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2013 Update to the Malaria Vaccine Technology Roadmap

Introductory text

This text represents the result of a review process facilitated by WHO, and working with the malaria vaccine funders group, to update the vision and strategic goal of the Malaria Vaccine Technology Roadmap. Originally launched at the 2006 WHO Global Vaccine Research Forum, and supported by the malaria vaccine funders group, the roadmap has formed a strategic framework underpinning the activities of the global malaria vaccine R&D community.

Substantial changes in malaria epidemiology are now being observed in many, but not all, settings following reduction in malaria transmission(1) in association with scaling-up of malaria control measures. Reduced transmission is associated with a shift in the peak age of clinical malaria to older children(2) and therefore the median age of hospitalization due to malaria has increased(3, 4) in some settings**.**

In response to the recognition that the epidemiological and malaria control status have changed markedly since 2006, and acknowledging substantial changes in the strategic direction for malaria research, the roadmap has been updated to encompass the current goals of prevention of malaria disease and deaths, accompanied by consideration of the accepted goals of incremental malaria elimination and ultimately global eradication. The expanded vision and strategic goals reflect these ambitious aims of the global malaria community.

The 2015 Landmark goal remains in place, unchanged, as follows “By 2015, develop and license a first generation malaria vaccine that has a protective efficacy of more than 50% against severe disease and death and lasts longer than one year.” Furthermore, the 11 priority areas in research, vaccine development, key capacities, policy and commercialization, all remain in place unchanged.

The priority areas outlined in the Malaria Vaccine Technology Roadmap will be updated only as necessary to reflect the new Vision and Strategic Goals, and taking into account the major progress in many of the areas since 2006.

It is noted that the following goal has been set as an indicator of success for the Global Vaccine Action Plan of the Decade of Vaccines by the 2012 World Health Assembly “Proof of concept for a vaccine that shows greater than or equal to 75% efficacy for HIV/AIDS, tuberculosis, or malaria by 2020”.

Keeping the roadmap up-to-date in future

Further reviews of the vision and strategic goals will occur at least every 5 years in light of the epidemiological and control situation at that time and progress in the development of new tools and technologies. Changes will be made only if necessary.

The malaria vaccine community should work with the malaria control and elimination communities to ensure products under development are suitable for use alongside current WHO recommended malaria prevention, diagnostic and treatment measures.

Vision

Safe and effective vaccines against *Plasmodium falciparum* and *Plasmodium vivax* that prevent transmission, disease and death to enable malaria eradication

Strategic Goals

By 2030, license vaccines targeting *Plasmodium falciparum* and *Plasmodium vivax* and encompassing the following two objectives, for use by the international public health community[1]:

1) Malaria vaccines with a protective efficacy of at least 70-80%[2] against clinical malaria, suitable for administration to appropriate at-risk groups in malaria-endemic areas.[3]
2) Malaria vaccines that reduce transmission[4] of the parasite and thereby substantially reduce the incidence of human malaria infection to achieve elimination in multiple settings. The vaccines should be suitable for administration to people of all ages in mass campaigns[5]

[1] While vaccines that meet or exceed these targets are acknowledged as being of major public health significance, those that do not fully meet these targets may still have substantial value. Any licensed, available malaria vaccine will undergo assessment for evidence-based policy recommendation by WHO.

[2] Relative efficacy estimates may be provided where a vaccine is tested against a licensed, available first generation malaria vaccine. In this case WHO will evaluate whether the relative efficacy estimates can be considered analogous to absolute efficacy of >70-80% (ie analogous to >70-80% efficacy from trials conducted with a traditional control arm)

[3] The efficacy measure will be an absolute reduction in incidence of all episodes of clinical malaria over at least 2 years. Booster doses will be required no more frequently than annually.

[4] The new transmission-related strategic goal does not apply only to sexual stage/mosquito antigen vaccines but to any vaccine capable of interrupting malaria transmission .

[5] For this goal the endpoints will be set through the process for development of preferred product characteristics for malaria vaccines. Although these metrics are centrally important to this goal, there is no consensus available to set the criteria at the time of this update.

Background to WHO malaria vaccine Preferred Product Characteristics

Vaccine R&D should address an unmet public health need. To do this, the unmet need must be identified and defined, and product development plans put in place. The strategic goals above provide guidance on the two highest priorities in terms of public health need for malaria vaccines.

Two sets of WHO preferred product characteristics (PPCs) will be developed in 2013-2014. The WHO PPCs will provide guidance on the characteristics of malaria vaccines that could meet the two strategic goals of the Roadmap, and could be programmatically suitable for use in malaria-endemic settings. Any malaria vaccine which becomes available for use in malaria-endemic countries will undergo evidence-based policy assessment by WHO through the standard policy processes. Those vaccines not meeting the WHO PPCs are not excluded from consideration for policy recommendation and pre-qualification by WHO. However the PPCs provide information on the desired characteristics of vaccines to meet the public health need, and to lower the burden on developing country immunization and malaria control programmes.

Target audience for this update:

- The Vision and Strategic Goals are aimed at senior leadership within international and national donor, financing and public health agencies, as well as governments of malaria-endemic countries.
- The Strategic Goals are also of interest to malaria vaccine developers in academia, government agencies, public-private partnerships and industry.
- The WHO malaria vaccine Preferred Product Characteristics are aimed at a technical audience in research & development in industry, public-private partnerships, academia and government agencies, who have an interest in development of malaria vaccines to meet the public health need in developing malaria-endemic countries.

Malaria Vaccine Technology Roadmap Priority Areas

Re-stated below are the original 11 Priority Areas. Those which are out of date will be reworded through a joint process between WHO and the malaria vaccine funders group.

Research

1. Develop a standard set of immunological assays with standardized procedures and reagents to enable comparisons of the immune responses of vaccines.

2. Standardize clinical trial design and assessment to allow comparison of data and to determine correlates of protection.

3. Use state-of-the-art approaches, including functional genomics, to characterize the biological functions of proteins at the interface of host-parasite interactions and to identify novel potential antigen candidates.

4. Develop web-based information-sharing tools to strengthen connections between the laboratory and the clinic.

Vaccine Development

5. Establish a systematic approach for prioritizing sub-unit vaccine candidates using accepted pre-clinical criteria.

6. Pursue multi-antigen, multi-stage, and attenuated whole-parasite vaccine approaches.

Key Capacities

7. Establish readily accessible formulation and scale-up process development capacity for malaria vaccines.

8. Build and broaden good clinical practice (GCP) clinical trial capacity in Africa and other malaria-endemic regions to accommodate the growing number of trials required for malaria vaccine development.

Policy and Commercialization

9. Establish and maintain country-level dialogues to facilitate decision-making on malaria vaccine policy.

10. Secure sustainable financing for future procurement of vaccines.

11. Develop novel regulatory strategies to expedite approval while ensuring safety.

References

1. WHO. World Malaria Report. 2011. Available from: www.who.int/malaria.
2. Carneiro I, Roca-Feltrer A, Griffin JT, Smith L, Tanner M, Schellenberg JA, et al. Age-patterns of malaria vary with severity, transmission intensity and seasonality in sub-Saharan Africa: a systematic review and pooled analysis. PLoS ONE. 2010;5(2):e8988.
3. O'Meara WP, Bejon P, Mwangi TW, Okiro EA, Peshu N, Snow RW, et al. Effect of a fall in malaria transmission on morbidity and mortality in Kilifi, Kenya. Lancet. 2008 Nov 1;372(9649):1555-62.
4. Ceesay SJ, Casals-Pascual C, Erskine J, Anya SE, Duah NO, Fulford AJ, et al. Changes in malaria indices between 1999 and 2007 in The Gambia: a retrospective analysis. Lancet. 2008 Nov 1;372(9649):1545-54.