Federal Democratic Republic of Ethiopia
Ministry of Health

Malaria Laboratory Diagnosis and Clinical Case Management Quality Assurance Manual for Malaria Elimination in Ethiopia

MAY 2017
Addis Ababa

Malaria Laboratory Diagnosis and Clinical Case Management Quality Assurance Manual for Malaria Elimination in Ethiopia

MAY 2017
Addis Ababa

Foreword

Ethiopia has launched sub-national malaria elimination in March 2017. To effectively implement the elimination efforts, it was necessary to develop and use guidelines to inform and guide implementers and health care workers. The availability of these documents will also standardize the work on malaria elimination across the country in both private and public sectors.

The effort of developing standardized guidelines is a significant input to the elimination efforts. Therefore, all partner organizations and all health care facilities at all levels and places are expected to use this manual. We should note that as this is the first of such efforts, this manual is updatable and can be revised at any time given that there are significant developments in the field.

Once more, the Ministry of Health appreciates the contribution of its partners to the development of this manual and urges all those who are involved in malaria elimination efforts to use this manual for ensuring the right diagnostic procedures are followed.

Acknowledgements

The Federal Ministry of Health would like to thank the National Malaria Control Program for overall coordination of the process, and WHO/AFRO for sponsoring the workshop that developed this manual.

The Ministry also would like to acknowledge the contributions made by Malaria Control and Elimination Partnership in Africa (MACEPA) at Program for Appropriate Technology in Health (PATH), WHO, Columbia University - ICAP in Ethiopia, and the Ethiopian Public Health Institute (EPHI).

The following individuals are acknowledged for their contributions in the preparation of the manual:

Name	***Organization***
Abnet Abebe	EPHI
Adugna Abera	EPHI
Anderson Chinorumba	WHO/AFRO
Berhane Tesfaye	PATH/MACEPA
Degu Mehari	FMOH
Dereje Dillu	FMOH
Desalegn Nega	EPHI
Gezahegn Tesfaye	PATH/MACEPA
Gudisa Asefa	FMOH
Hailemariam Lemma	CHAI
Hiwot Solomon	FMOH
Hiwot Teka	PMI/USAID
Kebede Etana	FMOH
Mekonnen Tadesse	ICAP in Ethiopia
Samuel Girma	PMI/USAID
Worku Bekele	WHO-Ethiopia
Yonas Petros	ICAP in Ethiopia

Contents

List of Tables

List of Figures

List of Abbreviations

AFRO	African Regional Office
API	Annual Parasite Incidence
CHAI	Clinton Health Access Initiative
DBS	Dried Blood Spot
DNA	Deoxyribo-Nucleic Acid
EDTA	Ethylene Diamine Tetra -acetic Acid
EHNRI	Ethiopian Health and Nutrition Research Institute
ELISA	Enzyme-Linked Immunosorbent Assay
EPHI	Ethiopian Public Health Institute
EQA	External Quality Assurance
FMHACA	Food, Medicines and Health Care Administration and Control Authority
FMOH	Federal Ministry of Health
FIND	Foundation for Innovative New Diagnostics
G6PD	Glucose 6 Phosphate Dehydrogenase
ICAP	Institute for AIDS Care and Treatment at Columbia University
IQC	Internal Quality Control
IPLS	Integrated Pharmaceuticals Logistics System
ISO	International Organization for Standardization
LAMP	Loop-mediated isothermal Amplification
LLIN	Long Lasting Insecticidal Net
MACEPA	Malaria Control and Elimination Partnership in Africa
MRDT	Malaria Rapid Diagnostic Test
NMCP	National Malaria Control Program
PATH	Partnership for Appropriate Technology in Health
PCR	Polymerase Chain Reaction
PFSA	Pharmaceuticals Fund and Supply Agency
PMI	President's Malaria Initiative
PT	Proficiency Testing
QA	Quality Assurance
QC	Quality Control
RDT	Rapid Diagnostic Test
RRL	Regional Referral Laboratory
SLMTA	Strengthening Laboratory Management Towards Accreditation
SOP	Standard Operating System
TDR	Tropical Disease Research
TOT	Training of Trainers
USAID	U.S. Agency for International Development
WBC	White Blood Cell
WHO	World Health Organization

Definition of Terms

Terms	Definitions
Quality Control	Refers to measures that must be included or carried out during each assay run to verify or ensure that the test is working properly.
External Quality Assessment	A system by which a laboratory's performance is checked objectively by an external agency or facility or a reference laboratory.
Malaria Elimination	The interruption of local mosquito-borne malaria transmission in a defined geographical area, i.e. zero incidence of locally contracted cases.
Corrective Action	Action taken to eliminate the cause(s) of an existing nonconformity, defect, or other undesirable situation in order to prevent recurrence.
Preventative Action	Action taken to eliminate the cause(s) of a potential nonconformity, defect, or other undesirable situation in order to prevent occurrence.
Accreditation	Procedure by which an authoritative body gives formal recognition that a body or person is competent to carry out specific tasks.
False Positive Rate	Is the proportion of test results that indicates the presence of malaria parasites, when actually there are no malaria parasites.
Invalid Rate	The proportion of particular test devices that do not show the control line after the recommended incubation time during testing.
Lot Testing	Quality control testing of a product lot (batch) after release from the manufacturing site.
Microscopist	A person who uses a microscope to read blood films to confirm the diagnosis of malaria and reports the findings.
Panel Detection Score	A score between 0 and 100, calculated as the proportion of times malaria RDT gives a positive result on all tests from both lots tested against samples of parasite panels at a specific parasite density.
Parasite Density	Number of parasites per microliter of blood detected by microscopic examination of peripheral blood films.
Proficiency Testing	Evaluation of participant's performance against pre-established criteria.
Quality Assurance	A planned and systematic set of activities focused on providing confidence that quality requirements are being met.
Quality Control	A set of activities or techniques for continuously assessing laboratory work and the emergent results to ensure that all quality requirements are being met.
Quality Management System	Management system to direct and control an organization with regards to quality.
Sensitivity	A measure of the probability for correctly identifying a person with malaria parasites.
Specificity	A measure of the probability for correctly identifying a person with no malaria parasites.

1. INTRODUCTION

1.1 Malaria Epidemiology in Ethiopia

Malaria is one of the main public health problems in Ethiopia. *Plasmodium falciparum* and *P. vivax* are the two most dominant malaria parasite species in Ethiopia and are prevalent in all malaria endemic areas with their relative frequency varying in time and space within a given geographical range. Approximately 60% of the total population lives in areas at risk of malaria. According to Ethiopia's Federal Ministry of Health (FMOH), out of the total 2,627,182 malaria cases reported in 2014/2015, 2,210,298 (84.1%) were confirmed by either microscopy or rapid diagnostic tests (RDT), and out of which, 1,415,150 (64.0%) were *P. falciparum* and 795,148 (36.0%) were *P. vivax*. The other two species (*P. malariae* and *P. ovale)* are very rare and are presumed to account for <1% of all confirmed malaria cases.

1.2 Structure of Malaria Diagnostic Services in Ethiopia

The laboratory services in Ethiopia are divided into 4 levels:

- Level IV– Ethiopian Public Health Institute (EPHI), National reference laboratory, technical research arm of the FMOH
- Level III- Regional reference laboratories, Federal specialized referral hospital laboratories, and Uniformed Forces hospital laboratories and Central Blood Bank Laboratory
- Level II - Regional referral, zonal and district hospital laboratories
- Level I - Health center laboratories and health posts. These are illustrated in the figure below.

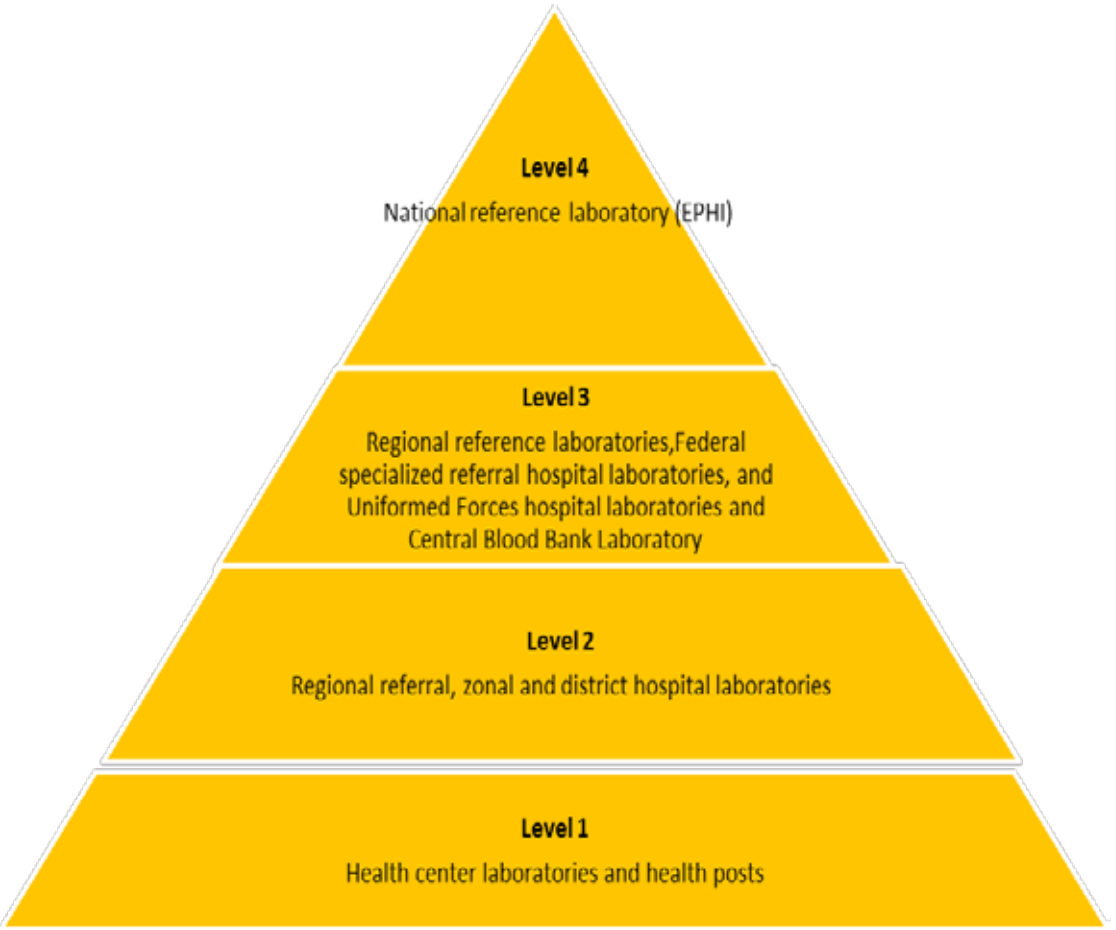


Figure 1. Ethiopia laboratory structure

1.3 Laboratory Quality Management Systems

The MOH/EPHI has recognized the importance and need to establish quality management systems in all laboratories based on ISO 15189 standards, which sets the requirement for quality and competency of medical laboratories. In this view, many public and private laboratories have already been ISO15189 assessed by different accrediting bodies and partners supporting accreditation. The remaining laboratories are working towards accreditation through initiatives such as strengthening laboratory management towards accreditation (SLMTA). There is a high degree of awareness among laboratory personnel on the ISO 15189 standard, with many laboratory personnel trained on 'Understanding ISO15189 standard'.

2. DIAGNOSTIC TOOLS FOR ELIMINATION

Prompt and accurate diagnosis will be performed for all suspected malaria cases using microscopy or RDTs. Microscopy is performed in health centers and hospitals where as RDTs are performed at health posts. In addition, specialized tests will be available for molecular diagnosis of cases, drug efficacy studies and contact screening.

During Phase I (optimization phase) of malaria elimination diagnosis with either RDT (health post) or microscopy (health center and hospitals) will be mandatory in all health facilities. Other sensitive tests may be introduced as they become endorsed for use by the WHO and available in the country.

In Phase II (pre-elimination phase) a national laboratory quality management system will be put in place and all health facility laboratories in elimination targeted areas will be part of external quality assessment scheme. The national and regional referral laboratories will take the lead in implementing the external quality assessment system per the guideline. In Phase III and IV (elimination and prevention of reintroduction phase) all available routine and advanced (molecular) techniques will be used.

It is important for all the diagnostic steps for the different methods (pre-analytical, analytical and post analytical) to be performed accurately. Therefore, standard operating procedures (SOPs) will be available in all testing facilities for all the tests performed. SOPs on performing diagnostic tests and job aids have been described in the manual for the laboratory diagnosis of malaria version 1.

To detect and treat asymptomatic cases during malaria elimination, RDT will be performed and dried blood spot specimen will be collected and transferred to regional or national reference laboratories for molecular testing. If the patient is positive for malaria by RDT at health posts after treatment within the past 28 days, s/he will be referred to higher health facilities for better evaluation by microscopy.

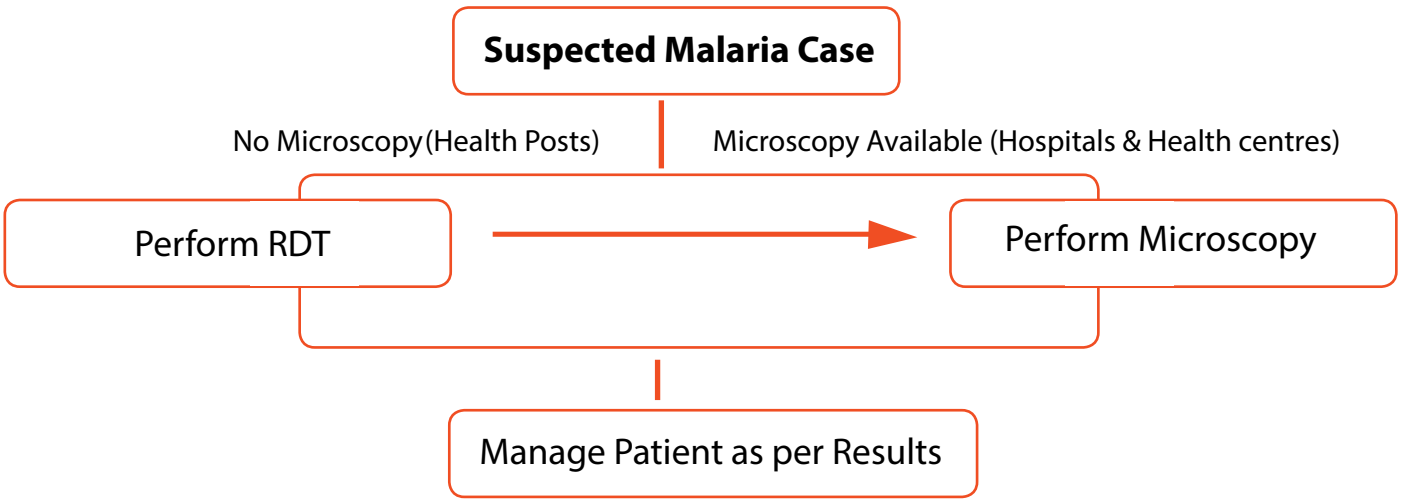


Figure 2. Malaria testing algorithm

2.1 Microscopy

Microscopy remains the gold standard for routine malaria diagnosis. Its advantages include:

- allows differentiation of malaria species and parasite stages
- allows quantification of parasite density
- allows assessment of drug efficacy
- can be used to diagnose other diseases

However, the quality of the microscopy remains unsatisfactory in the absence of essential quality supplies and competent personnel. Hence, a robust and regular training and quality assurance program will be implemented

2.1.1 Use of Microscopy

- Initial diagnosis of suspected malaria cases
- Follow up of patients on malaria treatment
- Drug efficacy studies

2.1.2 Specimen Type

- Thick and thin blood films

2.1.3 Reporting

- No haemo-parasites seen
- If malaria parasites seen, report :
  - Plasmodia species
  - Stage of malaria parasites with particular emphasis on presence of gametocytes
  - Count parasites/µl of blood

2.1.4 Responsibilities of testing personnel

Laboratory personnel performing microscopy are responsible for:

- Staining, examination and reporting of blood film results
- Submitting monthly consumption data to supplies department
- Ensuring proper storage of laboratory supplies and equipment
- Performing Internal Quality Control (IQC)
- Participating in external quality assessment (EQA) programs.
- Accurate, regular and complete reporting

2.2 Rapid Diagnostic Test

In Ethiopia, the prevalent plasmodium species are *P. falciparum* and *P. vivax*. As a result, the recommended RDTs are those that can pick both *falciparum* and *vivax*. RDTs have several advantages that include:

- RDTs can diagnose malaria using finger prick blood and are easy to use
- RDTs do not need specialised buildings or equipment.
- RDTs give results within a short time, usually around 20 minutes

Unlike other diagnostic tests that are performed in the laboratory setting, malaria RDTs present special challenges, including:

- Rapid malaria testing is conducted by healthcare professionals who do not have specific laboratory experience.
- IQC samples for RDTs are not available in the market
  - Proficiency testing for RDTs is not available
  - Estimation of parasite density cannot be performed
  - Stage of the parasite cannot be determined
  - Histidine-rich protein-2/3 gene deletion in some of P. facliparu*m* detecting RDTs

As a result of these challenges, there is a need for a robust training program of these non-laboratory staff members to provide them with all the needed laboratory skills, including specimen collection and safety and emphasis on procuring quality products, pre-and post-shipment lot testing and ensuring the recommended transportation and storage conditions.

2.2.1 Use of RDTs

- Diagnosis of suspected malaria cases at health posts
- Screening of contacts

***N.B**: RDTs should not be used for follow up of patients for treatment outcome since RDTs remain positive for several days after successful treatment.*

2.2.2 Specimen Type

- Capillary Blood
- EDTA Blood

2.2.3 Reporting

- Report as per manufacturer's instruction

2.2.4 Responsibilities of testing personnel

Health workers performing RDTs are responsible for:

- Performing malaria RDT as per manufacturer's instructions
- Submitting monthly usage data to the supplies department
- Ensure proper storage of RDTs
- Making a blood smear and DBS during follow up of patients on treatment
- Sending all blood films and DBS to the nearest laboratory
- Accurate, regular and complete reporting
- Participate in EQA (onsite evaluation) of RDT
- Take part in RDT Competency Assessment

2.3 Glucose 6- Phosphate Dehydrogenase Rapid Test

Radical treatment of *P. vivax* involves the use of primaquine, which can cause hemolytic anemia in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency. Primaquine can be given to vivax patients without testing for G6PD enzyme with strict and close follow up. This approach may change through time. If there are reports of hemolysis problem in patients who take primaquine for vivax treatment, then G6PD testing will be done on samples collected from a given focus with reports of suggestive hemolysis.

2.3.1 Specimen Type

- Capillary Blood
- EDTA Blood

2.3.2 Reporting

- Report as per manufacturer's instruction.

2.3.3 Responsibilities of testing personnel

Health workers performing G6PD rapid tests are responsible for:

- Performing G6PD RDT as per manufacturer's instructions
- Submitting monthly usage data to the supplies department
- Ensure proper storage of G6PD RDTs
- Accurate, regular and complete reporting

2.4 Advanced molecular tests

2.4.1 Malaria PCR

National and regional referral laboratories are responsible for performing PCR using available PCR platforms.

2.4.1.1 Use of PCR

- For differentiating recrudescence and new infections on suspected treatment failure cases.
- To investigate parasite epidemiology from surveys.
- To assess common drug resistance genes of plasmodium parasites such as K13 gene for ACT and Pvmdr1 and Pvcrt-o for Chloroquine).
- To assess the presence of plasmodium sporozoites in mosquitoes gut and salivary gland.
- Contact screening.

2.4.1.2 Specimen type

- DBS
- EDTA whole blood

2.4.1.3 Reporting

- Positive/Negative
- Plasmodia species
- Presence of drug resistance genes

2.4.1.4 Responsibilities of testing personnel

Laboratory personnel performing PCR are responsible for:

- Processing samples as per PCR SOP/ manufacturer's instructions
- Ordering laboratory supplies and equipment from the supplies department
- Submitting monthly consumption data to supplies department
- Ensuring proper storage of laboratory supplies and equipment
- Performing IQC
- Accurate, regular and complete reporting

2.4.2 Loop-mediated Isothermal Amplification

Loop-mediated isothermal amplification (LAMP) of DNA is a molecular technology platform. The Pan (genus) specific primers detect target DNA sequence well conserved in all plasmodia species while the *P. falciparum* and *P. vivax* specific primers are specific for *P. falciparum* and *P. vivax* respectively. While having almost similar sensitivity and specificity to PCR, LAMP is superior in sensitivity and specificity to microscopy. The advantage is that it can be used in fieldwork.

2.4.21 Use of LAMP

- Screening of contacts
- Surveys

2.4.2.2 Specimen type

- EDTA whole Blood
- Heparinized Blood
- DBS

2.4.2.3 Reporting

- Positive/Negative
- Parasite species
- Presence of drug resistance genes

2.4.2.4 Responsibilities of testing personnel

Laboratory personnel performing LAMP are responsible for:

- Sample analysis as per LAMP SOPs/ manufacturer's instructions
- Ordering laboratory supplies and equipment from the supplies department
- Submitting monthly consumption data to the supplies department
- Ensuring proper storage of laboratory supplies and equipment.
- Performing IQC
- Accurate, regular and complete reporting

3. THE QUALITY ASSURANCE PROGRAM

In order to support and facilitate quality assurance of microscopy and RDT in the context of malaria elimination, a comprehensive quality assurance (QA) program which comprises all the processes necessary to ensure that the results are accurate, from blood collection to the delivery of the results will be implemented.

Organizational Structure of Quality Assurance Program

A hierarchical organizational structure of the quality assurance program based on the structure of the laboratory services and functions of the different levels will be used to coordinate all the QA activities. This is described in figure 3 below.

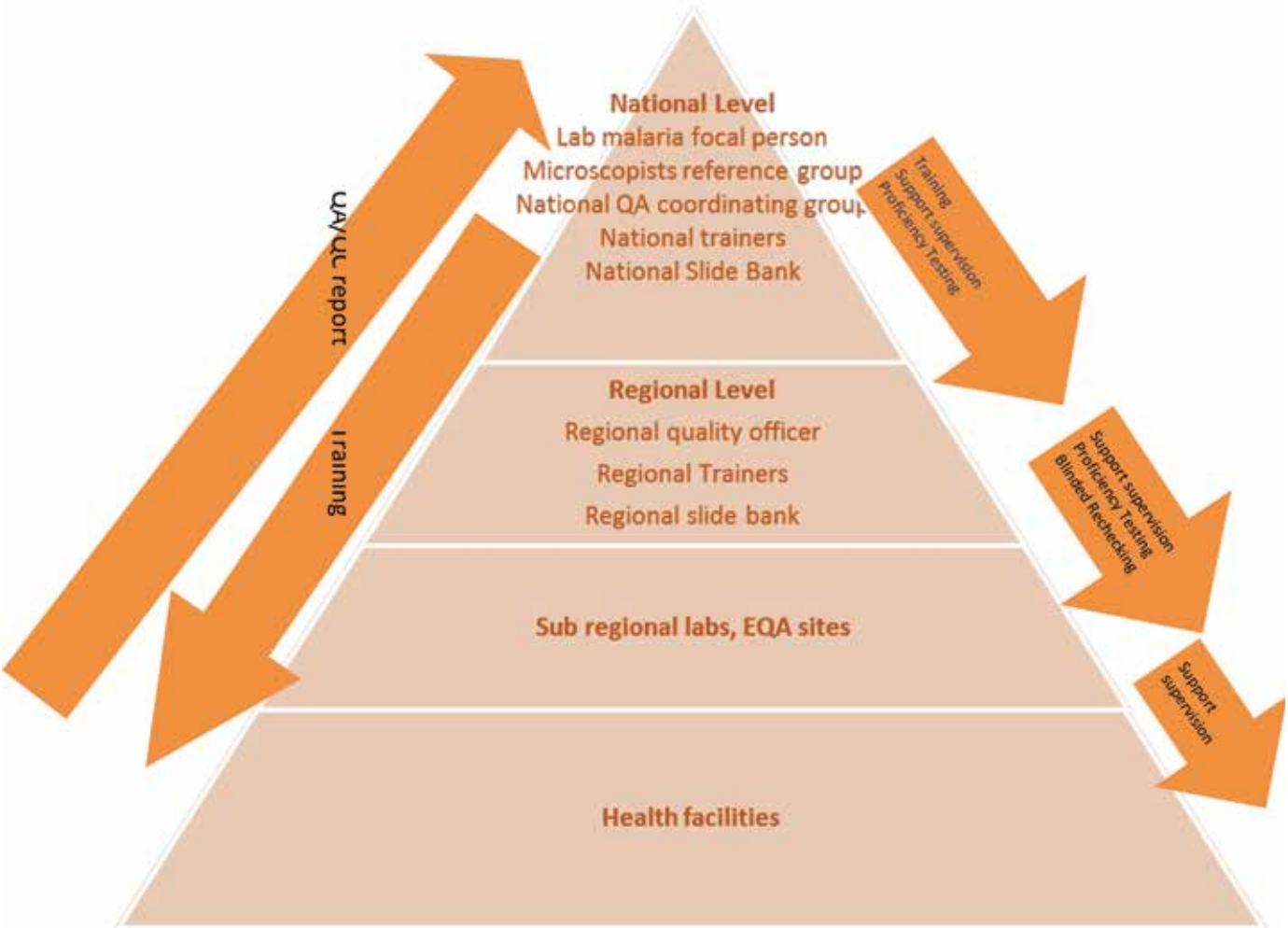


Figure 3. The Structure of the Quality Assurance Program

3.1 Roles and responsibilities of national bodies

3.1.1 National Reference Laboratory

The national reference laboratory is located in the premises of the EPHI, an autonomous federal government office accountable to the FMOH. It is responsible for coordinating medical laboratory diagnostic services in Ethiopia. In addition, the institute undertakes research, based on national public health research agenda, on priority health and nutrition problems, and generates, absorbs and disseminates scientific and technological knowledge to improve the health of the public. EPHI's responsibilities include the following:

- Provide training of trainers on malaria microscopy
- Develop national guidelines and manuals
- Maintain national malaria slide bank
- Provide proficiency testing to regional laboratories, uniformed forces and federal hospitals
- Compile and present summary reports on the EQA program implementation to the stakeholders
- Set supervision standards; develop/review checklists
- Conduct on-site evaluation to all regional reference laboratories (RRLs) and federal hospitals
- Perform lot testing for malaria RDT
- Perform advanced tests such as PCR, sensitive ELISA, Serology
- Conduct community and health facility based malaria operational researches such as regular antimalarial drug resistance monitoring, malaria indicator surveys, and monitoring the of efficacy of chemicals used for IRS and LLINs
- Malaria monitoring and evaluation through Public Health Emergency Management (PHEM) system

3.1.2 National Malaria Laboratory Diagnosis and Quality Assurance Coordinator

The National Malaria Laboratory Diagnosis and Quality Assurance Coordinator is a senior laboratory personnel with extensive knowledge of the national malaria control program (NMCP) and proven skills in malaria microscopy and RDT diagnosis. He/ she is appointed at national level and is a member of the WHO Certified Expert Malaria Microscopists Reference Group and reports to EPHI head and NMCP. His/her responsibilities include:

- Acting as a communication link between the NMCP and the Laboratory Services
- Working closely with national reference laboratory in coordinating EQA activities among the different laboratories and different programs.
- Monitoring and evaluation of laboratory plan for malaria diagnostic activities.
- Organizing microscopy training workshops for medical laboratory personnel

3.1.3 National Malaria Laboratory Diagnosis and Quality Assurance Coordinating Committee

The National Malaria Laboratory Coordinating Committee is made of senior laboratory personnel from national laboratory, private sector, representatives of WHO Certified Expert Malaria Microscopists Reference Group, and Pharmaceutical Fund and Supply Agency (PFSA) and is chaired by the Technical Supervisor of national laboratory. Its responsibilities include:

- Coordinating the activities of multiple partners
- Resource mobilization, partner coordination and budget preparations
- Develop and review laboratory policies on malaria diagnosis
- Preparing and overseeing implementation plans
- Monitoring and Evaluation

3.1.4 WHO Certified Expert Malaria Microscopists Reference Group

These are laboratory personnel who have been trained and certified by WHO as expert **Malaria Microscopists.** Their roles include:

- Training laboratory personnel on malaria microscopy
- Rechecking of blood smears
- Onsite supervisory visits on malaria microscopy
- Assist in surveys where examination of blood smears is required
- Develop and review the RDT and microscopy training packages, job aids and Standard Operating Procedures (SOPs)
- Conduct competency assessment on malaria microscopy

3.1.5 Food, Medicine and Health Care Administration and Control Authority

The Food, Medicine and Health Care Administration and Control Authority (FMHACA) regulates the registration and licensing of in-vitro diagnostics among other products. These include laboratory equipment, reagents and RDTs. The authority is also mandated to approve and regulate *In-vivo* studies including clinical trials on new and already existing antimalarial drugs and also to register and provide license for laboratory professionals.

3.1.6 Pharmaceutical Fund and Supply Agency

PFSA is the national procurement body for medical commodities. Its responsibilities include:

- Quantifying, procuring, storage and distribution of laboratory commodities including RDTs.
- Monitoring the quality of laboratory commodities during storage and transportation

3.2 Roles and responsibilities of regional bodies

3.2.1 Regional Reference Laboratory

The regional reference laboratories are mandated by regional health bureaus to support and strengthen the laboratory services of respective regions. With regard to malaria elimination, regional reference laboratories are responsible to:

- Provide basic training on malaria microscopy and RDT for health facilities under their catchment
- Establish and maintain regional malaria slide bank
- Provide proficiency testing to peripheral laboratories
- Conduct blinded rechecking of slides of their catchment facilities
- Conduct their own internal quality control on malaria microscopy
- Compile and present summary reports on the EQA program implementation to the national reference laboratory
- Conduct on-site evaluation, supportive supervision and mentoring at peripheral health facilities
- Prepare Giemsa stock solutions, check the quality and distribute to peripheral facilities
- Conduct advanced test such as PCR and ELISA
- Adopt SOPs developed at national level

3.2.2 Regional Malaria Laboratory Diagnosis and Quality Assurance Quality Officer

The regional laboratory quality officer is senior laboratory personnel with extensive knowledge of the NMCP and proven skills in malaria microscopy and RDT diagnosis. His/her responsibilities include:

- Acting as a communication link between the regional malaria laboratory services and regional malaria control program as well as the link between regional laboratory service and national reference laboratory

- Coordinating EQA activities among the different health facilities in the region
- Organizing microscopy training workshops for laboratory personnel
- Checks laboratory documents and modifies based on new updates

3.2.3 Sub Regional and EQA sites Laboratories

The national reference laboratory will strengthen certain health facility laboratories with satisfactory performance in EQA to act as centers of excellence within the region. Where available, these "EQA sites" will perform the following responsibilities.

- Perform EQA to peripheral laboratories
- Assist peripheral laboratories in carrying out corrective and preventative actions
- Mentoring of peripheral laboratories in quality management system development and implementation
- Report to regional laboratories

3.2.4 Health center and health post

Health center and health post level diagnostic tests include malaria microscopy at health center and malaria RDT at health post level. The diagnostic tests at this level provide confirmatory diagnosis for malaria, in accordance with the national guidelines

Health centers and health posts are responsible for performing malaria testing as per set national guidelines and standard operating procedures. This include following manufacturer's instructions and performing the tests under the right infrastructural and environmental requirements. In addition, health centers and health posts are responsible for reporting malaria data to the district health office.

3.3 National Documents

EPHI develops and regularly reviews all documents (guidelines, manuals, SOPs) for all activities. These address the pre-analytic, analytic and post analytic processes of all laboratory tests. All laboratories and laboratory personnel should adhere to these documents.

3.4 Malaria Microscopy

3.4.1 Quality Control

All laboratories shall comply with the requirements of ISO 15189 for their internal quality control. This includes daily control and monitoring of each stage of testing by laboratory personnel to ensure that all tests are performed accurately and precisely.

3.4.2 Equipment Maintenance

Each laboratory will perform daily equipment maintenance on microscopes, pH meters and weighing balances. This should include cleaning of equipment after use and performing manufacturer's recommended scheduled maintenance. This information shall be recorded on equipment maintenance log sheets and reviewed on a regular basis. See annex 8.1 and 8.2

3.4.3 Staining Reagent Preparation

Stock Giemsa stain should be diluted with buffered distilled water to obtain a pH of 7.0 to 7.4, with the optimum being 7.2. It should be prepared when needed and should be discarded within 8 hours of preparation. Both the stock and working solution should be stored at room temperature (18°C to 26°C) taking into consideration manufacturer's recommendations. The stock solution should be kept in the original dark glass bottle in a cool, dry, shady place, away from direct sunlight. The pH of the buffers and the working solution should be checked by a pH meter and recorded in the reagent preparation log sheets which will be reviewed on a regular basis. See annex 8.3.

3.4.4 Staining

Each new Giemsa working solution should be checked for quality by using known positive and negative malaria control slides. Malaria-positive blood will be used to prepare positive control thick and thin films, which can be stored (for up to 2 weeks in a cool, dark, dry area) and stained at the same time for each batch of patient slides each day. Before examining the stained patient slides, the quality control (QC) slides are checked for the quality of red-cell staining to control the buffer quality, and white blood cells (WBCs) are examined for staining of nuclei and granules and of parasite

chromatin and red cell inclusions, if present. If the QC slides are satisfactory, the patient slides can be examined with confidence. This information will be recorded on the staining internal quality control reporting sheet. See annex 8.4

3.4.5 Review and corrective action

All IQC data will be reviewed on a regular basis and preventative and/or corrective actions carried out when necessary. This will involve a detailed root cause analysis where nonconformance is detected.

3.4.6 External Quality Assessment

EQA is a process by which a laboratory's performance is checked objectively by an external agency or facility or a reference laboratory. This can be achieved through panel testing or blinded rechecking of slides for microscopy; and review of laboratory performance by on-site supervision. Both public and private health facility laboratories are expected to participate in the regional EQA program.

3.4.6.1 Proficiency Testing

Proficiency testing (PT) refers to the process by which laboratories (known as the "test laboratories") perform malaria microscopy on a set of prepared slides received from the national and/or regional reference laboratory. This exercise will be used to check the laboratories' blood film preparation and staining process as well as the competency of the technicians to recognize and identify malaria parasites present.

The national reference laboratory will have well characterized and validated blood film slides and will provide PT to RRLs. The national reference laboratory will prepare feedback and communicate results to RRLs. The national reference laboratory will review PT results of regional reference laboratories and their catchment health facilities and prepare summary reports for dissemination to stakeholders.

Regional reference laboratories will use well characterized and validated blood film slides from regional or national slide bank to provide PT to sub-regional laboratories and health facility laboratories. PT is conducted three times a year for all laboratories. They prepare and communicate feedback to participant laboratories. The regional reference laboratories will also prepare summary report and share with regional stakeholders and the national reference laboratory.

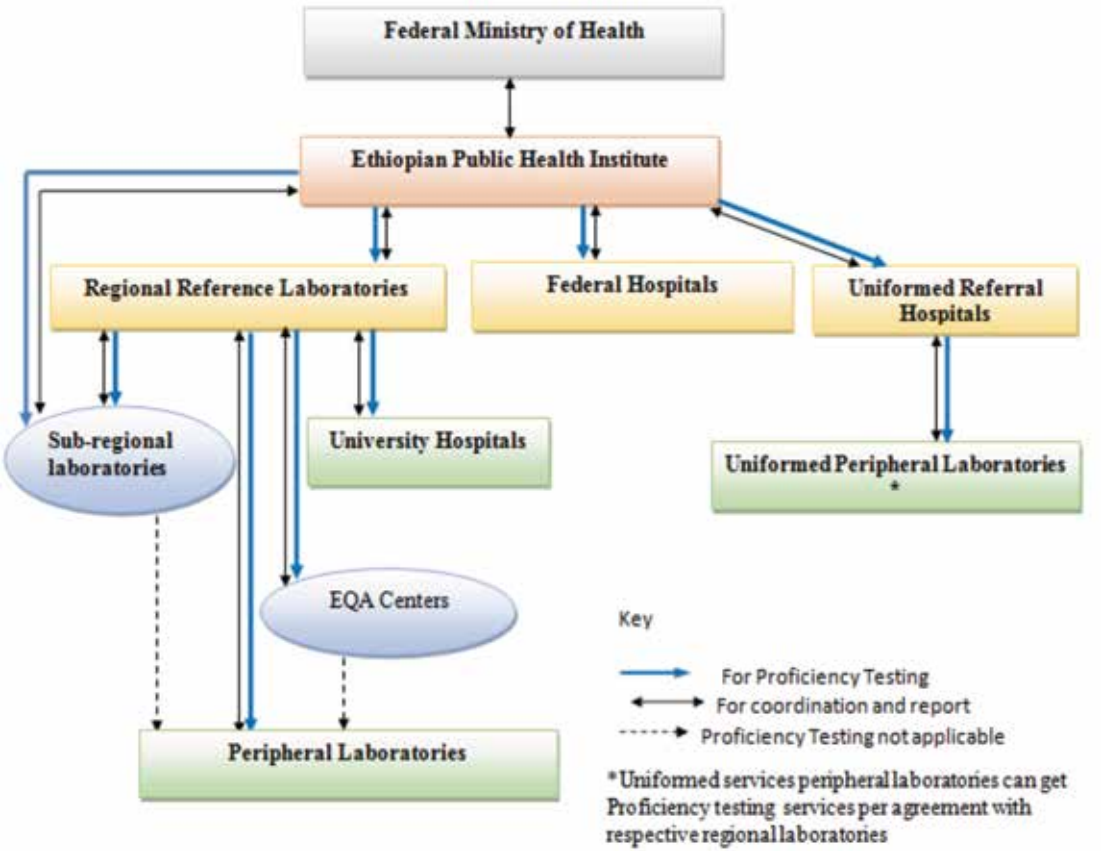


Figure 4. Structure of panel testing

The national reference laboratory shall monitor the competency of its entire expert microscopists involved in the slide rechecking program, by individually enrolling them in a regular PT scheme three times a year. The national reference laboratory shall keep a database of PT performance reports and share PT reports with National Malaria Laboratory coordinator and NMCP.

The PT schemes will be conducted as per the Malaria Laboratory Diagnosis External Quality Assessment Scheme Guidelines.

3.4.6.2 Blinded Rechecking of Blood Films

Blinded rechecking is an important component of Ethiopian malaria laboratory diagnosis quality assurance program. It will be used to assess blood film preparation, quality of staining, and accuracy of the result. Rechecking reflects the true performance of laboratories offering routine diagnostic services at health facility level. It also detects major deficiencies in laboratory performance due to incompetence, poor equipment, poor reagents, poor infrastructure or poor work practices.

The national reference laboratory shall coordinate the implementation of blinded rechecking program in the country including blinded rechecking of malaria blood slides for federal hospitals. The regional reference laboratories coordinate the implementation of blinded rechecking program in their respective region. Blinded rechecking of blood films is conducted quarterly for all laboratories. All summary reports on the performance of peripheral laboratories shall be shared with regional stakeholders and the national reference laboratory. Blinded rechecking is performed as per the Malaria Laboratory Diagnosis External Quality Assessment Scheme Guidelines.

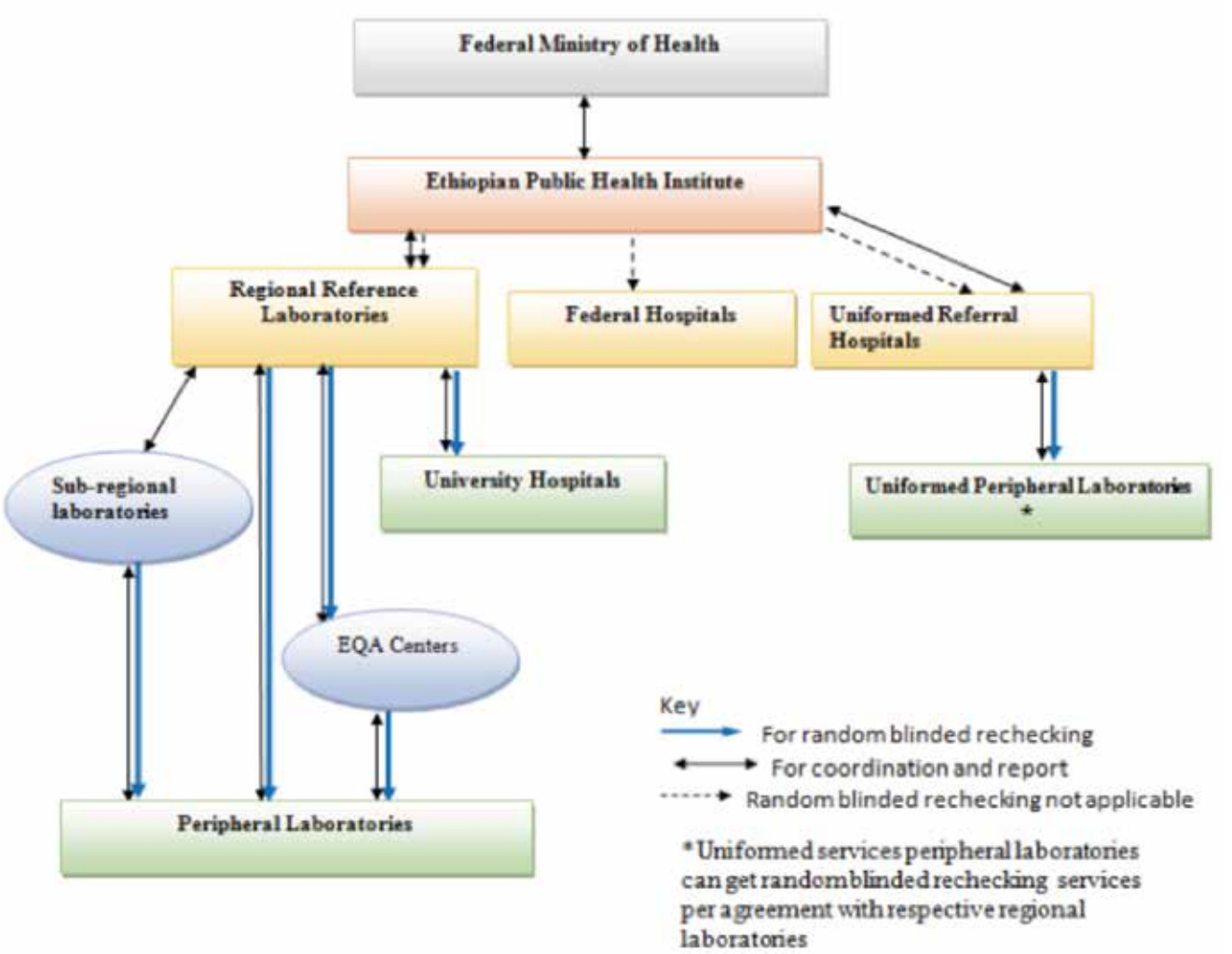


Figure 5. Structure of blinded rechecking

3.4.6.3 On-site supportive supervision

On-site supportive supervision will be performed with a standardized supervisory checklist that provides an overview of malaria microscopy diagnostic services at the site (see Annex 8.5). The aim of the on-site supportive supervision is to identify and correct deficiencies in laboratory supplies storage and inventory, basic procedures, equipment, quality of reagents, training status of the laboratory staff, review of laboratory practical skills, work load, safety and waste disposal system, performance of internal QC and result record keeping practice.

Sufficient time must be allotted for the visit to include observation of all the work associated with malaria microscopy, including preparing blood films, staining, reading of films by the laboratory personnel and examining a few stained *positive* and *negative* films by supervisors to observe the quality of film. This will be followed by giving feedback to the site coupled with intensive coaching/ mentoring to correct all identified deficiencies.

The national reference laboratory shall perform on-site supportive supervision to regional laboratories at least biannually. The regional reference laboratory shall perform on-site evaluation and support supervision to peripheral laboratories at least biannually. Summary reports of onsite visits should be forwarded to the national reference laboratory. On-site supportive supervision will be performed as per the Malaria Laboratory Diagnosis External Quality Assessment Scheme Guidelines.

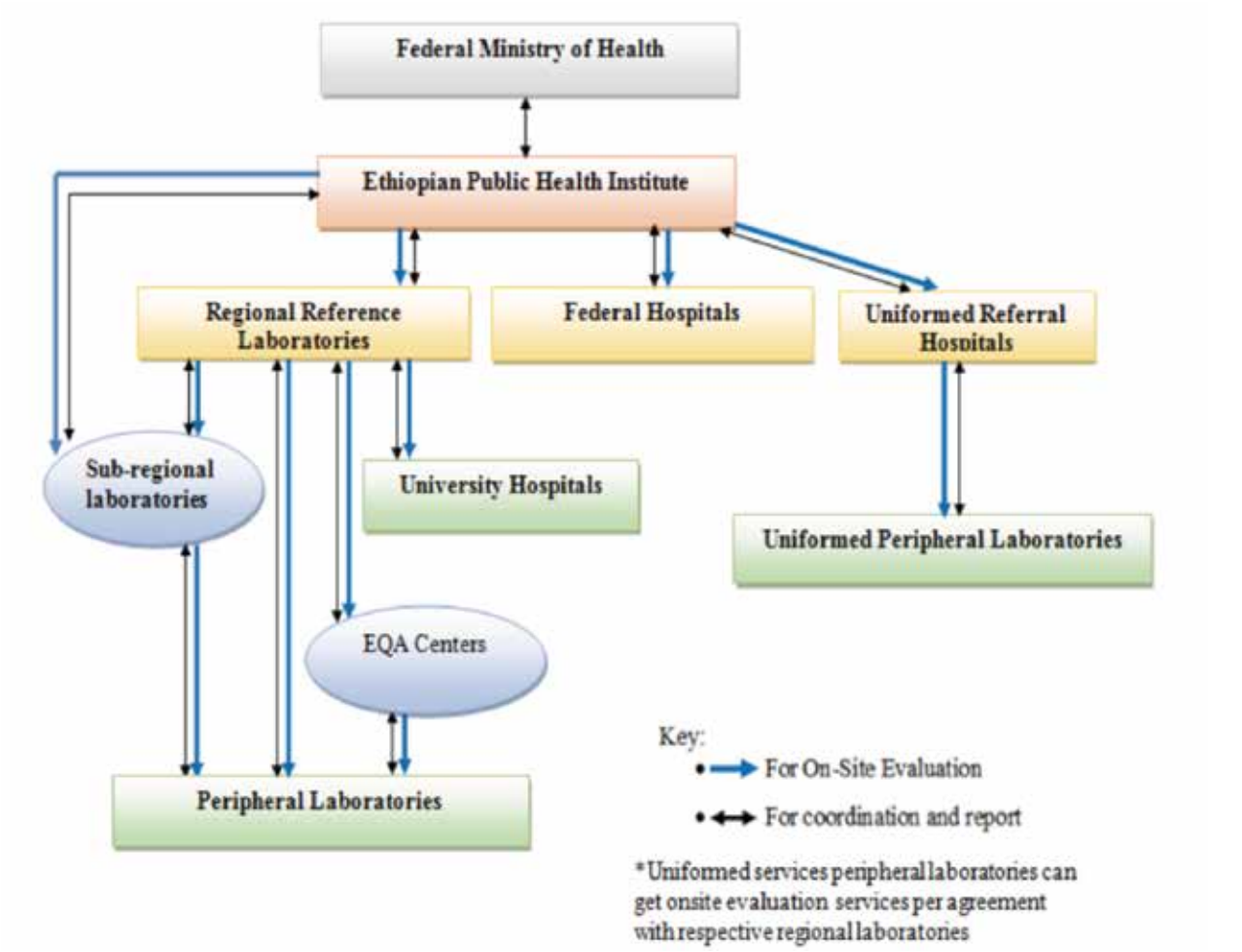


Figure 6. Structure of on-site supportive supervision

3.5 Malaria and Glucose 6-Phosphate Dehydrogenase Rapid Tests

The malaria rapid diagnostic test (mRDT) and glucose-6-phosphate dehydrogenase (G6PD) rapid tests are fairly easy to perform but errors can arise if the test kits are not stored properly, test procedure not performed correctly or results not interpreted correctly. In addition, the infrastructure of the testing facility plays a key role, e.g.

- Room size/testing area
- Ambient temperature
- Direct sun light
- Work surface
- Availability of a timing device

All these parameters will be assessed to ensure quality rapid test results.

Pre-and post-shipment lot testing of malaria RDTs will be performed on all procured batches and will be coordinated by EPHI. See annex 8.6 for lot testing procedure and form.

3.5.1 Quality Control for mRDTs and G6PD tests

All testing facilities shall store testing kits and reagents at manufacturer's recommended environmental conditions. This shall include, but not limited to, monitoring storage and testing/ assay temperatures for the test kits. The test device pouch should be checked for any damage before testing. The color of the desiccant pouch should be checked each time a test device is opened and it should conform to the manufacturer's recommendations. The test should be considered invalid if the control band does not appear for the malaria RDT and if there is no or incomplete blood migration for the G6PD rapid test, and in such cases the test should be repeated with a new test device. Invalid results, poorly performing kit devices and damaged kits should be recorded in the mRDT or G6PD rapid test quality control sheet.

3.5.2 External Quality Assessment for mRDTs and G6PD tests

Currently the only available external quality assessment activity for mRDTs and G6PD rapid tests is on-site supportive supervision.

3.5.3 Onsite Evaluation and Supportive Supervision for mRDTs and G6PD tests

On-site evaluation will be performed on all testing facilities performing malaria rapid tests and G6PD rapid test using standardized supervisory checklists (see annex 8.7). The aim of the onsite supportive supervision is to identify and correct deficiencies in:

- Storage facilities of rapid tests
- Availability of supplies and equipment (e.g. timers, thermometers, etc.)
- Testing infrastructure at facility
- Safety and waste disposal system
- Usage of the testing procedures
- Interpretation and recording of results

All deficiencies identified will be discussed with the facility and intensive coaching and mentoring will be given to correct the identified deficiencies. Where applicable, the necessary recommendations will be made which might include retraining of personnel.

The peripheral laboratories shall conduct on site supportive supervision to all health posts within their catchment area at least biannually. All reports should be forwarded to the regional reference laboratory and a copy retained in the facility.

3.6 Advanced Molecular Malaria Tests

3.6.1 Quality Control

IQC of PCR, LAMP and other advanced tests shall be performed as per the requirements of ISO15189 in line with the manufacturer's recommendations. All IQC data shall be recorded and reviewed on a regular basis.

3.6.2 External Quality Assessment

EQA of the national and regional reference laboratory performing advanced tests shall be part of the national and broader international EQA schemes. It is important to note that the laboratories are working towards ISO15189 accreditation and hence participate in national and international on site assessments and PT.

4. TRAINING

One of the most important factors in ensuring accurate and reliable malaria test results is the availability of appropriately trained staff to perform microscopy, RDT testing, advanced molecular tests and the various quality assurance activities. Training sessions will be performed using appropriate trainers and curriculums at the different testing levels. Trainings will be conducted for both public and private sector personnel.

4.1 Curriculums

Several training curriculums are available in Ethiopia to cater for training of trainers, microscopy and the rapid tests. Microscopy curriculums are developed at national level and reviewed regularly for updates. New training curriculums will be developed as needed upon introduction of new diagnostic tools.

4.2 Training of Trainers

This curriculum is meant for microscopy national training of trainers (TOT) and is designed to equip them with knowledge on how to facilitate trainings in addition to microscopy and RDT knowledge. It is a 5-day training. The curriculum has the following modules:

- Training Basics
  - How to facilitate an interactive lecture
  - How to facilitate activities and discussion
  - How to facilitate laboratory skills session
- Microscopy
  - Overview of malaria
  - Microscope parts, care and handling
  - Laboratory safety and precaution
  - Specimen collection and preparation of blood films, preparation of stains and blood film staining
  - Malaria microscopy: Examination and species identification
- Malaria RDTs
  - Overview
  - How to perform RDTs
  - Types: Multi-/single species identifying RDTs
  - Other information related to RDTs
- Recording and reporting
- Quality assurance of malaria laboratory diagnosis
- Managing supplies required for malaria laboratory diagnosis
- Practical session

4.3 Basic Malaria Microscopy Training

The basic malaria microscopy has been conducted in Ethiopia for several years. The curriculum is designed at national level and used to train laboratory technologists at various levels.

This curriculum is meant as refresher training for all laboratory personnel. It is designed to equip laboratory personnel with knowledge on parasite identification, species differentiation and quantification. In addition, it is also an opportunity to equip them with the latest national policy changes and guidelines. It is a 4-day training and has the following modules:

- Microscopy
  - Overview of malaria epidemiology
  - Microscope parts, care and handling
  - Laboratory safety and precaution
  - Specimen collection and preparation of blood films, preparation of stains and blood film staining
  - Malaria microscopy: Examination and species identification
- Recording and reporting
- QA of malaria laboratory diagnosis

- Managing supplies required for malaria laboratory diagnosis
- Practical session

4.4 Basic Malaria RDT Training

Training of laboratory technologists is carried out based on the curriculum prepared at national level. RDT training is part of the practical guide: Malaria prevention and control training module developed by the ministry of health in 2013.

4.5 Trainers

4.5.1 National Trainers

National trainers are trained by WHO certified expert microscopists. They are responsible for training regional trainers.

4.5.2 Regional Trainers

Regional trainers are trained by national trainers and are responsible for training within their regions. Regional trainers will be supported by WHO certified expert microscopists.

5. EQUIPMENT AND SUPPLIES MANAGEMENT

Equipment and supplies for diagnosis of malaria can vary considerably by type, specifications and manufacturers. They are directly related to the final test results, hence choosing quality products is essential. EPHI will come up with specifications for equipment and supplies for PFSA to procure. Equipment, supplies and testing procedures shall be standardized to facilitate sustainable procurement, maintenance and training programs.

5.1 Procurement

Below is the flow of procurement processes in Ethiopia for public facilities. Private facilities are expected to do their own procurement. Fig 7 below shows the procurement process for public sector facilities.

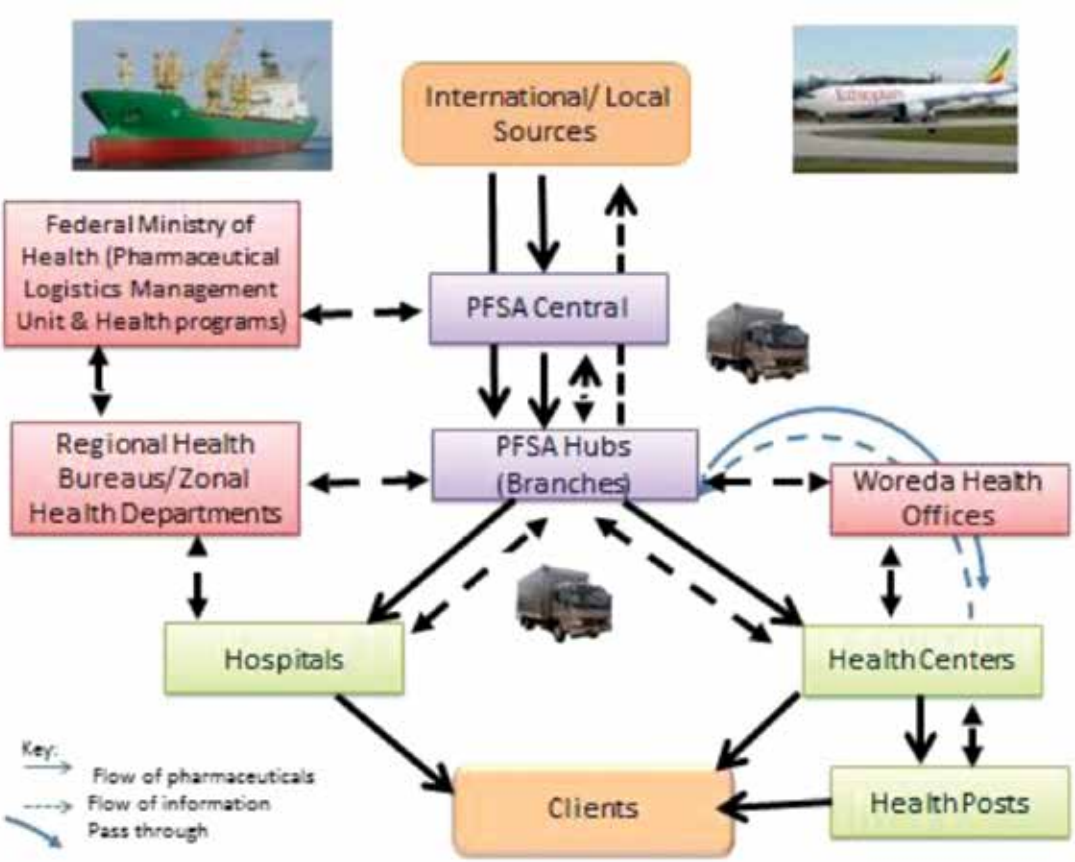


Figure 7. Flow of Pharmaceuticals & Information in the Integrated Pharmaceutical Logistics System

5.2 Specification

5.2.1 Microscopes

All facilities performing microscopy are equipped with high quality microscopes purchased from reputable dealers. These should be well serviced and maintained for accurate malaria diagnosis. Minimum standards for microscopes are listed in Annex 8.8.

5.2.2 Slides

Plain glass slides with a 20 mm frosted end area and ground edges are recommended for making blood films for malaria microscopy. Each slide measures 76X26X1mm. Slides should be scrupulously free from grease, dust, moisture and fungus. The slide box should always be kept closed with the desiccant pouch inside. Slide boxes should always be kept away from moisture and dust. Slides should be washed, dried and wrapped if oily, dusty or suspected to be contaminated with fungus.

5.2.3 Stains

The recommended stain in Ethiopia for malaria microscopy is Giemsa stain. Giemsa stain is considered to be the most reliable stain in routine practice due to its applicability to both thick and thin smears, its stability and its consistency and reproducible staining results over a range of temperatures. The specifications of the Giemsa stain are listed in Annex 8.9.

5.2.4 pH meters

Quality pH meters that read to 2 decimal places will be used to check the pH of buffers and staining solutions. All pH meters will be calibrated routinely or as per manufacturer's directions**.**

5.2.5 Thermometer

A thermometer should be available in all laboratories to continuously measure the temperature of the refrigerator, laboratory and storage room of laboratory supplies.

5.2.6 RDTs

The procurement of RDTs will be based on WHO/FIND/TDR panel detection scores- sensitivity, specificity, false positive rate and invalid rate. The following **minimum specifications** (Table 1) will be used:

Table 1. Minimum specifications for the procurement of RDTs

CHARACTERISTIC	REQUIRED SPECIFICATION
Target species	Pf, Pv and other (*P. ovale* & malariae)
Test format	Cassette
Test type	Pf, Pv and pan (*P. ovale* & malariae)
Minimum Panel Detection Score for Pf at 200 parasites/µL	75%
Minimum Panel Detection Score for PV at 200 parasites/µL	75%
Maximum False Positive rate	10%
Maximum Invalid Rate	5%
Temperature Stability	Up to 45°C

5.2.7 Dry blood spot card

Filter paper for collection of dry blood spots will be available

5.2.8 Timers

Timers will be used for timing the staining and procedure for performing malaria RDTs. Cellphones are not recommended for safety reasons.

5.2.9 Safe waste management system

All Laboratories should have waste containers for infectious and non- infectious solid waste, and sharp containers which will be used for disposal of lancets and others including needles.

5.2.10 Stock management

Stock management at all levels is through use of bin cards and stock cards.

6. QUALITY ASSURANCE PROGRAM MONITORING

The performance of the QA program will be monitored at all levels of implementation. The national level and the individual regions should set achievable targets in each financial year depending on their resources, malaria epidemiological picture and work load and monitor progress of their activities accordingly. The following indicators (Table 2) will be used.

Table 2. List of indicators for monitoring quality assurance program

Indicator	Target	Frequency of Measuring	Level
Number of WHO certified expert malaria microscopists (level 1&2)	12	Every three years	National
Proportion of RDT batches pre and post shipment lot tested	100%	Annually	National
Proportion of RDT batches tested post distribution	100%	Annually	National
Proportion of laboratories participating in Proficiency Testing	75 %	Three times a year	National & Regional
Proportion of laboratories participating in blinded rechecking of blood films	100%	Quarterly	National & Regional
Proportion of laboratories visited for onsite support supervision	100%	Biannually	National & Regional
Proportion of health posts visited for malaria RDT onsite support supervision	100%	Biannually	National & Regional
Number of laboratory personnel trained in malaria microscopy	100%	Biennial	National & Regional
Proportion of laboratories participating in Proficiency Testing scoring ≥80%	100%	three times a year	National & Regional
Proportion of laboratories participating in blinded rechecking scoring ≥80%	100%	Quarterly	National & Regional
Number of personnel trained in RDT	100%	Biennial	National & Regional
Proportion of RDT performing sites scoring >80% in onsite support supervision	100%	Biannually	National & Regional

7. QUALITY ASSURANCE OF CLINICAL MALARIA CASE MANAGEMENT

Quality assurance of clinical case management refers to regular assessment of malaria diagnosis and treatment practices tied with improvement plans so that malaria case management practice is as per the recommendation of the national malaria guidelines. Quality assured laboratory test result is one of the inputs for quality assured clinical case management, and clinicians need additional inputs like appropriate training and desktop references. Audits are important tools to assess and continuously improve the quality of malaria case management.

Recommendations of the national malaria guidelines

- All malaria suspected patients should be tested for malaria with recommended testing methods: malaria suspect is a patient who has fever and lives in malaria endemic area or has history of travel to malaria endemic area in the past 30 days. In pre-elimination and elimination phases malaria suspect includes people living within 100 m radius of a confirmed malaria case. Clinicians should ask all febrile patients for malaria risk (living in malaria endemic area or travel to malaria endemic area). All patients who are suspected to have malaria should be tested with RDT if they are seen in health post or microscopy if they are seen at health center or hospital level
- All patients with confirmed malaria should be treated with the recommended specific antimalarial drug and supportive care:
    - Uncomplicated *P. falciparum* cases should be treated with Artemether-lumefantrine (AL) and single dose primaquine (PQ) to clear the gametocytes and reduce onward transmission. G6PD testing is not required. Primaqine is contraindicated in pregnancy, infants less than six months old, women breast feeding infants less than six months and in people with known hypersensitivity to PQ. AL is contraindicated in first trimester pregnancy and such patients are treated with quinine tablets
    - Uncomplicated *P. vivax* cases will be treated with chloroquine (CQ) and radical cure PQ unless contraindicated. For implementation purpose, radical cure will be started at elimination targeted districts and will be scaled up nationwide when feasible. PQ is recommended to be started at the time of CQ initiation. See the annex for protocol and register of radical cure PQ
    - Uncomplicated mixed P. falciparum and P. vivax infection is treated with AL and single dose PQ if the diagnosis is with RDT and AL plus radical cure PQ if the diagnosis is with microscopy. AL and PQ are contraindicated during first trimester pregnancy and such patients will be treated with quinine tablets
    - Complicated and severe malaria is treated with IV/IM Artesunate followed by full course AL
- All patients with malaria should be given the following key messages
    - He/she has got malaria
    - The medication has to be taken as prescribed completely (full dose)
    - Early treatment is important to prevent severe illness and death due to malaria
    - Take/give enough food and fluid (especially fatty meal to enhance drug absorption and to avoid risk of hypoglycemia).
    - To return to the health facility if fever persists or patient is still sick after 72 hours or any time before 72 hours if condition worsens
    - Malaria is transmitted by mosquitoes
    - Malaria can be prevented by using insecticide treated nets, eliminating

mosquito breeding places, and protecting sprayed houses from re plastering

- All patients with malaria (clinical or confirmed) should be recorded on tally sheets or registers
- All patients with negative test result should be evaluated for other causes of fever
- All pregnant women with malaria should be treated according to the national guideline
    - Uncomplicated P. falciparum
        - First trimester: Quinine tablets
        - Second and third trimesters: AL
    - Severe malaria
        - First trimester: parenteral Artesunate followed by quinine tablets
        - Second and third trimesters: Parenteral Artesunate followed by AL
- All health care providers of malaria should be trained on malaria case management
- Patients with severe malaria should get first dose in the OPD (with in the first 2 hours)
- Referred severe malaria cases should get pre-referral treatment

Clinical audit is a preferred way of ensuring that these recommendations are implemented as per the guideline. Chart review will be conducted to assess diagnosis and treatment of malaria cases. Clinician-patient interaction will be observed to assess the degree to which key messages are delivered and important job aids are available. Pharmacist-patient interaction will also be observed to assess adherence support. A standardized audit tool shall be used to audit malaria case management services. The assessment will be followed by quality improvement plan with responsible bodies and time line. The quality assessment cycle will be conducted every quarter for each facility and the quality unit of the health facility will be responsible to conduct the assessments

Audit tool

Health post level

Review malaria (or relevant) register

- Number of patients seen in the previous month
- Number of malaria suspected patients that are tested for malaria with RDT
- Number of patients with confirmed malaria that are treated according to the national guideline
- Number of patients with negative test result that are treated with antimalarial drugs
- Number of pregnant women with malaria that are treated according to the national guideline
- Observe febrile patient HEW interaction
    - Number of interactions observed
    - Number of patients with malaria that are given key messages
    - Number of patients with malaria (clinical or confirmed) that are recorded on registers

Review the ICCM register, if available (previous one month) and document the following

- Number of children seen in the previous month
- Number of children with fever
- Number of febrile children that are tested for malaria with RDT
- Number of children diagnosed with malaria
- Number of children treated according to the national guideline
- Number of tested children without malaria who are treated with antimalarial drugs

Summary of findings

Strengths

Weaknesses

Recommendations with responsible person and timeline

Health center and hospital level

Review 5 charts of severe malaria cases (since last quality assessment) and identify 20 consecutive patients with fever from adult OPD register, 20 from pediatric OPD register and determine the following:

- For severe malaria charts
    - Number of severe malaria charts reviewed
    - Number of patients who were given IV/IM Artesunate
    - Number of patients who were shifted to AL after at least 24 hours of treatment
    - Number of patients with severe malaria who got first dose of IM/IV Artesunate in the OPD (with in the first 2 hours)
    - Number of referred severe malaria cases who were given pre-referral treatment
    - Number of severe malaria cases that die in the hospital
- Charts of identified febrile cases
    - Number of malaria suspected patients that are tested for malaria with microscopy
    - Number of malaria suspected patients that are tested for malaria with RDT
    - Number of patients with confirmed malaria that are treated according to the national guideline
    - Number of patients with negative test result that are treated with antimalarial drugs
    - Number of pregnant women with malaria that are treated according to the national guideline
- Observe febrile patient clinician interaction
    - Number of interactions observed
    - Number of patients with malaria that are given key messages
    - Number of patients with malaria (clinical or confirmed) that are recorded on tally sheets or registers
    - Review the IMNCI register (previous one month) and document the following
- Number of children seen in the previous month
- Number of children with fever
- Number of febrile children that are tested for malaria with microscopy
- Number of febrile children that are tested for malaria with RDT
- Number of children diagnosed with malaria
- Number of children treated according to the national guideline
- Number of tested children without malaria who are treated with antimalarial drugs

Summary of findings

Strengths

Weaknesses

Recommendations with responsible person and timeline

8. REFERENCE

Federal Ministry of Health. National Malaria Strategic Plan 2014 – 2020. June 2014, FMOH, Addis Ababa.

Ethiopian Health and Nutrition Institute. Malaria Laboratory Diagnosis External Quality Assessment Scheme Guidelines, 2009. EHNRI, Addis Ababa, Ethiopia

National Department of Health. National Malaria Diagnosis Quality Assurance Guidelines. 2011. Department of Health, Pretoria.

World Health Organization. Malaria Microscopy Quality Assurance Manual. WHO, 2015

Ministry of Health. Malaria Microscopy Quality Assurance Guideline. 2007. Draft. Zanzibar.

Ministry of Health. Malaria QA/QC Laboratory Manual, Botswana Laboratory Services.

Ethiopian Public Health Institute. Malaria Laboratory Diagnosis External Quality Assessment Scheme Guidelines, 2015, EPHI, Addis Ababa, Ethiopia (Under Printing).

Federal Ministry of Health of Ethiopia. HSDP IV Annual Performance Report EFY 2006 (2013/2014). FMOH, 2014. Report No.: Version 1.

PFSA. Standard Operating Procedures Manual For The Integrated Pharmaceuticals Logistics System In Health Facilities Of Ethiopia, Second Edition, Addis Ababa, Ethiopia, November, 2015

WHO. A Framework For Malaria Elimination, World Health Organization 2017.

EHNRI. Manual For The Laboratory Diagnosis Of Malaria, First Edition, Ethiopian Health and Nutrition Research Institute, Ministry of Health September, 2012, Addis Ababa

EPHI. Master plan for the Public Health Laboratory System in Ehiopia, second edition, 2009, Addis Ababa.

9. ANNEXES

Annex 9.1. Light microscope preventive maintenance form

Month/Year:		Equipment #:					Serial #:			Location:	
Date	Operator's Name	**DAILY MAINTENANCE (ü)**					**MONTHLY MAINTENANCE (ü)**			**Supervisor Review**	
		Remove oil from objectives	Clean stage	Clean condenser	Turn off light	Cover microscope	Clean body of microscope	Clean eyepieces, objectives & condenser	Remove & clean slide holder	Initials	Date
1											
2											
3											
4											
5											
6											
7											
8											
9											
10											
11											
12											
13											
14											
15											
16											
17											
18											
19											
20											
21											
22											
23											
24											
25											
26											
27											
28											
29											
30											
31											

Annex 9.2. Weighing balance equipment preventive maintenance form

Clean balance on each day of use

Equipment #:	Serial #:	Location:

Month/Year:					**Month/Year:**				
Date	Operator's name	Cleaned? (ü)	Supervisor review		Date	Operator's name	Cleaned? (ü)	Supervisor review	
			Initials	Date				Initials	Date
1					1				
2					2				
3					3				
4					4				
5					5				
6					6				
7					7				
8					8				
9					9				
10					10				
11					11				
12					12				
13					13				
14					14				
15					15				
16					16				
17					17				
18					18				
19					19				
20					20				
21					21				
22					22				
23					23				
24					24				
25					25				
26					26				
27					27				
28					28				
29					29				
30					30				
31					31				

In order to carry out maintenance, review instructions described in the SOP and the equipment user's manual. Any problem or malfunction detected must be reported to the supervisor. Record any equipment failure or problem on Equipment Problem Summary Form.

Annex 9.3. Giemsa working solution preparation log sheet

Preparation date	Buffered Distilled Water		Giemsa stock		pH of working solution (7.2±0.2)	Tech Initials & Date	Supervisor Initials & Date
	Lot #	Expiry date	Lot #	Expiry date			

Frequency: Perform QC on each batch of working Giemsa stain prepared

Materials: Use known positive and negative malaria slides

Annex 9.4. Giemsa Stain Internal Quality Control Result Recording Form

Region: _____ Zone_____ Woreda: _____ Facility: _____

Sr. No.	Date QC Blood film Prepared	Storage Temp. of QC Blood Film	Date of opening of Giemsa Stock solution	Date IQC Performed	IQC Blood Film ID	IQC Blood Film Type (Positive or Negative Control)		IQC Result (Passed or Failed)	Corrective Action Taken (if it is failed)	Name & Signature (who performed IQC)	Remark
						Neg	Pos.				

IQC will be performed

- For every new batch of Giemsa stain solution.
- Regularly
- When unexpected staining result observed while examining blood film.

QC Passed Means

- The background should be clean and free from debris
- The color of erythrocytes is a pale green pink.
- Leukocytes nuclei are a deep rich purple.
- Malaria parasites are well defined with deep-red chromatin and pale purplish, blue cytoplasm

Storage temp. of QC blood film

- Below zero ˚c (Recommended) or
- Room temp.

Comments: _____
_____

Reviewed by: _____
Sign._____

Date: _____

NOTE:

- Frequency: Perform QC on each batch of working Giemsa stain prepared
- Materials: Use known positive and negative malaria slides

Annex 9.5. Supervisory Checklist for Malaria Microscopy Laboratory Service

Region_____

Zone_____ Woreda_____

Name of health facility _____

Name of laboratory department head_____
_____

Tel. No_____

Fax_____

Date of onsite supervision conduct
ed_____

1. Training

No	Questions	Responses				
	Total No. Of lab staff___ Number of laboratory personnel trained on malaria microscopy___	Name of trained staff in the fiscal year	When was s/ he trained? (mm/yyyy EC)	How long was the training? (# of Days)	Who provided the training? (Organization)	Comments
	Comments					

2. *Malaria microscopy laboratory format and supplies*

	Are the following malaria microscopy formats and other materials available?	Items	1. = Available and being used 2. = Available, but not used 3. = Not Available	
		Malaria microscopy guideline		
		SOP for malaria microscopy		
		Laboratory result log book		
		Job aids		
		Weakly /monthly report form for malaria		
	Are the following reagents and other	Item	1 = Available and being used	Enough for the
	Laboratory commodities available?		2 = Available, but not used 3= Not Available 4= Not Applicable	coming 4 Months 1= Yes 2=No
		Absolute methanol		
		Absorbent cotton wool		
		Beaker/volumetric flask		
		Binocular microscope with electric source of light		
		Brown bottle		
		Distilled water		
		Drying rack		
		Funnel		
		Giemsa powder/Giemsa stain stock solution		
		Glass beads		
		Glycerol		
		Immersion oil		
		Timer		
		Lens cleaning solution		
		Lens paper		
		Measuring cylinder		
		Microscope slides		
		Glass-writing pen/lead pencil		
		Slide boxes		
		Staining rack		
		Staining jar		
		Tally counter		
		Tissue paper		
	Reagents labeled with its name, date of preparation and expiry date (observation)		1-Yes 2- No	

I.

3. Equipment

	How many electric binocular microscopes do you have?	Brand name (for the first EQA cycle but for other cycle fill this column if there is New arrival)	# Functional	# Non Functional	Specific problem (examine stained blood film slide to fill this column)	Remar
		Total				

4. Malaria microscopy skill assessment

	Who is responsible for sample collection?	1. Laboratory personnel 2. Non laboratory personnel 3. If non laboratory personnel, specify	☐ ☐
	Which type of blood film do you use for malaria diagnosis?	1. Always thin smear 2. Always thick smear 3. As necessary 4. Always both (in the same slide or separate slide)	☐ ☐ ☐
	Quality of thick and thin films? (observation)	1. Excellent 2. Good 3. Poor	☐ ☐
	How do you dry the film?	1. Air dry 2. Heat dry	☐
	Which part of the film (thin or thick) do you fix?	1. Thin 2. Thick 3. Both	☐ ☐
	How many fields do you examine to report a negative result (no parasites)?	1. <25 2. 50 3. 100 4. 200 5. _____	☐ ☐ ☐ ☐
	Do you report positive results by identifying species and parasite stages?	1. Species only 2. Stages only 3. Both 4. None	☐ ☐ ☐
	Do you quantify positive results (parasite density)?	• Yes • No • If yes, which method specify _____	☐

	When using WBC method, how many WBC do you count to quantify a parasite load?	1. 50 WBC 2. 100 WBC 3. 200 WBC 4. 500 WBC 5. Not applicable	☐ ☐ ☐ ☐
	Do you clean the microscope or objective lenses prior to starting microscope reading and at the end of the day?	1. Yes 2. No	☐
	What do you use for microscope lens cleaning?	1. Cotton 2. Lens paper 3. Tissue paper 4. Other _____	☐ ☐ ☐
	Which reagent do you use for blood film staining?	1. Giemsa 2. Wright 3. If other, specify_____?	☐ ☐
	For Giemsa stain		
	Do you prepare the stock reagent or use ready-made reagent?	1. Preparing reagent 2. Readymade reagent	☐
	How often do you prepare the working reagent?	1. Every 24 hrs 2. Prior to staining 3. Other specify_____	☐ ☐
	What is the commonly used reagent container to store the stock stain?	1. Brown bottle 2. Any transparent bottle 3. If other, specify _____	☐ ☐
	Where do you store the stock reagent?	1. Away from direct sunlight and moisture in lockable 2. cabinet Other, specify_____	☐
	Have you ever interrupted malaria laboratory services due to shortages of reagents, supplies and microscope problem?	1. Yes 2. No If yes, 1. Cause of interruption_____ 2. For how long _____ 3. How many times in the last 4 months _____	☐ ☐ ☐ ☐

	Have you experienced some difficulties with your microscope during the last 4 months?	1= Yes 2= No If yes, 1. with the Stage 2. with the objective 3. other specify,_____	☐ ☐ ☐ ☐
	Do you have an inventory list of supplies and stains?	1. Yes 2. No	☐
	How often do you receive supplies like stains and others?	1. Monthly 2. Every 6 months 3. Once a year	☐ ☐
	Do you have difficulties receiving your supplies?	1. Yes 2. No 3. If yes, why _____	☐ ☐
	Do you store patient blood (with EDTA) known to have parasites	1. Yes 2. No	☐
	Do you keep slides for rechecking?	1. Yes 2. No 3. If no, why? _____	☐ ☐
	Have you been supervised in the past 6 months?	1. Yes 2. No 3. If yes, specify the supervisor _____	☐ ☐
	Is a standard laboratory register book in use?	1. Yes 2. No 3. If not, why? _____	☐ ☐
	Is a standard laboratory request form in use?	1. Yes 2. No 3. If not, why? _____	☐ ☐

5. Quality Assurance

	Internal Quality Control (QC) Practiced			
	Do you prepare positive and negative slides for reagent quality control purposes?	1. 2.	Yes No, if no why? _____	☐
	When do you conduct internal quality control for malaria microscopy?	1. 2 3. 4. 5.	Weekly Monthly Upon opening of new batch_ During unusual staining results Others, Specify _____	☐
	Are stained slides ever rechecked by a person in the laboratory?	1. 2.	Yes No, if no why? _____	☐
	EQA practiced			
	Are stained slides validated regularly, and feedback obtained?	1. Yes 2. No, if no why? _____		☐
	Do you participate in an EQA scheme, and is feedback obtained	1. Yes 2. No, if no why? _____		☐

6. Safety and waste Disposal

	Are gloves and gowns worn while performing the procedure?	1. Yes 2. No, if no why? _____		☐
	Are a safety box/sharp container and non-sharp container available and placed in the right position?	1. Yes 2. No, if no why?_____		☐
	Is the working area clean and decontaminated before/after procedures?	1. 2.	Yes No, if no why? _____	☐
	Is waste disposed of in the appropriate container (sharp material to sharp container and non-sharps to non-sharp container)?	1. 2.	Yes No, if no why? _____	☐

2. How many blood film slides have been examined during the last four months?

Year	***Positive***					***Negative***	**Total**
	Malaria				Other Hemoparasite (specify)		
	Pf	*Pv*	Mixed Pf and Pv	Others			

3. SUPERVISORS' COMMENTS (best practices, major problems identified, suggested solutions) on MALARIA MICROSCOPY

BEST PRACTICES: _____

_____

_____

_____

MAJOR PROBLEM IDENTIFIED: _____

_____

_____

_____

SUGGESTED SOLUTIONS: _____

_____

_____

_____

SUPERVISORS

NAMESIGNATURE

1._____ _____

2._____ _____

3._____ _____

Annex 9.6. RDT Lot Testing Procedure

Materials

1. WHO/FIND Form 2.02: Malaria RDT lot test Request form
2. 100 RDT kits
3. Shipment boxes
4. Ice packs
5. Temperature monitoring devices

Procedure

1. Complete form 2.02 at least 2 weeks prior to date of shipment arrival.
2. Email completed form to Malaria_rdt@who.int and copy to the Lot testing coordinator, nora.champouillon@finddiagnostics.org.
3. File the hard copy of completed form 2.02
4. A form and instructions will be sent to you, complete with details regarding the volume of RDTs required and the instructions for shipment.
5. Return the completed request form to the lot testing coordinator.
6. Upon arrival of test kits, select 100 RDT kits (number requested by coordinator), preferably from different boxes in different shipment pellets.
7. Monitor storage temperature if RDTs are to be kept prior to shipment.
8. Pack RDT kits in boxes and insert a temperature monitoring device. Include a copy of the hard copy of form 2.02 and temperature monitoring chart.
9. Complete airway bill and ship to the address provided by the lot testing coordinator.

Annex 9.7. RDT on Site Support Supervision Checklist

MALARIA RDT ON-SITE SUPPORTIVE SUPERVISION CHECKLIST

GENERAL INFORMATION	
NAME OF FACILITY:	
NAME OF HEALTH DISTRICT:	
NAME OF TESTING PERSONNEL:	
PROFFESSION OF TESTING PERSONNEL:	
NAME OF ASSESSOR (S):	
DATE OF ASSESSMENT:	
TESTS KITS IN USE	

1. INFORMATION ON TESTING PERSONNEL

For each step below, tick Yes, No or Cannot determine			
	Yes	No	Cannot Determine
1.1 Was the testing personnel trained in Malaria Rapid Diagnostic Testing?			
1.2 Is the testing personnel confident in the results of the Malaria RDT?			
1.3 When was the last on site assessment for malaria RDT done?			
1.4 How many years have the testing personnel been performing malaria RDT?			
1.5 How many tests does the testing personnel perform per month on average?			

2. DEMONSTRATION/OBSERVATION OF MALARIA RDT PROCEDURE

Was this test done on a real patient? Circle the correct answer: 1=Yes 2=No.	1 Y	2 N		Comments	
For each step below, circle 1 if the Health worker performed the step correctly, circle 2 if the Health Worker performed the step incorrectly, circle 3 if the Health worker skipped the step, circle 4 if not evaluated					
2.1 Assemble all the required accessories (kits, 70% alcohol swab, dry cotton swab, buffer, pipette, sharps container, lancet & gloves)?	1	2	3	4	
2.2 Use clean testing basin/ surface for the pipette and dry cotton swab?	1	2	3	4	
2.3 Put on new pair of gloves?	1	2	3	4	
2.4 Check expiry date on test kits and buffer?	1	2	3	4	
2.5 Write patient's name/ ID on test kits?	1	2	3	4	
2.6 Place testing cassette on a level surface?	1	2	3	4	
2.7 Clean finger with antiseptic / alcohol?	1	2	3	4	
2.8 Allow finger to dry before pricking it?	1	2	3	4	
2.9 Use a sterile lancet for finger prick?	1	2	3	4	
2.10 Puncture off center on the fingertip?	1	2	3	4	
For each step below, circle 1 if the Health worker performed the step correctly, circle 2 if the Health Worker performed the step incorrectly, circle 3 if the Health worker skipped the step, circle 4 if not evaluated					
2.11 Dispose lancet in sharps bin immediately after pricking finger?	1	2	3	4	
2.12 Avoided air bubble during sample collection?	1	2	3	4	
2.13 Collect enough blood with the collection device for testing?	1	2	3	4	

2.14 Dispense blood with device correctly?	1	2	3	4		
2.15 Put correct volume of blood on testing device?	1	2	3	4		
2.16 Dispose blood collection device in a biohazard bag immediately?	1	2	3	4		
2.17 Dispense buffer with bottle in an upright position?	1	2	3	4		
2.18 Dispense the correct number of drops of buffer?	1	2	3	4		
2.19 Incubated the test for the right amount of time?	1	2	3	4		
2.20 Read Test results correctly?	1	2	3	4		
2.21 Interpret the results correctly?	1	2	3	4		
2.22 Record results in register?	1	2	3	4		
2.23 Dispose gloves, wrappers, alcohol swabs and desiccant safely?	1	2	3	4		

		Yes	No	Comment
Testing Facility	Is there consistent testing temperature monitoring?			
	Is there consistent storage temperature monitoring?			
	Is lighting sufficiently available in all testing rooms?			
	Are all Kits in use within the stated shelf life?			
	Are SOPs available where testing is performed?			
Purchasing and Inventory				
	Are functional timers available for use where testing is performed?			
	Are buffers available?			
	Are kits and reagents stored under appropriate environmental conditions?			
	Is space adequate for storage of kits and accessories?			
	Are personnel following "first expiry, first out" method when managing stock?			
	Where there any stock outs in the past 6 months?			
	Is there a procedure for re-ordering kits and accessories?			
Records	Are results interpreted and recorded according to protocols?			
	Are records kept in a safe and secure place?			

3. CHALLENGES
3.1 What are the challenges that the health care worker faces in the process of doing his/her duties?

Annex 9.8. Microscope Minimum Requirements

- Microscope must be completely UL*, CSA* and CE* tested, listed, and approved to ensure fire and/or shock safety.
- Must have10x/18mm eyepieces.
- Must have auto compensating Siedentopf style binocular with diopter scale for interpupillary distance (must have visible diopter scales).
- Must have 4-position reversed nosepiece of metal construction with internal ball bearing stops. External clip system not acceptable.
- Must have 4x HI-Plan, 10x HI-plan, 40x HI-plan, and 100x oil HI-plan par focal and par centered infinity corrected objectives.
- Mechanical stage must be of built-in design with metal rack and pinion X-Y drives. No polymer belts, metal cables, timing belt systems or non-metallic components are acceptable in the drive mechanism. Coaxial controls must be low mounted for ease of use.
- Pre-aligned Abbe condenser with graduated iris diaphragm wheel with markings to show where iris aperture should be set for each objective magnification.
- Focus drive must be a self-tensioning, three ball design of all metal construction. Fine focus must have graduations of 100 divisions and 3 microns per division. Focusing knobs on both sides must have these markings.
- All gears throughout the microscope: mechanical stage, focus, condenser rack and pinion must be made of metal, brass, stainless steel or aluminum – no plastic components.
- Illumination system must be designed for 12v/35w tungsten halogen 2,000 hour average life bulbs.
- Microscope must have hinged lamp door that is angled to help prevent breakage. Sliding "drawer" type bulb covers not acceptable for safety reasons.
- Must have blue filter fixed into its mount, not loose. In Koehler kits, lollipop filters have "locking slots" to prevent them from falling out when tilted.
- Microscope base temperature must not exceed 37 degrees centigrade using a 12v/20w halogen lamp at full voltage for 6 hours.
- Power supply must be voltage sensing 85-265 volts with surge suppression and soft start lamp control.
- Lamp intensity must be conveniently located in stand armrest and controlled via an illuminated rotating wheel.
- Stage finger assembly is to be slide friendly that does not damage or break slides.
- Microscope must have ergonomic design.

***UL:** Underwriters Laboratories Inc.
***CSA:** Canadian Standards Association
***CE:** Conformance European

Annex 9.9. Stock Giemsa Reagent Minimum Requirements

Aspect	Specification
Container	Brown glass bottle
Appearance Color	Dark Green to Very Dark Green and Black and Green-Black
Appearance Form	Powder or Crystals
Concentration	0.67M
Formulation (When not commercially prepared)	Glass beads, 3.0 mm 30.0 ml Absolute methanol, acetone-free 270.0 ml Giemsa stain powder (certified) 3.0 g Glycerol 140.0 ml
Wavelength 647 - 653 nm	Absorbance ≥ 0.6
Wavelength 520 - 526 nm	Absorbance ≥ 0.3
Wavelength 288 - 294 nm	Absorbance ≥ 0.3
Wavelength 243 - 249 nm	Absorbance ≥ 0.2

Annex 9.10. Form 2.02: Malaria RDT Lot-Test Request Form (17-7-2011)

TRANSPORT DETAILS

REQUESTING INSTITUTION *(Institution/Organization requesting for testing)*	
SENDING INSTITUTION *(if different from the Requesting Institution)*	
DATE SENT *(dd/mm/yyyy)*	

RDT DETAILS

RDT PRODUCT NAME (as in product insert)	MANUFACTURER	CATALOGUE NUMBER	LOT NO.	EXPIRY DATE dd/mm/yyyy	QUANTITY PROVIDED	
					NO. OF BOXES	NO. OF TESTS/ BOX
(Delete/extend rows as necessary.)						

Temperature monitor included in the shipment: Yes☐ No☐ (Not routinely included)
If "yes" send the monitor together with RDTs to the testing institution (RDT QC laboratory)

TESTING DETAILS: Sending institution should insert the number of RDTs sent and an explanatory note in blank cells below if the number of RDTs sent varies from the specified number through prior agreement.

Minimum number of RDTs required per lot	The number of RDTs sent may be varied for non-routine testing. Discuss with lot-testing coordinator and insert details below
Pf-only RDTs: 100 tests	
Combination RDTs: 150 tests	
Additional comments from the requestor	

CONTACT DETAILS FOR RECEIPT OF RESULTS:

(Delete/extend columns as necessary.)

CONTACT PERSONS NAME			
POSITION			
INSTITUTION/ADDRESS			
TEL. /FAX NO.			
EMAIL ADDRESS			

***NOTE**: This form should be sent by email prior to sending the RDTs to Malaria_rdt@who.int and the lot-testing coordinator (at June 2010, nora.champouillon@finddiagnostics.org) or the email contact specified on the WHO RDT website www.wpro.who.int/sites/rdt). Include also a hard copy with the RDTs. A summary of results report will be published regularly and this will include the product name but the procurer agency name will be excluded*

Annex 9.11. Protocol for Primaquine radical cure for P. vivax at Health Post Level

Plasmodium vivax accounts for 33% of malaria cases in Ethiopia (MIS, 2011). It is characterized by frequent relapses and the administration of primaquine radical cure reduced relapses by 40% during 15 months of follow up (WHO). The FMOH is planning to introduce primaquine for *plasmodium vivax* as radical cure. It will be a phased approach where selected districts will implement initially followed by all elimination targeted districts and finally all over the country. The safety of primaquine is not yet fully established and this approach will help to scale up this important intervention. This document outlines the standard protocol to be used at health post level.

Mode of implementation

It will be implemented in selected districts from malaria elimination districts. The experience will be systematically documented. This will help us to learn from limited sites before going to scale.

Dose and administration of primaquine

Primaquine is given for patients with *plasmodium vivax*. It may be repeatedly administered if the patient has repeated attacks of *plasmodium vivax* malaria. Primaquine will be given at a dose of 0.25 mg/kg body weight per day for fourteen days. It should be administered with food to prevent the gastrointestinal side effects

Body weight (kg)	Mg based on 0.25mg/kg	Number of 15mg tablets PER DAY FOR 14 DAYS
5-14	1.25 to 3.5	¼
15-24	3.75 to 6	½
25-34	6.25 to 8.5	½
35 -60 and more	8.75 to 15	1

Adverse Events

Primaquine is generally well tolerated.

- Dose-related gastrointestinal discomfort, including abdominal pain, nausea and vomiting (Administration with food improves tolerability).
- The most important adverse effect is hemolysis in some patients. This adverse event may be seen occasionally in Ethiopian patients. Fortunately, primaquine is eliminated from the body rapidly, so that hemolysis stops once the drug is stopped.

Contraindications

- Known hypersensitivity to primaquine
- Women breast feeding infants less than six months old
- Infants less than six months
- Pregnancy

- Use the following checklist to reasonably rule out pregnancy

Nº	Questions	Yes	No
1	Did your last menstrual period start within the past 7 days?		
2	Have you abstained from sexual intercourse since your last menstrual period or delivery?		
3	Have you been using a reliable contraceptive method consistently and correctly since your last menstrual period or delivery?		
4	Have you had a baby in the last 4 weeks?		
5	Did you have a baby less than 6 months ago, are you fully or nearly fully breast feeding, and have you had no menstrual period since then?		
6	Have you had a miscarriage or abortion in the past 7 days?		

Interpretation:

If the client answered **YES** to ***at least one of the questions*** and she is free of signs or symptoms of pregnancy (see below), you can be reasonably sure she is not pregnant.

If the client answered **NO** to ***all of the questions***, pregnancy cannot be ruled out using the checklist. Refer her to health center for pregnancy test or wait until the next menstrual cycle to start primaquine.

Signs and symptoms of pregnancy

- Increased frequency of urination
- Increased sensitivity to odors
- Mood changes
- Weight gain
- Nausea and/or vomiting
- Breast tenderness
- Fatigue

Procedure

- The health extension worker will assist the patient to select treatment supporter from the household or neighborhood. The treatment supporter will assist the patient in taking all courses of the primaquine.
- The health extension worker will provide health education and client education material for patients and treatment supporters
- The patient will come to the health post for follow up at prescheduled days. The day of initial treatment is designated as day zero. The patient will be seen at the health post at days 3, 7 and 13 to check symptoms of anemia and urine color.
- The symptoms of anemia are fatigue, palpitation or dyspnea (shortness of breathing) on exertion
- Additionally ask for the symptoms of malaria (fever) at each visit
- Observe the urine of the patient with the Hillmen colour chart
- Hillmen urine color estimation for haemoglobinuria: urine should be placed in a clear glass container and held up against a white piece of paper, in a well illuminated area, before estimating the colour compared to the Hillmen Colour Chart. Urine colour estimation should be carried out as soon after voiding as possible. A score of 5 or above is considered evidence of haemoglobinuria.

Hillmen Urine Colour Chart

When to stop PQ (Refer patient to health center)

- Symptomatic anemia
- Urine color: a score of 5 or above on the Hillmen urine colour chart

Documentation and follow up

Federal Ministry of Health
Follow up Register for Primaquine Radical cure
For Health posts

Identification	Day	Date	Number of Chloroquine doses taken	Number of AL doses taken (if applicable)	Number of primaquine doses taken	Fever (Yes/No)	Fatigue on exertion (Yes/No)	Palpitation (Yes/No)	Dyspnea on exertion (Yes/No)	Urine color score on Hillmen color chart	**Action taken** 1. Appoint for next visit 2. Support aherence to medications 3. If patient has fever, managed according to the national guideline 4. Patient has fatigue on exertion and referred to health center 5. Patient has palpitation and referred to health center 6. Patient has dyspnea on exertion and referred to health center 7. Patient has urine color score of more than 5 and referred to health center	Date of Next visit	On day 13, write the number of days the patient took primaquine
Name: MRN:	0 3 7 13 Unscheduled visit												
Name: MRN:	0 3 7 13 Unscheduled visit												
Name: MRN:	0 3 7 13 Unscheduled visit												
Name: MRN:	0 3 7 13 Unscheduled visit												

Annex 9.12. Protocol for Primaquine radical cure for P. vivax at Health Center and Hospital Levels

Plasmodium vivax accounts for 33% of malaria cases in Ethiopia (MIS, 2011). It is characterized by frequent relapses and the administration of primaquine radical cure reduced relapses by 40% during 15 months of follow up (WHO). The FMOH is planning to introduce primaquine for *plasmodium vivax* as radical cure. It will be a phased approach where selected districts will implement initially followed by all elimination targeted districts and finally all over the country. The safety of primaquine is not yet fully established and this approach will help to scale up this important intervention. This document outlines the standard protocol to be used at health post level.

Mode of implementation

It will be implemented in selected districts from malaria elimination districts. The experience will be systematically documented. This will help us to learn from limited sites before going to scale.

Indications for PQ

Primaquine is to be used at selected elimination targeted areas for all patients diagnosed with *Plasmodium vivax* malaria. It should also be given for patients diagnosed with mixed infection using microscopy

Dose and administration

Primaquine is given for patients with *plasmodium vivax*. It may be repeatedly administered if the patient has repeated attacks of *plasmodium vivax* malaria. Primaquine will be given at a dose of 0.25 mg/kg body weight per day for fourteen days. It should be administered with food to prevent the gastrointestinal side effects

Body weight (kg)	mg	Number of 15mg tablets
	based on 0.25mg/kg	PER DAY FOR 14 DAYS
5-14	1.25 to 3.5	¼
15-24	3.75 to 6	½
25-34	6.25 to 8.5	½
35 -60 and more	8.75 to 15	1

Adverse Events

Primaquine is generally well tolerated.

- Dose-related gastrointestinal discomfort, including abdominal pain, nausea and vomiting (Administration with food improves tolerability).
- The most important adverse effect is hemolysis in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency. The degree of hemolysis is proportional to the dose, duration of exposure, and degree of G6PD deficiency. A study conducted by EPHI showed the nonexistence of African and Mediterranean variants of G6PD which are expected to be present in Ethiopia. Fortunately, primaquine is eliminated rapidly, so that hemolysis stops once the drug is stopped.

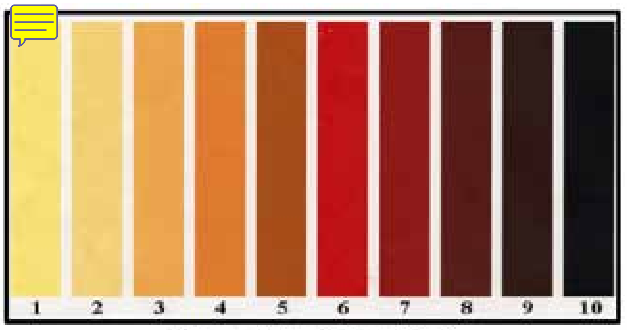
Contraindications

- Known hypersensitivity to primaquine
- Women breast feeding infants less than six months old
- Infants less than six months
- Pregnancy: do pregnancy test to rule out pregnancy

Procedure

- The health worker will assist the patient to select treatment supporter from the household or neighborhood. The treatment supporter will assist the patient in taking all courses of the primaquine.
- The health worker will provide health education and client education material for patients and treatment supporters
- The patient will come to the health center/ hospital for follow up at prescheduled days. The day of initial treatment is designated as day zero. The patient will be seen at the health facility at days 3, 7 and 13 to check symptoms of anemia, urine color and hemoglobin measurement.
- Ask for anemia symptoms at each visit. The symptoms of anemia are fatigue, palpitation or dyspnea (shortness of breathing) on exertion
- Measure hemoglobin on days 0, 3, 7 and 13

- Ask for the symptoms of malaria (fever) at each visit
- At each visit observe the urine of the patient with the Hillmen colour chart
    - Hillmen urine color estimation for haemoglobinuria: urine should be placed in a clear glass container and held up against a white piece of paper, in a well illuminated area, before estimating the colour compared to the Hillmen Colour Chart. Urine colour estimation should be carried out as soon after voiding as possible. A score of 5 or above is considered evidence of haemoglobinuria.



Hillmen Urine Colour Chart

When to stop PQ (refer patient to hospital)

- Hemoglobin < 5 g/dL
- Hemoglobin drop of >50% of the baseline
- Hemoglobin < 7 g/dL AND Hemoglobin drop from baseline of >25%
- Symptomatic anemia
- Urine color: a score of 5 or above on the Hillmen urine colour chart

Documentation and follow up

Federal Ministry of Health
Follow up Register for Primaquine Radical cure
For Health centers and hospitals

Identification	Day	Date	Number of Chloroquine doses taken	Number of AL doses taken (if applicable)	Number of primaquine doses taken	Fever (Yes/No)	Fatigue on exertion (Yes/No)	Palpitation (Yes/No)	Dyspnea on exertion (Yes/No)	Urine color score on Hillmen color chart	Hemoglobin	**Action taken** 1. Appoint for next visit 2. Support aherence to medications 3. If patient has fever, managed according to the national guideline 4. Patient has symptoms of anemia and managed/referred to hospital 5. Patient has urine color score of more than 5 and managed/referred to hospital 6. Patient has significant drop in hemoglobin and managed/referred to hospital	Date of Next visit	On day 13, write the number of days the patient took primaquine	Remark
Name:	0														
	3														
	7														
MRN:	13														
	Unscheduled visit														
Name:	0														
	3														
	7														
MRN:	13														
	Unscheduled visit														
Name:	0														
	3														
	7														
MRN:	13														
	Unscheduled visit														
Name:	0														
	3														
	7														
MRN:	13														
	Unscheduled visit														