Malaria vaccine research and development: Malaria Vaccine Advisory Committee (MALVAC) meeting planning

Initiative for Vaccine Research and Global Malaria Programme
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Background

The WHO Global Malaria Programme (GMP) coordinates WHO’s efforts to control and eliminate malaria. Important progress has been realized over the last decade, and the Global Technical Strategy provides a framework for accelerating progress in the reduction of malaria disease and mortality, moving towards elimination and preventing resurgence between 2016 and 2030. Yet, malaria remains responsible for a massive burden of disease and death and, as such, is an important public health priority. The availability of a highly effective malaria vaccine would greatly strengthen the prospects for further, sustained public health gains.

The WHO Initiative for Vaccine Research (IVR) provides guidance in the field of vaccine research and development (R&D) against priority diseases. Public health targets and advice on research avenues are outlined in preferred product characteristics (PPC) and R&D technical roadmap documents. The latest version of the WHO Malaria Vaccine R&D Technical Roadmap was produced in 2013. Since then, the malaria vaccine landscape has evolved in several major ways.

- One product (RTS,S/AS01) has received a favourable scientific opinion from the European Medicines Agency (EMA), having demonstrated moderate levels of protection against uncomplicated and severe malaria in Phase III clinical evaluation. Pilot implementation studies will soon begin in order to further evaluate the effectiveness, safety and feasibility of implementation through routine health systems.

- Other studies will assess the role of the RTS,S/AS01 vaccine when administered before or at the beginning of the malaria season in highly seasonal transmission areas and evaluate the potential of RTS,S/AS01 in South-East Asia. When tested against controlled human malaria infection (CHMI), the administration of a delayed, fractional dose of RTS,S has shown the potential to increase the vaccine’s efficacy. The role of dose- and schedule-associated changes to the vaccination regimen will be further evaluated in CHMI and natural exposure studies.

- A new RTS,S-like particle, R21, has been developed. Product characteristics and early experimental evaluation suggest that there are significant differences from RTS,S, warranting further evaluation.
• New evidence has been generated using live sporozoite immunizations, tested in multiple studies using CHMI or natural exposure.

• The evaluation of other malaria vaccine candidates continues with trials of promising blood-stage and sexual-stage candidate vaccines. Vaccine strategies against *Plasmodium vivax* malaria are being developed and moving into early clinical evaluation.

• Developments in experimental design have seen an increase in the use of CHMI studies and trials involving a second or delayed challenge in order to assess durability of protection. Platforms for CHMI studies have been developed within malaria-endemic countries. A low-dose blood-stage infection model has shown great potential for the measurement of vaccine-induced blood-stage immunity. Progress has been made in the set-up of a human malaria transmission experimental model fit for evaluating the transmission-blocking activity of sexual-stage vaccines.

• Major and rapid changes in malaria epidemiology are being seen at the global level, under constant pressure from malaria control and elimination efforts. Rapid progress is being made in the science of and pathway to malaria elimination.

In this generally evolving context, it is important to reconsider the role of malaria vaccines in the future technical framework for malaria control and elimination.

The Malaria Vaccine Advisory Committee (MALVAC) was established to provide expert input to help WHO articulate its vision and recommendations on malaria vaccine development.

It is timely for MALVAC to reconvene in order to assist WHO in the prioritization of specific malaria vaccine R&D avenues and thus support robust future policy decisions. The state-of-the-art in malaria vaccine development should be reviewed, and priority targets and preferred clinical development pathways should be redefined based on the review of new evidence, consideration of recent activities and changed public health priorities. An updated vision for the role of vaccines in future malaria control and elimination efforts needs to be articulated.

The high-level objectives of the malaria vaccine consultation, MALVAC meeting and the ensuing work are the following:

**A WHO vision for malaria vaccines**

• Discuss current trends in malaria epidemiology;

• Develop an integrated vision of the role of vaccines in the projected future technical framework for malaria control and elimination;

• Map out the status of malaria vaccine development, recent progress and challenges;

• Discuss potential malaria vaccine use in different epidemiological contexts;
• Update the priority targets as expressed in the malaria vaccine R&D technical roadmap;

• Discuss the vaccines’ value propositions: what are the vaccine profiles that can realistically play a role in the foreseeable future (i.e., around 2030)?

• Develop a vision for *P. vivax* vaccines;

• Consider the potential effect of vaccines on the development and spread of drug resistance.

**Research and development avenues**

• Provide guidance on the design of early proof-of-concept studies and optimal use of CHMI models, including transmission models;

• Determine the preferred late-stage evaluation strategies for second-generation malaria vaccine candidates and advise on the safety, efficacy and implementability evidence base required for WHO policy decisions;

• Discuss research standards in light of the status of RTS,S/A01;

• Discuss evaluation strategies for vaccines aimed at interrupting transmission.