

WHO recommends that the pilot implementations use the 4-dose schedule of the RTS,S/AS01 vaccine in 3–5 distinct epidemiological settings in sub-Saharan Africa, at subnational level, covering moderate-to-high transmission settings. In the pilot implementation schedules, the malaria vaccine should be given as a 3-dose initial series with a minimum interval between doses of 4 weeks, followed by a 4th dose at 15–18 months after the 3rd dose. The 1st dose should be administered as close as possible to age 5 months and the 3rd dose should be completed by 9 months of age.