

Session 4: Malaria vaccine implementation programme (MVIP)

Executive summary

1. Background

In January 2016, WHO published its position paper for RTS,S/AS01, the first malaria vaccine, officially adopting the joint recommendation by SAGE and the Malaria Policy Advisory Committee (MPAC). WHO recommends pilot implementation of the RTS,S vaccine in distinct settings in sub-Saharan Africa in order to generate critical evidence to enable decision-making about potential wider scale use.

2. Purpose of session 4

The aim of this session is two-fold:

- 1) To provide a comprehensive update to SAGE on how the recommendation for pilot implementation has been taken forward by WHO since 2016. Following a brief recap of the considerations that have led to the recommendation for pilots, the malaria vaccine implementation programme (MVIP) will be presented and a status update of preparatory activities given.
- 2) To provide an update on the development of the policy decision framework for RTS,S/AS01 which was first presented to SAGE during the breakfast meeting in October 2017.

3. Malaria vaccine implementation programme – progress update

Following the WHO recommendation for pilot implementation in January 2016, a team at WHO, with support from PATH, developed a funding proposal which was submitted to prospective donors in view of securing the required resources for the MVIP. Funding commitments from Gavi, the Vaccine Alliance, the Global Fund to Fight AIDS, Malaria and Tuberculosis and Unitaid were secured and donor agreements fully signed by the end of 2017.

Following a WHO call for expression of interest, three countries (Ghana, Kenya, Malawi) were selected to participate in the MVIP, introducing the RTS,S/AS01 malaria vaccine in pilot implementations.

The MVIP aims to support the introduction of the vaccine in selected areas of the three countries through routine immunization programmes and to evaluate the outstanding questions related to the public health use of the vaccine. The MVIP consists of three components:

- **Vaccine introduction:** National immunization programmes in Ghana, Kenya, and Malawi will lead the pilot introduction of the malaria vaccine in areas with moderate to high malaria transmission. The aim is to reach approximately 360 000 children per year in the selected areas.
- **Pilot evaluation:** A master protocol has been developed and will be implemented by country-based research partners to evaluate: (1) the programmatic feasibility of delivering RTS,S/AS01 with new immunization contacts, including the fourth dose in the second year of life; (2) the vaccine's impact on mortality and (3) the vaccine's safety in the context of routine immunization, with an emphasis on meningitis and cerebral malaria.

- **GSK Phase 4 study:** The GSK-sponsored observational Phase 4 studies form part of the RTS,S/AS01 Risk Management Plan agreed between GSK and EMA to further assess vaccine safety, effectiveness and impact in routine use. The WHO-led pilot evaluation has been designed to complement the GSK Phase 4 study that will take place in a small sub-set of the pilot areas.

The MVIP will be implemented over approximately 6 years from 2017 to 2022. Preparatory work for regulatory approval, vaccine introduction and pilot evaluation has started in all countries. RTS,S/AS01 introduction is anticipated in 2018 in the first country, upon confirmation of readiness of all relevant components.

4. Framework for policy decision

SAGE welcomed the idea of developing a framework for policy decision for RTS,S/AS01. The framework will aim to clarify how data collected through the MVIP might be used to inform future policy. Criteria will be established that would likely lead to a favorable or an unfavorable recommendation for vaccine use. Discussion and deliberation on the framework by SAGE and MPAC 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 programme end (2022). Examples of the type of questions that will be presented as part of the framework include :

- What constitutes ‘favorable implementation data’? In particular, what levels of coverage (especially of the fourth dose) achieved in a routine setting would be considered good public health value?
- If impact on severe disease is demonstrated despite only moderate vaccine coverage levels, would WHO recommend vaccine implementation?
- 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?

To help with question 1 above, two modelling groups (Swiss TPH and Imperial College) have been engaged to assist in estimating the impact on severe malaria and mortality of different vaccine coverage levels that might be achieved in the MVIP. Feedback from IVIR-AC was sought in March 2018 to ensure that the methods and assumptions of the modeling work proposed for the framework for policy decision are appropriate.

SAGE will be presented with a status update on this work and asked for feedback on the proposed inputs and output measures for modelling.