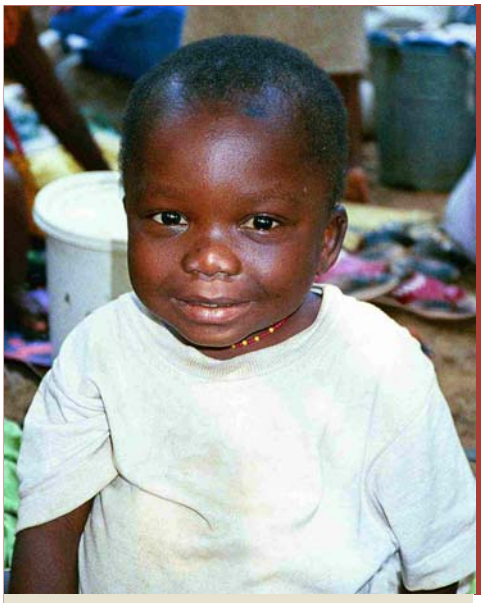

Annual Report to the US Agency for International Development

October 1, 2006 – September 30, 2007

malaria vaccine initiative

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PATH
A catalyst for global health

Executive Summary

The PATH Malaria Vaccine Initiative (MVI) carried out the following activities from October 1, 2006, through September 30, 2007. The cooperative agreement (CA) between PATH and the US Agency for International Development (USAID) was signed on October 8, 2004. Subsequent conversations led to a defined scope of work and budget submitted November 23, 2004, and approved by USAID on December 3, 2004. For the USAID fiscal year of 2006, a scope of work was submitted on October 21, 2005, and approved on January 6, 2006. For the subsequent USAID fiscal year of 2007, a scope of work was submitted on July 6, 2007, and approved on July 16, 2007.

John McNeil, MVI's CA principal, has had preliminary meetings with USAID (Dr. Carter Diggs) to begin a bilateral strategic planning process for the following year's activities.

Scientific and Technical Activities

MVDB MSP1-C (3D7 + FVO) Recombinant Protein Vaccine

The Malaria Vaccine Development Branch (MVDB) at the National Institute of Allergy and Infectious Diseases/National Institutes of Health (NIAID/NIH) produced two alleles (3D7 and FVO) of merozoite surface protein 1 (MSP1) that were co-formulated with alum or alum+CpG (Coley 7909). The formulations were evaluated in two dose groups (40 µg and 80 µg). The trial was conducted through an MVDB contract with the Johns Hopkins University (the trial site is at George Washington University in Washington, DC) and was designed to characterize the immune responses generated by the different doses and formulations. The trial was completed in the spring of 2007 and demonstrated that the vaccine formulations were safe and induced high titers of binding antibodies to MSP1-C1. The addition of CpG increased the magnitude of the induced immune response as measured by binding. MVI will not support further development of MSP1-C1 alone, however, on the basis of a weak functional antibody (growth inhibition assay) response and in keeping with MVI's policy of not developing blood-stage candidates as stand-alone vaccines unless they demonstrate very potent functional responses. MVDB has decided independently to cease support also for MSP1-C1 as a stand-alone candidate vaccine.

ELISA Service Center

In 2007, the ELISA Service Center analyzed 600 sera samples and developed a new circumsporozoite protein (CSP) assay under the Commercial Test Agreement between the Walter Reed Army Institute of Research (WRAIR) and MVI. Furthermore, the Principal Investigator of the ELISA Service Center participated in a workshop on blood-stage assays in February 2007. The high-quality work of this lab was presented and attracted the interest of another funder, the European Malaria Vaccine Initiative (EMVI). Planning is now underway, with EMVI's support, to expand the capabilities of the ELISA Service Center to include assay development, investigator training, and technology transfer in future years. The hope is to expand to an ELISA Global Reference Center operating out of WRAIR and the Kenya Medical Research Institute (KEMRI).

Leads Identification System

MVI set out to establish a means to identify antigens that, while still in preclinical testing, show promise as vaccines in their own right or as enhancers for RTS,S, the most clinically advanced vaccine candidate. During 2007, MVI entered into one-year agreements with two online information delivery services, ABIS Group and BioCentury Publications, and with two interactive online database services, Nerac, Inc. and Knowledge Express. While ABIS Group and BioCentury Publications have proven themselves useful to the Business Development team, providing information from reliable industry, government, and news sources in the most user-friendly manner, the Nerac and Knowledge Express databases have not. Consequently, MVI will only renew its agreements with ABIS and BioCentury.

In the future, MVI plans to selectively contract with other information services in order to augment its leads identification system, keeping those that best meet the organization's needs. These services will be chosen based on staff members' personal experience, input from industry contacts, and referrals from colleagues. First among these will be Life Science Analytics, Inc.'s MedTRACK Biomedical Corporate Intelligence Database and the Thomson Corporation's Investigational Drugs database (IDdb), both potential replacements for the Nerac and Knowledge Express services.

New Opportunity Assessment Process and Implementation

MVI has successfully implemented the planned New Opportunity Assessment Process, as illustrated in Figure 1 below. Thus far, 15 new opportunities have been assessed and Business Development Teams have been established to conduct in-depth due diligence for 6 of these. Those that receive a "go" recommendation will be presented to senior management at MVI and the USAID Malaria Vaccine Development Program (MVDP) with the intent of bringing them into the MVI and/or USAID MVDP vaccine portfolios.

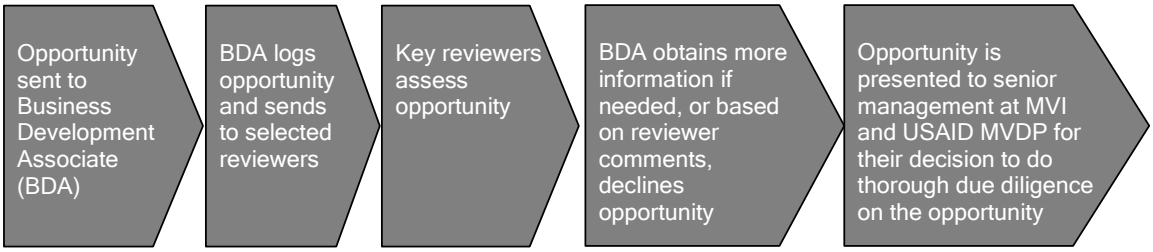

Figure 1. Schematic representation of the New Opportunity Assessment Process.

MVI will be evaluating the effectiveness of the process and associated Leads Identification System on a quarterly basis, following the first six months of operation.

Malaria Vaccine Decision-Making Framework

The Malaria Vaccine Decision-Making Framework (DMF) project initiated by MVI's Policy and Access unit in 2006 intends to encourage decision-makers from malaria-endemic countries and their partners to start early preparations for a decision on the use of a malaria vaccine when it becomes available.

The international health community and malaria-endemic countries are working hard to increase the coverage of current malaria control interventions in an effort to significantly reduce the toll of malaria. Introducing a new intervention, such as a malaria vaccine, has the potential to considerably complement the impact of these current interventions. In this changing environment, ministries of health will need to define early the relevant information that will support the decision on the use of a malaria vaccine in their health systems.

The DMF is a tool developed jointly by MVI, the World Health Organization (WHO, both headquarters staff and the Regional Office for Africa, WHO/AFRO), malaria and immunization experts from several African countries, and research institutions, to guide countries' decisions on introducing a malaria vaccine into national health systems. It outlines data and processes—at national, regional, and global levels—that countries have deemed important to know or have in place, respectively, in order to make a decision about a future malaria vaccine.

In 2006, a generic framework for decision-making was developed and then subsequently validated in six countries (Gabon, Ghana, Kenya, Mali, Mozambique, and Tanzania) through a series of two-day country consultations. During each consultation, participants adapted the generic DMF to fit their country-specific needs and developed an action plan for implementing the DMF.

In 2007, MVI's main objective was to build upon this momentum and:

- Support the countries consulted in 2006 to begin implementing their DMF-related action plans.
- Consolidate the country-specific DMFs into a draft regional DMF.
- Present the draft regional DMF at a regional meeting jointly organized by WHO and MVI for its validation and endorsement by national decision-makers as a common tool for policy decisions on malaria vaccine.
- Following this endorsement at the regional level, support two to four additional countries to use the regional DMF in preparing for a decision about a future malaria vaccine.
- Develop a global advocacy strategy to engage national and global partners to support the implementation of global DMF data and processes.
- Continue to share information about the DMF with stakeholders.

The work described here was implemented by MVI staff, together with part-time support from Ms. Kaitlin Christensen through a sub-agreement with Energetics. Ms. Christensen has been collaborating with MVI on the DMF work since 2006 when she was based in Nairobi, Kenya.

MVI is grateful for USAID's financial and technical support of this work in 2007. This work has also been partially financed by the Bill & Melinda Gates Foundation.

Implementation of 2007 activities

Support countries in implementing DMF action plans

Analysis of the different near-term plans of action developed by countries during 2006 consultations revealed that a common activity prioritized by countries was the establishment of Technical Advisory Groups (TAGs) for Malaria Vaccines. Those TAGs would facilitate country-level consultation and dialogue between the scientific community, policymakers, and other stakeholders during ongoing research and development of a malaria vaccine.

In 2007, MVI initiated follow-up with the six countries (Gabon, Ghana, Kenya, Mali, Mozambique, and Tanzania) that held consultations in 2006 to support them in setting up such TAGs. Three countries have begun to implement this activity: Tanzania and Kenya organized their first TAG meetings in April and October 2007, respectively, to define membership and a plan of activities; Mozambique initially planned its meeting for September 2007, but this was postponed. To support the implementation of the TAG and additional DMF-related activities in Mozambique, MVI recruited a locally-based resource person (a participant from the 2006 Mozambique DMF consultation) on a part-time basis. MVI has also started working with public health experts in Mozambique and Kenya to support and advocate for the DMF process, as part of its efforts to encourage greater engagement at the country level for the DMF.

MVI also has had extensive exchanges with ministries of health in Gabon, Ghana, and Mali about next steps, including convening of TAGs. These countries were unable to move on specific next steps in 2007 and the challenges facing WHO (noted elsewhere in this report) limited its ability to help advance the work in these countries. Next steps for these countries are noted in the plans for 2008.

Consolidate the country-specific DMFs into a draft regional DMF

The six country-specific DMFs were analyzed and synthesized to create a draft regional DMF, which can be used by any malaria-endemic country in the Africa region to aid decision-making about malaria vaccines. The draft regional DMF is documented in a report highlighting the common national and global data and processes identified during the consultations. A copy of this report will be sent under separate cover and is also available at www.malvacdecision.net. It is currently being translated into French and Portuguese for the regional meeting.

Validate the regional DMF at a WHO- and MVI-convened meeting

WHO, whose mandate is to provide technical advice to ministries of health for policy adoption and implementation, has been an important partner in the DMF since the inception of the project. WHO is represented on the DMF Steering Committee and has served as a co-host at each of the DMF country consultations. In 2006, MVI provided support to WHO to organize and participate in country consultations. In 2007, an agreement was proposed to continue this collaboration, specifically to organize with MVI a high-level, regional meeting to discuss the regional DMF and validate it as a regional tool for decision-making about malaria vaccines. Unfortunately,

WHO/AFRO began a major restructuring and transition in December 2006, which included loss of most of its malaria staff, including all those who had worked on the DMF in 2006. During this transition period, the WHO/AFRO headquarters office relocated from Harare to Brazzaville; a new director of the Division of AIDS, Tuberculosis and Malaria was appointed; and a new regional advisor for Malaria was appointed. Moreover, the position of focal person for malaria prevention activities remained vacant until July 2007. Because of this transition, WHO/AFRO has postponed the regional DMF meeting several times. Following discussions with the director of the Division of AIDS, Tuberculosis and Malaria, it was agreed that this meeting should be held in early 2008. MVI is exploring, in parallel, options for implementing the regional meeting through other regional organizations such as the African Malaria Network Trust (AMANET) or INDEPTH/the Malaria Clinical Trials Alliance.

Support two to four additional countries to use the regional DMF

Initially, MVI planned to roll out the regional DMF to additional African countries after its validation at the regional meeting. Despite the delay in organizing the regional meeting as explained above, a consultation was organized in Ethiopia in April 2007. This consultation resulted in a country-specific DMF based upon the draft regional framework. In terms of subsequent application of the DMF to the most clinically advanced vaccine candidate, RTS,S, consultation participants determined that they will be better placed to move forward with planning activities with the availability of Phase 3 data in 2010. The Ministry of Health of Burkina Faso has agreed to organize a consultation in the coming months, at a date to be agreed with the government and key partners.

Develop a global advocacy strategy

MVI is currently developing an advocacy strategy targeting global and regional stakeholders in order to increase awareness of and support for the DMF process and its implementation at the country level. This strategy is still under development and will be finalized by the end of 2007.

Share information about the DMF

MVI shared the draft regional DMF with African immunization and malaria control program managers at three WHO-sponsored sub-regional meetings: National Immunization Programme Managers (South and East Africa), National Immunization Programme Managers (West Africa), and Malaria Annual Planning and Review (South and East Africa).

At the international level, the DMF has been presented at a range of fora, including at the Global Health Council's annual conference in May 2007 and at a briefing convened by USAID in June 2007.

MVI has also updated existing materials and developed additional materials for use in documenting, and advocating for, the DMF process, including a DMF Fact Sheet, a report documenting the DMF process, and a report documenting the Ethiopia country consultation, as well as updates to information on the DMF website (www.malvacdecision.net).

Finally, MVI has continued to convene and chair regular teleconferences for the DMF Steering Committee in order to keep Steering Committee members, and by extension, the organizations that they represent, engaged in the process.

Constraints and challenges

MVI faced several challenges this year that affected the implementation of DMF activities. Though malaria control and immunization program managers expressed a strong interest in continuing to collaborate with MVI on DMF activities, they were limited in their ability to follow-through on commitments. In other instances, we experienced unforeseen delays in attaining approval from national authorities to host meetings. This was not interpreted as a desire to avoid the process, but rather that more pressing or immediate health issues were higher priority.

We also experienced significant challenges in collaborating with WHO/AFRO (as described earlier). Despite these challenges, WHO/AFRO remains a critical partner in this process, and MVI will continue to work in partnership with its representatives, while exploring ways to ensure that planned meetings are held and commitments fulfilled. To this end, MVI has consulted with the director of AIDS, Tuberculosis and Malaria in an effort to gain high-level acceptance for the DMF process. MVI also is looking at alternate organizations with a presence in Africa to convene ongoing work around the DMF. Potential partners include regional organizations, such as AMANET, as well as academic, nongovernmental, and professional entities in individual countries.

Conclusion

Despite the challenges encountered, MVI has made progress in analyzing the results of the 2006 country consultations, developing a draft regional framework which can serve as a tool for all sub-Saharan African countries with endemic malaria, improving awareness of the DMF among national and regional stakeholders, and beginning to implement key elements of the DMF in countries that were consulted in 2006.

Moving forward, MVI will work to meet several objectives:

- Continue collaboration with 2006 DMF participants.
- Expand engagement of important national groups, such as the Interagency Coordination Committees for Immunization, the Country Coordinating Mechanism for malaria, and other health sector groups.
- Mobilize the political support that public health professionals need in order to prepare their countries for rapid introduction of a future malaria vaccine.

Proposed next steps

Several near-term activities will complement the achievements made during 2007:

- Presentation of the finalized global advocacy plan to the DMF Steering Committee.
- Formation of a TAG in one additional country in 2007 (Mozambique).
- One additional two-day, in-country meeting in 2007 (Burkina Faso).

- Analysis of malaria and immunization policies in two countries (Burkina Faso and Malawi) and updating of existing information on malaria and immunization policies in seven countries (Ethiopia, Gabon, Ghana, Kenya, Mozambique, Senegal, and Tanzania).
- In partnership with WHO/AFRO, or an alternate, regionally-based organization, implementation in early 2008 of a high-level regional meeting to present and discuss the regional DMF and to develop a plan for implementing the DMF in countries that do not host a country consultation.
- Putting in place strategies, aside from collaboration with WHO, for convening consultations in individual countries, as well as exploring structures other than TAGs to advance DMF-related activities in individual countries.
- Monitoring and evaluation of ongoing and new activities, such as progress by TAGs in planning for malaria vaccines.

MVI is also pursuing the possibility of hosting additional DMF country consultations in early 2008.

Financial Review

PATH's quarterly financial report will be submitted per the agreement terms.