

International Reference Center for Malaria Serology

The Project: Enhancing Assays for Malaria Antigens

The PATH Malaria Vaccine Initiative (MVI) and the US Agency for International Development (USAID) are working together to enhance the ability of enzyme-linked immunosorbent assays (ELISAs) and other laboratory tools to evaluate the potential of new vaccine candidates. As part of this initiative, MVI and USAID are supporting the International Reference Center for Malaria Serology Laboratory (MSL) within the US Military Malaria Vaccine Program (USMMVP). The MSL is the only international reference center that performs ELISAs using vaccine-grade malaria plate antigens.

The Potential: Standardized Data Informs Decisions

The MSL provides the global malaria vaccine community with access to several standardized and highly reproducible assays. Data obtained using standardized MSL assays allow the scientific community to compare antigen-specific immunogenicity among vaccine candidates. This facilitates cross-study comparisons to inform vaccine development decision-making and helps to reduce investment risk.

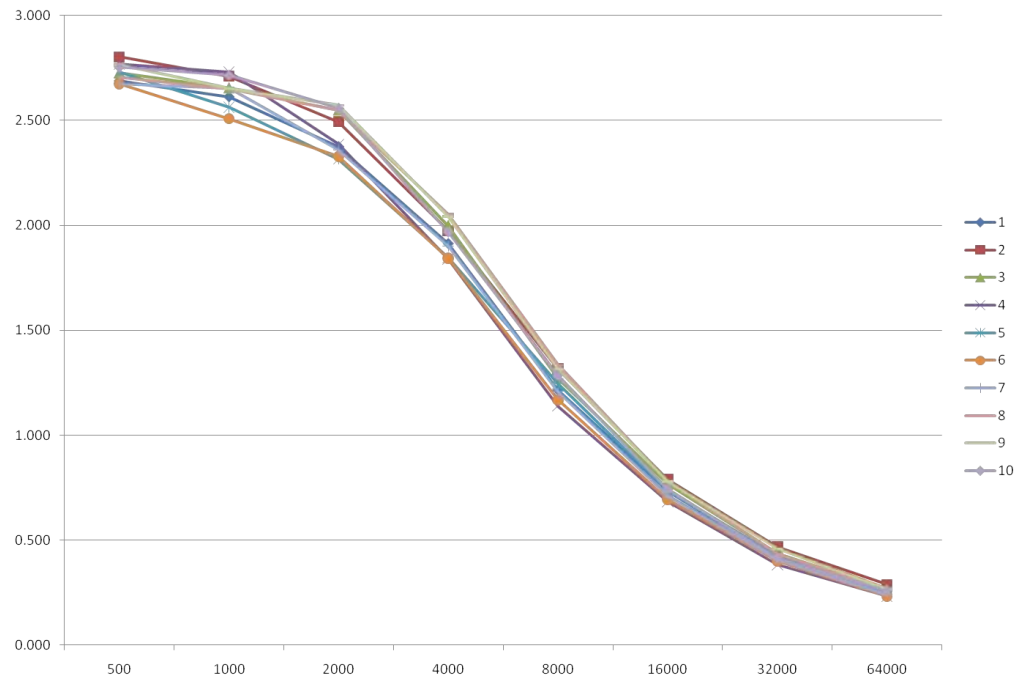
Laboratory structure. The MSL, located at the Walter Reed Army Institute of Research (WRAIR), operates in compliance with Good Clinical Laboratory Practices (GCLP) according to the British Association of Research Quality Assurance. The MSL has the following staff:

- Laboratory Director to oversee all work and collaborate with external partners.
- Quality Assurance/Quality Control (QA/QC) Manager to oversee strict data management and quality control.
- Laboratory Manager with more than 22 years of international laboratory experience in malaria and tropical diseases to manage sample storage and ensure smooth laboratory function.
- Four qualified ELISA operators.

Development of standardized, highly reproducible ELISAs. As a key facility within the USMMVP, the MSL has years of experience in developing and standardizing ELISAs. Assays are subject to a standard ELISA development protocol, standard operating procedures, and continuous quality assurance and control in accordance with GCLP guidance. As a result, MSL assays are extremely

robust and highly reproducible (see Figure 1 below). The facility performs ELISAs on both clinical and pre-clinical samples using peptides or vaccine-grade recombinant proteins as plate antigens.

Figure 1. Single operator quality control sample titration curve from qualification ELISAs performed on ten consecutive days.



New plate antigens are under development. The facility currently performs ELISAs for the following malaria antigens:

Plasmodium falciparum:

- Apical merozoite antigen 1 (3D7)*+
- Merozoite surface protein 1 (3D7*+ and FVO*)
- Circumsporozoite protein*+
- Liver-stage antigen 1*
- CelTOS

Plasmodium vivax:

- Circumsporozoite protein*

*Human assays that have been fully optimized; +Quantitative assays ($\mu\text{g/ml}$)

Operator qualification. In order to run clinical trial samples on standardized ELISAs, an operator must complete a rigorous qualification process on each individual assay. The process includes initial assay qualification and quarterly maintenance of qualification using quality control panels. In order to maintain assay qualification, assays must be performed accurately within established precision limits.

Volume. Despite rigorous QA/QC requirements for MSL assays, each ELISA operator can process up to 350 samples per month.

Contact us.

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Other technologies for characterizing vaccine-induced antibodies. The MSL is currently exploring other technologies to further distinguish the humoral response induced by malaria vaccines against whole sporozoites and malaria antigens, to include immunofluorescence assays (IFAs), description of antibody isotypes and IgG subclasses, and measurement of antibody affinity. Available technologies include *P. falciparum* sporozoite IFA, Attana® biosensor, and Luminex®. The laboratory welcomes collaborations with external partners for novel research to further characterize vaccine-induced antibodies.

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

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

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