

## Evaluation technologies – Generating reliable data for decision-making

### The need

**Understanding the immune responses to malaria vaccines** that contribute to protective immunity is key to accelerating malaria vaccine development. For this reason, continued investment in immunological assays, challenge models, and other evaluation technologies that can help to clarify protective immune responses in people remains a critical need.

PATH's Malaria Vaccine Initiative (MVI) makes data-driven decisions in managing our portfolio of vaccine approaches and has invested in the establishment of reference and service laboratories, and supported development of new evaluation tools, to ensure generation of reliable data. Continued development of effective evaluation technologies, which is essential for MVI to execute its strategy successfully, supports both preclinical and clinical projects.

### Assay development

**In cases where tools do not exist to measure relevant immune responses**, MVI engages research groups in developing and optimizing immunological assays to improve our ability to develop strong vaccine candidates.

### Challenge models

**Malaria vaccine developers have been fortunate** to have access to a human challenge model—known as controlled human malaria infection or CHMI—to evaluate the protective efficacy of pre-erythrocytic vaccines in early clinical trials. In CHMI studies, relatively small numbers of volunteers are exposed to the bites of infected mosquitoes in a safe, highly controlled environment. The immune responses in protected versus non-protected volunteers are compared to determine key differences. CHMI studies in malaria are possible because malaria infection can be readily treated with no long-term consequences, if managed appropriately.

The CHMI model has been critical for informing malaria vaccine development, and MVI and partners are working to capitalize on these efforts by evaluating human challenge models for their potential to assess the efficacy of transmission-blocking vaccines via the measurement of onward transmission to mosquitoes.

### Immune correlates

**Given the lack of understanding of the specific immune responses** associated with protection against parasite infection (as well as preventing parasite transmission), MVI has placed increasing emphasis on identifying immune correlates of protection. We are generating new hypotheses about the mechanisms of vaccine-induced protection. Multiple efforts are under way to characterize the humoral and cellular responses to vaccine candidates in our portfolio.

## Reagent generation

**Variability in procedures and types of assays** hinders comparability among vaccine candidates. MVI supports several efforts aimed at identifying high-quality reference reagents and acceptance of common methodologies.

## Reference centers

**MVI has identified several laboratories with strong backgrounds** in performing standardized assays and has engaged them in assay support activities for the benefit of the entire malaria vaccine development community. Activities include blinded testing of preclinical and clinical samples using standardized assays that enable comparison between different formulations and delivery platforms, as well as development of additional assays, as needed, to evaluate novel antigens. MVI-supported reference centers include the Standard Membrane Feeding Assay Reference Center at the Laboratory of Malaria and Vector Research (US National Institutes of Health/National Institute of Allergy and Infectious Diseases) and an immunology reference center established in collaboration with the International AIDS Vaccine Initiative and its Human Immunology Laboratory at Imperial College London.

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**PATH's MALARIA VACCINE INITIATIVE (MVI)** accelerates malaria vaccine development and catalyzes timely access in endemic countries, toward a world free from malaria. Standing at the intersection of malaria and immunization, MVI is part of PATH's Center for Malaria Control and Elimination and PATH's Center for Vaccine Innovation and Access. Learn more at [www.malariavaccine.org](http://www.malariavaccine.org).