

Briefing document: The status of the global malaria vaccine pipeline

This document was developed by the PATH Malaria Vaccine Initiative in consultation with the World Health Organization, United Nations Children's Fund, GAVI Alliance, Global Fund to Fight AIDS, Tuberculosis and Malaria, Bill & Melinda Gates Foundation, and Roll Back Malaria Partnership.

- More than 40 malaria vaccine candidates are moving through the development process globally, with 16 of these candidates in clinical trials.
- GlaxoSmithKline Biologicals' RTS,S—the malaria vaccine candidate closest to licensure—is targeted for submission to regulatory authorities by 2011. Second-generation vaccine candidates are unlikely to be available until after 2015.
- After decades of effort, RTS,S, the most advanced vaccine candidate, has demonstrated only partial efficacy—a reflection of the scientific challenges of developing vaccines against the parasitic disease. However, studies show that even a partially efficacious malaria vaccine could be a valuable, public-health tool.
- A major challenge to the development of malaria vaccines is the difficulty of moving products from the research stage into critical, clinical-trial and development pathways.
- Market incentives that serve to “pull” development of malaria vaccines are critical complements to public-sector “push” funding.

The field of malaria vaccines is dynamic—with more than 40 candidates under development, including 16 in clinical trials. (See Figure 1.)

- GlaxoSmithKline Biologicals' RTS,S candidate vaccine is scheduled to enter Phase 3 trials in 2008. Published data¹ suggest that RTS,S could have 35% efficacy against clinical disease in children for at least 18 months and 49 percent efficacy against severe malaria for the same time frame. More recent data, following the same subjects in Mozambique and presented at the November 2007 conference of the American Society of Tropical Medicine and Hygiene, suggest that efficacy could be maintained for at least four years.
- While intensive work is underway to develop a more efficacious, second-generation vaccine, such a vaccine is not expected until sometime after 2015.

¹ Alonso PL, Sacarlal J, Aponte JJ, et al. Duration of protection with RTS,S/AS02A malaria vaccine in prevention of *Plasmodium falciparum* disease in Mozambican children: single-blind extended follow-up of a randomised controlled trial. *The Lancet*. 2005; 366:2012–2018.

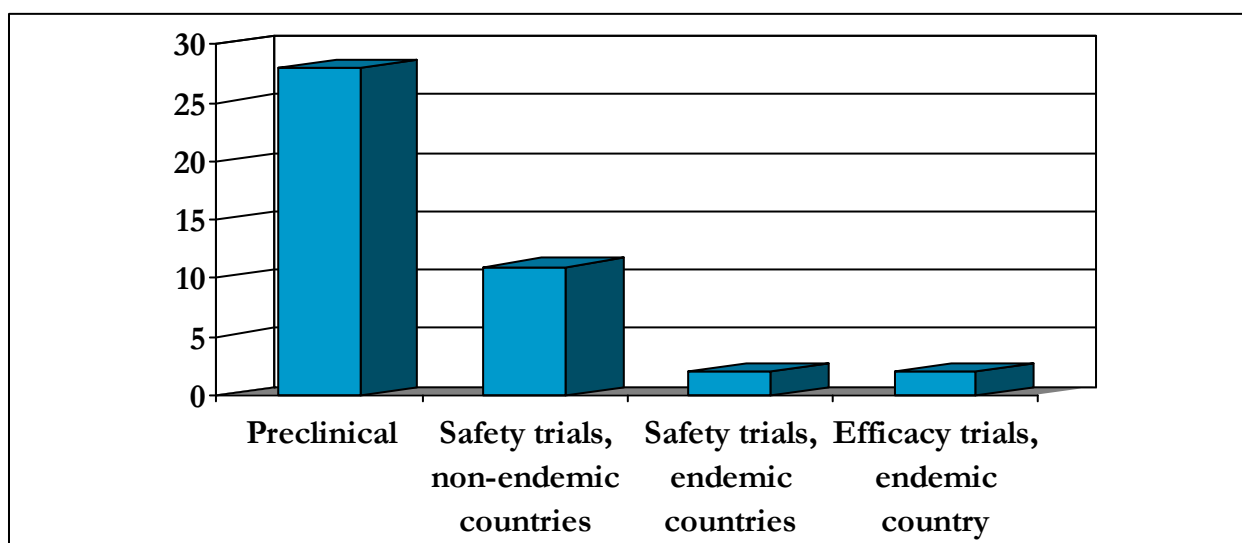


Figure 1. Status of malaria vaccine development, October, 2007²

Although progress on developing vaccines against the malaria parasite has accelerated in recent years, significant scientific challenges remain.

- No vaccine has ever been developed for human use against parasites—pathogens with much greater complexity than viruses and bacteria.
- There are no known correlates of immunity for malaria vaccines; therefore, vaccine candidates can only be shown to work (or not work) by going through clinical trials. The need for an empirical process makes malaria vaccine development expensive and time consuming.
- Much remains to be understood about how to optimally stimulate the human immune system with malaria vaccines.

A major challenge to the development of malaria vaccines is the difficulty of attracting partners with expertise in product development. History has shown that such partners play a critical role in moving vaccine candidates from the research stage into clinical-trial and development pathways.

- Traditionally, work on malaria vaccines has resided in academic and military-research institutions and not within pharmaceutical companies. This is due to:
 - The limited financial return anticipated from a market that is primarily in Africa.
 - The major technological and scientific challenges involved in developing malaria vaccines.

² Moran M, Guzman J, Ropars A, et al. *The malaria product pipeline: planning for the future*. London, United Kingdom: The George Institute for International Health; 2007. Available at: http://www.thegeorgeinstitute.org/iih/research/health-policy/publications/publications_home.cfm. (Modified by MVI to reflect updated portfolio)

- The novel characteristics of malaria vaccines and the complicated regulatory and uptake pathways, which increase the risk that the products may never provide commercial returns.

Push funding from the public sector for research and development is critical and should be increased. In addition, market incentives or “pull” mechanisms are needed to drive development of highly efficacious vaccines for Africa.

- Anticipation of future purchasing from the GAVI Alliance, the Global Fund to Fight AIDS, Tuberculosis and Malaria and from similar major financing initiatives increase the credibility of a future market for malaria vaccines.
- Malaria vaccines are under consideration for an Advance Market Commitment, which, if implemented, could encourage industry commitment while providing predictable price indications to facilitate country planning.