

PATH's Malaria Vaccine Initiative

SITUATION

Malaria is caused by a parasitic infection transmitted by mosquitoes. Approximately half of the world's population is at risk of malaria, with more than 200 million cases occurring every year. Of the more than 400,000 deaths from malaria in 2016, nearly 90 percent occurred in Africa, and the vast majority were among children younger than five years of age. Most deaths were caused by *Plasmodium falciparum*, the malaria parasite deadliest to humans. The disease can damage the nervous system, kidneys, and liver, and severe cases can quickly lead to death. Malaria vaccines could make an important contribution to reducing the burden of disease and death among young children as well as to regional elimination efforts and eventual eradication of the malaria parasite.

While consistent use of effective insecticides, insecticide treated nets, prompt diagnosis, and antimalarial drugs saves lives, further reducing the impact of malaria will require additional interventions, such as vaccines. Immunization is one of the most effective and cost-effective health interventions available, and vaccines against common childhood diseases such as polio and measles already save the lives of millions of children every year. A range of new tools—including vaccines—will be needed to control, eliminate, and eventually eradicate malaria.

OUR HISTORY

PATH's Malaria Vaccine Initiative (MVI) was founded in 1999 on the premise that although promising malaria vaccine approaches existed, they required additional support to get out of the laboratory and on a path toward clinical testing. Scientists had long demonstrated that immunization against malaria was biologically feasible—which is significant given there are no available vaccines targeting human parasitic infections. However, efforts were hampered by financial hurdles and gaps in product development expertise needed to effectively manage a portfolio of diverse vaccine approaches.

When MVI was created, several academic and governmental organizations and pharmaceutical companies had already been working on approaches to develop vaccines with the potential to have an impact on malaria. We catalyzed the acceleration of those efforts by providing funds as well as logistical and technical support to advance promising projects into clinical development.

PROGRESS

Today, we maintain a diverse portfolio that encompasses early-stage identification of vaccine targets, preclinical, clinical (translational research and translational development), and advanced clinical projects. At any one time, we work with more than 50 partners and has more than 100 project agreements in place. In 2017, half a dozen vaccine concepts were in preclinical or clinical development or undergoing regulatory review.



Samuel Oduor, Chief Community Relations Officer for the Kombewa Clinical Research Center, Kenya, and son. Photo credit: PATH/Jordan Gantz

Our longest-standing collaboration has been with GSK, developer and manufacturer of RTS,S/AS01 (RTS,S), the first, and to date, only vaccine to demonstrate a protective effect against malaria in young children in a Phase 3 trial. Together with a network of African research centers, GSK and MVI advanced RTS,S through Phase 2 and Phase 3

trials, involving more than 19,000 trial participants, 15,459 of whom were enrolled in the pivotal Phase 3 efficacy and safety trial (2009–2014). The Phase 3 trial showed that, over four years of follow-up, RTS,S prevented approximately 4 in 10 (39%) cases of malaria and 3 in 10 (29%) cases of severe malaria among young children who received four doses of the vaccine. In January 2016, the World Health Organization (WHO) recommended RTS,S for pilot implementation in settings of moderate-to-high malaria parasite transmission in Africa. The WHO's recommendation followed a positive scientific opinion for RTS,S from the European Medicines Agency (EMA). In late 2018, parts of three countries—Ghana, Kenya, and Malawi—are expected to begin providing the vaccine to young children through routine health services, as part of the WHO-coordinated Malaria Vaccine Implementation Programme.

HOW WE WORK

MVI's vaccine development efforts are broadly consistent with the vision of the 2013 *Malaria Vaccine Technology Roadmap*, which calls for the development of vaccines that prevent disease and death, and those able to prevent parasite transmission to enable malaria eradication. Thus, in addition to approaches that build on RTS,S by seeking to prevent the parasite from infecting humans, our range of vaccine approaches includes those that seek to block malaria parasite transmission from humans to mosquitoes. We also support the assessment of monoclonal antibodies (mAbs), in human volunteers, to inform the development of vaccines designed to interrupt parasite transmission between mosquitoes and humans.

Most new projects come to MVI as preclinical feasibility studies, with only a limited number advancing to the much more expensive stage of clinical development. With dozens of projects underway at any one time, our goal is to advance only the most promising vaccine candidates, while continuing to build on the knowledge gained from each project and thereby maximize the potential for success.

In addition to our direct support for vaccine development, we work in other areas. A key priority is to ensure the development of evaluation technologies to assess the potential efficacy of vaccine components. We also work to increase the flow of resources to the field and define acceptable vaccine product characteristics, catalyze the availability of vaccines once licensed, and identify the information decision-makers need prior to introducing a vaccine. To accomplish all of this, we work closely with many partners, including universities, corporations, intergovernmental organizations, and US government agencies. These efforts are now further enabled by the establishment of PATH's Center for Vaccine Innovation and Access, of which MVI is a part. CVIA brings together PATH's expertise across every stage of vaccine research, development, and introduction to make lifesaving vaccines widely available to women, children, and communities across the world.

THE NEED FOR INVESTMENT

The future of malaria vaccine development remains promising. However, continued progress requires continued investment, if the international community is to succeed in eradicating the parasite responsible for causing malaria. The required funding for malaria programs and malaria R&D is increasingly at risk, as government donors, in particular, wrestle with budgetary and political pressures, exacerbated by a diverse set of global health and humanitarian emergencies. More than ever, others are needed at the table, so that we can stay the course until eradication is achieved.

PATH is the leader in global health innovation. An international nonprofit organization, we save lives and improve health, especially among women and children. We accelerate innovation across five platforms—vaccines, drugs, diagnostics, devices, and system and service innovations—that harness our entrepreneurial insight, scientific and public health expertise, and passion for health equity. By mobilizing partners around the world, we take innovation to scale, working alongside countries primarily in Africa and Asia to tackle their greatest health needs. Together, we deliver measurable results that disrupt the cycle of poor health. Learn more at www.path.org.

PATH'S MALARIA VACCINE INITIATIVE (MVI) accelerates malaria vaccine development and catalyzes timely access in endemic countries, toward a world free from malaria. Standing at the intersection of malaria and immunization, MVI is part of PATH's Center for Malaria Control and Elimination and PATH's Center for Vaccine Innovation and Access, which brings together PATH's expertise across every stage of vaccine research, development, and introduction to make lifesaving vaccines widely available to women, children, and communities across the world. Learn more at www.malariavaccine.org and <http://sites.path.org/cvia>.