Subregional networks of antimalaria drug efficacy and resistance in Eastern Africa and Horn of Africa countries

Meeting report, Kampala, Uganda,
9–10 November 2023

World Health Organization

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This publication contains the meeting report of the subregional networks of antimalaria drug efficacy and resistance in Eastern Africa and Horn of Africa countries and does not necessarily represent the decisions or policies of WHO.

Contents

Abbreviations

ACT	artemisinin-based combination therapy
AL	artemether–lumefantrine
ASAQ	artesunate–amodiaquine
ASPY	artesunate–pyronaridine
CQ	chloroquine
DP	dihydroartemisinin–piperaquine
GLURP	glutamate-rich protein
Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria
LSHTM	London School of Hygiene and Tropical Medicine
MSP1	merozoite surface protein-1
MSP2	merozoite surface protein-2
NMP	national malaria programme
PCR	polymerase chain reaction
PfK13	*Plasmodium falciparum Kelch-13*
PMI	U.S. President's Malaria Initiative
PQ	primaquine
TES	therapeutic efficacy studies
WHO	World Health Organization

Executive summary

The World Health Organization (WHO) Global Malaria Programme organized a meeting on 9–10 November 2023 in Kampala, Uganda, bringing together countries in the WHO African Region (Eritrea, Ethiopia, Kenya, Rwanda, South Sudan, Uganda and United Republic of Tanzania) and the WHO Eastern Mediterranean Region (Djibouti, Somalia, Sudan and Yemen). The objective was to provide a platform for countries to share data and encourage generation of high-quality, up-to-date information on the efficacy of and resistance to antimalarial drugs in order to guide treatment policy. The attendees included representatives from national malaria programmes (NMPs), research groups, funding partners and multilateral organizations.

The agenda included technical updates on malaria case management and tools for monitoring antimalarial drug efficacy and resistance. Countries shared recent data from therapeutic efficacy studies (TES) and on molecular resistance markers. They reported generally high efficacy of artemisinin-based combination therapies (ACTs), although the efficacy of artemether–lumefantrine (AL) at some sites in Uganda and United Republic of Tanzania had been lower than expected. Delayed parasite clearance on day 3 associated with *Plasmodium falciparum Kelch-13 (PfK13)* mutations was reported from Eritrea, Rwanda, Uganda and United Republic of Tanzania. Challenges in implementing TES and insights from surveillance of molecular marker were also discussed, with calls for robust genotyping methods and algorithms to distinguish relapses from new infections.

Timely sharing of data with NMPs was considered essential for rapid decision-making. Each country presented their plans for TES in 2024–2025, including the numbers of sites, the drugs to be tested, financial resources, gaps and needs. Recommendations were agreed by discussion and group work to guide future work.

Recommendations:

- **Improve the quality of TES implementation:** Ensure the quality of TES, particularly by raising the standards of microscopy, through continuous training and certification in programmes such as external competence assessment of malaria microscopists, adherence to standardized protocols and tools, centralized procurement of quality-assured TES commodities and robust TES monitoring and support.

- **Improve genotyping methods:** Explore and integrate advanced molecular techniques, such as amplicon deep sequencing, for polymerase chain reaction (PCR) in routine TES. This approach could ensure more precise, comprehensive differentiation of recrudescence from new infections in areas of high transmission, thus improving understanding of the efficacy of and resistance to antimalarial drugs.

- **Facilitate timely data-sharing:** Data from TES and on resistance markers should be shared with the NMP to enable timely decisions. Collaboration and agreements among research institutions and the NMP should be encouraged to ensure rapid data-sharing.

- **Digitize data collection:** Use digitized data collection tools to improve efficiency and the accuracy and accessibility of information from TES.

- **Strengthen and support malaria resistance networks:** Promote collaboration by using networks for antimalarial drug resistance and surveillance of efficacy to foster exchange of knowledge, resources and experience among participating countries.

- **Mobilize resources for capacity building:** Secure resources to strengthen technical and infrastructural capacity in countries. Explore innovative cost-sharing methods, such as establishing regional molecular surveillance laboratories, to ensure sustained support for antimalarial research and surveillance.

- **Integrate TES into national strategic plans and routine surveillance mechanisms:** Such integration will improve country ownership, coordination and effective implementation of TES.

- **Develop and implement strategies to manage artemisinin resistance:** Comprehensive strategies based on national assessments of antimalarial drug resistance are required.

Background

The therapeutic efficacy of antimalarial drugs must be monitored to obtain data for formulating evidence-based policies for malaria treatment in endemic countries. WHO recommends that the efficacy of both first- and second-line ACTs be assessed at least every 2 years at designated sentinel sites in each country.

Partial resistance to artemisinins has now been confirmed in four African countries – Eritrea, Rwanda, Uganda and United Republic of Tanzania – and is probably present in others. There is also concern about the development of resistance to some of the key partner drugs used in ACTs, which are used to treat millions of malaria cases.

In November 2022, WHO launched a strategy to address antimalarial drug resistance in Africa, which emphasized the importance of strengthening surveillance of antimalarial drug efficacy and resistance *(1)*. Regular meetings of antimalarial drug efficacy and resistance monitoring networks in the Greater Mekong Subregion and the WHO Eastern Mediterranean Region have played a key role in providing data and updates on treatment policies. While similar networks were once active in Africa, most have not been convened since 2017–2018.

To renew regional collaboration, the WHO Global Malaria Programme organized a meeting on 9–10 November 2023, in Kampala, Uganda, bringing together representatives from countries in the WHO African Region (Eritrea, Ethiopia, Kenya, Rwanda, South Sudan, Uganda and United Republic of Tanzania) and the WHO Eastern Mediterranean Region (Djibouti, Somalia, Sudan and Yemen).

Objectives

The aim of the meeting was to provide a platform for countries to share high-quality, up-to-date data on the efficacy of and resistance to antimalarial drugs as a basis for treatment policy. The specific objectives of the meeting were to:

- update countries on current tools for monitoring antimalarial drug efficacy and resistance;
- review the most recent data on antimalarial drug efficacy and resistance and evaluate gaps in surveillance; and
- plan high-quality studies of therapeutic efficacy and drug resistance

The agenda of the meeting is provided in Annex 1 and the list of participants in Annex 2.

Opening session and remarks

The meeting was opened under the chairmanship of Daniel Kyabayinze, Director, Health Services, Uganda, who welcomed participants.

Subregional networks have historically played a pivotal role in increasing both the quantity and quality of efficacy studies and driving changes in treatment policy across countries by facilitating sharing of data and evidence. Significant reductions in malaria have been achieved over the years, due largely to widespread deployment of more effective fixed-dose ACTs. Recent reports of increased recurrence of *P. falciparum* during follow-up are, however, raising concern.

The meeting would discuss changes in the efficacy of currently recommended ACTs and address study challenges, explore funding opportunities, foster collaboration

with research institutions and ensure timely data-sharing. Additionally, the meeting would draw on experiences in the WHO Eastern Mediterranean Region in extending work beyond drug resistance to include surveillance of *HRP2-3* gene deletions. A focus throughout the meeting would be on the role of surveillance in providing actionable insights.

Session 1. Update on case management

Malaria case management from the WHO perspective

The WHO malaria guidelines highlight the critical importance of parasitological diagnosis of all suspected cases and test results within 2 h of a patient's presentation. For treatment of uncomplicated *Plasmodium falciparum* malaria, ACTs are the preferred option. Six ACTs are currently recommended: AL, artesunate–amodiaquine (ASAQ), artesunate–mefloquine, dihydroartemisinin–piperaquine, artesunate–sulfadoxine–pyrimethamine and artesunate–pyronaridine (ASPY).

In cases of uncomplicated non-falciparum malaria, either an ACT or chloroquine (CQ) may be used. The guidelines also recommend prevention of relapse with a course of primaquine for eligible patients. Exceptions include individuals with glucose-6-phosphate dehydrogenase deficiency, who should instead take a weekly dose for 8 weeks. Primaquine is contraindicated for pregnant women and infants < 6 months of age.

Treatment failure can result from drug resistance, inadequate exposure to a drug (due to factors such as suboptimal dosing, poor adherence, vomiting or poor absorption or metabolism) or from use of substandard medicines. If treatment failure occurs within 28 days, an alternative ACT with proven effectiveness should be administered. Treatment failure after 28 days may indicate either re-infection or recrudescence. As many routine clinical settings lack molecular tools to differentiate re-infection from recrudescence, such cases are generally treated as new infections with first-line medication.

For severe malaria, injectable artesunate is the optimal treatment. A new WHO field guide on pre-referral management of children is available online *(2)*. WHO consolidated guidelines for malaria are also available online and via a mobile app *(3)*. The guidelines include investment in the quality of care and ensuring proper implementation of malaria treatment protocols.

Session 2. Tools to monitor antimalarial drug efficacy and resistance

Current tools for monitoring efficacy and resistance of antimalarial drugs

Monitoring the efficacy of antimalarial drugs is essential to ensure that they remain effective for treatment of uncomplicated malaria. The TES protocol is used to evaluate first- and second-line drugs for *P. falciparum* and *P. vivax*, including with WHO's latest genotyping methods, to differentiate between recrudescence and new infection. The standard protocol includes comprehensive guidelines on study design, ethical considerations, treatment schedules and follow-up procedures.

The latest WHO guidance for distinguishing between recrudescence and new infection now recommends use of the markers merozoite surface protein-1 (MSP1), merozoite surface protein-2 (MSP2) and one microsatellite (Poly-α, Pfpk2 or TA1), replacing the

previous MSP1, MSP2 and glutamate-rich protein (GLURP). This approach is advised for areas of Africa with low, moderate and high transmission, while GLURP remains recommended for regions outside Africa.

TES data entry, analysis and application were described, including interpretation of treatment failure rates and molecular markers. Quality control monitoring is essential to maintain high standards in TES. The WHO TES monitoring checklist — used at the beginning, during and end of a study to ensure adherence to protocols in study implementation and data processing — was presented.

The speakers described challenges at various stages of TES, from preparation to data-sharing. During preparation, country teams often underestimate the time required for preparing a protocol, ethical approval, material procurement, administration of funding and team training. Issues such as missing the malaria transmission season, using referral hospitals instead of primary-care facilities and small numbers of malaria cases at study sites can result in low recruitment rates or high dropout.

Challenges in recruitment include enrolling patients who are outside the inclusion criteria, unsupervised dosing (e.g. with AL), inadequate documentation, inaccurate parasite identification and insufficient blood samples. Civil unrest and emergencies can further disrupt studies, causing site abandonment or loss of materials. Quality control issues, such as delays in slide reading, non-compliance with WHO slide procedures and different genotyping methods, obviate comparison of data among studies.

Issues in data entry and analysis include lack of double data entry and of data cleaning and no explanation of loss to follow-up or withdrawals. Timely sharing of data with NMPs and WHO is crucial for policy-making and for tracking global trends. These challenges must be addressed to ensure the accuracy and reliability of TES results, which allow effective malaria control strategies.

Malaria molecular surveillance and PCR correction

Molecular surveillance of malaria is necessary to monitor markers of resistance to antimalarial drugs, *HRP2* and *HRP3* deletions, insecticide resistance and parasite genetics in regions in which transmission is decreasing or being eliminated. Techniques for molecular surveillance were discussed, including conventional PCR for detection, high-volume quantitative PCR for low-density infections and whole genome sequencing to identify novel markers. Markers of resistance in *P. falciparum*, such as *PfK13* for artemisinin and the *P. falciparum* chloroquine resistance transporter gene for chloroquine, have been identified, although there are no validated markers for some ACT partner drugs. Further research is required to link molecular markers with treatment response in TES.

PCR-corrected treatment outcomes are necessary to assess the efficacy of antimalarials. Various genomic techniques were presented and their sensitivity, robustness and marker diversity discussed. Comparisons of genotyping methods (capillary electrophoresis, sequencing machines and targeted amplicon sequencing) showed differences in sensitivity; MSP1 and MSP2 were identified as highly sensitive, diverse markers. Microsatellites such as poly-alpha and PfPK2 are alternatives to GLURP, although neither detects minority strains in multiclonal infections. PfPK2 is more sensitive for minority strains but lacks the genetic diversity of poly-alpha. Thus, there is no ideal microsatellite marker for high-transmission areas. A consensus on optimal PCR correction techniques and an external quality assurance programmes are necessary to ensure the quality of data in all laboratories.

Comparative analyses of PCR correction methods consistently show that markers such as MSP1 and MSP2 are more diverse than microsatellites. Targeted amplicon

sequencing, while the most reliable method, is expensive. Until this method becomes more accessible in Africa, an expert WHO panel recommends use of MSP1, MSP2 and a microsatellite (poly-alpha, Pfpk2 or TA1) in areas with moderate-to-high transmission, while low-transmission regions can continue to use MSP1, MSP2 and GLURP.

Session 3. Country presentations on recent therapeutic efficacy studies of antimalarial drugs

Djibouti

Djibouti has not yet conducted a TES. The national team, with technical support from WHO, has now prepared a protocol, obtained ethical approval and trained a team. They are awaiting the transmission season to begin TES activities during the main transmission period in February 2024.

Eritrea

TES have been conducted routinely at four western sites: Shambuko, Tekombia, Goluj and Agordat. The TES for ASAQ in 2019 showed high efficacy (94–97.9%); however, an increase in the appearance of the PfK13 622I variant was observed, from 13.3% in 2016 to 21% in 2019, among pre-treatment isolates. The study also confirmed partial resistance of *P. falciparum* to artemisinin, along with *hrp-2/3* gene deletions. The most recent TES, in 2022, showed a PCR-uncorrected ASAQ efficacy of 87% at one site and of 95–99% at the remaining sites; genotyping is pending. The main challenges to TES were difficulty in achieving adequate sample sizes, limited human resources, low *P. vivax* case numbers, budgetary constraints, difficulty in procuring study materials and lack of molecular monitoring capacity in the country.

Ethiopia

The Ethiopian Institute of Public Health has conducted TES at 11 sites during the past two decades. In the TES in 2020–2021, AL showed > 90% efficacy in Shewrobit, Metehara, Arba Minch and Hamusite. The TES in 2022–2023, however, indicated PCR-uncorrected efficacy rates > 90% for both AL–primaquine (PQ). The main challenges are budget constraints, lack of standardized training and difficulty in obtaining reagents and supplies.

Kenya

In a TES in 2016–2017 to evaluate the efficacy of AL and dihydroartemisinin–piperaquine (DP), adequate clinical and parasitological response rates were 88.5% for AL on day 28 and 93.0% for DP on day 42. Day 0 samples were analysed for known *PfK13* mutations, but none was detected. Molecular surveillance in 2021 indicated a very low prevalence of *R539T* and *R561H* mutations. Challenges in conducting TES included high staff turnover, limited microscopy capacity, equipment delays, data management issues, rising costs, delays in ethical approval and fewer malaria cases, which affected patient recruitment.

Rwanda

Periodic TES have consistently shown the high efficacy of ACTs. The TES in 2018–2019 confirmed the efficacy of AL but showed delayed parasite clearance associated with the validated R561H mutation, indicating the emergence of partial resistance to artemisinins. Surveillance of resistance markers has since shown a nationwide increase in PfK13 mutations. In a study in 2022–2023 to monitor the efficacy of four ACTs, AL, ASAQ, DP and

APSY, recruitment was delayed, and adjustments were made, such as extending the age limit, broadening the criteria for parasitaemia and involving community health workers. Preliminary (uncorrected) results show 84% AL efficacy, with 12.5% parasitaemia on day 3 at the Masaka site. A study in several locations confirmed 100% efficacy of AL. Challenges include delayed enrolment and lack of updated guidelines. Despite the increase in PfK13 mutations and slower parasite clearance, baseline treatments remain effective. Plans are under way to update the national guidelines, potentially introducing multiple first-line treatments.

Somalia

Monitoring the therapeutic efficacy of nationally recommended ACTs has helped to shape the treatment policy, leading to replacement of artesunate–sulfadoxine–pyrimethamine with AL as first-line treatment and introduction of DP as second-line treatment in 2016. Studies in 2017 at two sites found high efficacy rates of > 99% for both first- and second-line treatment. Somalia has, however, faced challenges in implementing TES, primarily due to security issues, which restricted access to three of the four sentinel sites, while low transmission at one site also affected data collection. Additional challenges included staff shortages and limited capacity for data analysis.

South Sudan

South Sudan planned to conduct a TES on ASAQ and AL, its first- and second-line treatments, at four sentinel sites (Jonglei, Central Equatoria, Northern Bahr el Ghazal and Western Equatoria) in 2023. The challenges include lengthy ethical approval.

Sudan

Since 2004, Sudan has monitored the efficacy of ACT in Kassala, Gadarif, Sinnar, White Nile, South Kordofan, South Darfur and West Darfur and adjusted treatment guidelines as necessary. Studies in 2019–2020 in four states showed 100% efficacy for both AL and DP. TES conducted at seven sites between 2021 and 2023 faced significant challenges, with data collection interrupted and data lost due to the civil war. Studies in 2016 and 2019–2020 showed a 5.3–7.5% prevalence of the validated PfK13 mutation (R622I) in Gadarif and 2.2% in Sennar, although parasites were cleared by day 3. This result shows the importance of continuous monitoring of the efficacy of ACT, PfK13 mutations and day 3 positivity rates. The main challenge to programme implementation remains the ongoing civil conflict.

Uganda

The TES framework in Uganda for 2022–2023 covered five sites: Busia, Agago and West Nile, which have already been studied, and proposed sites in Kanungu and Karamoja. The sites were chosen according to previous results and surveillance data. The study assessed the efficacy of AL, DP, ASAQ and PA. It showed PCR-corrected efficacy rates for AL of < 90% at Busia and Arua and 97% at another site. At 42 days, DP showed 95% efficacy, ASAQ nearly 100% and ASPY < 90% in Arua. PfK13 mutation analysis indicated a significant, 21% prevalence of C469T in Agago. The challenges included limited funding and delayed enrolment due to intermittent lower malaria incidence.

United Republic of Tanzania

TES was conducted at eight routine sentinel sites, with additional special sites included as necessary. Studies at four sites in 2021 and four in 2022 showed an efficacy > 94% at seven sites and 89.9%, just below the 90% threshold, at one site. ASAQ was consistently effective at > 98%. A molecular marker survey in 2021 showed a high prevalence (22.5%) of the validated PfK13 R561H mutation in the Kagera region, near the borders of Rwanda

and Uganda. The TES in Kagera in 2022 also showed a high prevalence of the R561H mutation, linked to day 3 positivity, confirming partial resistance to artemisinins in the country. The main challenge for TES remains slow recruitment of patients due to low malaria incidence rates at some sentinel sites, which increases the cost of TES.

Yemen

There are five sentinel sites in the country, but physical access remains challenging due to the ongoing conflict. A study in 2020 and 2023 at two sites showed high efficacy (100%) for AL. No PfK13 mutations were detected in 2020, and the samples from 2023 are being analysed. Challenges persist in TES implementation due to the civil war, with logistical difficulties, especially in sample transport, compounded by limited courier options.

Session 4. Surveillance of molecular markers of antimalarial resistance – country examples

Horn of Africa Network for Monitoring Antimalarial Treatment: Experience of country support

The Horn of Africa Network for Monitoring Antimalarial Treatment (HANMAT) supports member countries in monitoring antimalarial drug efficacy and resistance. The support includes assessment of the effectiveness of ACT treatments and surveillance for resistance markers. HANMAT also encourages collaboration among member countries, including sharing of resources and expertise to build capacity and strengthen regional work against malaria drug resistance. Collaborative initiatives, including partnerships with the London School of Hygiene & Tropical Medicine (LSHTM), have provided data on the presence of *hrp2* and *hrp3* deletions in Eritrea, Somalia and Yemen. In Eritrea, parasites were identified with both deletions and the *Pfk13* R622I mutation. In Somalia, two samples showed the *R622I* mutation, whereas none were detected in Yemen.

Challenges in Somalia and Yemen include lack of security for sample collection and inconsistent quality of laboratory results. Recommended strategies to address these issues include standardizing field and laboratory protocols, engaging in external quality assurance programmes and investing in capacity building. The work of the LSHTM points to the importance of understanding the fitness and transmission dynamics of parasite mutations and of sustained funding for capacity-building in the region.

Experience from Uganda

The more than 20-year collaboration between Uganda and the University of California at San Francisco on antimalarial drug resistance demonstrates the advantages of close partnerships with local stakeholders and ministries of health. Over a decade of local capacity-building has been instrumental in generating data on genetic changes in malaria parasites across Uganda.

In Tororo, the prevalence of known resistance markers was studied over time. After introduction of AL, markers of reduced susceptibility to lumefantrine and increased sensitivity to CQ became more common. Between 1999 and 2015, no validated markers for artemisinin resistance were found; however, between 2016 and 2022, *PfK13* mutations began to appear, increasing in both frequency and geographical spread. In 2023, targeted deep sequencing suggested that Ugandan parasites probably originated from an African lineage rather than a South-East Asian one.

Sustained operation of molecular surveillance sites ensures early detection of resistance markers, allowing timely responses to changes in parasite populations. Strong partnerships, both local and international, are essential to overcome funding challenges and enhance understanding of evolving drug resistance patterns.

Experience from United Republic of Tanzania

The Malaria Molecular Surveillance Tanzania Project began in 2020 in 13 regions. Its aim was to enhance malaria molecular surveillance capacity in the country, particularly with respect to drug resistance. By 2023, the project had been extended to all 26 regions, covering over 150 health facilities, with collection of more than 55 000 samples. The objectives included mapping the genetic diversity of malaria parasites, monitoring drug resistance, and tracking *HRP2* gene deletions. A significant achievement was establishment of a fully equipped laboratory capable of next-generation sequencing. Emphasis on technology transfer resulted in disengagement from support from the USA, with local teams conducting independent analyses and bioinformatics.

Spread of the *R561H* mutation was documented in Kagera, from three districts in 2021 to five by 2023, with a notable increase in the *A675V* mutation. *PfCRT* mutations were also concentrated in Kagera, near Burundi, where ASAQ is commonly used. The high prevalence (22.5%) of the *R561H* mutation in Kagera in 2021 prompted a targeted TES in 2023, which confirmed partial resistance to artemisinins and indicated that a mitigation strategy should be planned. In the next phase, malaria-specific molecular surveillance will change to integrated molecular surveillance, including vector and human genomics. The challenges included building a dedicated team, ensuring a gender balance and managing the complexities of sample collection.

Session 5. Country planning of TES and resistance monitoring

Support from the U.S. President's Malaria Initiative

The U.S. President's Malaria Initiative (PMI) is active in 27 countries in Africa and supports TES at about 75 sites in 20 countries over 3 years, with close adherence to WHO recommendations. Protocols are rigorously reviewed to ensure compliance, and PMI provides standardized training materials, standard operating procedures and checklists, including a "starter checklist" to ensure consistent TES results. PMI is also involved in molecular surveillance through the Partnership for Antimalarial Resistance Monitoring network. The strategy emphasizes moving testing from the global North to endemic regions by training and supporting local laboratories.

Support from the Global Fund to Fight AIDS, Tuberculosis and Malaria

The Global Fund provides funding to national programmes and partners in the design, execution and reporting of TES. In its work with national programmes, the three main priorities are: securing sufficient funding, avoiding duplication and gaps and collecting actionable data. International collaboration and regional coordination are essential to ensure a continuous, unified response. Harmonization among TES funders such as the Global Fund and PMI enhances resource efficiency and prevents overlap. Challenges include prioritization of TES, delays due to limited capacity and issues of data quality. Delayed procurement of ACTs and over-reliance on certain ACTs indicate that diverse treatment options should be available. Successful partnerships and capacity-building are necessary to address these challenges, with ongoing dialogue, regional networks and collaboration to close gaps, facilitate policy changes and accelerate policy implementation.

National plans for TES and resistance monitoring

Participants from each country had been asked to prepare their plans for TES during 2024–2025. On a standardized template, they outlined key components, such as the drugs to be tested, sites, species, available resources, funding gaps, technical requirements and additional requirements (e.g. for training, monitoring, data analysis). The plans, summarized in Table 1, were presented and discussed in plenary.

Table 1. National plans for conducting TES during 2024–2025

Country	Species	Drug(s)	No. of sites	Funding source	Molecular laboratory	Other requirements (e.g. technical, training, monitoring, data analysis)
Djibouti	*P. falciparum*	AL	1	WHO	WHO collaborating laboratory	Protocol development, training, clinical monitoring, data review and analysis, PCR and marker analysis
Eritrea	*P. falciparum*	AL	4	Global Fund	WHO collaborating laboratory	Test drugs, filter paper, PCR and marker analysis
	P. vivax	AL	4	?	WHO collaborating laboratory	
Ethiopia	*P. falciparum*	AL, CQ–PQ, DP, ASPY	5	Global Fund, Ministry of Health, PMI-USAID, Africa CDC* and World Bank	National laboratory	Technical support, filter papers, PCR reagents
	P. vivax	AL, CQ–PQ, DP, ASPY	4 new			
Kenya	*P. falciparum*	AL, DP	To be determined	PMI	National laboratory	Protocol development, training, molecular analysis, data analysis and enhancement of laboratory capacity
Rwanda	*P. falciparum*	AL, DP, ASPY	6	PMI	National laboratory	Sequencing machine and reagents, training of laboratory technicians and data scientist
Somalia	*P. falciparum*	AL	2	Global Fund	WHO collaborating laboratory	Protocol development, quality control and data analysis, PCR and marker analysis
South Sudan	*P. falciparum*	AL, ASAQ	4 4	Global Fund and WHO	WHO collaborating laboratory	Support to protocol development, training, study implementation, quality control and data analysis, PCR and marker analysis
Sudan	*P. falciparum*	AL	4	Global Fund	WHO collaborating laboratory	Support to protocol development, data analysis, PCR and marker analysis

Country	Species	Drug(s)	No. of sites	Funding source	Molecular laboratory	Other requirements (e.g. technical, training, monitoring, data analysis)
Uganda	*P. falciparum*	To be determined	8	PMI and US CDC**	National laboratories	
United Republic of Tanzania	*P. falciparum*	AL, ASAQ, DP	9	PMI	National laboratories	Explore outsourcing or enhancing capacity for capillary electrophoresis and microsatellite analysis for genotyping
Yemen	*P. falciparum*	AL	2	Partial funding from World Bank	WHO collaborating laboratory	Support to protocol development, training, study implementation, quality control, data analysis, PCR and marker analysis

* African Center for Disease Control and Prevention

** US Center for Disease Control and Prevention

Panel discussion on improving data collection, data quality and timely data-sharing in countries

The panel comprised representatives of PMI, LSHTM and the NMPs of Kenya, Rwanda and Uganda. The moderator was Andrea Bosman. The session addressed challenges in data collection, quality and sharing and support mechanisms for improving them.

Question 1: To representatives from Kenya, Rwanda and United Republic of Tanzania: What support is required to improve data collection, specifically in the context of TES?

Response: The panellists said that existing tools should be examined and standardized to ensure consistency. A central platform for data sharing could be established so that NMPs could access and use data for decision-making swiftly, without relying on lengthy publication processes.

The panellists also said that TES and resistance testing should be integrated into national malaria strategies rather than considered as special projects. Regular collection of high-quality data was crucial to maintain effective case management. Health workers should be encouraged and their work acknowledged in order to motivate them. The panel proposed that a platform be created for sharing data, independent of workshops, to ensure clear agreement among the programme, the principal investigator and users of the data.

Question 2: To the representative of PMI: What additional support is required to improve data collection, data quality and sharing?

Response: Drawing on years of experience in TES, the PMI representative noted challenges in quality assurance and supervision, including infrequent field visits and gaps in documentation, which led to inconsistent data. More frequent, systematic supervision was required, with thorough documentation. PMI is changing to use of electronic study forms and patient records, which will allow principal investigators to monitor data in real-time, reduce travel and improve data oversight.

Question 3: To Professor Beshir: Given your experience in supporting TES, what changes do you envision to improve data collection, quality and sharing?

Response: Khaled acknowledged current challenges, such as delays in data processing, and reiterated that digitalization would provide access to real-time data. He stressed the importance of high-quality inputs (e.g. reagents, filter papers) from reliable suppliers and maintenance of proper storage conditions. Training and retraining of laboratory technicians, particularly in microscopy, are essential for accurate, high-quality data.

Recommendations from the meeting

Participants were separated into three groups to deliberate on recommendations: group 1, Somalia, Sudan and Yemen; group 2, Eritrea, Ethiopia, Kenya and South Sudan; and group 3, Rwanda, Uganda and United Republic of Tanzania. Partners were invited to join the groups. Each group presented its deliberations in a plenary session.

The recommendations for enhancing monitoring of antimalarial drug efficacy for timely responses are as follows.

- **Improve the quality of TES implementation:** Ensure the quality of TES, particularly by raising the standards of microscopy, through continuous training and certification in programmes such as external competence assessment of malaria microscopists, adherence to standardized protocols and tools, centralized procurement of quality-assured TES commodities and robust TES monitoring and support.

- **Improve genotyping methods:** Explore and integrate advanced molecular techniques, such as amplicon deep sequencing, for polymerase chain reaction (PCR) in routine TES. This approach could ensure more precise, comprehensive differentiation of recrudescence from new infections in areas of high transmission, thus improving understanding of the efficacy of and resistance to antimalarial drugs.

- **Facilitate timely data-sharing:** Data from TES and on resistance markers should be shared with the NMP to enable timely decisions. Collaboration and agreements among research institutions and the NMP should be encouraged to ensure rapid data-sharing.

- **Digitize data collection:** Use digitized data collection tools to improve efficiency and the accuracy and accessibility of information from TES.

- **Strengthen and support malaria resistance networks:** Promote collaboration by using networks for antimalarial drug resistance and surveillance of efficacy to foster exchange of knowledge, resources and experience among participating countries.

- **Mobilize resources for capacity building:** Secure resources to strengthen technical and infrastructural capacity in countries. Explore innovative cost-sharing methods, such as establishing regional molecular surveillance laboratories, to ensure sustained support for antimalarial research and surveillance.

- **Integrate TES into national strategic plans and routine surveillance mechanisms:** Such integration will improve country ownership, coordination and effective implementation of TES.

- **Develop and implement strategies to manage artemisinin resistance:** Comprehensive strategies based on national assessments of antimalarial drug resistance are required.

Closing remarks

Dorothy Achu, WHO Regional Office for Africa, thanked the organizers, participants and presenters for their valuable contributions, which had enhanced understanding of drug resistance and future planning. She noted the rising prevalence of markers of partial artemisinin resistance, while emphasizing that most ACTs remain effective. She stressed the urgency of addressing the threat posed by drug resistance and expressed gratitude for the networking opportunities presented by the workshop and support from partners.

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3. WHO guidelines for malaria, 16 October 2023. Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/373339). License: CC BY-NC-SA 3.0 IGO. The latest version of the guidelines is also available online at: https://app.magicapp.org/#/guideline/LwRMXj.

1 All references accessed on 29 January 2025.

Annex 1. Agenda

Day 1 (9 November 2023)		
Opening session		
09:00–09:45	Opening remarks, introduction and objectives	Andrea Bosman
Session 1: Update on case management		
10:30–11:00	Update on malaria case management from WHO perspective	Peter Olumese
11:00–11:20	Discussion	
Session 2: Tools to monitor antimalarial drug efficacy and resistance		
11:20–12:15	Current tools for monitoring efficacy and resistance of antimalarial drugs	Charlotte Rasmussen Marian Warsame
12:15–12:40	Malaria molecular surveillance and PCR correction	Christian Nsanzabana
12:40–13:00	Discussion	
Session 3: Country presentations on recent therapeutic efficacy of antimalarial drugs (results and challenges)		
14:00–14:45	• Yemen (10 min) • Djibouti (10 min) • Somalia (10 min) • Discussion (15 min)	Country teams
14:45–15:30	• Sudan (10 min) • Eritrea (10 min) • Ethiopia (10 min) • Discussion (15 min)	Country teams
16:00–16:45	• South Sudan (10 min) • Kenya (10 min) • United Republic of Tanzania (10 min) • Discussion (15 min)	Country teams
Day 2 (10 November 2023)		
Session 3 (continued): Country presentations on recent therapeutic efficacy of antimalarial drugs (results and challenges)		
09:00–09:35	• Uganda (10 min) • Rwanda (10 min) • Discussion (15 min)	Country teams
Session 4: Surveillance of molecular markers of antimalarial resistance – country examples		
09:35–09:55	Experience of country support	Khalid Bashir
10:15–10:35	Experience from Uganda	Melissa Conrad
10:35–10:55	Experience from United Republic of Tanzania	Deus Ishengoma
10:05–11:20	Discussion	
Session 5: Country planning of TES and resistance monitoring		
11:20–11:50	Partner support to antimalarial drug efficacy and resistance	Global Fund, PMI
11:50–12:00	Discussion	
12:00–12:05	Introduction to group work	Marian Warsame

12:05–12:45	Group work on developing country plans for TES in 2024–2025	Country teams
12:45–13:00	Summary of countries' plans	Marian Warsame
14:00–15:00	Panel discussion on supporting countries to improve data collection, data quality and timely data sharing	
15:00–15:45	Group work on recommendations	
16:00–16:30	Presentation of the recommendation	
16:30–17:00	Close of the meeting	

Annex 2. List of participants

Country representatives

Khansaa Abdelmoneim, Federal Ministry of Health, Sudan

Bosco Agaba, Infectious Diseases Research Collaboration, Uganda

Abdi Abdillahi Ali, National Malaria Programme, Ministry of Health Development, Somaliland, Somalia

Gudissa Assefa Bayisa, National Malaria Control Programme, Ethiopia

Bokretsion Gidey, Ethiopian Public Health Institute, Ethiopia

Regina Kandie, Case Management Unit, National Malaria Control Programme, Kenya

Kibor K. Keitany, National Malaria Control Programme, Kenya

Daniel J. Kyabayinze, Health Services – Public Health, Uganda

Abdallah S. Lusasi, National Malaria Control Programme, United Republic of Tanzania

Catherine Maiteki-Sebuguzi, National Malaria Control Division, Ministry of Health, Uganda

Dhel Nhomachot Manot, National Malaria Control Programme, South Sudan

Selam Mihreteab, National Malaria Control Programme, Ministry of Health, Eritrea

Ahmed Abdulgadir Mohamed, Ministry of Health, Sudan

Jean Louis Ndikumana, Malaria Prevention Unit at the Rwanda Biomedical Center, Rwanda

Jean Damascene Niyonzima, Malaria Case Management, Rwanda

Samwel L. Nhiga, National Malaria Control Programme, United Republic of Tanzania

Jimmy Opigo, National Malaria Control Programme, Uganda

Joseph Panyuan Puok, National Malaria Control Programme, South Sudan

Saga Mohamed Roble, National Malaria Control Programme, Ministry of Health and Human Services, Somalia

Gerald Rukundo, Uganda Mortality Surveillance Project, National Institute of Public Health, Uganda

Zaynab Said Nor, Ministry of Health, Puntland State of Somalia, Somalia

Shija Joseph Shija, Zanzibar Malaria Elimination Programme, United Republic of Tanzania

Ibrahim Yacob, Malaria Control Unit, Gash Barka Zone, Eritrea

Rapporteur

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Partners

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Victor Asua, Infectious Disease Research Collaboration, Uganda

Migbaru Keffale Bezabih, Armauer Hansen Research Institute, Ethiopia

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Jane Achan, Malaria Consortium, United Kingdom of Great Britain and Northern Ireland

Craig Bonnington, Malaria Consortium, United Kingdom of Great Britain and Northern Ireland

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Mehul Dhorda, Specimen Management Laboratory, Mahidol–Oxford Tropical Medicine Research Unit, Thailand

Chris Ebong, Infectious Disease Research Collaboration, Uganda

Ingrid Etoke, Global Heath – Malaria, Bill & Melinda Gates Foundation, United Kingdom of Great Britain and Northern Ireland

Anne Gasasira, National Institute of Medical Research Complex (African Leaders Malaria Alliance), Uganda

Kevin Griffith, Office of Communications, U.S. President's Malaria Initiative, United States of America

Deus Ishengoma, National Institute for Medical Research, United States of America

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Kefas Mugitu, Shinda Malaria project, United Republic of Tanzania

Joaniter Nankabirwa, Infectious Diseases Research Collaboration, Uganda

Christian Nsanzabana, Swiss Tropical and Public Health Institute, Switzerland

Sam Nsobya, Molecular Research Laboratory, Infectious Disease Research Collaboration, Uganda

Nekoye N. Otsyula, Global Medical Affairs, Malaria, Networks for Voluntary Services, Kenya

Elias Phiri, Malawi–Liverpool–Wellcome Trust Clinical Research Programme, Malawi

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Grazielle Scudu, Clinton Health Access Initiative, United States of America

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Pierre Tchamdja, West African Health Organization, Burkina Faso

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Jovin Kitau, Malaria Technical Officer, United Republic of Tanzania

Ranjbar Kahkha Mansour, Medical Officer, Malaria and Vector-borne Disease Control, Uganda

James Dan Otieno, National Professional Officer, Malaria Epidemics, Kenya

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Ghasem Zamani, Regional Malaria Adviser, WHO Regional Office for the Eastern Mediterranean

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