Background to development of vaccine roadmaps, to include priority areas for research, product development, capacities, and policy and commercialization

Roadmaps as a Vehicle for Addressing Large-Scale Public Health Challenges:

Lessons from the Malaria Vaccine Technology Roadmap
Presentation outline

• The lead up to the first version of the roadmap
  • A major shift
  • The update
  • Lessons learned?
The lead up to
The Malaria Vaccine Technology Roadmap

• Step 1: The call to action by a normative body:

  • Scientists have been working for decades to develop a preventive malaria vaccine. While they have successfully demonstrated that such a vaccine is possible, many challenges continue to impede progress on the road to an effective malaria vaccine. As a result, WHO through an advisory group called for a collective effort to explore and address the challenges. This effort resulted in the Malaria Vaccine Technology Roadmap process.
The lead up to
The Malaria Vaccine Technology Roadmap

- Step 2: Sponsorship of the process:

  - The Malaria Vaccine Technology Roadmap process was jointly sponsored by the Bill & Melinda Gates Foundation, the PATH Malaria Vaccine Initiative (MVI), and the Wellcome Trust. A Roadmap Working Group, consisting of representatives of the sponsors and IVR, guided the process. Members of the malaria vaccine funders group served as active participants and advisors. Energetics Incorporated assisted with the coordination of the process.
The lead up to
The Malaria Vaccine Technology Roadmap

• Step 3: The drafting process:
  • Through five meetings and over the course of a year and a half, more than 230 experts representing 100 organizations from 35 countries identified the challenges facing malaria vaccine development, established a vision and goal, and developed a shared plan to accelerate malaria vaccine development. A consultation through the internet sought input from an even wider malaria vaccine community.
The lead up to The Malaria Vaccine Technology Roadmap

• Step 4: The synthesis process:
  
  • A set of key experts reviewed the results of the meetings and provided recommendations about which activities could serve as strategic areas of investment to accelerate significantly the development of a malaria vaccine.
  
  • Based on further discussions with the malaria vaccine funders group, these recommendations were collated into the four key priority areas.
  
  • The product was the Malaria Vaccine Technology Roadmap.
The Malaria Vaccine Technology Roadmap

circa 2006

The Malaria Vaccine Technology Roadmap was launched in 2006 at the WHO Global Vaccine Research Forum and established a shared Vision, Strategic Goal (2025), and Landmark (2015) for development of malaria vaccines. The Roadmap also identified 11 Priority Areas in four categories: Research, vaccine development, key capacities, policy, and commercialization.

The Malaria Vaccine Technology Roadmap
Circa 2006

Vision

The malaria vaccine community will develop an effective vaccine that prevents severe disease and death caused by *Plasmodium falciparum* malaria in children under five in sub-Saharan Africa and other highly endemic regions. Efficient global coordination and collaboration will stimulate the malaria vaccine pipeline and accelerate progress towards this achievement.

Priorities circa 2006

- Prevent severe disease and death
- *P. falciparum*
- Children under five
- Sub-saharan Africa and other highly endemic countries
Strategic Goal

- By 2025, develop and license a malaria vaccine that has a protective efficacy of more than 80% against clinical disease and lasts longer than four years.
The Malaria Vaccine Technology Roadmap
Circa 2006

**Landmark**

- 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.

[http://www.malariavaccine.org/files/Malaria_Vaccine_TRM_Final_000.pdf](http://www.malariavaccine.org/files/Malaria_Vaccine_TRM_Final_000.pdf)
The Malaria Vaccine Technology Roadmap

**Circa 2006**

**Priorities** To achieve the vision and goals, the malaria vaccine community identified 11 priority areas that, if pursued, could accelerate the pace of progress. These priorities, composed of both new initiatives and ongoing efforts that require additional resources, represent the top priorities of the community. The priorities fall into four categories:

- Research
  - Vaccine Development
- Key Capacities
- Policy and Commercialization
Presentation outline

• The lead up to the first version of the roadmap
• A major shift
• The update
• Lessons learned?
“Any goal short of eradicating malaria is accepting malaria; it’s making peace with malaria; it’s rich countries saying: ‘We don’t need to eradicate malaria around the world as long as we’ve eliminated malaria in our own countries.’ That's just unacceptable.”

Melinda Gates, 2007
Malaria: The problem and the progress

The available tools:
- Insecticide-treated bed nets
- Indoor residual spraying
- Improved case management
- Rapid diagnosis and treatment

The burden:
- 3.3 billion at risk of malaria
- ~215 million cases/year; 86% in sub-Saharan Africa
- ~655,000 deaths/year; mostly African children < 5 yo

Mortality rates 2000–2010

Adapted from: WHO World Malaria Report 2011
Malaria: The unmet need

Control & Elimination

Preventing disease & death

Presentation outline

• The lead up to the first version of the roadmap
• A major shift
• The update
• Lessons learned?
Rationale to update the Roadmap

• “The need to update the Roadmap Vision and 2025 Strategic Goal in response to a number of changes since 2006, including changes in the strategic role of malaria vaccines and changes in malaria epidemiology and control status.”

• “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 with other tools and technologies. Changes will be made only if necessary. Should projects aimed at either of the 2 strategic vaccine goals reach major milestone performance indicators, such as proof of concept of efficacy, this will trigger a WHO-led consultative process to develop new Landmark goals for late stage development of these vaccines.”

2 http://www.who.int/vaccine_research/diseases/malaria/Roadmap_update_for_second_public_consultation.pdf
Updating the Malaria Vaccine Technology Roadmap: Expanded Vision

**Expanded vision**
- Includes *P. vivax*
- Not restricted to children under five
- Includes all malaria-endemic regions
- Includes vaccines that interrupt transmission
- In conjunction with other malaria interventions, contemplates elimination

**Vision**
Safe and effective vaccines against *Plasmodium falciparum* and *Plasmodium vivax* that prevent disease and death and prevent transmission to enable malaria eradication.
By 2030, license vaccines targeting *Plasmodium falciparum* and *Plasmodium vivax* that encompass the following two objectives, for use by the international public health community:

**Revised goal for disease prevention**

- Protective efficacy of >75% (reduced from 80%)
- Duration of at least 2 years (reduced from 4 years)
- Children and adults (expanded from <5 yo)
- Includes all malaria-endemic areas (expanded from SSA)
By 2030, license vaccines targeting *Plasmodium falciparum* and *Plasmodium vivax* that encompass the following two objectives, for use by the international public health community:

**New goal for reducing transmission**

- Reduce incidence of malaria infections
- Achieve elimination in multiple settings
- All ages
- Mass campaigns

Development of malaria vaccines that reduce transmission of the parasite and thereby substantially reduce the incidence of human malaria infection. This will enable elimination in multiple settings. Vaccines to reduce transmission should be suitable for administration in mass campaigns.
Updated priority areas

Research

1. Develop 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.
3. Use state-of-the-art approaches to identify novel potential candidate vaccine targets.
4. Confirm candidate vaccine targets and mechanisms of protection, using controlled human malaria infection models as appropriate.
5. Ensure that results from all funded malaria vaccine clinical trials are publicly available within 12 months of the last visit of the last subject for the primary endpoint, and encourage public sharing of all funded nonhuman primate studies within 12 months of completion of the primary immunological endpoint.

Development

6. Establish a systematic approach for prioritizing vaccine candidates (including multi-antigen, multi-stage, and attenuated whole-parasite vaccine approaches). Candidates will be prioritized, taking into account PPCs, back-validation from clinical to nonclinical models, immune correlates, and/or head-to-head comparisons.
7. Develop immunological correlates of vaccine-induced protection and surrogate efficacy endpoints to advance vaccine development and licensure timelines.

Key Capacities

8. Access to low-cost vaccine manufacturing under current Good Manufacturing Practices (cGMPs) for late-stage development and commercial production.
9. Promote sufficient and sustainable Good Clinical Practice (GCP) clinical trial, regulatory, and ethics capacity in malaria-endemic regions to accommodate a variety of clinical trials (including clinical trials with human-to-mosquito transmission endpoints) required for malaria vaccine development.
10. Develop approaches to address the need for appropriate, post-approval pharmacovigilance and effectiveness testing capacity in malaria-endemic regions in order to ensure timely malaria vaccine introduction and implementation.

Policy and Commercialization

11. Ensure data are available to support timely, evidence-based decision-making by national immunization and malaria control programs.
12. Develop and encourage responsible stewardship and support for malaria vaccine development and implementation through appropriate project management and investment strategies (e.g., through developing a business case).
13. Develop novel regulatory strategies to expedite approval while ensuring quality and safety.

http://www.who.int/immunization/topics/malaria/vaccine_roadmap/en/
Presentation outline

• The lead up to the first version of the roadmap
• A major shift
• The update
• Lessons learned?
Lessons learned?

• Normative bodies (Malaria TRM = WHO) can provide an important forum for input, synthesis, launching and sustaining the roadmap

• Plan to refresh the roadmap based on new data and/ change in strategy (and do so in a timely manner), but change only what is necessary

• Map target audiences and include elements tailored to each