MALARIA VACCINE INITIATIVE

ISSUE BRIEF

MVI's strategy for developing next-generation malaria vaccines

In late 2009, the PATH Malaria Vaccine Initiative (MVI) unveiled a new strategy that sets the stage for an aggressive push targeting the long-term goal of eliminating and eradicating malaria. The MVI strategy represents a multi-pronged approach to developing the next generation of malaria vaccines. The international community in 2006 set a long-term goal of having a malaria vaccine by 2025 that is at least 80 percent effective against clinical disease and lasts longer than four years.

In addition to this long-term goal, international experts in malaria vaccine development put forth an intermediate goal in the "Malaria Vaccine Technology Roadmap," published by the World Health Organization in 2006. This intermediate goal is the development of a "first generation" malaria vaccine that is at least 50 percent effective against severe disease and death and lasts more than one year. This intermediate goal could soon be satisfied by GlaxoSmithKline Biologicals' (GSK Bio) malaria vaccine candidate, RTS,S. Currently in Phase 3 clinical testing, this vaccine was found during Phase 2 testing to be 53 percent effective against clinical disease in young children. Currently being developed through a partnership among MVI, GSK Bio, and study centers located across Africa, RTS,S could soon be a landmark achievement for the malaria community. However, even given the success of RTS,S, the road to elimination and eradication of malaria requires filling the vaccine pipeline with promising new candidates that both build on the success of RTS,S and take different paths toward immunization.

Cultivating new approaches

MVI has numerous feasibility studies underway to develop the vaccine candidates of the future, with most focused on developing specific vaccine components. Only the most promising of these will advance to clinical development.

Like RTS,S, many of these studies are focused on the pre-erythrocytic approach, which aims to trigger the immune system to defend against the parasite as soon as it enters a person's bloodstream or infects liver cells. This prevents the parasite from maturing and multiplying in the liver, reentering the bloodstream, and infecting red blood cells.

Another approach targets the malaria parasite when it is most destructive: at the blood stage, when the parasite replicates rapidly in red blood cells. Blood-stage vaccines are not expected to block all infection. Instead, they aim to decrease the number of parasites in the blood, reducing

the severity of malaria. MVI will continue to make limited investments in this area, but sees the fruit of this effort as yielding additional components that could be combined with a pre-erythrocytic vaccine, for example, to further boost its effectiveness.

Targeting the mosquito and the most widespread form of malaria

MVI is also looking for vaccine candidates that block the transmission of malaria from mosquitoes to humans. Transmission-blocking vaccines attempt to interrupt the life cycle of the parasite by inducing antibodies that prevent the parasite from maturing in the mosquito after it bites a vaccinated person. Transmission-blocking vaccines would not prevent people from getting malaria, but they could significantly limit the spread of infection.

While malaria caused by *Plasmodium falciparum*—the deadliest parasite to humans—is the principal target of MVI's efforts, approaches targeting the more widespread *P. vivax* malaria parasite are also a part of the strategy. Vaccines targeting both parasites—whether separately or in combination—are needed if the eradication goal is to be reached.

Developing tools to measure success

As the number of potential malaria vaccine candidates increases, scientists will need new and better technologies to assess their potential efficacy and decide which should go forward. MVI is supporting the refinement and development of both laboratory tools and methodologies for evaluating vaccine candidates in humans. For example, MVI is supporting development of the Human Challenge Center at the Seattle Biomedical Research Institute, which offers early-stage testing in humans of the safety and efficacy of malaria vaccine candidates.

Continuing need for collaboration

Over the past ten years, MVI has worked with a wide range of partners and the numbers continue to grow. The program seeks collaborators both inside and outside the malaria research community, investing aggressively in approaches and technologies that are at earlier stages of development. This approach involves many smaller investments in projects that are evaluated as quickly as possible for their feasibility, another way that MVI seeks to maximize efficiency and use of scarce resources.

This partnership-based approach has yielded positive results, as seen in the advancement of RTS,S to a Phase 3 trial, the upgrading of clinical trial and research capacity in locations across Africa, and the decisions by several African countries to put in place mechanisms to facilitate informed decision-making on malaria vaccine use, once one becomes available.

MVI's scientific work is aimed at filling a kind of "toolbox" containing the components for highly effective vaccines against malaria. To succeed, MVI needs internal flexibility to reallocate resources to the most promising projects, and robust and sustained funding that supports this approach to development of next-generation malaria vaccines.

THE PATH MALARIA VACCINE INITIATIVE (MVI) is a global program established at PATH through an initial grant from the Bill & Melinda Gates Foundation. MVI's mission is to accelerate the development of malaria vaccines and ensure their availability and accessibility in the developing world. MVI's vision is a world free from malaria. For more information, visit **www.malariavaccine.org**.

PATH is an international nonprofit organization that creates sustainable, culturally relevant solutions, enabling communities worldwide to break longstanding cycles of poor health. By collaborating with diverse public- and private-sector partners, PATH helps provide appropriate health technologies and vital strategies that change the way people think and act. PATH's work improves global health and well-being. For more information, visit **www.path.org**.