Summary of Key Points

Malaria Vaccine: WHO Position Paper
January 2016
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*).

- In 2015, an estimated 438,000 people died of malaria, 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.

- Morbidity with *P. falciparum* can range from mild febrile illness to life-threatening disease with coma, respiratory distress, severe anaemia or circulatory shock.
Background

- **Malaria transmission:**
  - Vector-borne disease transmitted through the bites of Anopheles mosquitoes

- **Treatment:**
  - Artemisinin-combination therapy

- **Prevention:**
  - Long-lasting insecticidal nets (LLIN) and the use of indoor residual spraying of insecticides (IRS)
  - Intermittent preventive treatment (IPTp) in pregnancy
  - Seasonal malaria chemoprevention (SMC) in highly seasonal areas
Vaccines

- More than 30 *P. falciparum* malaria vaccine candidates are at either advanced preclinical or clinical stages of evaluation.

- Until now, only the RTS,S/AS01 vaccine has completed Phase 3 evaluation and received a positive regulatory assessment by the European Medicines Agency (EMA) in July 2015*.  

Efficacy of RTS,S/AS01

- Vaccine efficacy against all episodes of clinical malaria over the whole trial period (approximately 4 years) was 26.2% (95% CI 20.8, 31.2) among participants who received a 3-dose schedule starting at 5–17 months of age. Among those who received the 4-dose schedule overall vaccine efficacy was 39.0% (95%, CI: 34.3, 43.3).

- Vaccine efficacy was lower at every time point in those first vaccinated at 6–12 weeks of age compared to those first vaccinated at 5–17 months of age.
Safety of RTS,S/AS01

- 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.

- This 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, despite considerable scale-up of these interventions, malaria transmission, morbidity and mortality remain high in many endemic settings. Prevention needs to be strengthened still further and new tools are needed.
WHO Position

- The RTS,S/AS01 vaccine has been evaluated in a large Phase 3 trial and received a positive regulatory assessment.

- However, a number of uncertainties 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 Position

- 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.

- Based on the efficacy data from the Phase 3 trial, WHO does not recommend the use of the RTS,S vaccine in the younger (6–12 weeks) age category, as the vaccine efficacy was found to be low in this age category.
Implementation considerations

- The pilot implementations should be done in phased designs and in the context of ongoing high coverage of other proven malaria control measures.

- The pilot implementations should involve sufficiently large populations, followed for an adequate duration, with rigorous evaluation.

- Appropriate training and communication materials for the general public and for health workers should be developed and disseminated.
Monitoring and evaluation

Careful evaluation should be conducted to allow:

- Assessment of operational feasibility of providing the malaria vaccine in the target age-group at the recommended 4-dose schedule in the context of health service delivery in various countries;

- Evaluation of the impact of the vaccine on child mortality, including measures to determine the impact of the vaccine when added to concomitant malaria interventions, by sex;

- Surveillance of adverse events following vaccination, with an emphasis on meningitis and cerebral malaria including by sex and using standardized case definitions;

- Systematic compilation of evidence on the functioning of the immunization programme, adherence to currently recommended malaria control measures, and broader health system functioning and community engagement, including evidence of any adverse effects of vaccine implementation on other malaria control measures.
For more information on the Malaria Vaccine: WHO position paper, please visit the WHO website:

www.who.int/immunization/documents/positionpapers