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EXTERNAL EVALUATION OF THE USAID MALARIA VACCINE DEVELOPMENT PROGRAM

May 2016

This publication was produced at the request of the United States Agency for International Development. It was prepared independently by Peter Nsubuga, MD, Mark Polhemus, MD, and Deepak Gaur, PhD.

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2012.

External Evaluation of the USAID Malaria Vaccine Development Program

May 2016

Evaluation Mechanism: AID-OAA-C-14-00067

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This document (Report No. 072-16-001) is available online. Online documents can be found on www.ghpro.dexisonline.com. Documents are also made available through the Development Experience Clearinghouse (<http://dec.usaid.gov>). Additional information can be obtained from:

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This document was submitted by Dexis Consulting Group and The QED Group, LLC, to the United States Agency for International Development under USAID Contract No. AID-OAA-C-14-00067.

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ACRONYMS

Ad	Adenovirus
ASOI	GSK proprietary adjuvant
3D7	<i>Plasmodium falciparum</i> clone 3D7 (from isolate NF54)
AMA	Apical merozoite antigen
BMGF	Bill & Melinda Gates Foundation
CSP	Circumsporozoite surface protein
CeTOS	Cell-traversal protein for ookinetes and sporozoites
CHMI	Controlled human malaria infection
DMID	Division of Microbiology & Infectious Diseases
DOD	Department of Defense
EVI	European Vaccine Initiative
FVO	<i>Plasmodium falciparum</i> Vietnam Oak-Knoll Clone
GH	Bureau for Global Health, USAID
GH Pro	Global Health Program Cycle Improvement Project
GLA-SE	Glycolipid A Stable Emulsion Adjuvant
GMP	Good Manufacturing Practices
GSK	GlaxoSmithKline
HIDN	Office of Health, Infectious Diseases and Nutrition, USAID
HIV	Human Immunodeficiency Virus
IDRI	Infectious Disease Research Institute, Seattle
LMVR	Laboratory of Malaria & Vector Research (NIAID, NIH)
ME-TRAP	Multi-epitope thrombospondin-related anonymous protein
MF59	Novartis adjuvant
MIDRP	Military Infectious Diseases Research Project
MSP	Merozoite surface protein
MVDP	Malaria Vaccine Development Program
MVI	Malaria Vaccine Initiative
NAMRU	Naval Medical Research Unit Six, Lima, Peru
NIAID	National Institute for Allergy and Infectious Diseases
NIH	National Institutes of Health
NMRC	Naval Medical Research Center
PAD	Project Appraisal Document
PATH	Program for Appropriate Technology in Health
PfSpz	<i>Plasmodium falciparum</i> sporozoite whole organism vaccine
RTS,S	Pre-erythrocytic CSP-based vaccine
R&D	Research and development
SCG	Scientific Consulting Group
TBV	Transmission-blocking vaccine
USAID	United States Agency for International Development
USMMVP	U.S. Military Malaria Vaccine Program
VLP	Virus-like particle
VZV	Varicella zoster virus
WEHI	Walter and Eliza Hall Institute
WHO	World Health Organization
WRAIR	Walter Reed Army Institute of Research

EXECUTIVE SUMMARY

The United States Agency for International Development (USAID) Malaria Vaccine Development Program (MVDP) is currently authorized under MVDP Project Appraisal Document (936-6000), approved in July 2012 and amended in April 2014 to an end date of September 20, 2019.

Through previous authorizations, USAID has supported the development of malaria vaccines for the past five decades. This program has grown from basic and academic malaria research to a translational research program involving a range of activities from preclinical testing to human clinical trials. The last evaluation of the MVDP was organized in 2003. In October 2015, USAID commissioned an external evaluation team with the mandate to assess the MVDP's accomplishments since the last evaluation and to address the following three questions:

1. What has been the value added of the MVDP to the current status of malaria vaccine development?
2. How is the MVDP complementary to other programs funding malaria vaccine development?
3. Given the historical role of the MVDP, is this role critical going forward, or, given the changing funding environment for malaria vaccine development, should the focus of the USAID MVDP strategy be modified?

Through the MVDP, USAID continues to be a major funder and supporter of malaria vaccine development efforts across the globe. The program has forged strong alliances with many partners that have dedicated malaria vaccine programs, including the Bill & Melinda Gates Foundation (BMGF), universities and individual researchers. USAID leverages the expertise and vaccine investments of other sources, including the United States Military [both the Walter Reed Army Institute of Research (WRAIR) and the Naval Medical Research Center (NMRC)], the National Institutes of Health (NIH), Program for Appropriate Technology in Health (PATH) Malaria Vaccine Initiative (MVI) and several groups based in the UK and Australia.

Overall, the MVDP is perceived as an outstanding program that has taken a unique funding position in the malaria vaccine portfolio and filled a major void that has developed over the past decade or so from the shift in focus of other major malaria vaccine funders such as the BMGF. Despite limited funds, the program has been remarkably productive over the past decades and has received excellent reviews from its partners and stakeholders, as well as the external agencies/investigators in malaria vaccine development that formed the pool of key informants for the evaluation. This program has been run in an exceptional manner and is rated as highly successful in effectively leveraging funds with key partners and advancing projects that would have otherwise lacked crucial funding. Thus, the USAID MVDP has emerged as a very significant player in the global efforts to develop a successful malaria vaccine.

SUMMARY OF FINDINGS AND CONCLUSIONS

What has been the value added of the MVDP to the current status of malaria vaccine development?

- The MVDP has added significantly to the process of developing a malaria vaccine.
- The MVDP has used its limited resources to catalyze the process through strategic research on the continuum of malaria vaccine development, particularly in the approach of pre-erythrocytic and blood stages. The key informants and a significant portion of the survey respondents felt it was an important funder within the malaria vaccine community and played a unique role in a critical niche that otherwise would not be addressed within the global arena of malaria vaccine development.

- The MVDP's focus on key preclinical and early clinical development efforts, which are not usually funded by other entities, has supported critical decisions to down-select or advance early vaccine candidates.
- It was widely felt by evaluation respondents that additional malaria funding for the MVDP would advance and speed the progress of malaria vaccine development efforts.

How is the MVDP complementary to other programs funding malaria vaccine development?

- The MVDP does not have enough funding to support an entire vaccine development effort, so its flexible and focused support has been seen as desirable and effective in critical research areas that lack other funding sources. Effective strategic partnerships have leveraged available funds, recognizing that the MVDP focuses on acquiring evidence that could stimulate funding for advanced vaccine development. The MVDP has a unique niche as a catalyst in the malaria vaccine development community, using its expertise and flexible funding to support policy and science.
- The MVDP's role is significant, complementary to the role of other funders, and cost-effective due to its ability to leverage other funding. It was repeatedly noted by the Scientific Consulting Group (SCG), survey respondents and key informants that Dr. Diggs and Dr. Soisson are critical to the MVDP's success in this role and have provided valuable scientific experience for several programs. Many informants felt that Dr. Diggs and Dr. Soisson are so critical that a succession plan needs to be developed to ensure continued integration of MVDP leadership and expertise with current partners.
- The longstanding partnership with WRAIR and NMRC has been highly effective. Additionally, the MVDP has been involved with, and leveraged funding through, some of the most prominent malaria vaccine groups across the world, including NIH, Oxford and the Walter and Eliza Hall Institute (WEHI). Importantly, it has also partnered with other policy and funding organizations to exert significant influence on the policy and science behind malaria vaccine development.
- The financial relationship with MVI and ability to leverage its expertise and funding has changed with the ending of the USAID cooperative agreement with MVI. It is not clear how the lack of a funding relationship between USAID and MVI will impact the MVDP-MVI relationship. Survey respondents and key informants indicated a clear desire for a mechanism for partners outside the Department of Defense (DOD) to interact with the MVDP. In part due to the prolonged award process for the new MVDP non-U.S. Government partner (the Leidos MVDP contract), survey respondents were not sufficiently aware of this new partner and the possibilities of engaging with it. Leidos' pipeline development activities and vaccine development projects outlined in its work plan may ultimately support collaboration with non-DOD partners, but at the time the evaluation was conducted, it was not clear to many how this would work.

Given the historical role of the MVDP, is this role critical going forward, or, given the changing funding environment for malaria vaccine development, should the focus of the USAID MVDP strategy be modified?

- The MVDP's focus is aligned with the Malaria Vaccine Technology Roadmap endorsed by the Malaria Vaccine Funders Group.
- There are other malaria funders focused on basic research, epidemiology, disease prevention and treatment, as well as vaccines for reducing transmission, but few support the development of vaccines that reduce malaria morbidity and mortality. This remains a critical area, according to the Malaria Vaccine Technology Roadmap, SCG assessments, survey respondents and key informants. The MVDP is one of the few funders in this space, and its role is becoming more

critical. The MVDP is appropriately focused on the development of pre-erythrocytic and erythrocytic vaccines to prevent and control clinical disease.

- RTS,S¹, as it is currently understood, has significant limitations, and recently the WHO recommended further evaluation of RTS,S/AS01² in a series of pilot implementations, addressing several gaps in knowledge before considering wider country-level introduction. WHO does not recommend the use of the RTS,S vaccine in the younger (6-12 weeks) age category, as the vaccine's efficacy was found to be low in this age group.
- It was unanimous among survey participants and key informant interviews that an improvement or alternative to RTS,S was necessary and that work on vaccines that reduce morbidity and mortality is required.
- The SCG is well composed, has a strong role in the scientific monitoring of the MVDP and supports its current direction. If the focus of the USAID MVDP strategy is modified, the SCG is staffed and positioned to contribute to the new strategy.

RECOMMENDATIONS OF THE EVALUATION TEAM

The MVDP has contributed substantially to the process of malaria vaccine development, and stakeholders have found the program to serve an important catalyzing role within the malaria vaccine development community. It has facilitated successful partnerships with a variety of private and public malaria vaccine organizations and has been endorsed by the Malaria Vaccine Funders Group. The evaluation team suggests the following recommendations to continue and improve the valuable role that the MVDP plays in the global malaria vaccine community:

1. With the limited funding globally, which is focused on vaccines to impact malaria morbidity and mortality, the MVDP should continue to support this area and to evaluate where it can have the most impact as a funder. According to the survey and key informant interviews, the MVDP could have the greatest impact now by focusing on:
 - a. Continued evaluation of new antigens (pre-erythrocytic and blood-stage) that could be added to RTS,S or replace it
 - b. Methods to select which vaccine candidates to advance or down-select
 - c. Transitioning preclinical successes into clinical development through evaluation of vaccine platforms, funding Good Manufacturing Practices (GMP) lots, toxicology studies and evaluating vaccine efficacy in controlled human malaria infection (CHMI) models
2. In the continued evaluation of where the MVDP can have the most impact, an expanded role for the SCG should be considered. The SCG could play a prospective role in determining areas to fund and could meet in smaller groups more often to take stock of ongoing projects.
3. The MVDP should consider publishing or communicating its current mechanisms for collaborating with partners outside the DOD. The Leidos contract is the MVDP's current mechanism to extend its capabilities to entertain research and development efforts not available through the DOD or NIH, but it is not well understood currently in the greater malaria vaccine development community, including by some longstanding partners.
4. Plan for the long lead time it will take to train successors for Dr. Diggs and Dr. Soisson, who have served USAID admirably. A succession plan that reflects the need for continuity of the technical

¹ Pre-erythrocytic CSP-based vaccine

² GSK proprietary adjuvant

team and supports the continuation of MVDP's relationships and broad impact will be useful for USAID.

5. Evaluate current MVDP funding levels. The overall funding for malaria vaccine development is limited. The potential impact of MVDP funding has increased with the movement of BMGF funding to transmission blocking. The areas suggested for MVDP focus (GMP lot manufacturing, toxicology studies and CHMI trials) are expensive, multiyear endeavors. Thus, given the MVDP's unique role and critical niche in the malaria vaccine development community, increased funding could support more of the areas of research suggested as most important for MVDP funding and could speed vaccine development efforts through critical milestones.

I. EVALUATION PURPOSE AND EVALUATION QUESTIONS

The United States Agency for International Development (USAID) has supported the development of malaria vaccines for the past five decades. Over the years, this program has evolved from supporting basic research in academic settings to a more recent translational model involving a range of activities from preclinical testing to conducting clinical trials. The USAID Malaria Vaccine Development Program (MVDP) was last evaluated in 2003 by a team of five experts (Lynn Cates, Stephanie James, Gerald Jennings, Wayne Hockmeyer and Ripley Ballou).

The MVDP continues to be a major funder and supporter of malaria vaccine development efforts across the globe. It has forged strong alliances and leveraged its funds with major research groups that have been leading dedicated malaria vaccine programs, which include the United States Military [the Walter Reed Army Institute of Research (WRAIR) and the Naval Medical Research Center (NMRC)], the National Institutes of Health (NIH), Program for Appropriate Technology in Health (PATH) Malaria Vaccine Initiative (MVI), and several groups based in the UK and Australia.

An internal USAID portfolio review in 2014 recommended another evaluation of the MVDP to assess USAID's current and future unique role in the development of malaria vaccines, MVDP progress to date, ways to accelerate progress and ways to improve the program in the future. The intended audience for this evaluation includes the USAID Bureau for Global Health (GH), the Office of Health, Infectious Disease and Nutrition (HIDN) leadership and the MVDP staff, who would use the results to shape the program's future. Major decisions and policies of the program that may be affected include strategic direction, funding, scientific direction and partnerships formed.

In 2015, USAID authorized Dexis Consulting Group through the Global Health Program Cycle Improvement Project (GH Pro) to assemble an external evaluation team with the mandate to assess MVDP accomplishments over the past 12 years and to address three major questions:

- 1. What has been the value added of the MVDP to the current status of malaria vaccine development?** In addressing this question, the evaluation team was requested to consider the following points:
 - Whether or not MVDP activities have achieved their anticipated strategic results
 - The relevant importance of MVDP contributions to malaria vaccine discovery and development
 - If the MVDP fills a critical niche that otherwise would not have been addressed within the global arena of malaria vaccine development
- 2. How is the MVDP complementary to other programs funding malaria vaccine development?** In addressing this question, the evaluation team was requested to consider the following points:
 - USAID's effectiveness in coordinating with its funded MVDP partners
 - If MVDP staff have been effective in coordinating with other malaria vaccine donors
 - Complementarity of the MVDP with other efforts by funded partners and the malaria vaccine development enterprise at large, and how this can be enhanced
- 3. Given the historical role of the MVDP, is this role critical going forward, or, given the changing funding environment for malaria vaccine development, should the focus of the USAID MVDP strategy be modified?** The context provided for this question was as follows:

- Currently, a large proportion of malaria vaccine funding worldwide is devoted to vaccines as tools to facilitate malaria elimination, in contrast to the USAID MVDP focus on enhancing malaria control.
- A licensed, partially effective vaccine with a relatively short duration of action targeting malaria control may be available in 2016.

The external evaluation team laid out a plan for the evaluation during a team planning meeting in October 2015. Steps of the process were discussed with the USAID MVDP leadership and technical management team. Based on these discussions, the methodology adopted to complete the evaluation consisted of three parts:

1. Review of MVDP documents and Scientific Consulting Group (SCG) reports
2. A feedback survey of partner organizations, SCG members and malaria experts
3. One-on-one key informant interviews with leaders in the malaria vaccine development community

Based on the mandate provided, the evaluation team prepared an evaluation matrix outlining the illustrative indicators, data sources, data collection methods, sampling and selection criteria and data analysis methods. The details of the methodology are discussed in section 3, Evaluation Methods and Limitations.

2. PROJECT BACKGROUND

2.1. HISTORY

USAID has supported malaria vaccine development for more than 45 years. The MVDP was created in the late 1960s in response to the termination of the Malaria Eradication Program. Its history can be divided into four phases:

1. 1966–1974: Focus on single-center research and development with the objective of developing a malaria vaccine
2. 1974–1980: Establishment of a network of partners and a variety of research approaches to cell-based (sporozoite and merozoite) vaccines through further development of academic models in which protection had been demonstrated in small numbers of subjects
3. 1980–1988: Use of molecular approaches and the performance of a clinical trial of New York University's peptide vaccine at the University of Maryland's Center for Vaccine Development, the first peptide malaria vaccine to undergo clinical testing
4. 1988–present: Focus on the development of new vaccine candidates and progression to clinical trials to assess proof of principle

2.2. AUTHORIZATION AND FUNDING

When it was authorized through a project approval document by USAID in 1992, the Malaria Vaccine Development Project (936-6001) consolidated efforts of two earlier projects: the Malaria Immunity and Vaccine Research Project (931-0453) and the Malaria Field Trials Project (936-5967). It should be noted that all of these projects have been part of the MVDP. The MVDP is currently authorized by USAID under a Project Appraisal Document (PAD) (936-6000), which was approved in July 2012 and amended in April 2014. The PAD's ceiling is \$75,000,000, and its end date is September 20, 2019. The current annual obligation is \$7,100,000.

2.3. FOCUS

The overall aim of the USAID MVDP is to accelerate the development of malaria vaccines for disease control programs to alleviate further morbidity and mortality. The MVDP has supported vaccine approaches that target two stages of the parasite's life cycle: pre-erythrocytic (i.e., from injection of sporozoites from the mosquito through the liver stages) and erythrocytic (i.e., circulating merozoites in the human bloodstream that invade red cells). While the former targets sterile immunity (i.e., the absence of circulating blood-stage parasites), the latter focuses on preventing blood-stage disease. In the latter case, viable parasites may persist in the circulation, as is the case in naturally acquired immunity to malaria. In recent years, the MVDP has focused on building a pipeline from early preclinical vaccine development, through the regulatory process, and to clinical and field testing of vaccine candidates. The MVDP has supported production and testing of protein subunit vaccines, evaluation of new platform technologies for vaccine development, as well as adjuvant formulations, and development of vaccine strategies to overcome strain variability.

2.4. LANDSCAPE OF MALARIA VACCINE DEVELOPMENT

While there has not been a licensed vaccine for malaria previously, there is now potential that a licensed, partially effective vaccine with a relatively short duration of action targeting malaria control may be available relatively soon. The Phase III results of this vaccine, known as RTS,S/AS01, were submitted to the European Medicines Agency and World Health Organization (WHO). The European Medicines Agency's Committee for Medicinal Products for Human Use has adopted a positive scientific opinion for RTS,S/AS01 (Mosquirix), for use outside the European Union. However, before approving

licensure and countrywide implementation, the WHO has recommended further evaluation in a series of phased pilot implementations in select populations, which address several gaps in the knowledge of the true vaccine efficacy. A critical concern and major uncertainty that needs to be resolved is whether the protection demonstrated among the children 5-17 months old in the Phase 3 trial can be replicated in routine health systems, particularly due to the need for a booster dose schedule that will involve new immunization contacts.

The decision of the Bill & Melinda Gates Foundation (BMGF) to focus on malaria elimination and eradication has resulted in a major shift in the focus of malaria vaccine research. The adoption of this very long-term focus by much of the community will continue to play a role in strategic research planning as the long-term impact of malaria control efforts becomes clearer and new tools for control and elimination emerge.

Multiple organizations with well-established malaria vaccine development programs have advanced efforts that are vying for limited research and development funds. Globally, funding for malaria vaccine development is not sufficient to support the many efforts currently underway. In malaria vaccine development, researchers face a dearth of funding for later steps of vaccine development, such as process development, Good Manufacturing Practices (GMP) lots, toxicology studies and clinical trials. The NIH and other government research agencies do not easily fund these activities. More so, blood-stage vaccines are not getting any support except from USAID.

2.5. OPERATIONS

The MVDP is located in the Malaria Division of the GH Bureau's HIDN office. The management team that provides operational direction and oversight to the MVDP portfolio consists of Julie Wallace (Malaria Division Head), Lilia Gerberg and Susan Youll. Technical advice on the program is provided by two contract staff members (Drs. Carter Diggs and Lorraine Soisson).

2.6. PARTNERS

The global malaria vaccine development effort involves numerous stakeholders. The MVDP has established good working relationships with these organizations. Also, as it has made the transition from basic discovery in academic institutions to a widely diversified portfolio focused on efficiently moving vaccines to proof of principle, the MVDP has developed close partnerships with both the public and private sectors. It has employed a variety of mechanisms to support implementers, ranging from informal negotiations and sub-agreements with great flexibility, to more formal contracts, cooperative agreements and interagency agreements.

The MVDP currently has agreements with WRAIR, the NMRC, the National Institute of Allergy and Infectious Disease (NIAID), and the MVDP Leidos contract. A USAID MVDP cooperative agreement with PATH/MVI ended in September 2014.

Walter Reed Army Institute of Research: WRAIR's focus is on developing, producing and performing clinical and field evaluations of protein subunit vaccines. WRAIR, in collaboration with GlaxoSmithKline (GSK) and PATH/MVI developed RTS,S, the most advanced malaria vaccine. Currently, WRAIR's work with USAID is focussing on recombinant vaccines based on CSP³, CelTOS⁴, and AMA-1⁵. MVDP will provide a portion of the total budget for the United States Army's malaria vaccine development work at WRAIR.

³ Circumsporozoite surface protein

⁴ Cell-traversal protein for ookinetes and sporozoites

⁵ Apical merozoite antigen

Naval Medical Research Center: The NMRC has pursued DNA-based strategies in the past (in collaboration with Genvec and Alphavax) and currently is working on advanced vaccine construction and formulations, including pox and adenovirus vectored vaccines (in collaboration with Professor Adrian Hill, Oxford). In 2015, the MVDP provided a portion of the NMRC malaria program's total budget.

National Institute of Allergy and Infectious Diseases, NIH: Previously, the MVDP has provided considerable support to collaborative efforts with the NIH. Examples include Phase I testing of an early blood-stage vaccine formulation and the CSP multiple antigen peptide (in collaboration with New York University). The MVDP has also provided initial funding for the creation of the NIAID Malaria Vaccine Development Unit, now called the Laboratory of Malaria Immunology and Vaccinology. Recently, MVDP has supported a vaccine efficacy trial in Aotus monkeys for an antigen combination of AMA1 and RON2, and it continues to support the GIA reference laboratory, located in the Laboratory of Malaria and Vector Research (LMVR), NIAID, NIH.

MVDP Leidos Contract: In 2015, USAID awarded Leidos a five-year contract for providing scientific and management support for the MVDP activities. Leidos, formerly known as Science Applications International Corporation, is a science-based corporation and vaccine development contractor with strong links in the malaria community. It was the prime contractor from 2000–2014 for the Malaria Vaccine Production and Support Services contract with the NIH/NIAID Division of Microbiology and Infectious Diseases. Leidos has more than 13 years of experience building scientific alliances and managing a diverse portfolio of pharmaceutical, biotechnology and academic organizations, as well as contract manufacturing and contract research organizations, for vaccine and drug development contracts funded through the NIH and the Department of Defense (DOD).

Overall, the Leidos contract will provide management support (scientific, technical, administrative and regulatory) for the MVDP program across four different elements of protocol development, implementation, procurement and meeting support. Activities include (1) meetings with USAID to provide technical status updates and discuss contract deliverables and administration, (2) programmatic deliverables and financial reports, (3) management and archiving of MVDP data and documentation review, (4) subcontracts administration (e.g., generating scopes of work, preparing solicitations and reviewing proposals) and (5) overseeing technical implementation by subcontractors. The contract will undertake literature searches and surveys on topics specified by USAID to facilitate identification of funding opportunities prioritized by the USAID MVDP team and to provide comparator information regarding specific vaccine-development projects. Currently, USAID white paper requests and topic-specific scope requirements include a focus on the development of vaccine platform/adjuvant systems, CSP vaccine candidates, RH5 vaccine candidates, liver-stage vaccine epitope scouting/vaccine candidates and novel blood-stage candidates. The estimated costs for 2015-2016 contract activities total \$4.8 million.

3. EVALUATION METHODS AND LIMITATIONS

3.1. EVALUATION DESIGN AND METHODOLOGY

This was a retrospective evaluation through 2015. USAID and GH Pro developed a scope of work with terms of reference and questions and contracted with a three-person external consultant team to conduct the evaluation. The consultants collectively had several years of project evaluation and malaria vaccine experience. The team met with USAID and GH Pro staff at the evaluation's inception in October 2015 and developed a detailed work plan, including a refined scope, and a design matrix (Annex III). The evaluation questions, detailed in the design matrix, were as follows:

1. What has been the value added of the MVDP to the current status of malaria vaccine development?
2. How is the MVDP complementary to other programs funding malaria vaccine development?
3. Given the historical role of the MVDP, is this role critical going forward, or, given the changing funding environment for malaria vaccine development, should the focus of the USAID MVDP strategy be modified?

The team met every week to review progress and decide on appropriate next steps.

3.2. METHODS

The evaluation utilized a mixed-methods approach, with qualitative and quantitative data collection through document review, MVDP stakeholder and partner survey, and MVDP stakeholder and partner key informant interviews.

Document review: At the onset of the evaluation, the team requested all documents that were pertinent to answer the evaluation questions. USAID MVDP staff provided 59 documents, including project and meeting reports and contractual documents with USAID partners. Document review was conducted from November 2015 to February 2016.

Stakeholder and partner survey: The team developed a questionnaire to obtain answers to the evaluation questions and created a survey that was sent to previous and current MVDP grant recipients, malaria vaccine experts and malaria policy and funding organizations. The evaluators developed the list of survey respondents based on review of the MVDP documents and the evaluators' understanding of the previous and current stakeholders in malaria vaccine development. The team made every effort to ensure representation of the key stakeholders in malaria vaccine development. The questionnaire was self-administered (through SurveyMonkey), and the evaluators sent several reminders to ensure completion. The survey was conducted from December 2015 to January 2016. A total of 44 individual survey responses were obtained, of which 34 (77.2 percent) were complete.

Key informant interviews: The team selected a list of key informants from a list of previous and current MVDP partners and grant recipients and malaria vaccine experts. The team developed a key informant questionnaire, which was administered by interviewer. The team visited the key informants who were available for in-person meetings and interviewed others over the phone. During February 2016, the team interviewed a total of 26 key informants out of the 47 that were contacted.

Data collection and analysis: The data collected from the document review were entered into a database. The survey data were entered directly into an electronic database, which was transferred directly into MS Excel and Epi Info. The team members summarized key informant data into key themes.

3.3. THEMES FOR ANALYSIS

The analysis was organized to answer the evaluation questions. The team utilized results from each of the data collection methods to triangulate the information. Quantitative data were summarized into tables, charts and figures as appropriate. Qualitative data were summarized into themes to answer the evaluation questions. The results are presented for each evaluation question by data collection method: document review, survey and key informant interviews. The survey results included as many direct quotes as possible to provide background for the conclusions.

3.4. LIMITATIONS

Although the design and resources used were adequate to answer the evaluation questions, there were some limitations. First, many of the respondents were previous or current recipients of MVDP funding and could have views that were influenced by their role in the program. There may have been a natural bias to focus on program successes, although the team tried to tease out other critical points. Secondly, although several attempts were made to obtain answers from all the survey respondents, 54 did not respond, and their views could have been different from those who did answer. Thirdly, some of the key informants that were contacted were not available to be interviewed due to scheduling difficulties. Finally, the evaluation questions required the respondents to have adequate recall of events that occurred some time ago, or in some cases, when the respondent was not the one in charge of the project at that time. The team tried to triangulate sources of information to limit the effect of recall bias.

4. FINDINGS

4.1. EVALUATION QUESTION 1: What has been the value added of the MVDP to the current status of malaria vaccine development?

To address this question, the evaluators were asked to consider the following:

- Whether or not MVDP activities have achieved their anticipated strategic results
- The relevant importance of MVDP contributions to malaria vaccine discovery and development
- Whether or not the MVDP fills a critical niche that otherwise would not have been addressed within the global arena of malaria vaccine development

4.1.1 Question 1 findings from document review

The MVDP has had a significant impact on the current status of malaria vaccine development. The program is funding and involved in:

- Development of strategic goals and priorities for the malaria vaccine community
- Translational research supporting antigen progress towards vaccine candidates
- Advancing promising vaccine candidates through small lots of GMP material and early clinical trials, including Controlled Human Malaria Infections (CHMI)
- Evaluation of multiple vaccine platforms and approaches
- Publishing results of funded research activities and clinical trials

The SCG has repeatedly noted the critical niche MVDP fills within the global arena of malaria vaccine development and has listed significant accomplishments in malaria vaccine research and development in its reports.

Excerpts from SCG reports addressing whether the MVDP fills a critical niche:

“The mission of the MVDP is totally aligned with the USAID goal to address current public health problems in the developing world, and its policy of attempting to address perceived gaps in the global malaria vaccine development portfolio. The second of these two factors has taken on greater importance in the past few years as much of the malaria vaccine development effort globally, and in particular that of a major funder, the Bill and Melinda Gates Foundation, is now focused on strategies for blocking transmission as a part of an eradication campaign. It is critical considering the complexity of the malaria parasite target to sustain a diverse research portfolio, and that requires diverse sources of funding.” (*SCG Report 2015*)

“The MVDP maintains a very important position in the malaria vaccine development landscape by continuing to focus on the pre-erythrocytic and erythrocytic stages of vaccine development and attempting to address perceived gaps in the global malaria vaccine development portfolio including exploration of new platforms and new adjuvants. This focus is particularly important as some groups in the vaccine field, particularly those supported by the Bill and Melinda Gates Foundation, have concentrated on sexual stages of parasite development and efforts to interfere with transmission.

Progress with disease-modifying vaccines should reduce the risk of acquiring malaria and also reduce the severity of disease in all recipients, particularly children of endemic areas, the populations most vulnerable to this disease.” (*SCG Report 2015*)

Excerpts from SCG reports addressing MVDP contributions to malaria vaccine discovery and development:

“Overall, the SCG concludes that continued progress is being made on the major approaches in both the blood stage and pre-erythrocytic aspects of the USAID program and looks forward to the results of ongoing and proposed studies.” (SCG Report 2015)

“One such blood stage CHMI trial has been conducted in 2014 to assess the efficacy of the AMA13D7⁶/AS01B vaccine candidate in a collaborative effort between the University of Oxford, WRAIR, GSK, PATH-MVI, and USAID.” (SCG Report 2015)

“Preclinical investigations of the blood stage vaccine candidates EBA175 and Rh5 which are being conducted at the Walter and Eliza Hall Institute (WEHI) in Australia were part of the USAID/PATH-MVI partnership that ended in late 2014.” (SCG Report 2015)

“The NavOx work continues with the Navy performing a study comparing DNA/ChAd63 expressing CSP+AMA1 or CSP+AMA1+ME-TRAP⁷ with DNA/rAd5 expressing CSP+AMA1 in Ad5-seronegative subjects.” (SCG Report 2015)

“Studies conducted at WRAIR have been designed to address issues relating to overcoming the polymorphism of AMA1. In this regard, a rhesus study was conducted this past year to examine the immunogenicity of Quadvax, to see if a combination of four different AMA1 alleles would overcome the limitations of allelic diversity of the monovalent FMP2.1 AMA1 3D7 vaccine.” (SCG Report 2015)

“The MVDP also has supported some small animal studies in rodents to develop preclinical evaluative models to guide vaccine development. These models include the use of chimeric rodent malaria parasites expressing human malaria vaccine antigens such as MSPI-19⁸ and CSP. The models have been informative in preclinical evaluations of vaccine candidates as noted above in the study with RTS,S and FL [full-length] CSP and the SCG recommends continued support of these models if they continue to be of utility in facilitating vaccine development decisions for these vaccine antigens.” (SCG Report 2015)

“Humanized mouse models at the NMRC that incorporate hepatocytes, human stem cells, and erythrocytes to propagate human *P. falciparum* parasite stages have also been supported by MVDP. This model has been recently reported on and shown to support the full lifecycle of *P. falciparum* (Wijayalath W, et al., Malar J. 2014 13:386.)” (SCG Report 2015)

Summary of other key achievements:

Period	Field trials	Clinical trials	Vaccine conceptualization, actualization and preclinical evaluations
2010–2015	None	AMA1 CHMI Ad prime/MVA boost (2 trials) CelTOS/GLA-SE ⁹ CelTOS/AS01	CSP (3 formulations) AMA1 (3 formulations) CelTOS (many formulations) MSPI (many formulations)
1995–2010	1-MSPI (5 trials) 2-AMA1 (3 trials)	MSPI (US naïve) MSPI/RTS,S MSPI FVO ¹⁰ (US naïve) Ad25/Ad36 CSP	MSPI (many formulations)

⁶ *Plasmodium falciparum* clone 3D7 (from isolate NF54)

⁷ Multi-epitope thrombospondin-related anonymous protein

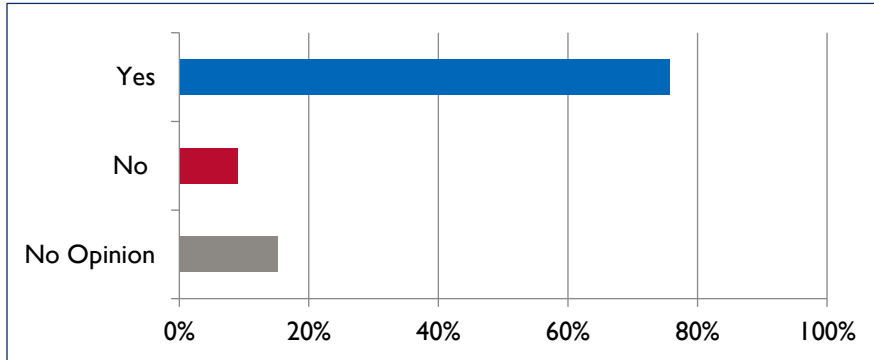
⁸ Merozoite surface protein

⁹ Glycolipid A Stable Emulsion Adjuvant

¹⁰ *Plasmodium falciparum* Vietnam Oak-Knoll Clone

4.1.2 Question 1 survey findings

Figure 1. Is the MVDP an important funder within the malaria vaccine community?

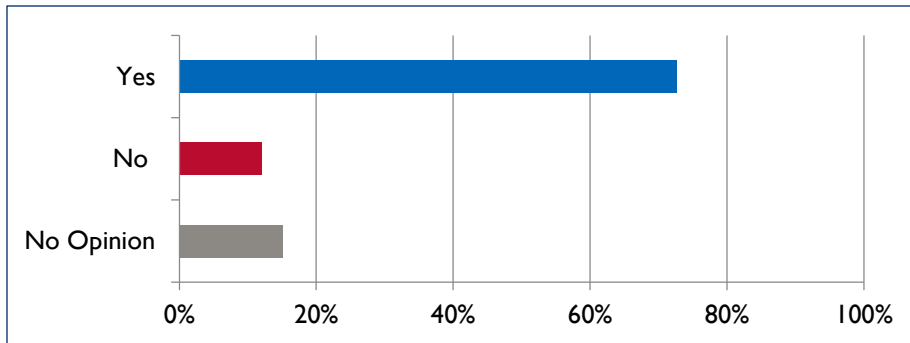


(n=33)

Direct quotes from survey respondents who answered “yes”
“USAID has provided critical leadership and seminal funding over a long period.”
“USAID has been particularly important in retaining a focus and funding on vaccines to prevent clinical malaria, as much of the community has shifted to elimination and eradication focus. The funding is essential and should be increased, if possible.”
“USAID MVDP has been a lifeline to the development of several important antigens that still have serious potential as components of a multi-stage, multi-antigen, second-generation malaria vaccine. USAID support for the military vaccine program, in particular, has kept an extremely important program active and contributing to progress toward an effective malaria vaccine.”
“USAID is funding critical efforts to improve and broaden malaria vaccine targets, increase vaccine efficacy of vaccines under development and establish/maintain vital malaria field reference centers.”
“With NIAID abandoning their dedicated, extramural malaria vaccine program, USAID has become the last government agency to try and bring industry (biotech) into solving this issue through funding efforts.”
“We depend heavily on USAID support for working on blood-stage and liver-stage vaccines that will be cost effective and accessible to the Army.”

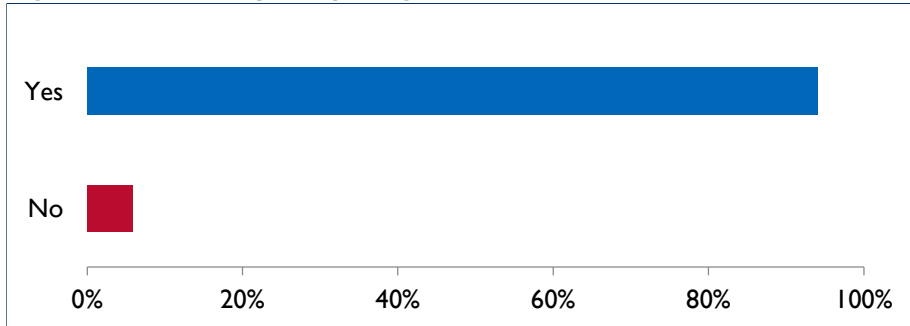
Direct quotes from survey respondents who answered “no”
“It supports programs worth pursuing, especially the U.S. Navy program. The conservative recycling of adjuvants and the same antigens in the U.S. Army program is not likely to yield progress. Bold, innovative steps are needed to spruce up the effort with single protein-based, single-antigen vaccines.”
“They give large amounts of money with no efficiency or strategy.”
“USAID MVDP only funds VERY limited projects—they have been funding blood-stage vaccines for over 20 years, with no significant success. Only recently have they started funding other aspects.”
“USAID MVDP has the potential to be an important funder, but I am not aware of any program in the last five years that it has funded that has been successful.”

Figure 2. Does the MVDP have a unique role or niche?



(n=33)

Figure 3. Is there any compelling reason for the MVDP to continue?



(n=34)

Direct quotes from survey respondents who answered “yes”
“The Military Program is worth maintaining.”
“The malaria vaccine community is struggling for funding on a daily basis. WE NEED MVDP TO CONTINUE.”
“A malaria vaccine is crucial to USAID goals, and no single organization will be able to develop a vaccine. Each organization focuses on its niches, and each might be successful.”
“Persistence is crucial.”
“Again, because they fill a unique niche”
“We do not say good-bye half-way—we must carry this to success...this is also an ethical requirement.”
“If it provides an independent science and data-based funding of novel approaches to the problem with a holistic view and a well-conceived risk and opportunity profile, just like a smart VC [venture capital] fund.”
“Any source of funding can be useful, but it needs to be efficiently managed.”
“MVDP has significant funds that can contribute to combatting malaria.”
“MVDP continues to be a strong voice for malaria vaccine development for global health and continues to provide important leadership. Its flexibility as a program allows it to take advantage of unique scientific and technical opportunities promptly.”
“There is a huge need for continued investment in malaria vaccine to prevent disease and death.”
“Yes. As above, MVDP has played an essential role in the field, and prospects for a successful vaccine would diminish in its absence.”

Direct quotes from survey respondents who answered “yes”
“MVDP fills an essential niche in funding and pushing forward vaccine efforts, building on theirs and others successes to effect improved vaccines. MVDP discontinuation would severely debilitate chances of finding, developing and fielding an effective malaria vaccine worldwide.”
“They have the power through their contractor to provide product development from bench to clinic. That is a unique capability and should be exploited for novel projects that do not get attention from other agencies.”
“Malaria vaccine is suffering severe lack of funding.”
“The funding of malaria vaccine work is low as it is and the loss of one more flexible funding body will only be detrimental to vaccine development.”
“It is important to keep USAID involved in these efforts for political and humanitarian reasons.”
“Yes–MVDP has an unmatched history of efficiently identifying, advancing and evaluating the most promising vaccine candidates. Further, the MVDP has the latitude and leadership to act without excessive bureaucracy.”
“There is a gap in funding that MVDP can fill if it wishes.”
“MVDP is among the few that understand the urgent need to develop an effective malaria vaccine. Their support for a malaria vaccine has led to the development and progress of many promising candidates that are either in early clinical trials or are in the process of one. The malaria vaccine development community urges the continued support from MVDP as they are an important partner in developing an eventual malaria vaccine.”
“USAID should continue to operate its program based on a mission distinct from DOD.”
“There is not a vaccine for malaria that meets target product profiles, duration of protection, against heterologous strains and species. The limited success of some recent vaccines (i.e., RTS,S and PfSPZ ¹¹), while encouraging, [does] not necessarily represent complete success stories. MVDP has played a pivotal role in malaria vaccine development. Their absence in the vaccine community will create a huge void in research, development and funding opportunities.”
“MVDP provides an alternative approach to that being championed by the large funders such as BMGF. It would be unfortunate if the field became completely aligned with the BMGF strategy—it may prove to be unsuccessful. A plurality of approaches is required.”
“The thinking behind the program is very different from other funders, and it has a commitment to long-term funding in a climate where many funders are looking for quick results to grab the headlines.”
“I think USAID’s mandate to prevent infection and disease offers a chance to reduce the burden of malaria in a way that other funders are not doing.”
“Investment in malaria vaccine development is trivial compared to the importance of the problem. MVDP has the potential to make a significant impact.”
“As already mentioned, USAID tends to fund different aspects than the other funders.”
“Developing a malaria vaccine is a high-risk, low-yield venture with minimal interest among for-profit, pharmaceutical.”
“Basic science (e.g., novel antigen discovery) can be funded by NIH, and pre-erythrocytic/ sexual stage vaccines can be funded by BMGF, but no other big funder for translation work of blood-stage vaccines.”
“Provide great funding source for the identification of vaccine candidates.”

¹¹ *Plasmodium falciparum* sporozoite whole organism vaccine

Direct quotes from survey respondents who answered “no”
“Unless USAID MVDP sets itself apart from the rest of the funders and does not copy others’ strategies with either the U.S. military or NIH, its value is limited. However, now is the time to set a new course with a new objective and pursue that objective with line-of-sight, milestones, similar to how the private sector operates.”

What would happen if MVDP funding does not continue?

Direct quotes from survey respondents
“Military Program would falter.”
“Large gaps in our research at NMRC. I believe it would be same for WRAIR.”
“Some promising projects will die.”
“Slower progress”
“A real loss to malaria vaccine development”
“I will guess a more balkanized approach to malaria vaccine development.”
“The loss of MVDP funding would be a significant blow to the malaria vaccine R&D [research and development] community, especially in the area of blood-stage vaccines. The flexibility and accelerated the pace of development that MVDP has brought to the field means that development would slow significantly in key areas.”
“Investment in a critical area of malaria vaccine development will be insufficient, and likely set the field back many years. Could ultimately result in a resurgence of disease and death attributable to malaria given the increasing failure of bed nets and ACTs.”
“Certain promising candidates and approaches would wither.”
“I believe it would set back, or stagnate, needed malaria research, testing, and deployment of an effective vaccine. The remaining funders are not capable (at certainly do not fund) the promising efforts that are sure to make a difference. Other funders are very narrowly focused, and MVDP efforts avoid this trap.”
“Less biotech will be engaged in helping apply novel technologies to develop an effective malaria vaccine.”
“It will be very difficult to carry out our work.”
“Successful malaria vaccine development will falter and be slower.”
“Vaccine development would significantly lag; more children would die.”
“There would be a gap in malaria vaccine development efforts.”
“The wait for a malaria vaccine would be longer.”
“Research and development of malaria vaccines will most definitely be impacted for the worse. The malaria vaccine community needs strong partners such as the USAID MVDP to realize the goal of eliminating malaria.”
“More delays in vaccine development, losses of critical scientific personnel”
“Large sectors of the product development and early preclinical development work would no longer receive support.”
“The focus of vaccine research would diminish in scope and may retard progress towards effective vaccine development.”

Direct quotes from survey respondents
“Malaria vaccine development would become dangerously focused on a very narrow vision of what is needed.”
“MVDP funding has already stopped for my organization, and we are now almost exclusively funded by BMGF.”
“The field would suffer.”
“Very little”
“Nothing except for decreased funding to U.S. military that would otherwise come to a halt. USAID has been instrumental in support of DOD malaria vaccine development activities.”
“Significant reduction in our program and shortfall in vaccine development”
“A key player in the R&D of a vaccine against malaria will be lost, and development activities will decrease, and timeline for vaccine development will significantly increase.”
“Most candidate antigens will not be screened.”

4.1.3 Question 1 findings from key informant interviews

Despite the broad range of organizations and research interests represented by the key informants, this group unanimously agrees that USAID MVDP plays a critical role as a funder of malaria vaccine development.

Significant funding is needed across all areas of malaria vaccine development. USAID MVDP is a valuable funder in the area of disease prevention and mortality reduction. While the amount of USAID MVDP funding is limited, it is critical to many ongoing efforts and becoming more critical as other funders focus resources on transmission blocking.

4.2. EVALUATION QUESTION 2: How is the MVDP complementary to other programs funding malaria vaccine development?

With limited potential malaria vaccine marketability to encourage research and development by the pharmaceutical industry, progress requires synergy and complementarity of public sector initiatives. Thus, to address this question, the evaluators considered the following:

- USAID’s effectiveness in coordinating with its funded MVDP partners
- If MVDP staff have been effective in coordinating with other malaria vaccine donors
- Complementarity of the MVDP with other efforts by funded partners and the malaria vaccine development enterprise at large, and how this can be enhanced

4.2.1 Question 2 findings from document review

The SCG has repeatedly lauded the effectiveness of USAID MVDP in coordinating with funded partners and other funding organizations. Examples from recent SCG reports are numerous:

“A feature of the successful USAID MVDP has been the leverage obtained through highly effective partnerships with a variety of investigators throughout the world.” (SCG Report 2015)

“Despite substantial budget reductions and unexpected delays in contract finalization, preparation or delivery of agents for trials, the USAID team led by Drs. Carter Diggs and Lorraine Soisson has performed outstanding work in maintaining important activities from vaccine concept development to preclinical development, and early clinical trials in experimental medicine. This work has ensured productivity throughout the past year and allowed USAID to continue its valuable contributions to malaria vaccine development into the future.” (SCG Report 2015)

“The SCG continues to note the excellent work of MVDP staff, particularly the contributions of Drs. Carter Diggs and Lorraine Soisson, who bring great credit to USAID, and the Malaria Vaccine Development Program. We note excellent return on investment in maximizing leverage of the funds provided to the investigators and building synergies of complementary programs and encourage continuing efforts to work with other funders to avoid unnecessary duplication of effort.” (SCG Report 2015)

“USAID MVDP also supported an *Aotus nancymae* monkey AMA1 vaccine trial conducted at NAMRU-6¹² in Peru in collaboration with LMVR/NIAID/NIH investigators.” (SCG Report 2015)

“The SCG noted that USAID provided 15% of total USMMVP¹³ funds for the fiscal year 2014 and 17% in 2015. These funds are leveraged to gain additional resources for the program, from Department of Defense (DoD) and non-DoD sources.” (SCG Report 2015)

“The WRAIR team, with USAID support, reached an agreement with GSK to compare their full-length CSP (FL CSP) construct formulated in Montanide and in AS01, and WRAIR's own "RTS,S-like" construct (lacking the N-terminus of CSP) in Montanide, head-to-head with RTS,S/AS01. This agreement represents a major achievement.” (SCG Report 2015)

“The SCG notes that the USAID MVDP continues to maintain very effective partnerships with a variety of investigators throughout the world, and congratulates management on initiating and fostering these links. In particular, interactions with the PATH/MVI program and Oxford University have been collegial and productive, enabling efficient leveraging of funds between the two groups.” (SCG Report 2014)

“We note excellent return on investment in maximizing leverage of the funds provided to the investigators and building synergies of complementary programs, and encourage continuing efforts to work with other funders to avoid unnecessary duplication of effort.” (SCG Report 2014)

“The SCG notes that this is a transitional time for the USAID Program. The long-standing Cooperative Agreement between USAID and the PATH/Malaria Vaccine Initiative is coming to an end this year and is being re-competed. Furthermore, the SCG notes that the leadership of both the Army and the Navy programs have changed with the smooth leadership transition to Dr. Eileen Villasante at the Navy and Dr. Norm Waters now leading the WRAIR program.” (SCG Report 2014)

“The USAID team led by Drs. Carter Diggs and Lorraine Soisson has successfully managed all these transitions, maintained productivity, and positioned USAID to continue its valuable contributions to malaria vaccine development into the future.” (SCG Report 2014)

“As always, the selection of programs and partners by the leadership team has allowed USAID to leverage its limited resources to maximize efforts to develop a malaria vaccine.” (SCG Report 2014)

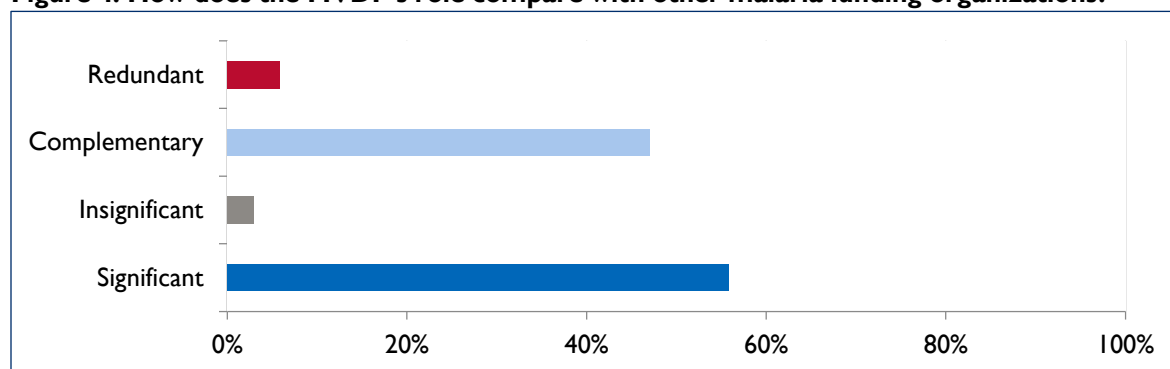
“As always, the SCG must point to the exceptional management of this program by Drs. Carter Diggs and Lorraine Soisson. Their comprehension of a difficult and complex field coupled with their hands-on management style, attention to detail, and collegial interactions make this program a model to emulate. Their important role in participating in meetings of funders of malaria vaccine development is recognized by WHO and other funding agencies.” (SCG Report 2014)

¹² Naval Medical Research Unit Six

¹³ U.S. Military Malaria Vaccine Program

4.2.2 Question 2 survey findings

Figure 4. How does the MVDP's role compare with other malaria funding organizations?



(n=34)

Direct quotes from survey respondents who answered “significant” or “complementary”
“Funding the military program has made progress in this program possible. The internal funding (MIDRP ¹⁴) is only enough to cover running costs, not to manufacture a product or conduct clinical trials. Without USAID, the military program would falter.”
“They have an important role in malaria vaccine development. Very well placed to contribute to ongoing research.”
“As BMGF has focused on TBV [transmission-blocking vaccine], USAID has maintained a focus on blood-stage vaccines and military partnerships.”
“They have entered a niche that is not fully covered by the other agencies.”
“Over the years, MVDP has played a critical role in promoting translational research and maintaining a focus on child health in developing countries.”
“It complements the strong focus on elimination/eradication, particularly from the Gates Foundation.”
“If not for MVDP support, some promising approaches and candidates would never have progressed or would have withered as other funders shifted direction.”
“BMGF has succeeded in creating a sclerotic bureaucracy that mirrors big government and has ceased to be a creative force. The military is a dedicated government lab that is focused on only what they have developed and, therefore, biased in their approach. NIH no longer has a dedicated extramural malaria vaccine program.”
“For our program MVDP support is critical for planning long term, all others tend to be focused on funding their scientific ideas and testing their hypotheses.”
“Politically connected to the interests of the U.S. Department of State”
“MVDP can fill in gaps left by larger funders and thus provide a complementary role.”
“The MVDP is more cost-effective than any of the other programs mentioned.”
“The strength of the USAID effort is its ability to operate its program with its mission and at the same time synergize with the DOD.”

¹⁴ Military Infectious Diseases Research Project

Direct quotes from survey respondents who answered “significant” or “complementary”
“MVDP plays a complementary role with the military malaria vaccine programs and has advanced several vaccines. These funds have been leveraged with internal DOD funding. These accomplishments could not have taken place without this long-standing partnership.”
“MVDP has the potential to play a significant role, because of its budget.”
“Our program leverages USAID funding with funding from other sources, and thus the price tag for a single funder is not too high and, therefore, affordable.”
“USAID is focusing on some vaccine candidate while others focus on other[s], thus each group is complementing each other.”
“Provide funding for the screening of candidate vaccines.”

Direct quotes from survey respondents who answered “insignificant” or “redundant”
“USAID[s] role was based more on testing scientific breakthroughs across the entire malaria community WW [worldwide], not parochial as the NIH or military programs.”
“MVDP has significant funds that can be used to fund vaccine development—however, at the moment, I feel they are extremely restrictive in who and what they fund.”
“In past USAID has mainly supported MVI, which is mainly supported by BMGF.”
“BMGF—diverted by too many secondary agendas—avoid the military, fund international efforts of less merit.”
“The funding available from MVDP has always been relatively modest about that of the larger funders.”
“Unfortunately, there are a lot of me-too projects. Why would USAID need another CSP-based vaccine when there is already one in RTS,S? Put aside petty jealousies and either work to improve RTS,S or change course on another approach, i.e., blood-stage vaccines only. Why does USAID exclude <i>P. vivax</i> vaccines, which is the most prevalent malaria species and is important to U.S. government interests worldwide? There is more to malaria than Pf in Africa. If USAID wanted a niche that stands it apart from other funders, then it should not copy other funders like PATH and EVI [European Vaccine Initiative], which are better funded. It should carve out an area no one else is funding so that complementary rather than competitive activities occur. USAID should not be tethered so close to NIH, as it seems like there are many vaccine projects that are alike.”

4.2.3 Question 2 findings from key informant interviews

The USAID MVDP was repeatedly described by key informants as a “catalyst.” The abilities to work across different research groups and to leverage funding from multiple sources are seen as program strengths. There is not enough funding in the USAID MVDP to support an entire vaccine development effort, so what was described as its flexible and focused support in critical research areas that lack other sources of funding is seen as desirable and effective. USAID MVDP funding in these areas has supported the advancement of projects to the point where other funding sources are available.

USAID MVDP support of the WRAIR and NMRC programs has been critical, and both look forward to broad USAID MVDP involvement in their programs going forward. It is widely felt that these have been successful relationships.

MVI valued the recent funding relationship with USAID MVDP, which was felt to be mutually beneficial. It allowed for coordinated support for some programs and expanded the malaria vaccine development expertise available to both USAID MVDP and MVI.

However, there was broad support among key informants for USAID MVDP to have a simple mechanism to evaluate potential new partners or new ideas. The best mechanism for doing this was admittedly unclear by most interviewed, and no single, well-tuned mechanism could be advanced. An NIH-like model based on responding to a request for proposals was felt to be the wrong approach, as it would require massive additional support and potentially take funding away from vaccine development efforts. Expanded use of the SCG was one option brought up by some informants, who felt the SCG could have a prospective role in deciding what the USAID MVDP evaluated and funded, in addition to its role in reviewing the program. This would clearly need detailed development before it could be evaluated as an option. Other informants felt that, because of its small and well-connected leadership team and longstanding relationships with other funders, the USAID MVDP is already appropriately positioned and informed to determine which partnerships and ideas to fund, and there just needs to be a simple mechanism to present new ideas. It was acknowledged that a “Rob Peter to pay Paul” scenario could arise, as currently there is fixed, limited USAID MVDP funding.

There was very broad support for the USAID MVDP leadership team. Drs. Carter Diggs and Lorraine Soisson were repeatedly recognized for their longstanding leadership in the malaria vaccine community. It was noted they had broad involvement in the community, from convening and policy roles to evaluation of specific vaccine platforms and candidates. With praise for the current, stable, expert leadership in the USAID MVDP, there was also wide support for investment in the leadership team of the future. Informants felt it would take years to develop someone to replace the current team.

4.3. EVALUATION QUESTION 3: Given the historical role of the MVDP, is this role critical going forward, or, given the changing funding environment for malaria vaccine development, should the focus of the USAID MVDP strategy be modified?

The context for this question is:

- Currently, a large proportion of malaria vaccine funding worldwide is devoted to vaccines as tools to facilitate malaria elimination, in contrast to the USAID MVDP focus on enhancing malaria control.
- A licensed, partially effective vaccine with a relatively short duration of action targeting malaria control may be available in 2016.

4.3.1 Question 3 findings from document review

The SCG has been clear in its reports that the current USAID MVDP focus is appropriate. Despite the changing environment, MVDP’s role is critical going forward, and the current focus should continue.

“The focus on elimination does not diminish the ongoing value of the approaches of the MVDP and several other groups that continue to work on the development of disease-modifying vaccines. They, as well as senior leaders of the Gates Foundation, agree that these vaccines would play a very important role in reducing morbidity and mortality in areas of current high transmission, such as Heartland Africa where malaria remains an enormous risk to children, their mothers, and any non-immune entrants to those areas. The need for different types of vaccines is mirrored in the malaria vaccine roadmap that has two strategic goals, one related to clinical disease and the other around interruption of transmission.” (SCG Report 2015)

“The SCG continues to believe that at a time when there is no transmission blocking vaccine close to deployment it would be premature to scale down on the search for an effective blood-stage vaccine. Indeed, as increasingly large proportions of the world, especially in Africa, declining immunity due to reductions in transmission, there is already evidence that epidemics of clinical disease in previously immune populations will become a major public health threat. In such circumstances any vaccine that includes components capable of limiting the development of clinical disease would be clearly desirable.” (SCG Report 2015)

4.3.2 Question 3 survey findings

Figure 5. Given the BMGF’s focus on a transmission-blocking vaccine, is there value in continuing to develop a vaccine that prevents disease?

Answer Choices	Responses	
Yes	100.00%	34
No	0.00%	0
Total		34

Direct quotes from survey respondents who answered “yes”
“A pre-erythrocytic stage vaccine that blocks infection will prevent disease and block transmission at the same time.”
“We need a highly protective vaccine for malaria to protect those in endemic areas as well as travelers. The focus of BMGF is a separate issue.”
“TBV may not work, and drugs and insecticides are failing. Vaccines are needed to help now and in future.”
“While the ultimate goal is eradication, lessening of disease is a worthy goal.”
“As long as there are disease and death in Africa, it is critical to continue blood-stage vaccines.”
“For high-burden countries and population groups, yes.”
“There will eventually be breakthrough transmission and thus asexual disease even if TB vaccine is brilliantly successful—the population would be of low naturally acquired immunity or zero immunity in young people to asexual disease—hence a very high morbidity and mortality that would cause the TB vaccine to be seen as a failure.”
“Transmission blocking requires high-level penetrance of the population. Doubtful to eliminate disease without a buffer.”
“TBV are just one part of the portfolio; as is well known, TBVs will not prevent individuals from suffering the consequences of the disease. Therefore, instead of focusing entirely on TBV significant efforts need to be put into developing more efficient ways of delivering pre-erythrocytic vaccines, which will help the recipients, and also, also serve in reducing transmission by reducing the extent the number of infected individuals.”
“Unless transmission can be completely interrupted, there will always be the concern that malaria could resurge, and therefore, there will be a need to prevent malaria disease.”
“Morbidity and mortality levels are still unacceptably high, and other interventions (drugs, bed nets) are showing signs of failure.”
“As a component of a vaccine that interrupts transmission, to improve the benefit to recipients, and anti-blood-stage activity may well enhance the ability of a multistage vaccine to interrupt transmission as well as preventing disease.”
“TBV hold great promise but is just one aspect needed to prevent malaria. Should TBV not cover the population or parasites/vector adapt, the population should not be left “unprotected” against malaria. Bed nets and a direct vaccine are needed to combat this disease.”
“The blocking of the transmission of the parasite has not been proven. TBV are completely theoretical and what is needed for preventing morbidity and mortality from malaria.”

Direct quotes from survey respondents who answered “yes”
“TBVs are unlikely to work due to the inability of humans to maintain high levels of antibodies needed to block 100 percent transmission, as indicated by several failed human trials. There are also no assays that measure actual transmission in the field; most in vitro assays look at oocyst counts rather than sporozoite transmission rates.”
“TBV are not likely to be completely effective, and there will still be clinical disease although transmission may be reduced.”
“Focus should not be transmission blocking exclusively, given the low likelihood that this type of vaccine ALONE could eliminate transmission.”
“The two approaches are complementary. A disease-preventing vaccine is a needed component until all transmission is stopped.”
“Until the parasite is eliminated, a vaccine that reduces the burden of disease while not increasing the parasite reservoir in the human host is still needed.”
“It is most important to prevent disease and death.”
“The ultimate goal of a malaria vaccine is to prevent the suffering and mortality caused by the parasite. For this to happen, a TBV has to be near 100 percent effective. Given that none of the current TBV candidates in clinical trials have been this effective, it would be prudent to continue developing vaccines that prevent clinical disease. To be effective, an eventual malaria vaccine will need to comprise components that target all the life cycle stages.”
“Uncertain efficacy against pre-erythrocytic stages requires alternative platforms.”
“Transmission-blocking vaccines have not been as effective in clinical trials as has been seen in animal models. Anti-disease vaccines can reduce morbidity and mortality, which will have a direct benefit to populations.”
“Classical studies in the 1960s showed that passive immunization of children with adult IgG had a profound effect on blood-stage parasitemia. We still have not identified the antigens that are the target of such IgG and shown that this effect can be replicated by vaccination. A vaccine that prevents death and disease is surely still a high priority.”
“Evolutionary theory suggests that the parasite will adapt to the introduction of vaccines and that elimination is far from being a realistic target. Malaria is likely to be with us for many decades (or more), and preventing people who acquire malaria from falling [ill] and dying is thus an important component of an effective vaccine.”
“The pathway to license a TBV may be long and complicated and may become more challenging once RTS,S is widely available. The availability of a next-generation vaccine with higher efficacy that can reduce infection and disease will have a more straightforward development pathway, and may be a very important public health tool as the incidence of malaria declines and the prevalence of non-immune individuals increases. I think USAID could help fulfill an important need in this area while the BMGF focuses on blocking transmission.”
“For an individual, no vaccine will entirely prevent infection and thus disease in 100 percent of recipients. It would be useful to have an anti-disease component for those who have breakthrough infections.”
“The development of a transmission vaccine is likely to be difficult and be well behind a pre-erythrocytic vaccine.”
“The premise above is wrong. BMGF wishes to interrupt transmission that leads to elimination. A pure TBV is only a small avenue toward that goal and is NOT the only viable approach. The USAID approach does not have vision or objectives that lead to either prevention of infection (which is the best way to prevent disease) or objectives that are aimed at preventing disease.”

Direct quotes from survey respondents who answered “yes”
“Preventing the spread of the disease will be of great value for reducing the cases of malaria (even in non-vaccinated subjects).”
“The purpose of a transmission-blocking vaccine and a vaccine to prevent malaria in the non-immune adults are different and complementary. Both vaccines type of vaccines need to be developed.”
“We should cover the whole population to make a TBV effective, and the vaccine should maintain high titers by itself, because many epidemiology studies have shown that natural infection cannot boost (or almost none) even Pfs48/45 and Pfs230 antibody responses. It is logical to try a “relatively easier” approach first.”
“To be effective, a malaria vaccine needs to cover the whole life cycle of the parasite.”

Figure 6. Given advances in RTS,S, is there a need for additional work on a vaccine to prevent disease?

Answer Choices	Responses	
Yes	100.00%	34
No	0.00%	0
Total		34

Direct quotes from survey respondents who answered “yes”
“RTS,S has been shown to be only partially protective with limited duration.”
“Effect of RTS,S is less than 50 percent; its effects on mortality are unknown.”
“RTS,S is partially effective”
“The importance of saving lives has to be primary as we await the elimination of malaria. RTS,S is not very effective in infants.”
“RTS,S technology reflects the best knowledge of 20 years ago! We know a lot more about malaria biology now. Asexual vaccine candidates today would be very different antigen constituents.”
“Poor long-term RTS,S protection”
“Recently, great strides have been made in improving the efficacy of RTS,S—however, if such efforts were made several years ago, we would have been further along and have had results from larger studies. All modifications were put on hold after the initial success. If time and money had been spent in refining the dose and schedule, we would have a vaccine with higher efficacy much earlier. Similarly, we need to continue working on alternate strategies so that we do not waste several more years in case a better candidate/regimen is found.”
“The RTS,S vaccine confers modest efficacy of short duration. We can and should do better with second-generation malaria vaccines to prevent disease.”
“A vaccine with high efficacy and longer durability of protection is needed (see WHO roadmap).”
“Efficacy is well below any reasonable target.”
“RTS,S, while reducing clinical cases, is not sufficiently protective to get to complete (90-100 percent) population protection and remains limited to <i>P. falciparum</i> (until proven otherwise).”

Direct quotes from survey respondents who answered “yes”
<p>“RTS,S has proven that the CSP molecule can protect, but improvements on it and the addition of a blood-stage vaccine is also critical. Further, considering that the access to RTS,S is limited, there should be an effort to develop a better molecule and a smarter adjuvant that is available to the community.”</p>
<p>“Cost and access and improvements”</p>
<p>“EVI has clearly identified [blood-stage] vaccines as a priority due to the lack of efficacy of RTS,S to prevent the transmission (lack of efficacy on parasitemia: as long as the parasite is circulating in the blood it can be transmitted) and the lack of good candidate for TBV sexual stage.”</p>
<p>“RTS,S, despite the publicity, is not an effective enough vaccine and only reduces clinical disease partially and probably not effective at reducing transmission significantly.”</p>
<p>“As indicated above, I think that that MORE work needs to be done to develop a blood-stage vaccine that reduces morbidity. This is especially critical at present, since rebounds in malaria morbidity and mortality are likely to increase with better vector control that reduces but does not irrevocably stop transmission. I work in western Kenya at present and believe that the communities where we are working are experiencing such a rebound at present.”</p>
<p>“It is a categorical imperative to continue to advance the pre-erythrocytic vaccines. RTS,S/AS01 in the extended boosted, reduced dose format is incredibly promising, and likely represents a significant advance over the present regimen. Also, other VLP [virus-like particle] antigens have yet to be systematically and empirically evaluated as combinations to augment CSP-based vaccines.”</p>
<p>“A vaccine that has a longer duration of protection and higher efficacy than the pediatric RTS,S is needed.”</p>
<p>“RTS,S has low efficacy. A high-efficacy, durable vaccine is needed.”</p>
<p>“The RTS,S vaccine still has long ways to go as it has only [around] 30 percent efficacy in infants and [around] 50 percent efficacy in older children. Furthermore, recent data suggest that polymorphisms in the CS protein may limit the vaccine efficacy, at least in some age groups. Moreover, this vaccine does not protect against clinical disease. However, a next generation RTS,S vaccine that overcomes many of the shortcomings could be an important part of an eventual multi-component malaria vaccine.”</p>
<p>“Financial viability of RTS,S is limited. The platform has never been optimized, and needed investment by GSK is doubtful.”</p>
<p>“Current vaccines, including RTS,S, have not shown long-lived immunity; furthermore, the RTS,S vaccine is solely focused on the 3D7 strain parasite, which is not naturally prevalent across field settings.”</p>
<p>“RTS,S provides some protection against infection and pre-erythrocytic stages but has no effect on asexual blood stage development. Therefore, there is a clear need to develop a vaccine that targets the stage responsible for the disease.”</p>
<p>“RTS,S does not fully prevent infection and will make only a small contribution to reducing mortality and morbidity.”</p>
<p>“If eradication is the ultimate goal, and in areas where transmission remains high, a vaccine that includes an anti-disease component should help reduce the numbers of parasites that proceed to sexual stage development and also introduce a level of immunity within a community that also protects immunized individuals and not just inducing antibodies that block human to mosquito transmission.”</p>

Direct quotes from survey respondents who answered “yes”
“The protective efficacy of RTS,S is lower than any licensed vaccine and is lost relatively rapidly. It is hard to understand where it will be used if ever used.”
“RTS,S is completely insufficient. It has limited durability.”
“Question 15 is biased to give but one answer. Of course, additional work is needed, but with dramatic decreases in clinical malaria over the past 15 years with proven tools that already exist, one could conceivably argue that a vaccine is not needed. Doubling down on proven interventions like antimalarial drugs and ITNs [insecticide-treated nets] will continue the downward trajectory toward elimination.”
“RTS,S is currently only protecting 30 percent in the field—and this is only a reduction in mortality. This is not a useful vaccine.”
“RTS,S is of no value to non-immune adults.”
“Based on the efficacy and duration of protection, I don't think many countries will use the RTS,S as a real vaccine.”
“RTS,S vaccine efficacy does not attain the WHO goal for use in transmission settings. Efficacy is comparable to the use of bed nets.”

Figure 7. Should the malaria vaccine community focus on both transmission blocking and disease prevention?

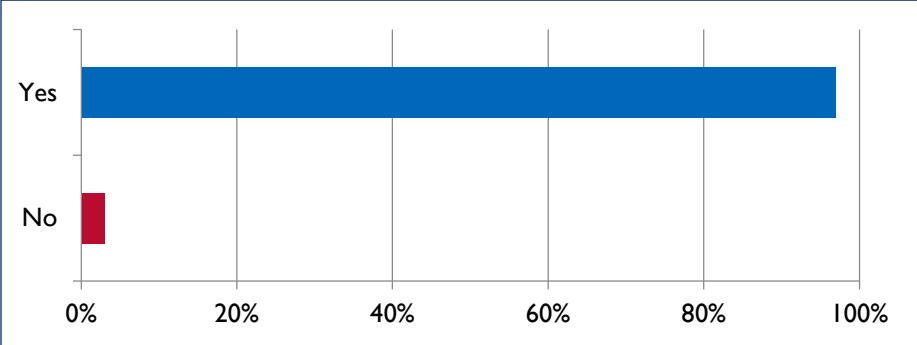
Answer Choices	Responses	
Yes	100.00%	34
No	0.00%	0
Total		34

Direct quotes from survey respondents who answered “yes”
“I am not a strong supporter of blood-stage antigen malaria vaccine development. I would suggest passive immunization as a stronger approach, or whole organism blood-stage vaccines (Michael Good, etc.)”
“We need to prevent infection/disease as well as prevent transmission. This is the surest way to move to eradication in my opinion.”
“All approaches should be pursued for such a staggering public health problem.”
“Both are relevant objectives.”
“And pre-erythrocytic vaccines. However, RTS,S is a pre-erythrocytic vaccine that is evaluated by its effect on disease, and it was not very effective.”
“As this is the most effective approach to reach elimination and eventually once eradication”
“They each will add value to each other.”
“It does not make any sense to put on hold vaccines that will prevent symptomatic infection.”
“Transmission blocking and disease prevention are complementary aspects of malaria control and elimination, and should be pursued concurrently.”

Direct quotes from survey respondents who answered “yes”
“Morbidity and mortality are still unacceptably high, and eradication will take many decades. A vaccine preventing clinical malaria will also be important during elimination/eradication campaigns, to prevent epidemics, as natural immunity will be very low.”
“These are not mutually exclusive. A vaccine that does both is far more attractive than one that does only one and not the other.”
“Malaria disease prevention efforts are making a positive impact. At least, until malaria is eradicated, disease prevention is needed to afford TBV its best chance of success. TBV will take some time to “take” sufficiently in a population to adequately cover/protect a population from disease. It is unknown the impact of foreign travelers (with or without malaria) on the success of TBV coverage (will it sufficiently blanket the population with international travelers bearing malaria disease, for instance?).”
“Both are important endeavors and should continue in parallel. Scientific lessons learned from all these efforts funnel to the greater understanding of the parasite life cycle and how to attack it.”
“But with emphasis on disease prevention”
“The probability of success of TBV is low when considering the attrition of the pipeline.”
“It will require both types of vaccines to be effective in areas of intractable high and moderate transmission.”
“A combination would decrease the spread of vaccine-resistant strains, thus extending the utility of the pre-erythrocytic components.”
“The ability of TBVs to reduce parasite burden to the point of extinction is theoretical and highly risky.”
“Disease prevention is attainable sooner than transmission blocking and is more important.”
“Absolutely. I think it goes together. A multi-component malaria vaccine targeting all life cycle stages will be needed to eliminate malaria. It is, however, important to emphasize the need for an effective vaccine that prevents disease, which is the single most important reason many of us work on malaria.”
“Future efficacy of pre-erythrocytic and blood-stage vaccines is unknown. Transmission-blocking candidate provides some mitigation should other candidates fail.”
“A broad portfolio of approaches may be necessary, since it is not clear as yet which vaccine will have the greatest impact, under which setting of endemicity. While there are encouraging results from recent clinical trials, it is too premature to consider that the malaria vaccine effort is done.”
“There is a clear need for anti-disease asexual blood-stage vaccines. While the theoretical benefit of transmission blocking is clear, this approach has not been properly validated at the population level. If BMGF put their resources into transmission-blocking vaccines, this allows other organizations to fund complementary approaches such as vaccines for disease prevention.”
“Both of these approaches will reduce disease burden and in combination may be more sustainable.”
“It depends on what is the ultimate goal of the USAID. If they are aligned with the BMGF on wanting to eradicate malaria, then treating cases and reducing transmission simultaneously would hopefully expedite both the reduction in the burden of disease and reduce transmission. “
“The primary focus should be a pre-erythrocytic stage vaccine that prevents infection, disease, and transmission. A blood-stage vaccine that reduces morbidity only will have a chance of being deployed if used with a highly effective pre-erythrocytic stage vaccine.”

Direct quotes from survey respondents who answered “yes”
“Blocking transmission is critically required to get toward elimination. Disease prevention alone will not get toward elimination, as it does not address the asymptomatic reservoir of parasites. Preventing infection through a pre-erythrocytic vaccine, which provides efficacy of greater than 80 percent with a long duration of one year, may be achievable.”
“Both approaches—reducing the infections and reducing the morbidity—[are] more promising than a single target alone.”
“Different population groups have different needs. Transmission-blocking vaccine will assist in disrupting the malaria life cycle and thus, help to achieve eradication of malaria, while a vaccine for prophylaxis will protect non-immune adults traveling to the endemic area as well [as] protect children from malaria. The war against malaria needs to be on different fronts.”
“Ten years ago, experts recommended NIAID malaria vaccine group to stop developing any TBV. We don’t know what will happen 10 years from now. Since it takes a long time for human resources development, I feel it is a wrong decision to terminate completely anti-blood stage vaccine development while weight can be changed from time to time.”

Figure 8. Should the MVDP continue to work on pre-erythrocytic and blood-stage based vaccines against *Plasmodium falciparum*?

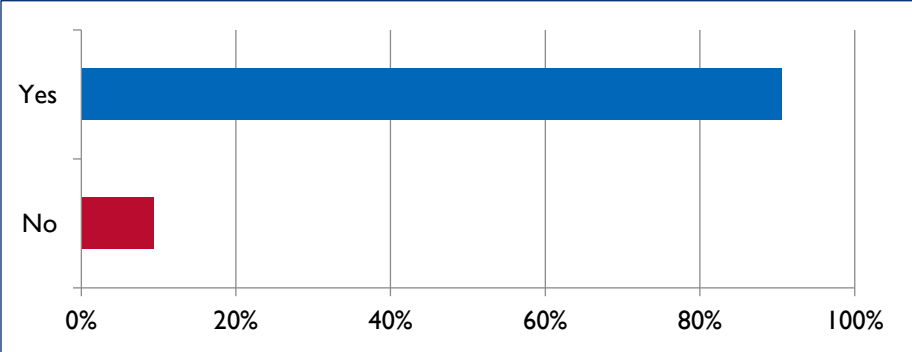


(n=33)

Direct quotes from survey respondents
“Pre-erythrocytic stage vaccines, in particular, offer the possibility of preventing infection, which would be a very good thing.”
“I believe that this is the approach through which we will develop the first highly effective malaria vaccine.”
“These vaccines have a strong rationale, and there is evidence that these targets can be protective in humans.”
“It is an important goal.”
“Again, it fills a unique niche in funding asexual blood stage.”
“Given all advances, we are in a favorable situation.”
“Malaria will evolve away from any single approach unless it provides 100.00 percent complete protection in all patients—and that isn’t happening in 10 years.”
“Blood-stage vaccines may not prove fruitful.”
“There is still much work to do in both areas, and they are complementary aspects.”
“These are important approaches. In particular, other donors are not adequately funding blood-stage approaches.”

Direct quotes from survey respondents
“I believe that the two most promising approaches are a subunit multistage, multi-antigen vaccine or a whole organism vaccine. The former will depend on having a menu of candidate antigens of different stages to arrive at the right combination.”
“An effective vaccine to <i>P. falciparum</i> is needed to eradicate malaria effectively.”
“Reduce the morbidity and mortality.”
“Blood stage is the one that causes death and disease, and it is the only stage whose antibodies can be boosted by natural infection.”
“There is a need for both types of vaccines.”
“Yes. There is too little serious global effort in this arena.”
“To fill the gap in funding”
“These are the stages most likely to save lives. We do not have proof of concept that transmission blocking is achievable in humans, and even if it works it may not be a deployable measure.”
“Again, USAID efforts synergize with DOD's program.”
“MVDP leveraged funding has created research teams with expertise in antigen discovery, product development, preclinical studies, clinical trials and clinical immunology. These efforts would be substantially affected by the loss of support from MVDP.”
“These areas still have the potential to make a highly significant contribution to malaria vaccine development.”
“It should focus more on pre-erythrocytic stage vaccines.”
“Only when pre-erythrocytic vaccines, that improve RTS,S. Any blood-stage vaccine must be added to RTS,S as there is no value [in] testing through phase 3 another vaccine, which will cost from 300-500 million dollars. Even then, there are NO blood-stage vaccines currently under development that show that it will make it past phase I trials.”
“Blood stages (as long as they are not directed against polymorphic targets such as AMA-1) can be the second line of defense when the pre-erythrocytic component of the vaccine fails.”
“Much is yet to be learned. Both types of vaccines need to be studied.”
“Best stage to prevent infection from occurring”

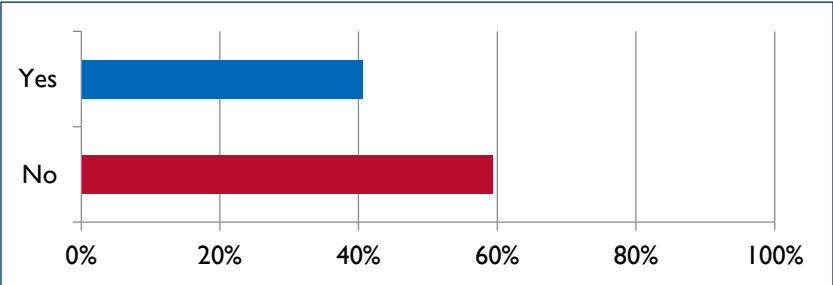
Figure 9. Should the MVDP work on new vaccine candidates?



(n=32)

Direct quotes from survey respondents	
	"I don't think CelTOS is going to jump from no protection to high-level protection."
	"Whole sporozoite vaccine platform"
	"There are few promising new candidates."
	"We need new vaccines."
	"Always important until successful"
	"You need to be broad in identifying where the true potential is."
	"MVDP need not focus on vaccine discovery per se, should focus on converting targets of immune responses into vaccine candidates that can undergo further evaluation."
	"I think this is critical, given the current global portfolio and the general failure of many leading approaches of the last decade (e.g., AMA1, MSP1, etc.)."
	"A core activity"
	"Discovering and developing novel vaccine candidates can broaden the target vaccine repertoire, improving the breadth of impact, and most likely is the best route to improving vaccine efficacy of promising vaccines currently being tested in clinical trials. Research to support what is valuable and what can supplement RTS,S, for instance, will pay off in the effort to eradicate malaria."
	"Attrition of pipeline"
	"This is critical if malaria vaccine development is to be successful."
	"We need to revisit blood-stage vaccines in the light of the weak justification for using RTS,S."
	"A systematic effort should be made to advance to phase I/2 trials 10 promising sporozoite/early hepatic antigens in VLP format."
	"Use very stringent target validation criteria to identify those that should go into clinical testing."
	"Better candidates are needed."
	"I'd like to see more support for <i>P. vivax</i> malaria vaccine discovery efforts funded by USAID, particularly in discovery and development of blood-stage culture of <i>P. vivax</i> ."
	"Only after a full evaluation of the current candidates and their down-selection"
	"Identification of new vaccine candidates is still a top priority."
	"We have very few candidates, and the newly emerging ones are very promising."
	"It should expand its repertoire."
	" <i>P. vivax</i> —no other funder is supporting this. Why would USAID exclude countries in Latin America, East Africa, India, Pacific Islands and SE Asia? It makes no sense."
	"Identify candidates to move into the design pipeline."

Figure 10. Should the MVDP work on adjuvants?



(n=32)

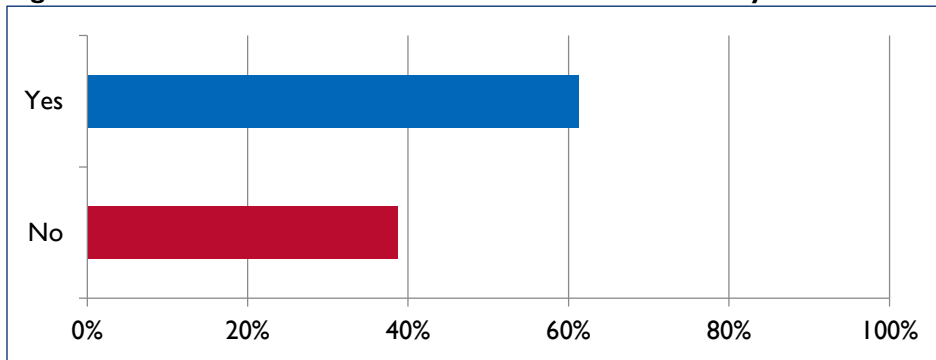
Direct quotes from survey respondents who answered “yes”
“We need new adjuvants.”
“Maybe. IDRI [Infectious Disease Research Institute, Seattle] makes adjuvants for the public sector. The other real need is to produce virus-like particles such as being done by Ali Salanti in Copenhagen.”
“There are hardly any good ones—only very few—in routine use.”
“Maybe critical”
“This is critical to improving vaccine candidates, especially on magnitude and durability of immune responses necessary for successful vaccines. This is not just a question of adjuvants, however, but more broadly of novel formulation and delivery systems, e.g., nanoparticles.”
“Resources permitting”
“While there are a few adjuvants eliciting strong impact on vaccine efficacy, they are limited by IP and toxicity. Adjuvants that can improve different vaccine platforms may thrust a moderately protective and very safe vaccine into a safe and strongly protective vaccine.”
“This is the means by which to break the t-cell exhaustion that is seen with most viable antigens (i.e., CSP).”
“This is an important area of research that is of general interest to vaccinology, not just malaria.”
“GSK should be compelled to share the AS01 adjuvant.”
“Make adjuvant available during in vitro assays.”

Direct quotes from survey respondents who answered “no”
“I am worried about the side effects of adjuvants. What we have on the shelf now is good enough. Too big a job for USAID to tackle.”
“Expensive and outside of USAID focus”
“Given MVDP’s limited financial investment, I would leave this to other, better-funded groups, and leverage their findings. Maximal resources should be applied to malaria-specific activities, such as target identification, lead identification, lead optimization, etc.”
“Too big a task for MVDP”
“Effort better left to industry”
“There are adjuvants currently in development that need to be fully characterized. Expertise in adjuvants formulation should be done through partnerships with formulation experts.”
“I think industry may be better suited to this. Good adjuvants will be generic—i.e., for use with lots of vaccines, not just malaria.”
“BMGF is heavily involved in this area.”
“If USAID wants to become another NIH, then go ahead and pour in [money] for new adjuvants, which take a minimum of 20-30 years to develop, test and get past safety concerns. They should focus on using adjuvants that already are state-of-art and approved for use (AS01 for malaria and VZV ¹⁵ , MF59 ¹⁶ for flu).”

¹⁵ Varicella zoster virus

¹⁶ Novartis adjuvant

Figure 11. Should the MVDP work on correlates of immunity?



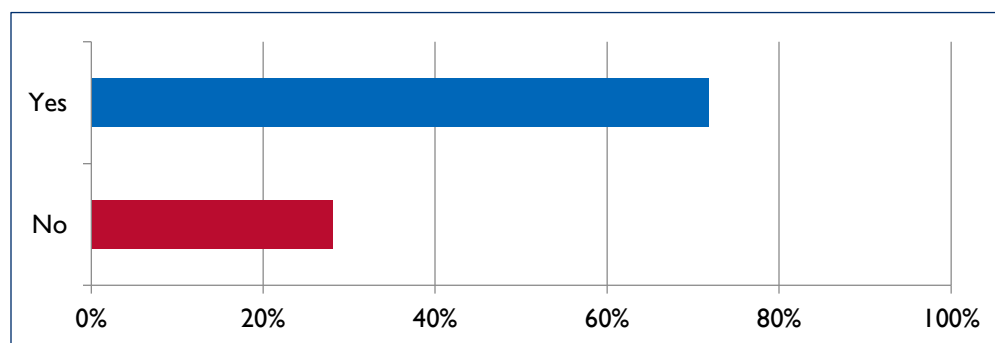
(n=31)

Direct quotes from survey respondents who answered “yes”
“Always useful to do—but should be subsidiary to larger efforts.”
“We need to understand this.”
“Always important to understand how the vaccine is working and help in pointing the way to other vaccines.”
“Key for trials and introduction...we need this.”
“This is necessary to guide rational vaccine design and development.”
“Critical to accelerate vaccine development efforts.”
“Important for early vaccine development”
“Useful endpoints for judging efficacy”
“Again, a logical synergy with DOD”
“The development of clinical challenge models enables a much more focused approach to facilitate the definition of correlates.”
“Understanding correlates of immunity will help inform rational vaccine design.”
“In my opinion, the most of the knowledge obtained from rodent model (including humanized mouse model) are a minor impact on real vaccine development, regarding correlates of immunity. This aspect should be tested more using CHMC model, but it is difficult to find a funder for such "research-translational" studies.”
“A correlate of immunity will allow the identification of good vaccine candidates.”

Direct quotes from survey respondents who answered “no”
“Seems outside USAID focus—focus should be tied closely to products.”
“Time sync and little past utility”
“There is an insufficient empiric effort to identify the prerequisite additional protective/partially protective antigens. Once found, then their correlates can be examined.”
“Leave this to NIH.”
“Natural immunity is pretty irrelevant to vaccine design.”
“In the absence of a protective vaccine, correlates of immunity are relatively non-informative. And animal models have not yet been fully validated to be predictive of human responses.”

Direct quotes from survey respondents who answered “no”
“This is a bit of a minefield, and MVDP needs to retain its focus on vaccine development.”
“Same as above. USAID should focus on translating basic findings to clinical trials.”
“The goal with MVDP should be in rapidly getting a candidate in the clinic, not correlates, which are a more academic endeavor.”
“Unless the immune mechanisms associated with protection (surrogate markers) or correlated with protection are known, the down-selection of vaccines is almost impossible and require[s] many expensive clinical trials.”

Figure 12. Should the MVDP work on exploring other technologies?



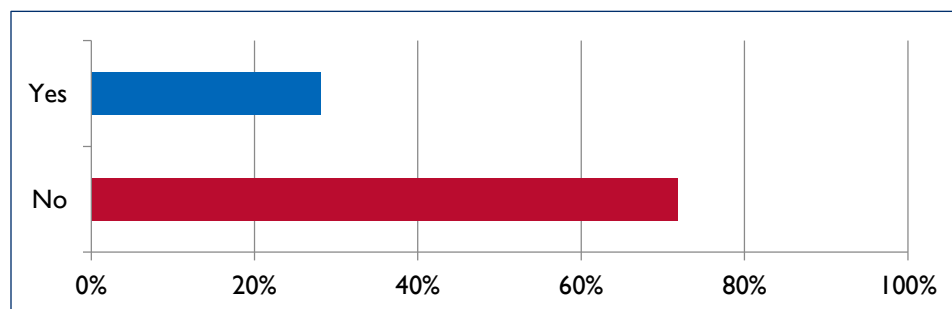
(n=32)

Direct quotes from survey respondents who answered “yes”
“Yes—whole organism vaccines, for example. There is a good chance Sanaria's vaccines will be licensed for use, and USAID will not even have participated. USAID should join the consortium and play a role.”
“If cost-effective and tied closely to products”
“If possible”
“VLP”
“Always, in order not to lose the link to recent advances”
“See answer to question 48, which also applies here. Also, novel vaccine delivery technologies need to be investigated.”
“In an opportunistic way and depending on resources”
“MVDP, in pursuing other new technologies, has helped develop a very promising niche in malaria vaccine development. Vaccines critical to RTS,S were first funded in part or totality by MVDP.”
“The risk is the advantage that government can afford.”
“Find, produce and test additional sporozoite/early hepatic antigens as VLPs.”
“Yes, to a degree. Malaria has most of the best technologies under assessment, but a watching brief is needed. Avoid hyped new approaches like RNA.”
“Absolutely. There is a constant need to evaluate current technologies and improve or develop new ones that will improve vaccine efficacy.”
“Where relevant to enhancing the immunogenicity of malaria vaccine candidates”
“Yes, but I don't think this should be a major focus.”
“New vaccine technologies other than recombinant subunit vaccines should be explored.”

Direct quotes from survey respondents who answered “yes”
“Currently, USAID supports with low confidence in the rationale the latest and greatest in vaccinology without input from immunologists. New technologies may push the limited success over the threshold and lead to an efficacious vaccine.”

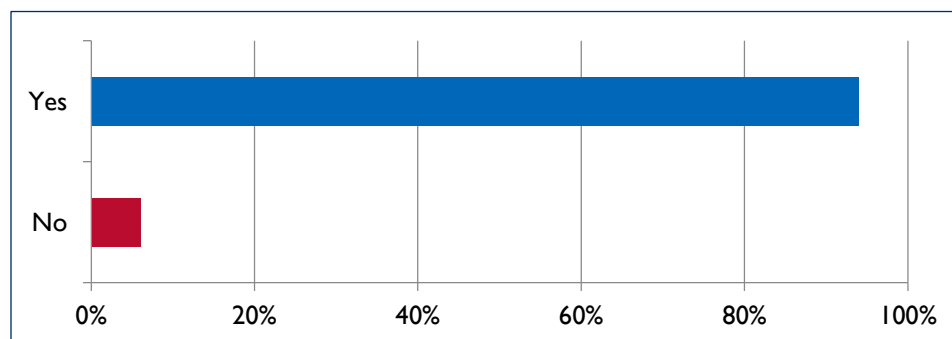
Direct quotes from survey respondents who answered “no”
“I would limit the focus to the malaria-specific elements and not invest heavily in platforms. Rather, suggest leveraging learnings from better-funded areas, such as HIV, cancer, etc., and applying them as needed.”
“Leave this to others.”
“Effort better left to academia and NIH. USAID could help accelerate work once proof of concept demonstrated.”
“While recognizing the need for new technologies, these are often in their infancy about clinical development and thus would require a much more significant investment in resources and funding.”
“This is NIH’s purview.”
“Stay focused.”

Figure 13. Should the MVDP work on building field sites?



(n=32)

Figure 14. Should the MVDP work on clinical trials?



(n=33)

Direct quotes from survey respondents who answered yes
"A key investment"
"We are significantly slowed in DOD research on PfSPZ Vaccine and PfSPZ-CVac because of lack of adequate funding."
"USAID should be taking promising candidates to the clinic, especially when other funders decline as being outside their scope."
"Needed"
"When there are vaccine candidates, clinical trial essential next step."
"Clinical trials represent an essential part of vaccine development, and MVDP should include this in its portfolio of activities. However, MVDP should seek to partner with other agencies, as clinical trials often require specialized infrastructure and can become quite expensive."
"Yes, where preclinical data are supportive. Particularly human challenge trials."
"Particularly early controlled human malaria infection trials of both pre-erythrocytic and blood-stage vaccines"
"MVDP is well positioned to test the vaccines they have helped develop."
"Fast to clinic allows the ultimate test of a vaccine's utility."
"POC in CHMI"
"Will be important for testing multistage multi-antigen subunit vaccines (in the future)."
"Yes. Especially phase 1/2 challenge trials, which have now been validated as having negative and positive predictive value for making go/no-go development decisions."
"Take advantage of CHMI."
"Essential—ow else can we determine what works?"
"Again, logical synergy with DOD."
"Clinical trials should be considered in conjunction with product development. Huge investments have been made in product development and preclinical studies, and following validation of an antigen or formulation; this should then lead to clinical trials."
"It is essential that early studies in humans are part of the development plan."
"But only [if] the budget increases substantially—might be better to engage with industry and MVI to do this."
"In many cases, preclinical models are not predictive of human outcomes, so expanding the opportunities for clinical testing of promising preclinical candidates will help guide development decisions."
"The only way to determine if a vaccine works is through clinical trials."
"Only by testing vaccines in humans do we learn something. They should devote 80 percent of their funding for early-stage manufacture and testing by answering questions that need answers."
"As we have no correlates of protection, clinical trials [are] the only way to assess vaccine efficacy. These trials should not be run solely in the malaria-endemic area, but first in malaria naïve individuals and then in the field."
"Limited to the challenge model"
"Since the last 15-20 years of studies have shown that animal model (including monkey challenge model in my opinion) is not so predictive in human[s]. Therefore, I think it is very important to test novel vaccine candidates in clinical trials as soon as possible. And to do that, support by MVDP will be very valuable."

4.3.3 Question 3 findings from key informant interviews

Despite the broad range of organizations and research interests represented by the key informants, there was unanimous agreement on the following two points:

1. RTS,S is not the final malaria vaccine product needed for the world, and efforts to improve it or develop something better are necessary.
2. Despite the recent high-visibility focus on transmission-blocking vaccines, there is still a critical need to continue vaccine development efforts focused on disease prevention and mortality reduction. It was repeatedly noted that this goes beyond individual opinion and is reinforced by planning documents supported by WHO, PATH/MVI and others.

While there was no consensus among the key informants on a specific approach to malaria vaccine development, it was widely felt that going forward, the malaria vaccine community will likely take a two-pronged approach focused on both transmission reduction and disease prevention/mortality reduction. This approach is supported by the Malaria Vaccine Technology Roadmap, which was originally launched in 2006 at the WHO Global Vaccine Research Forum and, in response to changing malaria epidemiology and control efforts, reviewed and updated in November 2013. The document is supported by the Malaria Vaccine Funders Group, an informal group of some of the key funders of malaria vaccine development, including the BMGF, the European and Developing Countries Clinical Trials Partnership, EVI, the European Commission, PATH/MVI, USAID, NIAID, the Wellcome Trust and WHO. Key informants indicated that there is still broad support for this document and approach. Key informants unanimously agreed that more work needs to be done, and disease prevention and mortality reduction will continue to be a focus area of the malaria vaccine development community.

Of the many areas that would benefit from USAID MVDP funding, the consensus from the key informant interviews was that the USAID MVDP could have the most impact by supporting four areas:

1. Continued evaluation of new antigens (pre-erythrocytic and blood-stage), which could be added to RTS,S or replace it
2. Correlates of protection and methods to help decide if a new vaccine candidate should continue to human-use trials in the field
3. Small vaccine lots made under GMP for human-use trials
4. Early-phase trials with a CHMI

While some felt that funding of new antigen discovery by MVDP would be valuable, the majority felt that funding to further the evaluation of the current pre-erythrocytic and blood-stage candidates across a variety of vaccine platforms would be of greater value.

The key informants did not support using USAID MVDP funds for adjuvant discovery or evaluation. Evaluation of an adjuvant candidate as part of a clinical trial for a specific vaccine candidate garnered some support, but not an evaluation of adjuvants as an independent effort—only if it made sense in the development plan of the vaccine candidate.

Some key informants advocated for USAID MVDP support of reference labs with preclinical assays that can be utilized by multiple programs. It was widely recognized that tools for preclinical evaluation of vaccine candidates that correlate with outcomes of field trials are limited. Supporting reference labs with “best-available” assays may aid in the standardization of information available for advancing or down-selecting a vaccine candidate.

The key informants did not support funding research efforts specifically focused on determining correlates of immunity. Other funding is available for this, and USAID MVDP funds could be better used in other areas with less funding.

Informants felt that proof-of-concept studies in humans with CHMI are a critical area for USAID MVDP funding. It was widely agreed that there is no single evaluation path for vaccine candidates and no clear set of go/no-go criteria that can be used to advance or down-select a vaccine candidate. Until there are preclinical evaluation tools that clearly correlate with outcomes of field trials, the CHMI will have a critical role in this space. However, to use the CHMI, there has to be a supportable decision to advance a promising candidate, completion of multiple regulatory requirements, a vaccine lot made under GMP ready for human use, and then funding to conduct the trial with CHMI. This is a complicated and expensive progression that is not being funded by many sources and an area that the USAID MVDP partnerships and funding could impact greatly. It was noted that USAID MVP has substantial experience in this progression and longstanding partnerships that can support each step in the progression, which makes the USAID MVDP uniquely equipped to focus in these areas.

5. CONCLUSIONS

5.1. EVALUATION QUESTION 1: What has been the value added of the MVDP to the current status of malaria vaccine development?

1. The MVDP has added significantly to the process of developing a malaria vaccine.
2. The MVDP has used its limited resources to catalyze the process through strategic research in the continuum of malaria vaccine development, particularly in the approach of pre-erythrocytic and blood stages. The key informants and a significant portion of the survey respondents felt the MVDP was an important funder within the malaria vaccine community and played a unique role in a critical niche that otherwise would not be addressed within the global arena of malaria vaccine development.
3. The MVDP's focus on key preclinical and early clinical development efforts, which are not usually funded by other entities, has supported critical decisions to down-select or advance early vaccine candidates.
4. It is widely felt that additional MVDP funding would advance and speed progress of malaria vaccine development efforts.

5.2. EVALUATION QUESTION 2: How is the MVDP complementary to other programs funding malaria vaccine development?

1. The MVDP does not have enough funding to support an entire vaccine development effort, so its flexible and focused support has been seen as desirable and effective in critical research areas that lack other sources of funding. Effective strategic partnerships have leveraged available funds, recognizing that the MVDP focuses on acquiring evidence that could stimulate funding for advanced vaccine development. The MVDP has a unique niche as a catalyst in the malaria vaccine development community, using its expertise and flexible funding to support policy and science.
2. The MVDP's role is significant, complementary to the role of other funders, and cost-effective due to its ability to leverage other funding. The SCG, survey respondents and key informants repeatedly noted that Drs. Diggs and Soisson are critical to the MVDP's success in this role and have provided key scientific experience for several programs. Many key informants felt that Drs. Diggs and Soisson were so critical that a succession plan needed to be developed to ensure continued integration of MVDP leadership and expertise with current partners.
3. The longstanding partnership with WRAIR and NMRC has been highly effective. Additionally, MVDP has been involved with, and leveraged funding through, some of the most prominent malaria vaccine groups worldwide, including NIH, Oxford and WEHI. Importantly, USAID MVDP has also partnered with other policy and funding organizations to exert significant influence on both the policy and science behind malaria vaccine development.
4. The financial relationship with MVI and ability to leverage MVI expertise and funding has changed with the contract to Leidos. It is not clear how this will impact the past MVDP/MVI relationship or replace MVI's role in expanding the portfolio of MVDP to include research and development efforts not available through the DOD. It was clear from survey respondents and key informant interviews that a mechanism for partners outside the DOD to interact with the MVDP was desired. Leidos' Pipeline Development Activities and Vaccine Development Projects outlined in its Malaria Vaccine Development Work Plan may ultimately support collaborations with non-DOD partners, but it was not clear to many, at the time of the surveys and interviews, how this would work.

5.3 EVALUATION QUESTION 3: Given the historical role of the MVDP, is this role critical going forward, or, given the changing funding environment for malaria vaccine development, should the focus of the USAID MVDP strategy be modified?

1. The MVDP's focus is aligned with the Malaria Vaccine Technology Roadmap endorsed by the Malaria Vaccine Funders Group.
2. Other malaria funders are focused on basic research, epidemiology, disease prevention, treatment and vaccines for reducing transmission, but few support the development of vaccines that reduce malaria morbidity and mortality. This remains a critical area, according to the Malaria Vaccine Technology Roadmap, SCG assessments, survey respondents and key informants. The MVDP is one of the few funders in this space, and its role is becoming more critical. The MVDP is appropriately focused on the development of pre-erythrocytic and erythrocytic vaccines to prevent and control clinical disease.
3. RTS,S, as it is currently understood, has significant limitations, and recently the WHO recommended further evaluation of RTS,S/AS01 in a series of pilot implementations, addressing several gaps in knowledge before considering wider country-level introduction. WHO does not recommend the use of the RTS,S vaccine in the younger (6-12 weeks) age category, as the vaccine efficacy was found to be low in this age group.
4. It was unanimous among survey participants and key informant interviews that an improvement or alternative to RTS,S was necessary and work on vaccines that reduce morbidity and mortality is required.
5. The SCG is well composed, has a strong role in the scientific monitoring of the USAID MVDP and supports its current direction. If the focus of the USAID MVDP strategy is modified, the SCG is staffed and positioned to contribute to the new strategy.

6. RECOMMENDATIONS

1. With the limited funding globally, which is focused on vaccines to impact malaria morbidity and mortality, the MVDP should continue to support this area and evaluate where it can have the most impact as a funder. Based on the surveys and key informant interviews, MVDP could have the greatest impact now by focusing on:
 - a. Continued evaluation of new antigens (pre-erythrocytic and blood-stage) that could be added to RTS,S or replace it
 - b. Methods to select which vaccine candidates to advance or down-select
 - c. Transitioning preclinical successes into clinical development through evaluation of vaccine platforms, funding GMP lots and toxicology studies and evaluating vaccine efficacy in CHMI models
2. In the continued evaluation of where the MVDP can have the most impact, an expanded role for the SCG should be considered. The SCG could play a prospective role in determining areas to fund and meet in smaller groups more often to take stock of ongoing projects.
3. The MVDP should consider publishing or communicating its current mechanisms for collaborating with partners outside the DOD. The Leidos contract may sufficiently extend the capabilities of the MVDP to entertain research and development efforts not available through the DOD, but currently this is not well understood in the greater malaria vaccine development community, including with some longstanding partners.
4. Plan for the long lead time it will take to train successors for Dr. Diggs and Dr. Soisson. USAID has been served remarkably and admirably by Drs. Carter Diggs and Lorraine Soisson. A succession plan that reflects the need for continuity of the technical team and supports the continuation of MVDP's relationships and broad impact will be useful to USAID.
5. Evaluate current funding levels for the MVDP. The overall funding for malaria vaccine development is limited. The potential impact of MVDP funding has increased with the movement of BMGF funding to transmission blocking. Many of the areas suggested for MVDP focus (GMP lot manufacturing, toxicology studies and CHMI human trials) are expensive, multi-year endeavors. Thus, given the unique role and critical niche MVDP has in the malaria vaccine development community, increased funding could support more of the areas of research suggested as most important for MVDP funding and speed vaccine development efforts through critical milestones.

ANNEX I. STATEMENT OF WORK

Global Health Program Cycle Improvement Project–GH Pro
Contract No. AID-OAA-C-14-00067

EVALUATION OR ANALYTIC ACTIVITY STATEMENT OF WORK (SOW)

August 17, 2015

INSTRUCTIONS: Complete this template in MS Word to develop a SOW for an evaluation, assessment, or other analytic activity. Please be as thorough as possible in completing this SOW. Your GH Pro technical advisor and project management team can assist you in developing your final SOW.

Refer to the USAID How-To Note: Developing an Evaluation SOW and the SOW Good Practice Examples when developing your SOW.

Note: When submitting this SOW, please also include relevant background documents that would assist in planning the analytic activity, such as a project descriptions, contract/agreements and implementing partner PMPs/reports.

I. TITLE: USAID Malaria Vaccine Development Program (MVDP) Evaluation (072)

II. Requester/Client

USAID/Washington
 Office/Division: GH/HIDN/MAL

III. Funding Account Source(s): (Click on box(es) to indicate source of payment for this assignment)

- | | |
|--|---|
| <input type="checkbox"/> 3.1.1 HIV | <input type="checkbox"/> 3.1.6 MCH |
| <input type="checkbox"/> 3.1.2 TB | <input type="checkbox"/> 3.1.7 FP/RH |
| <input checked="" type="checkbox"/> 3.1.3 Malaria | <input type="checkbox"/> 3.1.8 WSSH |
| <input type="checkbox"/> 3.1.4 PIOET | <input type="checkbox"/> 3.1.9 Nutrition |
| <input type="checkbox"/> 3.1.5 Other public health threats | <input type="checkbox"/> 3.2.0 Other (specify): |

IV. Cost Estimate: (Note: GH Pro will provide a final budget based on this SOW)

V. Performance Period

Expected Start Date (on or about): August 2015

Anticipated End Date (on or about): December 2015

VI. Location(s) of Assignment: (Indicate where work will be performed)

Washington, DC

VII. Type of Analytic Activity (Check the box to indicate the type of analytic activity)

EVALUATION:

Performance evaluation (Check timing of data collection)

Midterm Endline Other (specify): **Performance to date evaluation**

Performance evaluations focus on descriptive and normative questions: what a particular project or program has achieved (either at an intermediate point in execution or at the conclusion of an implementation period); how it is being implemented; how it is perceived and valued; whether expected results are occurring; and other questions that are pertinent to program design, management and operational decision making. Performance evaluations often incorporate before-after comparisons, but generally lack a rigorously defined counterfactual.

Impact evaluation (Check timing(s) of data collection)

Baseline Midterm Endline Other (specify):

Impact evaluations measure the change in a development outcome that is attributable to a defined intervention; impact evaluations are based on models of cause and effect and require a credible and rigorously defined counterfactual to control for factors other than the intervention that might account for the observed change. Impact evaluations in which comparisons are made between beneficiaries that are randomly assigned to either a treatment or a control group provide the strongest evidence of a relationship between the intervention under study and the outcome measured.

OTHER ANALYTIC ACTIVITIES

Assessment

Assessments are designed to examine country and/or sector context to inform project design, or as an informal review of projects.

Costing and/or economic analysis

Costing and Economic Analysis can identify, measure, value and cost an intervention or program. It can be an assessment or evaluation, with or without a comparative intervention/program.

Other analytic activity (Specify)

PEPFAR EVALUATIONS (PEPFAR Evaluation Standards of Practice 2014)

Note: If PEPFAR-funded, check the box for type of evaluation

Process evaluation (Check timing of data collection)

Midterm

Endline

Other (specify): _____

Process evaluation focuses on program or intervention implementation, including, but not limited to access to services, whether services reach the intended population, how services are delivered, client satisfaction and perceptions about needs and services, management practices. In addition, a process evaluation might provide an understanding of cultural, sociopolitical, legal, and economic context that affect implementation of the program or intervention. For example: Are activities delivered as intended, and are the right participants being reached? (PEPFAR Evaluation Standards of Practice 2014)

Outcome evaluation

Outcome evaluation determines if, and by how much, intervention activities or services achieved their intended outcomes. It focuses on outputs and outcomes (including unintended effects) to judge program effectiveness, but may also assess program process to understand how outcomes are produced. It is possible to use statistical techniques in some instances when control or comparison groups are not available (e.g., for the evaluation of a national program). Example of question asked: To what extent are desired changes occurring due to the program, and who is benefiting? (PEPFAR Evaluation Standards of Practice 2014)

Impact evaluation (Check timing(s) of data collection)

Baseline

Midterm

Endline

Other (specify):

Impact evaluations measure the change in an outcome that is attributable to a defined intervention by comparing actual impact to what would have happened in the absence of the intervention (the counterfactual scenario). IEs are based on models of cause and effect and require a rigorously defined counterfactual to control for factors other than the intervention that might account for the observed change. There are a range of accepted approaches to applying a counterfactual analysis, though IEs in which comparisons are made between beneficiaries that are randomly assigned to either an intervention or a control group provide the strongest evidence of a relationship between the intervention under study and the outcome measured to demonstrate impact.

Economic evaluation (PEPFAR)

Economic evaluations identifies, measures, values and compares the costs and outcomes of alternative interventions. Economic evaluation is a systematic and transparent framework for assessing efficiency, focusing on the economic costs and outcomes of alternative programs or interventions. This framework is based on a comparative analysis of both the costs (resources consumed) and outcomes (health, clinical, economic) of programs or interventions. Main types of economic evaluation are cost-minimization analysis (CMA), cost-effectiveness analysis (CEA), cost-benefit analysis (CBA) and cost-utility analysis (CUA). Example of question asked: What is the cost-effectiveness of this intervention in improving patient outcomes as compared to other treatment models?

VIII. BACKGROUND

Background of project/program/intervention:

History: USAID has supported malaria vaccine development for over 45 years. The Malaria Vaccine Development Program (MVDP) was created in the late 1960s in response to the termination of the Malaria Eradication Program. Its history can be divided into four phases:

- 1966–1974: Focus on single-center research and development with the objective of developing a malaria vaccine
- 1974–1980: Establishment of a network of partners and a variety of research approaches to cell-based (sporozoite and merozoite) vaccines through further development of academic models in which protection had been demonstrated in small numbers of subjects
- 1980–1988: Use of molecular approaches and the performance of a clinical trial of New York University’s peptide vaccine at the University of Maryland’s Center for Vaccine Development, the first peptide malaria vaccine to undergo clinical testing
- 1988–present: Focus on development of new vaccine candidates and progression to clinical trials to assess proof of principle

Authorization and funding: When it was authorized in 1992, the Malaria Vaccine Development Project (936-6001) consolidated efforts of two earlier projects: the Malaria Immunity and Vaccine Research Project (931-0453) and the Malaria Field Trials Project (936-5967). It should be noted that all of these projects have been part of the Malaria Vaccine Development Program. The MVDP is currently authorized under the MVDP Project Appraisal Document (936-6000), which was approved in April 2013 and amended in April 2014. The ceiling of the PAD is \$75,000,000 and the end date is September 20, 2019. The current annual obligation is \$7,100,000.

Focus: The USAID MVDP goal is to speed the development of vaccines for use as tools in control programs to further mitigate morbidity and mortality due to malaria. This goal is different from that of most other funders. Currently, a large proportion of malaria vaccine funding worldwide is devoted to vaccines as tools to facilitate malaria elimination and eradication. Thus, the MVDP focus fills what would otherwise be a serious gap in the global portfolio. The MVDP’s efforts focus on two stages of the parasite growth cycle: pre-erythrocytic (i.e., from injection from the mosquito through the liver stages) and erythrocytic (i.e., circulating in the human blood stream). While the former targets sterile immunity (i.e., absence of circulating blood stage parasites), the latter focuses on preventing blood stage disease. In the latter case, viable parasites may persist in the circulation, as is the case in naturally acquired immunity to malaria. In recent years, the MVDP has focused on building a pipeline from early preclinical vaccine development, through the regulatory process, and to clinical and field testing of vaccine candidates. The MVDP has supported production and testing of protein subunit vaccines, evaluation of new platform technologies for vaccine development, as well as adjuvant formulations, and development of vaccine strategies to overcome strain variability.

Landscape of malaria vaccine development: While there has not been a licensed vaccine for malaria previously, there is now potential that a licensed, partially effective vaccine with a relatively short duration of action targeting malaria control may be available in 2016. The Phase III results of this vaccine, known as RTS,S/AS01, have been submitted to the World Health Organization and the European Medicines Agency. These organizations are reviewing the data, and a decision regarding a recommendation for introduction of the vaccine into Africa is expected at the end of 2015.

As mentioned above, the decision of the Bill & Melinda Gates Foundation to devote essentially all its research and development support to tools to be used for elimination and eradication has resulted in a major shift in the focus of malaria research in general, as well as the impact on vaccine development. The adoption of this very long-term focus by much of the community will continue to play a role in strategic research planning as the long-term impact of malaria control efforts become clearer and new tools for control and elimination emerge.

Worthy of note is a current effort to develop a cell-based (sporozoite) vaccine based on the earlier demonstration of the induction of protection by irradiated sporozoites. Recent successful efficacy

trials of this investigational vaccine have attracted extensive international attention and numerous clinical and field investigations. However, obstacles to widespread implementation remain.

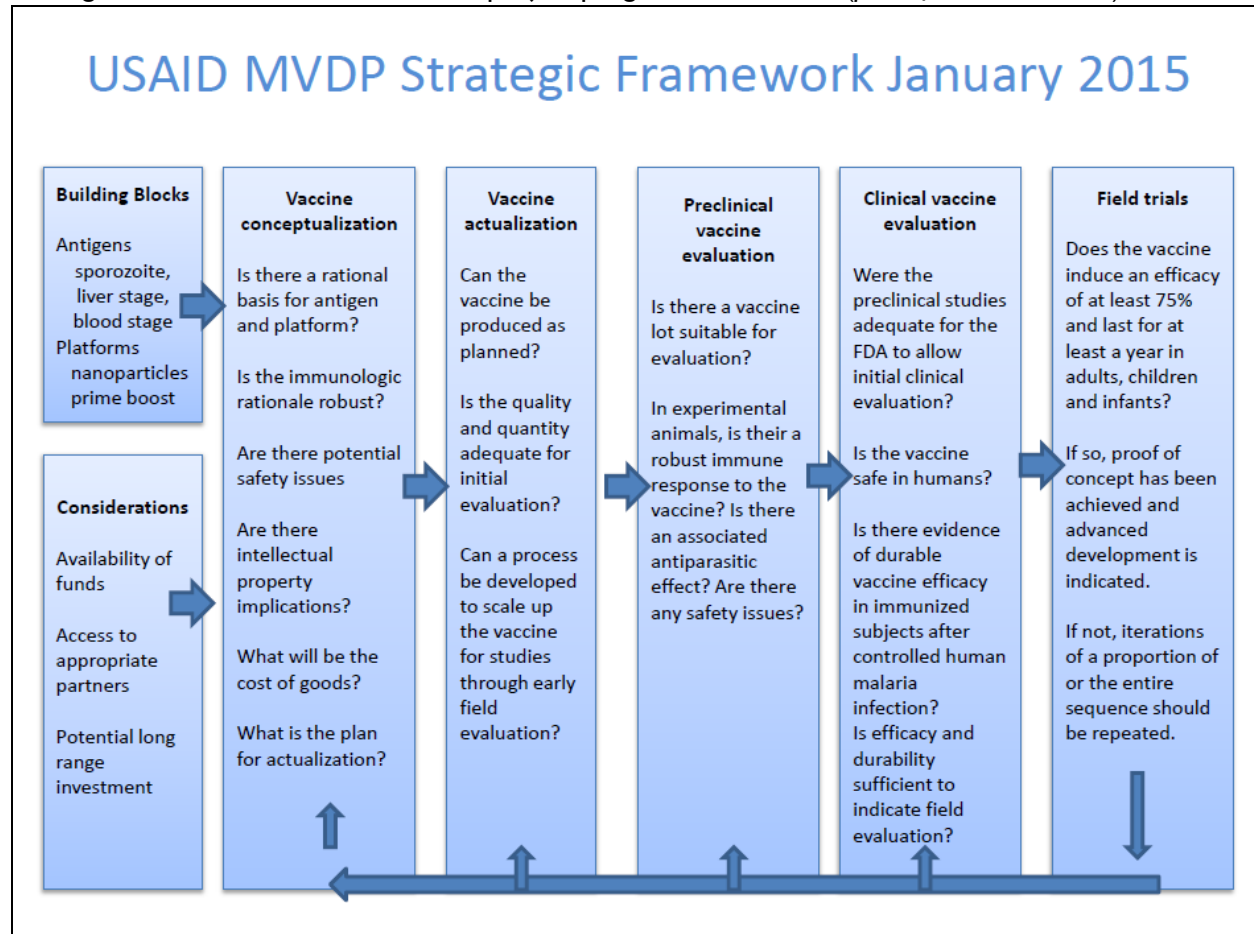
Operations: The MVDP is located in the Malaria Division of the Global Health Bureau's Office of Health, Infectious Disease and Nutrition (HIDN). Technical advice to the program is provided by two contract staff members (Carter Diggs and Lorraine Soisson).

Partners: The MVDP currently has agreements with the Walter Reed Army Institute of Research (WRAIR), the Naval Medical Research Center (NMRC), the National Institute of Allergy and Infectious Disease (NIAID), and Initiatives, Inc. A cooperative agreement with the Malaria Vaccine Initiative at PATH ended in September 2014.

Describe the theory of change of the project/program/intervention.

The desired goal of the MVDP is control of malaria due to *Plasmodium falciparum*. However, many factors and forces external to the MVDP will be required for realization of this outcome. Therefore, the proximal MVDP goal is to provide evidence of feasibility of development of a highly efficacious, durable and cost-effective vaccine that would enable activation of the many required externalities to come into play. Notably, the most difficult factor to engage is the capital to actualize the advanced vaccine development enterprise. However, many other inputs will also be required.

Strategic or Results Framework for the project/program/intervention (paste framework below)



What is the geographic coverage and/or the target groups for the project or program that is the subject of analysis?

The distal goal of incorporation of a vaccine into control programs will have global impact, with direct effect in the *P. falciparum* endemic areas. The proximal goal of proof of concept of a vaccine will have no immediate geographic effect.

IX. SCOPE OF WORK

A. **Purpose:** Why is this evaluation or analysis being conducted (purpose of analytic activity)? Provide the specific reason for this activity, linking it to future decisions to be made by USAID leadership, partner governments, and/or other key stakeholders.

The MVDP was evaluated in 2003. During the portfolio review in 2014, it was recommended to undertake another evaluation to assess: USAID's current and future unique role/niche in the development of malaria vaccines; the progress made to date by MVDP, as well as ways to accelerate progress; and ways to improve the program in the future.

B. **Audience:** Who is the intended audience for this analysis? Who will use the results? If listing multiple audiences, indicate which are most important.

USAID Global Health Bureau and HIDN leadership and MVDP staff

C. **Applications and use:** How will the findings be used? What future decisions will be made based on these findings?

The findings will be used to shape the program in future years. Future decisions affected may include strategic direction, funding, scientific direction and partnerships formed.

- D. **Evaluation questions:** Evaluation questions should be: (a) aligned with the evaluation purpose and the expected use of findings; (b) clearly defined to produce needed evidence and results; and (c) answerable given the time and budget constraints. Include any disaggregation (e.g., sex, geographic locale, age, etc.) that must be incorporated into the evaluation questions. **USAID policy suggests 3 to 5 evaluation questions.**

Evaluation Question
<p><i>What has been the value added of the MVDP on the current status of malaria vaccine development? To address this question, please consider the following:</i></p> <ul style="list-style-type: none"> – whether or not MVDP activities have achieved their anticipated strategic results – the relevant importance of MVDP contributions to malaria vaccine discovery and development – if the MVDP fills a critical niche that otherwise would not have been addressed within the global arena of malaria vaccine development
<p><i>How is MVDP complementary to other programs funding malaria vaccine development? With limited potential malaria vaccine marketability to encourage research and development by the pharmaceutical industry, progress requires synergy and complementarity of public sector initiatives. Thus, to address this question, please consider the following:</i></p> <ul style="list-style-type: none"> – USAID’s effectiveness in coordinating with its funded MVDP partners – if MVDP staff have been effective in coordinating with other malaria vaccine donors – complementarity of the MVDP with other efforts by funded partners and the malaria vaccine development enterprise at large and how it can be enhanced
<p><i>Given the historical role of the MVDP, is this role critical going forward or, given the changing funding environment for malaria vaccine development, should the focus of the USAID MVDP strategy be modified? The context for this question is: (1) currently, a large proportion of malaria vaccine funding worldwide is devoted to vaccines as tools to facilitate malaria elimination, in contrast to the USAID MVDP focus on enhancing malaria control; (2) a licensed, partially effective vaccine with a relatively short duration of action targeting malaria control may be available in 2016.</i></p>

Other Questions [OPTIONAL]

(Note: Use this space only if necessary. Too many questions leads to an ineffective evaluation.)

- E. **Methods:** Check and describe the recommended methods for this analytic activity. Selection of methods should be aligned with the evaluation questions and fit within the time and resources allotted for this analytic activity. Also, include the sample or sampling frame in the description of each method selected.

■ **Document review** (list of documents recommended for review)

SCG meeting reports 2003 MVDP Evaluation USAID-MVI Cooperative Agreement Final Report Scientific papers for work supported by USAID [suggested key papers to be provided via Google docs] Timeline with key milestones (2003–present) MVDP current agreement MVDP annual and quarterly reports MVDP performance monitoring plan with indicator data MVDP technical reports
--

Secondary analysis of existing data (list the data source and recommended analyses)

Data Source (existing dataset)	Description of data	Recommended analysis

Key informant interviews (list categories of key informants, and purpose of inquiry)

MVDP current project staff:

- Walter Reed Army Institute of Research (WRAIR)
- the Naval Medical Research Center (NMRC)
- the National Institute of Allergy and Infectious Disease (NIAID)
- Initiatives, Inc.

MVDP prior project staff:

- PATH

USAID PMI and GH/HIDN/MAL staff

Focus group discussions (list categories of groups, and purpose of inquiry)

Group interviews (list categories of groups, and purpose of inquiry)

Client/participant satisfaction or exit interviews (list who is to be interviewed, and purpose of inquiry)

Facility or service assessment/survey (list type of facility or service of interest, and purpose of inquiry)

Verbal autopsy (list the type of mortality being investigated (i.e., maternal deaths), any cause of death and the target population)

Survey (describe content of the survey and target responders, and purpose of inquiry)

Observations (list types of sites or activities to be observed, and purpose of inquiry)

Data abstraction (list and describe files or documents that contain information of interest, and purpose of inquiry)

Case study (describe the case, and issue of interest to be explored)

Rapid appraisal methods (ethnographic/participatory) (list and describe methods, target participants, and purpose of inquiry)

Other (list and describe other methods recommended for this evaluation, and purpose of inquiry)

If **impact evaluation**:

Is technical assistance needed to develop full protocol and/or IRB submission?

Yes No

List or describe case and counterfactual

Case	Counterfactual

X. ANALYTIC PLAN

Describe how the quantitative and qualitative data will be analyzed. Include method or type of analyses, statistical tests and what data are to be triangulated (if appropriate), for example, a thematic analysis of qualitative interview data, or a descriptive analysis of quantitative survey data.

The evaluation team will be responsible for coordinating the data analysis. The analysis will use social science approaches to answer the evaluation questions outlined above. The evaluation team should propose a robust analytic plan that generates robust evidence needed to answer the evaluation questions. Each team member will participate in the analysis and contribute to the interpretation of the data, as their area of specialty allows.

This evaluation will utilize primarily qualitative analyses in order to answer the evaluation questions stated within this SOW, as the document review and key informant interviews will produce qualitative data. However, many of the reports to be reviewed will contain quantitative data, and this evaluation team will be responsible to review and critique these findings and synthesize as appropriate.

Thematic review of qualitative data will be performed, connecting the data to the evaluation questions, seeking relationships, context, interpretation, nuances, homogeneity and outliers to better explain what is happening and the perception of those involved. Qualitative data will be used to substantiate and elaborate on the quantitative findings from this evaluation and pertinent reports/papers, and answer questions where other data do not exist.

Use of multiple methods that are quantitative and qualitative, as well as existing data (e.g., project reports and scientific papers) will allow the team to triangulate findings to produce more robust evaluation results.

XI. ACTIVITIES

List the expected activities, such as team planning meeting (TPM), briefings, verification workshop with implementing partners and stakeholders, etc. Activities and deliverables may overlap. Give as much detail as possible.

Background reading: Several documents are available for review for this evaluation. These include the MVDP RFA, proposal, agreement with modifications, annual work plans, M&E plans with performance monitoring plan (PMP), progress reports, routine reports of project performance indicator data, evaluation reports, technical reports and papers, and other project-generated reports and materials. Additionally, scientific papers and reports related to malaria vaccine development will be included in the reading materials. This desk review will provide background information for the evaluation team and will also be used as data input and evidence for the evaluation.

Team planning meeting (TPM): A three-day TPM will be held at the initiation of this assignment and before the data collection begins. The TPM will:

- Review and clarify any questions on the evaluation SOW
- Clarify team members' roles and responsibilities
- Establish a team atmosphere, share individual working styles, and agree on procedures for resolving differences of opinion
- Review and finalize evaluation questions

- Review and finalize the assignment timeline and share with other units
- Develop data collection methods, instruments, tools and guidelines
- Review and clarify any logistical and administrative procedures for the assignment
- Develop a data collection plan
- Draft the evaluation work plan for USAID's approval
- Develop a preliminary draft outline of the team's report
- Assign drafting/writing responsibilities for the final report

Evaluation plan: By the close of the TPM, the evaluation team will prepare a brief but detailed evaluation plan in response to SOW requirements and evaluation questions. In consultation with the USAID/GH/HIDN/MAL team, the detailed evaluation plan should identify the countries for site visits and individuals and stakeholders for in-depth interviews and should include each of the proposed data collection instruments (i.e., semi-structured interview guides, etc.). A draft of the detailed evaluation plan and data collection instruments should be submitted to the USAID/GH/OHS team for input prior to finalization.

Briefing and debriefing meetings: Throughout the evaluation, the team leader will provide briefings to USAID. The in-briefing and debriefing are likely to include all the evaluation team experts but will be determined in consultation with USAID/GH/HIDN/MAL. These briefings are:

- **Evaluation launch**, a call/meeting among the USAID/GH/OHS, GH Pro and the evaluation team to initiate the evaluation activity and review expectations. USAID will review the purpose, expectations and agenda of the assignment. GH Pro will introduce the team and review the initial schedule and other management issues.
- **In-briefing with USAID/GH/HIDN/MAL**, as part of the TPM. This briefing may be broken into two meetings: (a) at the beginning of the TPM, so the evaluation team and USAID can discuss expectations and intended plans; and (b) at the end of the TPM, when the evaluation team will present an outline and explanation of the design and tools of the evaluation. Also discussed at the in-briefing will be the format and content of the evaluation report. The time and place for this in-briefing will be determined between the team leader and USAID/GH/HIDN/MAL prior to the TPM.
- **In-briefing with MVDP**. The evaluation team will meet with MVDP to discuss the evaluation and expectations of involvement and cooperation of MVDP staff and partners. This meeting will also provide MVDP an opportunity to present the evaluation team an overview of the project.
- The team leader will brief the USAID/GH/HIDN/MAL **weekly** to discuss progress on the evaluation. As preliminary findings arise, the team leader will share these during the routine briefing, and in an email.
- A **final debriefing** between the evaluation team and USAID/GH/HIDN/MAL will be held at the end of the evaluation to present preliminary findings to USAID/GH/HIDN/MAL. During this meeting a summary of the data will be presented, along with high-level findings and draft recommendations. For the debriefing, the evaluation team will prepare a **PowerPoint presentation** of the key findings, issues and recommendations. The evaluation team shall incorporate comments received from USAID during the debriefing in the evaluation report. (*Note: preliminary findings are not final, and as more data sources are developed and analyzed these findings may change.*)
- **MVDP and stakeholder debrief/workshop** will be held following the final debrief with the USAID/GH/HIDN/MAL. The evaluation team will discuss with USAID who should participate.

Data collection: The evaluation team will conduct in-person and virtual interviews with key informants.

XII. DELIVERABLES AND PRODUCTS

Select all deliverables and products required on this analytic activity. For those not listed, add rows as needed or enter them under “Other” in the table below. Provide timelines and deliverable deadlines for each.

Deliverable / Product	Timelines & Deadlines (estimated)
<input checked="" type="checkbox"/> Launch briefing	TBD: August 2015
<input checked="" type="checkbox"/> Work plan with timeline	TBD: August 2015
<input checked="" type="checkbox"/> Analytic protocol with data collection tools	TBD: August 2015
<input checked="" type="checkbox"/> In-briefing with USAID	TBD: September 2015
<input checked="" type="checkbox"/> Routine briefings	Weekly/when needed
<input checked="" type="checkbox"/> Out-briefing with USAID	TBD: October 2015
<input checked="" type="checkbox"/> Findings review workshop with stakeholders with PowerPoint presentation	TBD: October 2015
<input checked="" type="checkbox"/> Draft report	TBD: November 2015
<input checked="" type="checkbox"/> Final report	TBD: November 2015
<input checked="" type="checkbox"/> Raw data	TBD: November 2015
<input type="checkbox"/> Dissemination activity	
<input checked="" type="checkbox"/> Posting report to the DEC	December 2015
<input type="checkbox"/> Other (specify):	

Estimated USAID review time

Average number of business days USAID will need to review deliverables requiring USAID review and/or approval? _____ business days

XIII. TEAM COMPOSITION, SKILLS AND LEVEL OF EFFORT (LOE)

Evaluation team: When planning this analytic activity, consider:

- Key staff should have methodological and/or technical expertise, regional or country experience, language skills, team leader experience and management skills, etc.
- Team leaders for evaluations must be external experts with appropriate skills and experience.
- Additional team members can include research assistants, enumerators, translators, logisticians, etc.
- Teams should include a collective mix of appropriate methodological and subject matter expertise.
- Evaluations require an evaluation specialist, who should have evaluation methodological expertise needed for this activity. Similarly, other analytic activities should have a specialist with related methodological expertise.
- Note that all team members will be required to provide a signed statement attesting that they have no conflict of interest, or describing the conflict of interest if applicable.

Team qualifications: Please list technical areas of expertise required for this activity.

The team as a whole should have the following competencies:

- Expertise in program evaluation
- General malariology
- Clinical management of malaria
- Technical grounding in malaria vaccine development

Note: One consultant may fill more than one key staff position, if s/he has the technical skills and meets the qualifications under both positions. If positions are combined, this will not increase the allotted level of effort (LOE) for the consultant,

List the key staff needed for this analytic activity and their roles. You may wish to list desired qualifications for the team as a whole, or for the individual team members.

Team leader: This person will be selected from among the key staff and will meet the requirements of both this and the other position. The team leader should have significant experience conducting project/program evaluations. S/He will manage a team of consultants in a comprehensive review of the MVDP, including the preparation of the evaluation report. S/he will be responsible for the overall organization of the report and the presentations. S/he will be the chief liaison with USAID. The team leader will provide guidance to other team members, assign appropriate tasks and ensure timely completion of specific tasks, as well as the entire assessment.

Roles and responsibilities: The team leader will be responsible for (1) managing the team's activities, (2) ensuring that all deliverables are met, are of high quality and submitted in a timely manner, (3) serving as a liaison between the USAID and the evaluation team, and (4) leading briefings and presentations. Furthermore, s/he should consult with USAID contacts regularly throughout this exercise to ensure progress is sound and key SOW issues are being addressed.

Qualifications: The team leader should have a solid technical background, and his/her strengths should accentuate the management skills and experience required in the SOW, including:

- Extensive experience in team leadership
- Able to provide technical and administrative leadership to the team
- Minimum of 10 years of experience in public health
- At least five years' experience in M&E, preferably on USAID projects/programs
- Excellent skills in planning, facilitation and consensus building
- Demonstrated experience leading an evaluation team
- Excellent interpersonal skills
- Excellent skills in project management
- Excellent organizational skills and ability to keep to a timeline
- Good writing skills
- Familiarity with USAID policies and practices
 - Evaluation policy
 - Results frameworks
 - Performance monitoring plans

Key Staff I Title: Malariologist

Roles and responsibilities: Serve as a member of the evaluation team, providing technical expertise on general malariology, malaria control and/or clinical management of malaria. S/He will participate in evaluation planning, data collection, data analysis, presentations and report writing.

Qualifications:

- At least five years' experience in general malariology, malaria control and/or clinical management of malaria
- Must be at the doctoral level or equivalent
- Training/experience in vaccine development is desirable
- Ability to work well on a team
- Good interpersonal communication skills
- Strong writing skills
- Familiarity with USAID program/projects is desirable

Number of consultants with this expertise needed: 1

Key Staff 2 Title: Vaccine development specialist

Roles and responsibilities: Serve as a member of the evaluation team, providing technical expertise on general malariology, malaria control and/or clinical management of malaria. S/He will participate in evaluation planning, data collection, data analysis, presentations and report writing.

Qualifications:

- At least five years' experience in vaccine or drug development
- Experience in the development of vaccines in government or industry
- Expertise in malariology desirable
- An advanced scientific degree in a field related to vaccine development
- Experience in vaccine development
- Ability to work well on a team
- Good interpersonal communication skills
- Strong writing skills
- Familiarity with USAID program/projects desirable

Number of consultants with this expertise needed: 1-2

Key Staff 3 Title: Evaluation specialist

Roles and responsibilities: Serve as a member of the evaluation team, providing quality assurance on evaluation issues, including methods, development of data collection instruments, protocols for data collection, data management and data analysis. S/He will ensure the highest level of reliability and validity of data being collected. S/He is responsible for all data analysis, ensuring all quantitative and qualitative data analyses are done to meet the needs for this evaluation. S/He will participate in all aspects of the evaluation, from planning to data collection, data analysis and report writing.

Qualifications:

- At least five years of experience in USAID M&E procedures and implementation
- At least eight years managing M&E, including evaluations
- Strong knowledge, skills and experience in qualitative and quantitative evaluation tools
- Experience in design and implementation of evaluations
- Experience in data management
- Experience using analytic software
- Experience evaluating health programs/activities, with experience in health systems and/or pharmaceutical sector evaluations preferred
- An advanced degree in public health, evaluation, research or related field
- Understanding of USAID contracting of centrally funded and bilateral projects preferred
- Ability to work well on a team
- Good interpersonal communication skills
- Strong writing skills

Number of consultants with this expertise needed: 1

Other staff titles with roles and responsibilities (include number of individuals needed):

Program assistant (GH Pro) will assist with gathering, organizing and reviewing documents, assist with setting up in-person and virtual interviews and meetings, and assist key evaluation staff as needed.

Will USAID participate as an active team member or designate other key stakeholders to as an active team member? This will require full time commitment during the evaluation or analytic activity.

- Yes – If yes, specify who:
 No

Staffing level of effort (LOE) matrix (optional):

This optional LOE matrix will help you estimate the LOE needed to implement this analytic activity. If you are unsure, GH Pro can assist you to complete this table.

- a) For each column, replace the label "Position Title" with the actual position title of staff needed for this analytic activity.
- b) Immediately below each staff title enter the anticipated number of people for each titled position.
- c) Enter row labels for each activity, task and deliverable needed to implement this analytic activity.
- d) Then enter the LOE (estimated number of days) for each activity/task/deliverable corresponding to each titled position.
- e) At the bottom of the table total the LOE days for each consultant title in the 'sub-total' cell, then multiply the subtotals in each column by the number of individuals that will hold this title.

Level of effort in **days** for each evaluation/analytic team member (*LOE days, TDY trips and deliverables will be finalized during the team planning meeting with the USAID client)

Activity/Deliverable		Evaluation/Analytic Team	
		Team Leader	Key Staff
Number of persons →		1	2
1	Launch briefing	.5	.5
2	Desk and data review	8	8
3	Team planning meeting	3	3
4	In-briefing with USAID GH/HIDN/MAL	1	1
5	In-briefing with MVDP, including preparation	1	1
6	Finalize data collection forms and procedures for all data collectors (circulate with USAID and GH Pro for quality assurance)	1	1
7	Data quality orientation and compliance workshop, including simulation to test reliability and validity of data collection tools	1	.5
8	Preparation/logistics for data collection	1	.5
9	Data collection	10	10
10	Data analysis and synthesis	4	4
11	Debriefing with USAID with presentation, including preparation	1	1
12	Incorporate USAID's feedback	.5	.5
13	MVDP stakeholders' workshop, including preparation	1	1
14	Draft evaluation report	6	5
15	GH Pro report quality assurance review and formatting		
16	Submission of draft report(s) to mission		
17	USAID report review		
18	Revise report per USAID comments	3	2
19	Finalization, formatting and submission of final report		
20	508 compliance review and editing		
21	Upload evaluation report to the DEC		
Sub-Total LOE (per person)		42	39*2
Total LOE		42	78

If overseas, is a six-day work week permitted? Yes No

Travel anticipated: List international and local travel anticipated and by which team members.

Consultants will travel to Washington, DC for key informant interviews and brief meetings

XIV. LOGISTICS

Note: Most evaluation/analytic teams arrange their own work space, often in their hotels. However, if Facility Access is preferred GH Pro can request it. GH Pro does not provide Security Clearances. Our consultants can obtain **Facility Access** only.

Check all that the consultant will need to perform this assignment, including USAID Facility Access, GH Pro work space and travel (other than to and from post).

USAID Facility Access
Specify who will require Facility Access: _____

Electronic County Clearance (ECC) (International travelers only)

GH Pro work space

Specify who will require work space at GH Pro: meeting space for TPM and other team meetings

Travel-other than posting (specify): Washington, DC

Other (specify): _____

XV. GH PRO ROLES AND RESPONSIBILITIES

GH Pro will coordinate and manage the evaluation team and provide quality assurance oversight, including:

- Review SOW and recommend revisions as needed
- Provide technical assistance on methodology, as needed
- Develop budget for analytic activity
- Recruit and hire the evaluation team, with USAID point of contact approval
- Arrange international travel and lodging for international consultants
- Request for country clearance and/or facility access (if needed)
- Review methods, work plan, analytic instruments, reports and other deliverables as part of the quality assurance oversight
- Report production: If the report is public, then coordination of draft and finalization steps, editing/formatting, 508ing required in addition to submission to the DEC and posting on GH Pro website. If the report is internal, then copy editing/formatting for internal distribution.

XVI. USAID ROLES AND RESPONSIBILITIES

Below is the standard list of USAID's roles and responsibilities. Add other roles and responsibilities as appropriate.

USAID Roles and Responsibilities

USAID will provide overall technical leadership and direction for the analytic team throughout the assignment and will provide assistance with the following tasks:

Before field work

- SOW:
 - Develop SOW.
 - Peer-review SOW.
 - Respond to queries about the SOW and/or the assignment at large.
- Consultant conflict of interest (COI): To avoid conflicts of interest or the appearance of a COI, review previous employers listed on the CVs for proposed consultants and provide additional information regarding potential COI with the project contractors evaluated/assessed and information regarding their affiliates.
- Documents: Identify and prioritize background materials for the consultants and provide them to GH Pro, preferably in electronic form, at least one week prior to the inception of the assignment.

- **Local consultants:** Assist with identification of potential local consultants, including contact information.
- **Site visit preparations:** Provide a list of site visit locations, key contacts and suggested length of visit for use in planning in-country travel and accurate estimation of country travel line-item costs.
- **Lodgings and travel:** Provide guidance on recommended secure hotels and methods of in-country travel (i.e., car rental companies and other means of transportation).

During field work

- **Mission point of contact:** Throughout the in-country work, ensure constant availability of the point of contact person and provide technical leadership and direction for the team's work.
- **Meeting space:** Provide guidance on the team's selection of a meeting space for interviews and/or focus group discussions (i.e., USAID space if available, or other known office/hotel meeting space).
- **Meeting arrangements:** Assist the team in arranging and coordinating meetings with stakeholders.
- **Facilitate contact with implementing partners:** Introduce the analytic team to implementing partners and other stakeholders, and where applicable and appropriate, prepare and send out an introduction letter for team's arrival and/or anticipated meetings.

After field work

- **Timely reviews:** Provide timely review of draft/final reports and approval of deliverables.

XVII. ANALYTIC REPORT

Provide any desired guidance or specifications for the final report. (See *How-To Note: Preparing Evaluation Reports*)

The **evaluation final report** must follow USAID's Criteria to Ensure the Quality of the Evaluation Report (found in Appendix I of the *USAID Evaluation Policy*).

- The report must not exceed 50 pages (excluding executive summary, table of contents, acronym list and annexes).
- The structure of the report should follow the evaluation report template, including branding found [here](#) or [here](#).
- Draft reports must be provided electronically, in English, to GH Pro who will then submit it to USAID.
- For additional guidance, please see the evaluation reports to the *How-To Note on Preparing Evaluation Draft Reports* found [here](#).

Reporting guidelines: The draft report should be a comprehensive analytical evidence-based evaluation report. It should detail and describe results, effects, constraints and lessons learned, and provide recommendations and identify key questions for future consideration. The report shall follow USAID branding procedures. **The report will be edited/formatted and made 508 compliant as required by USAID for public reports and will be posted to the USAID/DEC.**

The preliminary findings from the evaluation will be presented in a draft report at a full briefing with USAID/GH/OHS and at a follow-up meeting with key stakeholders. The report should use the following format:

- Executive summary: concisely state the most salient findings, conclusions and recommendations (not more than 2 pages)
- Table of contents (1 page)
- Acronyms
- Evaluation purpose and evaluation questions (1-2 pages)
- Project [or program] background (1-3 pages)
- Evaluation methods and limitations (1-3 pages)
- Findings
- Conclusions
- Recommendations

- Annexes
 - Annex I: Evaluation statement of work
 - Annex II: Evaluation methods and limitations
 - Annex III: Data collection instruments
 - Annex IV: Sources of information
 - List of persons interviewed
 - Bibliography of documents reviewed
 - Databases
 - [etc.]
 - Annex V: Disclosure of any conflicts of interest
 - Annex VI: Statement of differences [if applicable]

The evaluation methodology and report will be compliant with the USAID Evaluation Policy and Checklist for Assessing USAID Evaluation Reports

All data instruments, data sets, if appropriate, presentations, meeting notes and report for this evaluation will be presented to USAID electronically to the evaluation program manager. All data will be in an unlocked, editable format.

XVIII. USAID CONTACTS

	Primary Contact	Alternate Contact
Name:	Lilia Gerberg	Carter Diggs
Title:	Malaria Technical Advisor	Senior Technical Advisor
USAID Office/Mission	GH/HIDN/MAL	GH/HIDN/MAL
Email:	lgerberg@usaid.gov	cdiggs@usaid.gov
Telephone:	571-551-7431	
Cell Phone (optional)	571-225-1149	301-275-6092

List other contacts [OPTIONAL]

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XIX. REFERENCE MATERIALS

Documents and materials needed and/or useful for consultant assignment, that are not listed above

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XX. EVALUATION DESIGN MATRIX

This design matrix may be helpful for connecting your evaluation methods to questions. Often more than one method can be employed in an analytic activity to obtain evidence to address more than one question. A method should be listed by question when it will include specific inquiries and/or result in evidence needed to address this specific question.

Evaluation matrix

Evaluation questions	Illustrative indicators or other assessment criteria	Data source/ collection methods	Sampling/ selection criteria	Data analysis method

ANNEX II. EVALUATION METHODS AND LIMITATIONS

EVALUATION DESIGN

The evaluation was an assessment of performance to date. USAID and GH Pro developed a scope of work with terms of reference and questions and contracted with a three-person external consultant team to conduct the evaluation. The consultants collectively had several years of project evaluation and malaria vaccine experience. The team met with USAID and GH Pro staff at the evaluation's inception in October 2015 and developed a detailed work plan, including a refined scope, and a design matrix (Annex III). The evaluation questions, detailed in the design matrix, were as follows:

1. What has been the value added of the MVDP to the current status of malaria vaccine development?
2. How is MVDP complementary to other programs funding malaria vaccine development?
3. Given the historical role of the MVDP, is this role critical going forward, or, given the changing funding environment for malaria vaccine development, should the focus of the USAID MVDP strategy be modified?

The team met every week to review the progress of the survey and decide appropriate next steps.

METHODS

The evaluation utilized a mixed-methods approach, with qualitative and quantitative data collection through document review, MVDP stakeholder and partner survey and MVDP stakeholder and partner key informant interviews.

Document review: At the onset of the evaluation, the team requested all documents that were pertinent to answer the evaluation questions. USAID MVDP staff provided documents including project and meeting reports and contractual documents with USAID partners. The evaluators reviewed a total of 59 documents from November 2015 to February 2016.

Stakeholder and partner survey: The team developed a questionnaire to obtain answers to the evaluation questions and created a survey that was sent to previous and current MVDP grant recipients, key malaria vaccine experts and malaria policy and funding organizations. The evaluators developed the list of survey respondents from a review of the MVDP documents as well as an understanding of the previous and current stakeholders in malaria vaccine development. The team made every effort to ensure representation of the key stakeholders in malaria vaccine development. The questionnaire was self-administered (through SurveyMonkey), and the evaluators sent several reminders to ensure completion. The survey was conducted during December 2015 to January 2016. A total of 44 individual survey responses were obtained, of which 34 (77.2 percent) were complete.

Key informant interviews: The team selected a list of key informants from a list of previous and current MVDP partners and grant recipients and malaria vaccine experts. The team developed a key informant questionnaire that was administered by interviewers. The team visited key informants who were available for in-person meetings and interviewed others over the phone. During February 2016, the team interviewed a total of 23 key informants of the 40 that were contacted.

Data collection and analysis: The data collected from the document review were entered into a database. The survey data were entered directly into an electronic database, which was transferred directly into MS Excel and Epi Info. The team members summarized key informant data into key themes.

THEMES FOR ANALYSIS

The analysis was organized to answer the evaluation questions. The team utilized results from each of the data collection methods to triangulate the information. Quantitative data were summarized into tables, charts and figures, as appropriate. Qualitative data were summarized into themes to answer the evaluation questions. The results are presented for each evaluation question by data collection method: document review, survey and key informant interviews. The survey results included as many direct quotes as possible to provide background for the conclusions.

LIMITATIONS

Although the design and resources that the evaluators used were adequate to answer the evaluation questions, there were some limitations. First, many of the respondents were previous or current recipients of MVDP funding and could have views that were influenced by their role in the program. There may have been a natural bias to focus on program successes, although the team tried to tease out the points pertinent to the questions. Secondly, although several attempts were made to obtain answers from all the survey respondents, some did not respond, and their answers could have been different from those of the respondents who did answer. Thirdly, some of the key informants that were contacted were not available to be interviewed due to scheduling difficulties. Finally, the evaluation questions required the respondents to have adequate recall of events that occurred some time ago, or in some cases, when the respondent was not the one in charge of the project at that time. The team tried to triangulate sources of information to limit the effect of recall bias.

ANNEX III. DATA COLLECTION INSTRUMENTS

EVALUATION DESIGN MATRIX: OCTOBER 20, 2015, GH PRO MVDP EVALUATION

Evaluation questions	Illustrative indicators or other assessment criteria	Data source/data collection methods	Sampling/selection criteria	Data analysis method
What has been the value added of the MVDP to the current status of malaria vaccine development?				
<i>Whether or not MVDP activities have achieved their strategic results</i>	1. MVDP strategic plan with objectives or partnership policies	USAID/Data call USAID/Data call	<ul style="list-style-type: none"> • USAID principals • Principle investigators on funded projects 	Mixed (quantitative and qualitative) <ul style="list-style-type: none"> • Tables • Charts • Narrative
<i>The relevant importance of MVDP contributions to malaria vaccine discovery and development</i>	2. Funded activities	USAID/Data call		
<i>If the MVDP fills a critical niche that otherwise would not have been addressed within the global arena of malaria vaccine development</i>	3. Unique areas within malaria vaccine development as compared to other funders	Funded partners/Data call		
	4. Synergy (matching funds or other indicators)	Funded partners/Data call		
	5. Proportion of partners' portfolio that is funded by USAID	USAID/Data call Partners/Data call		
	6. Number of global partners that USAID has funded	USAID/Data call		
How is the MVDP complementary to other programs funding malaria vaccine development?				
<i>USAID's effectiveness in coordinating with its funded MVDP partners</i>	1. Written MVDP partnership model or strategy	USAID/Data call	<ul style="list-style-type: none"> • USAID project staff • Principal investigators on funded projects 	Mixed (quantitative and qualitative) <ul style="list-style-type: none"> • Tables • Charts • Narrative
<i>If MVDP staff have been effective in coordinating with other malaria donors</i>	2. Synergy (matching funds or other indicators)	USAID/Data call		
<i>Complementarity of the MVDP with other efforts by funded partners and the malaria vaccine development enterprise at large and how it can be enhanced</i>	3. Level of satisfaction by partners	Partners/Data call Partner survey		
	4. Coordination meeting reports or minutes	USAID		
	5. Level of MVDP funding against portfolio of: <ul style="list-style-type: none"> a. Known target antigens b. Preclinical vaccine evaluation c. Infrastructure for vaccine evaluation 	USAID USAID/Data call Funded proposals		

Evaluation questions	Illustrative indicators or other assessment criteria	Data source/data collection methods	Sampling/selection criteria	Data analysis method
Given the historical role of the MVDP, is this role critical going forward, or, given the changing funding environment for malaria vaccine development, should the focus of the USAID MVDP strategy be modified?				
<p>Context:</p> <p>(1) <i>Currently a large proportion of malaria vaccine funding worldwide is devoted to vaccines as tools to facilitate malaria elimination, in contrast to the USAID MVDP focus on enhancing malaria control.</i></p> <p>(2) <i>A licensed, partially effective vaccine with a relatively short duration of action targeting malaria control may be available in 2016.</i></p>	<p>I. Opinion of malaria vaccine development leaders (WHO, Wellcome Trust, BMGF, MVI)</p>	<p>Surveys Key informant interviews Existing articles, policies, plans</p>	<ul style="list-style-type: none"> • Survey respondents • Leaders of funding and partner organizations (e.g., Wellcome Trust, BMGF, MVI) • PubMed search of articles • Web search of policies 	<p>Mixed (quantitative and qualitative)</p> <ul style="list-style-type: none"> • Tables, charts, graphs with frequencies and proportions • Themes and direct quotations

ANNEX IV. SOURCES OF INFORMATION

KEY INFORMANTS INTERVIEWED

Graham Brown, MB, BS, MPH, PhD
Nossal Institute for Global Health
University of Melbourne
Victoria 3010, Australia

Kevin Marsh, MD
KEMRI-Wellcome Trust Research
Laboratories, Kilifi, Kenya

Vasee Moorthy, MA, BMBCh, MRCP, PhD
Acting Team Leader, Vaccine Development
World Health Organization
Geneva, Switzerland

Louis Miller, MD
Head, Malaria Cell Biology Section
Laboratory of Malaria and Vector Biology
NIAID/NIH
Rockville, MD 20852

Carole A. Long, PhD
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Patrick Duffy, MD
Chief, Laboratory of Malaria Immunology and Vaccinology
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Kathryn C. Zoon, PhD
Former Director, DIR, NIAID
Chief, Cytokine Biology Section
NIAID/NIH
Bethesda, MD 20892

Lee Hall, MD, PhD
Chief, Parasitology and International Programs Branch
NIAID/NIH

Dr. Chris Karp
Deputy Director, Global Health Discovery & Translational Sciences Program
Leader, Vaccines & Host-Pathogen Biology Team
Bill & Melinda Gates Foundation
Seattle, WA

Professor Marcel Tanner
Director Emeritus

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Professor of Pediatrics and Medicine
Director, Division of Global Pediatrics
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Minneapolis, MN 55414

James W. Kazura, MD
Director, Center for Global Health and Diseases
Director, International Affairs in Health Sciences
Professor of International Health, Medicine and Pathology
Case Western Reserve University
Cleveland, OH 44106

N. Regina Rabinovich
Director, Malaria Elimination Initiative, ISGlobal
Senior Advisor, Malaria Eradication Scientific Alliance
Department of Immunology and Infectious Diseases
Harvard School of Public Health
Boston, MA 02115

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Microbiologist, Department of Immunology
WRAIR
Silver Spring, MD 20910

Sheetij Dutta, PhD
Department of Immunology
WRAIR
Silver Spring, MD 20910

Eileen Villasante, PhD
Director, Malaria Program
Naval Medical Research Center
503 Robert Grant Avenue, Silver Spring, MD 20910-7500

Judith Epstein, MD
CAPT, USNR
Naval Medical Research Center, Malaria Program
Thomas L. Richie, MD, PhD
Formerly Naval Medical Research Center
Currently: Sanaria, Rockville, MD

Keith Limbach, PhD
Naval Medical Research Center, Malaria Program

Noelle Patterson, MS
Naval Medical Research Center, Malaria Program

Professor Adrian Hill
Jenner Institute
University of Oxford, UK

Dr. Christopher V. Plowe, MD, MPH
Professor and Chief, Malaria Section
University of Maryland School of Medicine
Baltimore, MD 21201

Dr. Stephen L. Hoffman
Former Director, Malaria Program
Naval Medical Research Center
Currently: CEO, Sanaria Inc., Rockville, MD

Dr. Dan Carucci
Former Director, Malaria Program,
Naval Medical Research Center
Currently: President, Global Health Consulting, Inc.
Washington, DC

Ashley Birkett, PhD
Director, Pre- and Early Clinical R&D
PATH Malaria Vaccine Initiative
Washington, DC 20001-2621

C. Richter (Rick) King, PhD
Director, Research and Development
PATH Malaria Vaccine Initiative

DOCUMENTS REVIEWED

1. MVDP SCG Reports (2004–2015)
2. MVDP 2012 Project Appraisal Document
3. PATH Malaria Vaccine Initiative (MVI) Final Report 2004–2014
4. 2003 USAID MVDP Evaluation Report
5. USAID-WRAIR Inter-Agency Agreements
6. USAID-NMRC Inter-Agency Agreements
7. USAID-NIAID Inter-Agency Agreements
8. Malaria vaccine: WHO position paper—January 2016

ANNEX V. CONSULTANT CONFLICT OF INTEREST STATEMENTS

GLOBAL HEALTH PROGRAM CYCLE IMPROVEMENT PROJECT

USAID NON-DISCLOSURE AND CONFLICTS AGREEMENT

USAID Non-Disclosure and Conflicts Agreement- Global Health Program Cycle Improvement Project

As used in this Agreement, Sensitive Data is marked or unmarked, oral, written or in any other form, "sensitive but unclassified information," procurement sensitive and source selection information, and information such as medical, personnel, financial, investigatory, visa, law enforcement, or other information which, if released, could result in harm or unfair treatment to an individual or group, or could have a negative impact upon foreign policy or relations, or USAID's mission.

Intending to be legally bound, I hereby accept the obligations contained in this Agreement in consideration of my being granted access to Sensitive Data, and specifically I understand and acknowledge that:

1. I have been given access to USAID Sensitive Data to facilitate the performance of duties assigned to me for compensation, monetary or otherwise. By being granted access to such Sensitive Data, special confidence and trust has been placed in me by the United States Government, and as such it is my responsibility to safeguard Sensitive Data disclosed to me, and to refrain from disclosing Sensitive Data to persons not requiring access for performance of official USAID duties.
2. Before disclosing Sensitive Data, I must determine the recipient's "need to know" or "need to access" Sensitive Data for USAID purposes.
3. I agree to abide in all respects by 41, U.S.C. 2101 - 2107, The Procurement Integrity Act, and specifically agree not to disclose source selection information or contractor bid proposal information to any person or entity not authorized by agency regulations to receive such information.
4. I have reviewed my employment (past, present and under consideration) and financial interests, as well as those of my household family members, and certify that, to the best of my knowledge and belief, I have no actual or potential conflict of interest that could diminish my capacity to perform my assigned duties in an impartial and objective manner.
5. Any breach of this Agreement may result in the termination of my access to Sensitive Data, which, if such termination effectively negates my ability to perform my assigned duties, may lead to the termination of my employment or other relationships with the Departments or Agencies that granted my access.
6. I will not use Sensitive Data, while working at USAID or thereafter, for personal gain or detrimentally to USAID, or disclose or make available all or any part of the Sensitive Data to any person, firm, corporation, association, or any other entity for any reason or purpose whatsoever, directly or indirectly, except as may be required for the benefit USAID.
7. Misuse of government Sensitive Data could constitute a violation, or violations, of United States criminal law, and Federally-affiliated workers (including some contract employees) who violate privacy safeguards may be subject to disciplinary actions, a fine of up to \$5,000, or both. In particular, U.S. criminal law (18 USC § 1905) protects confidential information from unauthorized disclosure by government employees. There is also an exemption from the Freedom of Information Act (FOIA) protecting such information from disclosure to the public. Finally, the ethical standards that bind each government employee also prohibit unauthorized disclosure (5 CFR 2635.703).
8. All Sensitive Data to which I have access or may obtain access by signing this Agreement is now and will remain the property of, or under the control of, the United States Government. I agree that I must return all Sensitive Data which has or may come into my possession (a) upon demand by an authorized representative of the United States Government; (b) upon the conclusion of my employment or other relationship with the Department or Agency that last granted me access to

PSN

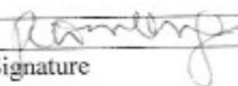
GLOBAL HEALTH PROGRAM CYCLE IMPROVEMENT
PROJECT

Sensitive Data; or (c) upon the conclusion of my employment or other relationship that requires access to Sensitive Data.

9. Notwithstanding the foregoing, I shall not be restricted from disclosing or using Sensitive Data that: (i) is or becomes generally available to the public other than as a result of an unauthorized disclosure by me; (ii) becomes available to me in a manner that is not in contravention of applicable law; or (iii) is required to be disclosed by law, court order, or other legal process.

ACCEPTANCE

The undersigned accepts the terms and conditions of this Agreement.

Signature		Date	4/13/2015
Name	GLOBAL VIVERA MD	Title	MEDICAL BIOETHICIST GLOBAL PUBLIC HEALTH SOLUTIONS

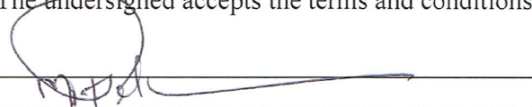
GLOBAL HEALTH PROGRAM CYCLE IMPROVEMENT
PROJECT

Sensitive Data; or (c) upon the conclusion of my employment or other relationship that requires access to Sensitive Data.

9. Notwithstanding the foregoing, I shall not be restricted from disclosing or using Sensitive Data that:
- (i) is or becomes generally available to the public other than as a result of an unauthorized disclosure by me;
 - (ii) becomes available to me in a manner that is not in contravention of applicable law; or
 - (iii) is required to be disclosed by law, court order, or other legal process.

ACCEPTANCE

The undersigned accepts the terms and conditions of this Agreement.



Signature

Date 17 Aug 2015

MARK E. Polhemus

Name

Dir, Center for Global Health
Title and Translational Science

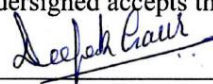
GLOBAL HEALTH PROGRAM CYCLE IMPROVEMENT
PROJECT

Sensitive Data; or (c) upon the conclusion of my employment or other relationship that requires access to Sensitive Data.

9. Notwithstanding the foregoing, I shall not be restricted from disclosing or using Sensitive Data that:
- (i) is or becomes generally available to the public other than as a result of an unauthorized disclosure by me;
 - (ii) becomes available to me in a manner that is not in contravention of applicable law; or
 - (iii) is required to be disclosed by law, court order, or other legal process.

ACCEPTANCE

The undersigned accepts the terms and conditions of this Agreement.



June 09, 2015

Signature

DEEPAK GAUR, PH.D.

Date

ASSOCIATE PROFESSOR
SCHOOL OF BIOTECHNOLOGY

JAWAHARLAL NEHRU UNIVERSITY

Name

Title NEW DELHI, INDIA

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<http://www.ghtechproject.com/resources>

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