Briefing Document: National decision-making framework for malaria vaccines

The return on investment for malaria vaccines:

preliminary estimates of public health impact in Africa

This is one of seven briefing papers produced for a country consultation to develop a decision-making framework for the use of future malaria vaccines. It was developed under the guidance of the consultation steering committee: Alan Brooks, PATH Malaria Vaccine Initiative (MVI); Dr. Carter Diggs, US Agency for International Development; Sarah Ewart, MVI; Dr. Dorothée Kinde-Gazard, Minister of Health, Benin; Annique Lennon, MVI; Dr. Rose Macauley, World Health Organization (WHO) Regional Office for Africa (AFRO); Dr. John Marshall, Consultant to PATH; Dr. Zarifah Reed, WHO; Dr. Magda Robalo, WHO AFRO; and Dr. Rick Steketee, PATH Malaria Control and Evaluation Partnership in Africa..

Contact the PATH Malaria Vaccine Initiative (info@malariavaccine.org) or Dr. Magda Robalo (robalom@whoafr.org) for more information.

This document was made possible in part by a grant from the Bill & Melinda Gates Foundation to the PATH Malaria Vaccine Initiative and through support provided by the Infectious Disease and Environmental Health Division, Bureau for Global Health, U.S. Agency for International Development, under the terms of Cooperative Agreement No. GHS-A-00-04-00016-00. The opinions expressed herein are those of the author(s) and do not necessarily reflect the views of the U.S. Agency for International Development.

I. Introduction

A malaria vaccine—if adequately funded by donors and supported by the governments of countries where malaria is endemic—has the potential to save millions of lives and greatly reduce the burden of malaria. Currently, despite the fact that the international community has long struggled to control the disease, the World Health Organization (WHO) estimates malaria kills more than one million people each year (mostly young children in sub-Saharan Africa) and contributes to the deaths of many others.

In 2005, the PATH Malaria Vaccine Initiative (MVI) worked with The Boston Consulting Group (BCG) and the Swiss Tropical Institute (STI) to conduct an impact analysis that quantified potential lives saved and the cost-effectiveness of hypothetical malaria vaccines under certain scenarios and assumptions. This paper details preliminary findings from the public health, or social impact, analysis and the implications for decision-makers, quantifying the potential impact of a malaria vaccine on malaria-related mortality and morbidity. It also assesses the potential impact of a vaccine in attaining established development goals.

II. Study overview

The analysis of public health impact was completed in three phases. In the first phase, the project team identified a set of key social return metrics and drivers on which to model the impact of a malaria vaccine. These metrics fell into three categories: health status metrics, socioeconomic status metrics, and financial status metrics.[1] The proposed metrics were evaluated in terms of the availability and relative robustness of data for use in an analysis.

In the second phase, the team integrated relevant findings from two other unpublished models—a malaria vaccine demand model from MVI and BCG and a mathematical malaria vaccine epidemiology model from STI—to create a foundation for calculating the impact of a malaria vaccine on the set of social metrics. The malaria vaccine demand model simulates potential demand throughout the world for various profiles of malaria vaccines, based on extensive primary and secondary research with leaders from countries where malaria is endemic and with donor and technical organizations. The mathematical malaria vaccine model simulates the transmission dynamics and epidemiology of a *Plasmodium falciparum* vaccine, estimating both the short- and long-term effects of malaria vaccines on the burden of disease.

The third phase of the analysis, conducted by MVI and BCG, included estimating the public health impact of a vaccine, according to the established social metrics, and its key sensitivities. These estimates may be considered conservative because they assume that the Millennium Development Goals have been achieved, substantially decreasing the malaria

[1] **Health status metrics** measure factors such as impact on infections or mortality. They are often described in terms such as “disability-adjusted life-years” and “infections averted.” Established development goals, such as the Abuja Targets and the Millennium Development Goals, also fit into this category. **Socioeconomic status metrics** include such measures as cost-effectiveness, and **financial status metrics** measure the impact on the health system, such as the cost of purchasing the vaccine.

burden. Representative output from this preliminary analysis is included below.

III. Key findings

A partial-efficacy vaccine can have a significant impact.

One of the key findings of our study is that a vaccine with partial efficacy (a blood-stage vaccine with efficacy of 50 percent against severe disease and a duration of efficacy of at least one year) can have a significant impact on the malaria burden. Based on estimated current levels of donor funding,[2] this vaccine could prevent an estimated 153 deaths per 100,000 infants vaccinated in Africa and save 4,910 disability-adjusted life-years (DALYs) per 100,000 in the same target group.[3] This analysis assumes that the intervention is delivered through the Expanded Programme on Immunization (EPI), an established delivery mechanism, and is thus relatively cost-effective, at US$4,711 per death averted and $144 per DALY saved. This compares well to published standards, such as WHO's guideline that interventions with a cost of $150 or less per year of life saved should be considered "attractive."[4] However, this number is quite low compared with the vaccine's potential, which can only be achieved with higher levels of implementation and infrastructure support than are found today.

Maximizing the impact of a partial-efficacy vaccine depends on implementation.

The potential social impact of a malaria vaccine is great, but achieving that impact requires effort and support. Current constraints, particularly those related to infrastructure, implementation, and funding, need to be eased for a vaccine to have the maximum impact. With improved support—such as a reduction in the delay between licensure of the vaccine and the earliest adoption by countries, wider adoption by countries, and improved EPI coverage rates—the impact of the vaccine increases remarkably. If the partially efficacious vaccine described above were implemented under such conditions,[5] the number of deaths averted could increase from 153 to 491 per 100,000 infants vaccinated in Africa, and the number of DALYs averted could increase from 4,910 to 15,547 per 100,000.

---

[2]This scenario assumes that Expanded Programme on Immunization coverage remains at current levels, that there is a five-year delay between vaccine licensure and introduction, and that US$1.2 billion in donor funds is available for the first 15 years of vaccine purchase and delivery—a figure extrapolated from and complementing current levels of donor funding for malaria interventions and immunization.

[3]Deaths averted and disability-adjusted life-years saved per year are averages of The Boston Consulting Group model's impact projections for the first 15 years of a vaccine launched in 2010. The disease burden projections used include impact on both direct and indirect malaria deaths and assume that the Millennium Development Goal of halving the number of malaria deaths by 2015 has been achieved through other prevention and control interventions.

[4]*Investing in Health Research and Development: Report of the Ad Hoc Committee on Health Research Relating to Future Intervention Options*. TDR/Gen/96.1. Geneva: World Health Organization; 1996.

[5]This scenario assumes that US$7.4 billion in cumulative donor funds would be available for the first 15 years of vaccine purchase and delivery, that there would be a three-year delay between licensure and introduction of the vaccine, and that Expanded Programme on Immunization coverage in Africa has expanded to reach 90 percent of the target age group.

A high-efficacy vaccine could have a tremendous impact, magnified further as coverage rates improve.

With minimal delay between licensure and adoption of the vaccine, widespread acceptance by countries, and improved EPI coverage rates, a highly efficacious vaccine (efficacy of 90 percent against clinical and severe disease, with minimal efficacy decay)[6] could be a powerful tool for reducing the malaria burden. Such a vaccine could prevent 5,482 deaths per 100, 000 infants vaccinated in Africa and save 193,926 DALYs (Table 1).[7] In a single peak year, this would mean a 66 percent reduction in the number of malaria deaths worldwide.

A highly efficacious, long-duration vaccine could have an estimated average cost-effectiveness in Africa of approximately $14 per DALY saved and $508 per death averted. Under WHO guidelines,[8] interventions that cost less than $25 to $30 per year of life saved should be considered "highly attractive."

In the absence of real improvements to infrastructure and implementation, even a highly efficacious vaccine would have considerably less impact. The number of child deaths averted in Africa each year would decrease from an estimated 5,482 to 1,432 per 100,000. Likewise, the number of DALYs saved would decrease from 193,926 to 50,323 per 100,000.

Table 1. The predicted impact of a malaria vaccine among infants vaccinated in Africa.

Level of implementation	No. of deaths averted per year[a]	Cost per death averted, US$	No. of DALYs saved per year[a]	Cost per DALY saved, US$
50% Efficacy				
Current[b]	153	4,711	4,910	144
Enhanced[c]	491	4,900	15,547	151
90% Efficacy				
Current[b]	1,432	432	50,323	12
Enhanced[c]	5,482	508	193,926	14

Note. DALY, disability-adjusted life-year; EPI, Expanded Programme on Immunization.
[a]Per 100,000 infants vaccinated in Africa.
[b]Assumes current levels of EPI coverage and funding comparable to current levels of donor funding for malaria interventions and immunization.
[c]Assumes that maximum EPI coverage levels have been reached and sufficient donor funding is available to meet all demand.

[6]This scenario assumes that such a vaccine would target *Plasmodium falciparum* and would be implemented in the Expanded Programme on Immunization for the public market with a three-dose schedule at US$7 per dose. We assume a post-licensure lag before implementation of three years in Africa and one year everywhere else. Projected coverage and uptake would mirror that of hepatitis B vaccine.

[7]Includes direct deaths (deaths directly attributable to malaria) averted and disability-adjusted life-years saved from 2010 through 2040 from a vaccine administered from 2010 through 2025.

[8]*Investing in Health Research and Development: Report of the Ad Hoc Committee on Health Research Relating to Future Intervention Options*. TDR/Gen/96.1. Geneva: World Health Organization; 1996.

IV. Implications for decision-making

These findings are preliminary, and additional work will be needed to validate this analysis. This will include further consideration of the estimates of vaccine effectiveness and updated estimates of malaria mortality based on implementation of malaria control interventions. Summary conclusions at this time include the following.

Both partial- and high-efficacy vaccines are likely to have roles in many countries.

The impact of partial- and high-efficacy vaccines will vary from country to country, but even a partial-efficacy vaccine will be an essential complement to other existing and future interventions in many malaria control and immunization programs. Both types of vaccine are cost-effective and significantly reduce the burden of one of the most serious public health problems for many African countries.

In the event that a partial-efficacy vaccine reaches the market, it is important to note that at-risk populations will need to be informed about the advantages of different ways to prevent malaria and that other methods (e.g., bednets, long-sleeved clothing) will remain particularly important, even for individuals who have been immunized.

A malaria vaccine's impact will depend on its implementation.

In addition to being safe and reliable, vaccines have historically offered a highly effective and cost-effective means of preventing disease and death. In most countries, existing immunization services targeting infants provide a highly effective, proven, and credible structure for reaching the population segments most in need of a malaria vaccine. Vaccines hold particular promise for malaria, thanks to recent technological advances and evidence demonstrating that immunizing children against the malaria parasite is feasible.[9]

However, the impact of the vaccine depends to a large extent on how successfully it is delivered to the people who need it. Improving delivery systems and infrastructure will allow a malaria vaccine, as well as other immunizations, to fulfill its potential for saving lives.

Early action is important.

National policymakers can take action now that will pave the way for successful malaria vaccine introduction in the future. Although immunization coverage rates have improved dramatically over the past few decades, there is still room for progress, and many rural populations are beyond the reach of current programs. Improving the reach and capacity of immunization programs will increase the future impact of malaria vaccines, as well as other immunizations. Donors and partner organizations will have a critical role in supporting countries as they determine which interventions to embrace and how to sustain them.

[9]Alonso P, Sacarlal J, Aponte JJ, et al. Efficacy of the RTS,S/AS02A vaccine against *Plasmodium falciparum* infection and disease in young African children: randomised controlled trial. *Lancet*. 2004;364:1411–1420.