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Innovations in Malaria Vaccine Development (IMV)
Addendum 03 to the USAID Global Health Broad Agency Announcement for Research and Development (2018)

I. Background

Despite successes in malaria control over the past several decades, over 436,000 people still die from malaria annually and the 2018 World Malaria Report[1] estimates 219 million cases of malaria in 2017. Malaria control programs face several challenges including drug and insecticide resistance and the need for sustained investment to maintain gains in malaria control. The development of a safe, effective, and durable malaria vaccine would provide an additional tool for global malaria control and elimination programs.

The RTS,S/AS01 (Mosquirix) vaccine, the only malaria vaccine evaluated in a phase III clinical trial, demonstrated vaccine efficacy of approximately 40% in children aged 5-17 months against clinical malaria.[2] The RTS,S/AS01 vaccine is currently entering advanced field trials under the malaria vaccine implementation program (MVIP) in Ghana, Kenya, and Malawi. While the RTS,S/AS01 vaccine showed a significant reduction in malaria cases in areas of high malaria burden in the phase III trial, the vaccine does not reach the World Health Organization (WHO) goal of a malaria vaccine that provides at least 75% protective efficacy against clinical malaria.[3] There are other vaccine candidates under development with some initial promising results; however in their current form they are also unlikely to meet the WHO goal stated above. For these reasons the United States Agency for International Development (USAID) supports the development of a “next-generation” malaria vaccine that demonstrates a high level of protective efficacy and durability as envisioned by the WHO and other global partners.

USAID initiated a Malaria Vaccine Development Program (MVDP) in the 1960s in response to the end of the first malaria eradication program with the goal of accelerating the development of efficacious, durable, and affordable vaccines for use in malaria control programs in endemic areas of the developing world. Several milestones in the malaria vaccine development pathway were achieved with support from the MVDP, including malaria parasite

[1] World Malaria Report 2018. Geneva: World Health Organization. 2018. Available from: https://www.who.int/malaria/publications/world-malaria-report-2018/en/
[2] RTS,S Clinical Trials Partnership. (2015). Efficacy and safety of RTS,S/AS01 malaria vaccine with or without a booster dose in infants and children in Africa: final results of a phase 3, individually randomised, controlled trial. *Lancet*, 386(9988),31-45.
[3] Malaria Vaccine Funders Group. Malaria Vaccine Technology Roadmap. 2013. Available from: http://www.euvaccine.eu/sites/default/files/uploads/Files/2-TRM_Update.pdf

culture, early development and clinical evaluation of circumsporozoite protein (CSP) and blood stage vaccines, and the first field trials of blood stage vaccines in East and West Africa. The USAID MVDP's investments have historically been through interagency agreements with U.S. government partners, including the Walter Reed Army Institute of Research (WRAIR), the Naval Medicine Research Center (NMRC), and the National Institute of Allergy and Infectious Diseases (NIAID). The USAID MVDP's investments have also included the non governmental / private sector including a cooperative agreement with PATH Malaria Vaccine Initiative (MVI) (2004-2014) and a contract with Leidos, Inc (2015-2020).

The USAID MVDP's research and development (R&D) portfolio currently includes vaccine development efforts pre-erythrocytic (sporozoite and liver) stage parasites, and erythrocytic (blood) stage parasites. Presently, USAID supports research toward an improved CSP vaccine by evaluating various vaccine display platforms, including a CSP virus like particle (VLP) containing helper T cell epitopes of diverse parasite strains and human leukocyte antigen (HLA) type reactivity and enhanced B cell epitopes. The USAID MVDP is also currently supporting the evaluation of a full-length CSP vaccine in a clinical trial. USAID has invested in liver stage vaccine efforts by NMRC and Oxford University to evaluate antigens expressed in the liver stage using a DNA-prime, chimpanzee adenovirus boost approach in a controlled human malaria infection trial. USAID also currently supports preclinical studies to evaluate additional potential highly conserved liver stage candidate antigens containing both CD4 and CD8 epitopes recognized by a broad repertoire of HLAs. USAID recently supported the Oxford University early stage clinical trial of the RH5 recombinant protein blood stage vaccine. Additionally, USAID supports preclinical studies of other blood stage antigens, including RH5 complex proteins, to build evidence sufficient to move forward along the vaccine development pipeline with these antigens. For more information on the USAID MVDP, please see: https://www.usaid.gov/what-we-do/global-health/malaria/research-innovation

II. Solutions Sought

USAID is seeking to enhance our malaria vaccine investments through a collaborative design process. The goal of USAID's MVDP is to demonstrate the proof of concept of a vaccine to reduce morbidity and mortality due to malaria caused by infection with *Plasmodium falciparum*. Target malaria vaccine end characteristics will include at least 75% efficacy and evidence of affordability. USAID intends to support efforts towards vaccines that have the potential to directly protect recipients against disease caused by *P. falciparum* such as vaccines that target the pre-erythrocytic (sporozoite and liver stage) and erythrocytic stages of the life cycle. The purpose of this Addendum is to solicit Expressions of Interest (EOI) for novel and innovative approaches to malaria vaccine development that would encompass preclinical development through proof of principle clinical studies to motivate advanced development of a deployable, effective malaria vaccine.

WHAT WE ARE LOOKING FOR:

USAID is looking for EOIs that clearly include one or more of the following:

- The potential to accelerate malaria vaccine development efforts and/or enhance the effectiveness of current malaria vaccine candidates targeting pre-erythrocytic (sporozoite and liver) and erythrocytic stages through strategic research, prototype vaccine development, preclinical, and early stage clinical testing (through proof of principle efficacy studies).
- A continuation or enhancement of USAID's current funded R&D activities (as described above) or that support novel approaches that could add or replace elements of current USAID MVDP R&D investments.

USAID encourages EOIs from potential partners who have access to systems that can obtain research materials and services including expert technical support for USAID and its collaborators in support of USAID's malaria vaccine R&D efforts.

WHAT WE ARE <u>NOT</u> LOOKING FOR:

- Basic research. Basic research is defined as research directed towards fuller knowledge or understanding of the fundamental aspects of phenomena and or observed facts without specific applications towards processes or products in mind.
- Primary antigen, platform, or adjuvant discovery research that is not a part of a coherent vaccine development program.
- Research to support vaccines against non-falciparum malaria parasite species.
- Proposed approaches involving standalone transmission blocking vaccine efforts.
- Proposed approaches for support of advanced development (i.e large efficacy or field studies) of current malaria vaccines.

III. Eligibility and applicant requirements

For the purposes of this Addendum, USAID seeks to engage with partners from the private sector, academic institutions, non-profit organizations, and other government agencies with demonstrated ability in vaccine development to identify novel and innovative approaches for malaria vaccine research and development during a co-creation Workshop.

All organizations must be formed and legally incorporated, have the capacity to successfully execute the activities in their respective areas of expertise, and be capable of receiving and administering award funding. Sole proprietorships are not eligible for funding.

A project can have only one Project Lead, who must be affiliated with the institution from which the EOI is being submitted. A Project Lead may only be listed on one (1) EOI to this Broad Agency Announcement. An institution may be the applicant on multiple applications, provided all EOIs have different Project Leads.

IV. Instructions for Expressions of Interest (EOIs)

EOIs will be reviewed against the applicable criteria; selected groups will be invited to participate in Stage 2 of the BAA process (see below under Selection Process).

EOIs must include the following:

1. A brief description of a creative and/or innovative idea/approach that has the potential to lead to the development of a new or improved malaria vaccine that targets pre-erythrocytic (sporozoites and liver stages) and/or erythrocytic stages of the life cycle through strategic research, prototype vaccine development, preclinical and/or early clinical evaluations;
2. A demonstrated expertise in vaccine development and a clear understanding of the most recent scientific evidence in the field of malaria vaccines or other infectious disease vaccine research;
3. A brief description of the advantages of the idea/approach compared to previous or ongoing malaria vaccine development efforts and summary of any preliminary data/results, if available;
4. The feasibility of the idea/approach to progress along the vaccine development pipeline towards early stage clinical studies, as well as potential use in malaria endemic countries in the developing world;
5. A brief description of your organization's ability to collaborate effectively with USAID and/or other U.S. government agencies, academic institutions, and/or private/public partners to conduct scientific research;
6. Clearly articulated contributions and areas of expertise of proposed partners or collaborations; and
7. A brief description of your organization's capacity to implement and manage the proposed project.

Instructions for the EOI:

All EOIs must be submitted in accordance with the following:

- If a respondent does not follow the instructions set forth herein, the respondent's EOI may be eliminated from further consideration.
- EOIs must be submitted in English.
- EOIs must be submitted electronically to ghmvdpbaa@usaid.gov only with a subject line "GH MVDP - [Name of respondent organization]. Facsimile or hardcopy submissions will not be accepted.
- Respondents must use 8.5 by 11 inch (or A4) paper, single spaced, Times New Roman 12 point font, and have margins no less than one inch on the top, bottom, and both sides. Number each page consecutively.
- EOIs must be 3-5 pages of narrative in length.
- EOIs must include a header with the following information:

    - Respondent Name/Group and contact information (address, telephone number, and email address)
    - Response Title
    - BAA Addendum Name/Number
- EOIs must be in .pdf or .docx format.
- Respondents must address willingness to participate and contribute to a co-creation workshop with USAID.
- All EOIs submitted in response to this Addendum are due no later than the closing date and time indicated in this Addendum. Late EOIs will not be considered.

DO NOT SUBMIT A BUDGET at the EOI stage.

USAID may, at any time and at its sole discretion, modify eligibility criteria with respect to individual applicants, and/or Project Leads, to the extent that such modifications do not materially undermine the review process. USAID will not pay for any EOI preparation costs.

V. Review of Submissions

A. Criteria

The following criteria will be applied to EOIs:

1. **Idea/Approach**: USAID will evaluate the scientific merit, creativity, feasibility, and potential impact of the idea/approach and its relevance to USAID's Solutions Sought (Section II).
2. **Collaboration**: USAID will evaluate your organization's ability to collaborate with USAID and other partners to conduct scientific research.
3. **Capacity**: USAID will evaluate your organization's ability to implement and manage the proposed research including any proposed partners or collaborators.

B. Selection Process

USAID will review and select EOIs submitted in accordance with the guidelines and criteria set forth in this Addendum. USAID reserves the right to disregard any EOIs that do not meet the guidelines.

Stage 1: USAID will review and select EOIs submitted in accordance with the guidelines and criteria set forth in this Addendum. EOIs must include all required information. Only complete EOIs will be considered. USAID reserves the right to disregard any EOIs that do not meet the submission guidelines. USAID is not obligated to issue a financial instrument or award as a result of this Addendum.

Stage 2: Based on the review of EOIs, selected EOI teams will be invited to join a co-creation workshop to be held in the Washington, DC area, in late August or early September, 2019. USAID will provide guidance to selected EOI teams regarding who should attend the co-creation workshop. USAID will also provide guidance to selected EOI teams regarding the number of invitations to the co-creation workshop that will be provided to each organization. USAID, Resource Partners[4] and EOI teams, as well as other select invitees, will gather to collaboratively develop concept papers for research addressing the development of next-generation malaria vaccines. Selected applicants should be prepared to travel to and participate in the workshop. Travel funding to the co-creation workshop will not be provided by USAID. Invitation to and participation in the co-creation workshops do not constitute a government commitment to fund an award.

Stage 3: Approximately one month after the co-creation workshop, final concept papers will be submitted to USAID for review and selection by the Peer and Scientific Review Board comprised of USAID and select Resource Partners, as appropriate. The Peer and Scientific Review Board will review concept papers and recommend which applicants should be considered Apparently Successful Partners and whether to move forward with the project including revisions/additions to the project, and potential partners and resources. All potential partners may not be selected to move forward to Stage 4.

Stage 4: After review and selection, concept papers may proceed to the Contracting/Agreement Officer Determination as described in the Broad Agency Announcement for Global Health.

VI. Timing and Expectations

EOIs must be submitted to ghmvdpbaa@usaid.gov by 5:00PM U.S. Eastern Standard Time on June, 21, 2019. Late submissions will not be considered.

Questions in regard to the Addendum must be submitted to ghmvdpbaa@usaid.gov by 5:00PM U.S. Eastern Standard Time on May 24, 2019.

USAID anticipates awarding one or more awards totaling up to $35,500,000 (USD) over five years. The number of awards and award size will ultimately depend on the scope of the concept. Note that this is only an estimated range, and the amounts could be smaller or greater depending on the concept.

USAID is not obligated to issue a financial instrument or award as a result of this Addendum. Any award is subject to the availability of funding and issues at the discretion of the United States Government.

[4] The term “Resource Partners” means participants in the co-creation workshop who did not submit an EOI (e.g., other U.S. government agencies).

VII. Information Protection

USAID's goal is to facilitate the research that is required to lead innovative, and potentially commercially viable, solutions. Understanding the sensitive nature of submitters' information, USAID will work with organizations to protect intellectual property.

EOIs should be free of any intellectual property that the submitter wishes to protect, as the EOIs will be shared with USAID partners as part of the selection process. However, once submitters have been invited to engage in further discussions, submitters will work with USAID to identify proprietary information that requires protection. Therefore, organizations making submissions under this Addendum hereby grant USAID a royalty-free, non-exclusive, and irrevocable right to use, disclose, reproduce, and prepare derivative works, and to have or permit others to do so to any information contained in the Expressions of Interest submitted under this Addendum. If USAID engages with the organization regarding its submission, the parties can negotiate further intellectual property protection for the organization's intellectual property. Organizations must ensure that any submissions under this Addendum are free of any third-party proprietary data rights that would impact the license granted to USAID herein. This Addendum falls under the USAID Global Health Broad Agency Announcement for Research and Development (2018).