

Update on RTS,S Malaria Vaccine Implementation Programme and framework for decision-making

March 2018, Geneva, Switzerland

Background

In January 2016, WHO published its first malaria vaccine position paper.¹ Following the advice from the MPAC and the Strategic Advisory Group of Experts (SAGE) on Immunization, WHO recommended pilot implementation of the RTS,S/AS01 malaria vaccine in order to address several outstanding questions related to the public health use of the vaccine.

The Malaria Vaccine Implementation Programme (MVIP) has been developed to support the introduction of the malaria vaccine in selected areas of the three pilot countries (Ghana, Kenya and Malawi) and the rigorous evaluation of the programmatic feasibility of administering the required four doses; the vaccine's impact on mortality; and its safety in the context of routine use.

The Programme is jointly coordinated by the Global Malaria Programme (GMP), the Immunization, Vaccines & Biologicals (IVB) department and the WHO Regional Office for Africa, collaborating closely with other WHO departments and country offices, the Ministries of Health in pilot countries, PATH and other partners. The malaria vaccine introduction is country-led. Relevant activities are coordinated with the vaccine manufacturer, GSK.

Update since October 2018

The critical cross-cutting elements of the MVIP are now in place to move the malaria vaccine implementation forward:

- In October 2017, WHO signed a Collaboration Agreement with PATH and GSK to define the roles and responsibilities of these partners in the MVIP. WHO and PATH are working together across various areas, including economic assessment and the qualitative assessment of the behaviour change that may occur during the introduction of the vaccine. GSK is manufacturing the vaccine and leading the Phase 4 studies to continue monitoring vaccine safety and effectiveness in routine use as part of the RTS,S/AS01 Risk Management Plan agreed with the European Medicines Agency. As part of the Collaboration Agreement, GSK has committed to supplying, without charge, sufficient quantities of the RTS,S/AS01 vaccine to enable sound implementation of the MVIP, up to a maximum of 10 million doses.

¹ World Health Organization. Malaria vaccine: WHO position paper – January 2016. Weekly Epidemiological Record. 2016;91:33–52 (<http://www.who.int/wer/2016/wer9104.pdf>).

- By mid-December 2017, all donor agreements between WHO and the three MVIP funders (Gavi, the Vaccine Alliance, the Global Fund and Unitaid) have been fully executed and funding is now available for phase 1 of the MVIP, through 2020.
- The hiring of dedicated staff in the WHO Regional Office for Africa and the pilot countries is moving forward.

All pilot countries have developed and submitted vaccine introduction plans and initiated preparatory activities related to communications, supply planning, and the strengthening of routine pharmacovigilance, among others.

Use of RTS,S/AS01 in the MVIP will require special approval from the national regulatory authorities (NRAs) of the three pilot countries prior to vaccine introduction. The three NRAs held a joint regulatory review in February 2018, convened under the African Vaccine Regulatory Forum (AVAREF). Timelines for the regulators' final decision on special approval have been agreed upon.

Progress has been made in the identification of research partners for the pilot evaluations. Following the WHO Request for Proposals (RFP), a lead bidder consortium of partners has been identified for each pilot country. The awards are subject to successful negotiations with prospective evaluation partners in order to bring budgets in line with available resources. These negotiations are expected to be completed shortly. The master protocol for the pilot evaluations, developed by WHO, was approved by the WHO Research Ethics Review Committee in February 2018.

The two key advisory bodies for the MVIP have been established: the MVIP Programme Advisory Group (PAG), the highest-level advisory body to WHO on MVIP-specific aspects, which convened for the second time in March 2018; and the MVIP Data Safety and Monitoring Board (DSMB), responsible for safeguarding the well-being of children vaccinated in the MVIP by providing advice and recommendations to WHO on issues concerning the safety of RTS,S. The DSMB met for the first time in February 2018. During Q1 2018 the MVIP team consulted with malaria and meningitis experts to obtain advice on the measurement of meningitis and cerebral malaria in MVIP sentinel hospitals in order to ensure appropriate design and methodologies for reliable diagnosis during the pilot.

Various elements need to be in place before vaccine introduction and pilot evaluations can begin in each country. The MVIP team is actively supporting the components within its remit (i.e., sentinel hospital surveillance, impact monitoring, etc.), while closely monitoring the aspects outside of its control and their impact on timelines (e.g., special approval by national regulators for use of the vaccine, competing priorities for the national Immunization Programmes, etc.). At present, the first vaccination is still expected to occur in 2018.

Framework for policy decision on RTS,S/AS01

The MPAC was in favour of a proposal, presented by the MVIP team at the last meeting in October 2017, to develop a framework for policy decision on RTS,S/AS01. The framework will aim to describe how data collected through the MVIP might be used to inform future policy by establishing criteria that would likely lead to a favourable recommendation for vaccine use. Discussion and deliberation on the framework by the SAGE and MPAC in future sessions will provide an opportunity to clarify the relative contribution of the collected data (e.g., feasibility as measured by vaccine coverage, impact on severe malaria, impact on mortality, safety) in light of potential changes in SAGE/MPAC membership between the

time the recommendation for pilots was made (2015) and the end of the programme (2022). Examples of the types of questions that will be presented as part of the framework include:

1. What constitutes ‘favourable implementation data’? In particular, what levels of coverage (especially of the fourth dose) achieved in a routine setting would be considered to have good public health value?
2. If impact on severe disease is demonstrated despite only moderate vaccine coverage levels, would WHO recommend vaccine implementation?
3. Is demonstration of impact on mortality through the MVIP required for a policy recommendation or would evidence of impact on severe disease and modelled impact on survival suffice?

Two modelling groups (Swiss TPH and Imperial College) have been engaged to assist in estimating the impacts on severe malaria and mortality of different vaccine coverage levels that might be achieved in the MVIP. A sub-group of WHO’s Immunization and Vaccines Related Implementation Research Advisory Committee (IVIR-AC) evaluated the impact models from these groups over a period of 4 years from 2011 to 2015. The IVIR-AC was therefore consulted again in March 2018 to ensure that the methods and assumptions of the modelling work proposed for the decision framework are appropriate to help answer the policy questions. The IVIR-AC will be consulted again in September before the framework is expected to be presented to the SAGE and the MPAC in the October 2018 meetings.

Contact

For more information, please contact:

Mary Hamel, MVIP lead, WHO HQ, Immunization, Vaccines & Biologicals, hamelm@who.int

David Schellenberg, Scientific Adviser, WHO HQ, Global Malaria Programme, schellenbergd@who.int