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# Clinical performance of novel malaria rapid diagnostic tests for the detection of malaria infections with pfhrp2/3 gene deletions in Ethiopia

**Submission date**
02/12/2025

**Recruitment status**
Recruiting

**Registration date**
08/12/2025

**Overall study status**
Ongoing

**Last Edited**
08/12/2025

**Condition category**
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

## Plain English summary of protocol

Background and study aims
Malaria rapid diagnostic tests (RDTs) usually detect a protein called histidine rich protein 2 (HRP2). However, some Plasmodium falciparum malaria parasites have hrp2/3 gene deletions, which can cause these tests to give false negative results. This leads to missed diagnoses, untreated cases, and continued disease spread. New RDTs are needed to address this challenge. The goal of this study is to evaluate two new RDTs — the STANDARD Q hs-Malaria P.f Ag and the STANDARD Q hs-Malaria P.f/P.v Ag — for their ability to detect P. falciparum infections with hrp2 /3 deletions.

Who can participate?
Patients aged 5 years or older attending clinics in Ethiopia who either have a fever (suspected malaria) or are confirmed positive for P. falciparum malaria by microscopy but negative by an HRP2-based screening RDT.

What does the study involve?
For suspected malaria patients, finger-prick blood will be collected for the routine malaria test at the clinic (microscopy or RDT) and the two new RDTs. For confirmed cases enrolled by screening, fingerprick blood will be collected for the new RDTs. All participants will have venous blood (from the arm) drawn for laboratory use. In the laboratory, the study will repeat the new RDTs, conduct additional comparator tests, and conduct the gold standard reference test for malaria. All clinical management of study participants will follow the standard of care for malaria diagnosis in Ethiopia. Venous blood will undergo confirmatory testing, including identifying genetic variation, sequencing of Plasmodium genes and quantifying antigens. Specimens will be stored frozen for testing of additional RDTs in the future.

What are the possible benefits and risks of participating?
There are minimal risks associated with participation in this study, mainly related to blood sample collection, such as slight pain or bruising. Participation will not benefit individuals

personally, but what is learned from this study may help others in the future who need testing for malaria.

Where is the study run from?
This study is being conducted by Addis Ababa University Aklilu Lemma Institute of Health Research (Ethiopia). Recruitment will take place in Oromia Region of Ethiopia at Haro Adi Health Center.

When is the study starting and how long is it expected to run for?
The study will recruit from October 2025 to Q1 2026.

Who is funding the study?
Bill and Melinda Gates Foundation (USA)

Who is the main contact?
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2. Stephanie Zobrist, Co-Investigator and Sponsor Representative, szobrist@path.org
3. Miraf Mesfin, Co-Investigator and Sponsor Representative, mmesfin@path.org

# Contact information

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# Additional identifiers

# Study information

### Scientific Title
Clinical performance evaluation of novel malaria rapid diagnostic tests for the detection of malaria infections with pfhrp2/3 gene deletions among febrile individuals in Ethiopia

### Acronym
ETH-mRDT

### Study objectives
Primary objective is to assess the sensitivity of the SD Biosensor P.f combo and P.f/P.v combo RDTs for the detection of P. falciparum infections containing hrp2 and/or hrp3 gene deletions.

Secondary objectives
1. To assess the sensitivity and specificity [altogether referred to hereafter as “diagnostic accuracy”] of the SD Biosensor P.f combo and P.f/P.v combo RDTs in intended use settings for detecting P. falciparum infections in capillary and venous whole blood samples collected prospectively from patients with confirmed or suspected malaria.
2. To assess the diagnostic accuracy of comparator tests (microscopy and the Rapigen BIOCREDIT Pf/Pv [pLDH/pLDH] test) in intended use settings for detecting P. falciparum infections in capillary and venous whole blood samples collected prospectively from patients with symptoms suggestive of malaria.
3. To establish a repository of frozen specimens for the evaluation of RDTs for their performance against P.falciparum specimens with known hrp2/hrp3 gene deletion status.

### Ethics approval required
Ethics approval required

### Ethics approval(s)
1. approved 04/04/2025, Aklilu Lemma Institute of Health Research- Institutional Research Ethics Review Committee (ALIHR-IRERC) (Aklilu Lemma Institute of Health Research Institutional Review Board, PO Box 1176, Sefere-Selam Campus, Addis Ababa, 1000, Ethiopia; +251 (0) 112763091; aklilu.lemma@aau.edu.et), ref: ALIHR IRERC/185/2017/25

2. approved 15/04/2025, WIRB Copernicus Group (1019 39th Ave. SE, Suite 120, Puyallup, 98374, United States of America; +1 (0)360-252-2447; clientcare@wcgclinical.com), ref: 1391503

3. approved 09/09/2025, National Research Ethics Review Board (PO Box 1367, Arada Sub-City, Addis Ababa, 1000, Ethiopia; +251 (0)111553133; info@moe.gov.et), ref: 8/246/84/25

## Primary study design
Observational

## Secondary study design
Cross sectional study

## Study type(s)

## Health condition(s) or problem(s) studied
Malaria

## Interventions
Index tests/investigational product:
1. STANDARD Q hs-Malaria P.f Ag Test
2. STANDARD Q hs-Malaria P.f/P.v Ag Test

Comparator tests:
1. Light microscopy: standard of care and research-grade
2. Standard of care RDT, if applicable
3. Comparator RDT: Rapigen BIOCREDIT Malaria Ag Pf/Pv (pLDH/pLDH)
4. An HRP-2 based RDT for screening

Reference test:
1. Real-time polymerase chain reaction (PCR) assay for quantification and species identification
2. Speciation of all malaria, P.vivax, P.falciparum

Confirmatory tests:
1. Research use only assay for quantification of malaria antigens
2. PCR testing for HRP2/HRP3 gene deletion in P. falciparum infections

## Intervention Type
Device

## Phase
Phase III

## Drug/device/biological/vaccine name(s)
STANDARD Q hs-Malaria P.f Ag Test, STANDARD Q hs-Malaria P.f/P.v Ag Test

## Primary outcome(s)
1. Sensitivity of the index tests on specimens with hrp2/hrp3 deletions measured using using the formula Sensitivity = TP/(TP+FN); TP = True positive (positive by PCR for P. falciparum or P. vivax and positive by the relevant RDT test line); FN = False negative (positive by reference PCR and negative by the relevant RDT test line), at after data collection is completed

2. Sensitivity and specificity of SD Biosensor P.f combo and the P.f/P.v combo RDTs for the detection of P. falciparum infections in patients with confirmed or suspected malaria. measured using the formulae Sensitivity = TP/(TP+FN) and Specificity = TN / (TN + FP) at after data collection is completed

3. Sensitivity and specificity of comparator tests (microscopy and the Rapigen BIOCREDIT Pf/Pv [pLDH/pLDH] test) for the detection of P. falciparum infections in patients with symptoms suggestive of malaria. measured using the formulae Sensitivity = TP/(TP+FN) and Specificity = TN / (TN + FP) at after data collection is completed

4. Specimen repository measured using establishing a repository of frozen specimens for the evaluation of RDTs for their performance against P.falciparum specimens with known hrp2/hrp3 gene deletion status at end of study

### Key secondary outcome(s))

### Completion date
30/01/2026

# Eligibility

### Key inclusion criteria
Inclusion criteria for cross sectional component:
1. Aged 5 years of age or older
2. Presenting at the study site with fever or a history of fever during the preceding 48 hours
3. Freely agreeing to participate by providing informed consent (and assent, as applicable)

Inclusion criteria for screening component:
1. Aged 5 years of age or older
2. Presenting at the study site with fever or a history of fever during the preceding 48-hours
3. Confirmed P. falciparum malaria positive by microscopy
4. Negative for P. falciparum malaria on a WHO-recommended HRP2-based RDT
5. Freely agreeing to participate by providing informed consent (and assent, as applicable)

### Healthy volunteers allowed
No

### Age group
Mixed

### Lower age limit
5 years

### Upper age limit
100 years

### Sex
All

### Total final enrolment
0

### Key exclusion criteria
Presence of symptoms and signs of severe illness and/or central nervous system infections as defined by WHO guidelines

### Date of first enrolment
06/10/2025

### Date of final enrolment
30/01/2026

## Locations

### Countries of recruitment
Ethiopia

## Sponsor information

### Organisation
Program for Appropriate Technology in Health

### ROR
https://ror.org/02ycvrx49

## Funder(s)

### Funder type

### Funder Name
Bill and Melinda Gates Foundation

### Alternative Name(s)
Bill & Melinda Gates Foundation, Gates Foundation, Gates Learning Foundation, William H. Gates Foundation, BMGF, B&MGF, GF

### Funding Body Type
Government organisation

### Funding Body Subtype
Trusts, charities, foundations (both public and private)

### Location
United States of America

# Results and Publications

## Individual participant data (IPD) sharing plan

### IPD sharing plan summary
Not expected to be made available