

**Project Title:** Evaluating for cross-reactivity in commercially available Malaria RDTs using a COVID-19 samples challenge, in Zambia.

**Project Dates:** Flexible 9-12 months On-site between (May 2024 – May 2025)

**Project Site:** Lusaka, Zambia (Matero Clinical Research Site (CRS), Macha Trust Research Center (MTRC) and Tropical Disease Research Center (TDRC)).

**Project Overview:** Malaria is a curable disease caused by the parasite plasmodium, in which patients may present with fever, chills, and flu-like illness and if left untreated, may cause severe complications even death (*Global Health and Division of Parasitic Diseases, 2020*). Children under 5 years, travellers and people that are immunocompromised (*CDC, 2021*). Given the similarities in clinical presentation between malaria and COVID-19, there has been a lot of emphasis on the importance of people in malaria-endemic regions who are febrile or display symptoms of COVID-19 being evaluated for malaria and to prompt the management required to prevent serious outcomes in individuals with COVID-19 and malaria co-infection (*Wilairatana et al. 2021*)(*WHO 2021*). According to the WHO, during the peak of the COVID-19 pandemic it was estimated that COVID-related disruptions led to about 13 million more malaria cases and 63 000 more malaria deaths (*WHO, 2022*).

Therefore, challenges of uncertainty in the diagnosis of malaria with respect to COVID-19 may not only result in mismanagement; underestimation or overestimation of both conditions, but also the risk of potentiating antimalarial drugs resistance due to over exposure during the COVID-19 pandemic. Some scientists have suggested that different antibodies certainly affect the sensitivity of different RDTs with respect to their target antigens leading to variability in the detection of the variable structures of HRP2 (*WHO 2019*) and higher-than-expected positivity of non-neutralizing IgG was observed to spike and receptor-binding domain antigens in a pre-pandemic sero-survey conducted on malaria-infected persons (*Jessica et al, 2022*) (*Lapidus et al. 2022*).

Serological research and immunological studies conducted in malaria-endemic regions should consider determining and/or understanding the background reactivity/assay. This would help account for any alterations in expected immune responses and making compensatory adjustments if required. In addition, having a better mechanistic understanding of the immunological interactions of the endemic diseases with other diseases or scientific interventions, may contribute to the development of more targeted and effective strategies to control diseases. Highlighting the complexities of parasite-host interactions, immune responses, and disease pathology in parasitic infections such as Malaria in endemic countries is a much-needed and important area of research in parasitic diseases endemic African countries.

**Project Summary:** In this study we aim to evaluate the performance of the commercially available diagnostic immunoassays for Malaria used as point-of-care in most of the out-patient-departments (OPD) and healthcare facilities in Zambia, using the malaria and COVID-19 samples challenge. The study will be a multi-center cross-sectional study. The Center for Infectious Diseases in Zambia (CIDRZ) in Lusaka, while working in collaboration with the Macha Trust Research Center (MTRC) in the Southern province and Tropical Disease Research Center (TDRC) on the Copperbelt province will conduct this study in Zambia. The study specific laboratory tests will be conducted at the laboratories in Lusaka at CIDRZ, in Southern province at Macha Trust Research Center (MTRC) and on the Copperbelt province at the Tropical Disease Research Center (TDRC). The study team will conduct the study required tests on the pre-pandemic malaria dried blood spots (DBS) stored at MTRC and TDRC; and COVID-19 samples collected during the COVID-19 pandemic at CIDRZ. The objectives include:

- To investigate for cross-reactivity in commercially available Malaria RDTs to PCR confirmed SARS-CoV-2 positive samples, including investigating the relationship with SARS-CoV-2 species, COVID-19 clinical presentation, COVID-19 vaccination status and age.

- To investigate using ELISAs whether there is cross-reactivity to SARS-CoV-2 associated with malaria exposure and we investigate the relationship with Plasmodium species, malaria infection status, and age.

### **Scholar Involvement:**

This will be a flexible 9 -12 months On-site between (May 2024 – May 2025). This will be broken down into 4-5 months of laboratory work between the 3 proposed sites. Two months of analysis of the results, including data cleaning (QA/QC). 2-3months of manuscript writing and publication.

#### a. Laboratory work (4-5 months)

During this time period the scholar will be assigned to the 3 different laboratories in the 3 different research organizations. This will be done in this order:

##### 1. COVID-19 sample process and training

This will be done at the CIDRZ laboratory in the capital city of Lusaka where the serum COVID-19 samples are stored. The scholar will be introduced to the CIDRZ structures and team. The scholar will be trained on the laboratory etiquette and assigned to the laboratory staff.

##### 2. Malaria samples processing and training

This will be done at the Macha Trust Research Center (MTRC) in the Southern province and Tropical Disease Research Center (TDRC) on the Copperbelt province in Zambia. This will involve the scholar travelling to the other study sites accompanied by the CIDRZ mentor. The scholar will then be introduced to the other mentors and the laboratory staff.

During this period the scholar will receive the necessary training on Good Clinical Practices and the sample processing methods. The Scholar will also be allocated time for hospital ward rounds.

#### b. Data QA/QC and analysis. (2 Months)

- During this period the scholar will be involved in the data cleaning process.
- Attend basic statistical analysis and methods training.

#### c. Manuscript writing and publication.

- The scholar will be expected draft the initial manuscript for review.
- Receive training on basic manuscript writing, literature review and referencing.
- Submission of the manuscript to research journals for publication as lead author.

#### d. The Center for Infectious Diseases house (CIDRZ) in-house activities

- The scholar is expected to attend the weekly scientific journal presentations.
- The scholar will be expected to present the scientific findings to the study team and the whole CIDRZ forum during the scientific journal meeting.

**Regulatory requirements for the project and plans for completing them:** Ethical approval will be acquired from The University of Zambia Biomedical Research Ethics Committee (UNZABREC), Zambia Medical Regulatory Authority (ZAMRA) and The National Health Research Authority (NHRA) before conducting the study. Every effort will be made to protect participant privacy and confidentiality to the

extent permitted by law. Study-related information will be stored securely at the CIDRZ Matero research site (CRS). All participant information will be stored in lockable file cabinets in areas with access limited to study staff. Data/ Sample collection, processing, and administrative forms, and other reports will be identified by a coded number only, to maintain participant confidentiality. All records that contain names or other personal identifiers, such as locator forms and informed consent forms, will be stored separately from study records identified by code number. Consent will be acquired from the participants before any study related procedures are conducted.

**Expected Deliverables:**

- HVTN – presentation
- Manuscript for submission

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