Federal Republic of Nigeria

National Guidelines for Diagnosis and Treatment of Malaria

ROLL BACK MALARIA

NATIONAL GUIDELINES FOR DIAGNOSIS AND TREATMENT OF MALARIA

Federal Ministry of Health
National Malaria and Vector Control Division
Abuja-Nigeria

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FOREWORD

Malaria has consistently topped the list of the public health diseases in the country, contributing significantly to high morbidity and mortality.
Over the years, the Federal Government has put several interventions in place to control the scourge of the disease, one of which is the improvement of malaria case management at all levels. A major threat to these efforts however was the emergence of resistance to available antimalarial medicines such as chloroquine and Sulphadoxine-Pyrimethamine. The Drug Therapeutic Efficacy Tests (DTET) on chloroquine and Sulphadoxine-Pyrimethamine in the six epidemiological zones in 2002 evidently showed the inability of these medicines to completely clear malaria parasites in the blood.
The introduction in 2005, of Artemisinin based Combination Therapy (ACTs) as treatment of uncomplicated malaria following the failure of chloroquine and Sulphadoxine-Pyrimethamine revolutionalized the treatment of malaria in the country. Presently ACTs are the most efficacious antimalarial treatment available globally.

In a renewed effort to control, the disease, emphasis has shifted from the vulnerable groups to the entire population at risk. In this case, colour coded and pre-packaged antimalarial medicines will now be deployed to the public sector and also at highly reduced cost to the private sector. By so doing, the medicines will be made available and affordable to the general populace.
One of the major highlights in the newly reviewed policy is the promotion of parasite based diagnosis in all age groups; in which case, all suspected cases of malaria shall be appropriately diagnosed where available, before treatment. This is expected to protect the medicine while also saving cost.
This updated guideline provides comprehensive information on chemoprophylaxis, preventive treatment, diagnosis and treatment of malaria as recommended by the country's National Policy on Diagnosis and Treatment of Malaria. The use of this document is therefore expected to provide information that will lead to the improvement in the management of malaria illness both at the health facility and at community levels.
The guideline would be widely disseminated to health care facilities; both private and public across Nigeria as an important step in standardizing their prescription practices. Accordingly, it is imperative for the health care providers in the country

to strictly comply with this guideline to harmonize malaria management practices within the country.

I would therefore encourage all health care providers at the various health facilities and within the community to avail themselves of the opportunities offered by this guideline with a view to "rolling back" malaria from Nigeria.

Prof. C.O. Onyebuchi Chukwu
Honourable Minister of Health

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We also appreciate the contribution of representatives of academic institutions and research centres for their quality inputs to the development of this document.
It is our hope that this document will provide the necessary guide required for the effective management of malaria in Nigeria.

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GLOSSARY

Artemisinin-based combination therapy (ACT): A combination of artemisinin or one of its derivatives with an antimalarial or antimalarials of a different class.

Asexual parasitaemia: The presence in host red blood cells of asexual parasites. The level of asexual parasitaemia can be expressed in several different ways: the percentage of infected red blood cells, the number of infected cells per unit volume of blood, the number of parasites seen in one microscopic field in a high-power examination of a thick blood film, or the number of parasites seen per 2001000 white blood cells in a high power examination of a thick blood film.

Cerebral malaria: Severe *P. falciparum* malaria with cerebral manifestations, usually including coma (Glasgow coma scale < 11, Blantyre coma scale < 3). Malaria with coma persisting for > 30 min after a seizure is considered to be cerebral malaria.

Cure: Elimination of the symptoms and asexual blood stages of the malaria parasite that caused the patient or caregiver to seek treatment.

Drug resistance: The World Health Organization (WHO) defines resistance to antimalarials as the ability of a parasite strain to survive and/or to multiply despite the administration and absorption of a medicine given in doses equal to or higher than those usually recommended but within the tolerance of the subject, provided drug exposure at the site of action is adequate. Resistance to antimalarials arises because of the selection of parasites with genetic mutations or gene amplifications that confer reduced susceptibility.

Gametocytes: Sexual stages of malaria parasites present in the host red blood cells.

Malaria pigment (haemozoin): A dark brown granular pigment formed by malaria parasites as a by-product of haemoglobin catabolism. The pigment is evident in mature trophozoites and schizonts. They may also be present in white blood cells (peripheral monocytes and polymorphonuclear neutrophils) and in the placenta.

Monotherapy: Antimalarial treatment with a single medicine (either a single active compound or a synergistic combination of two compounds with related mechanism of action).

Plasmodium: A genus of protozoan vertebrate blood parasites that includes the causal agents of malaria. *Plasmodium falciparum, P. malariae, P. ovale* and *P. vivax* cause malaria in humans. Human infections with the monkey malaria parasite, *P. knowlesi* have also been reported from forested regions of South-East Asia.

Rapid diagnostic test (RDT): An antigen-based stick, cassette or card test for malaria in which a coloured line indicates that plasmodial antigens have been detected.

Recurrence: The recurrence of asexual parasitaemia following treatment. This can be caused by a recrudescence, a relapse (in *P. vivax* and *P. ovale* infections only) or a new infection.

Recrudescence: The recurrence of asexual parasitaemia after treatment of the infection with the same infection that caused the original illness. This results from incomplete clearance of parasitaemia due to inadequate or ineffective treatment. It is, therefore, different to a relapse in *P. vivax* and *P. ovale* infections, and it differs from a new infection or re-infection (as identified by molecular genotyping in endemic areas).

Relapse: The recurrence of asexual parasitaemia in *P. vivax* and *P. ovale* malaria deriving from persisting liver stages. Relapse occurs when the

blood stage infection has been eliminated but hypnozoites persist in the liver and mature to form hepatic schizonts. After variable intervals of weeks to months, the hepatic schizonts burst and liberate merozoites into the bloodstream.

Severe anaemia: Haemoglobin concentration of < 5 g/100 ml (haematocrit < 15%).

Severe falciparum malaria: Acute falciparum malaria with signs of severity and/or evidence of vital organ dysfunction.

Uncomplicated malaria: Symptomatic infection with malaria parasitaemia without signs of severity and/or evidence of vital organ dysfunction.

LIST OF ABBREVIATIONS

AA: Artesunate - amodiaquine

ACTs: Artemisinin-based Combination Therapy

ADR: Adverse Drug Reaction

AL: Artemether - lumefantrine

CSF: Cerebrospinal fluid

DHP: Dihydroartemisinin - piperaquine

DOT Directly Observed Therapy

ECG: Electrocardiogram

FCT: Federal Capital Territory

GIT: Gastrointestinal Tract

G6PD: Glucose 6-Phosphate Dehydrogenase Deficiency

Hb: Haemoglobin

HBSS: Sickle Cell Haemoglobin

HIV: Human Immunodeficiency Virus

HRP-2: Histidine Rich Protein-2

IM: Intramuscular

IPT Intermittent Preventive Treatment

IV: Intravenous

LGA: Local Government Area

LLIN: Long Lasting Insecticidal Nets

MAPS: Malaria Action Programme for States.

MP: Malaria Parasite

NAFDAC: National Agency for Food and Drug Administration and Control

NGT: Nasogastric Tube

PCR: Polymerase Chain Reaction

PCV: Pack Cell Volume

PMVs: Private Patent Medicine Vendors

QA: Quality Assurance

QC: Quality Control

RDTs: Rapid Diagnostic Test

RMCs: Role Model Care-givers

SOPs: Standard Operating Procedures

SuNMaP: Support for National Malaria Programme

TNF: Tumor Necrosis Factor

USAID: United States Agency for International Development

WBCs: White Blood Cells

WHO: World Health Organization

EXECUTIVE SUMMARY

Malaria case management remains a vital component of the malaria control strategies. This entails early diagnosis and prompt treatment with effective antimalarial medicines recommended for use in the country. As part of the activities to scale up the diagnosis and treatment of Malaria in Nigeria, the National Malaria Control Programme reviewed the National Policy on Diagnosis and Treatment of Malaria in line with WHO recommendations. This guidelines has therefore been reviewed to reflect the changes and recommendations in the new policy document

This third edition of the guidelines emphasizes the importance of parasitological confirmation of malaria cases through microscopy or Rapid Diagnostic Test and also provides clear and easy-to-understand steps required in carrying out the listed procedures.

The summary of the key recommendations provided in these guidelines is presented below.

- Prompt parasitological confirmation by microscopy or RDTs is recommended in all patients suspected of malaria before treatment.
- Treatment solely on the basis of clinical suspicion should only be considered when a parasitological diagnosis is not accessible.
- Artemisinin-based combination therapies (ACTs) are the recommended treatments for uncomplicated *P. falciparum* malaria.
- The following ACTs are recommended for use in Nigeria Artemether-lumefantrine, Artesunate-amodiaquine,
- Artemisinin and its derivatives should not be used as monotherapy in the treatment of uncomplicated malaria
- Oral Quinine is the recommended medicine for the treatment of uncomplicated malaria in the first trimester and in children less than 5kg, however, ACTs can be used under supervision by the

health care provider

- ACTs is the recommended treatment of uncomplicated malaria in the second and third trimesters of pregnancy.
- Severe malaria is a medical emergency. After rapid clinical assessment and confirmation of diagnosis where feasible, commence immediate treatment with parenteral medication. Intravenous artesunate is preferred for the treatment of severe P.*falciparum* malaria
- Parenteral quinine or artemether is an acceptable alternative if artesunate is not available.
- Parenteral antimalarial medicines in the treatment of severe malaria should be administered for a minimum of 24 hours once started (irrespective of the patient's ability to tolerate oral medication earlier) and thereafter, complete treatment with a complete course of an ACT.
- In settings where complete treatment of severe malaria is not possible, patients should be given pre-referral treatment and referred immediately to an appropriate facility for further treatment. The recommended pre-referral treatment options include any of these; artesunate IM or rectal, and quinine IM.
- The recommended chemoprophylaxis for non immune visitors will be as available in the visitor's country of origin or as recommended in Nigeria.
- Sulphadoxine-Pyrimethamine is the recommended medicine for Intermittent Preventive Treatment in Pregnancy.

2.0. INTRODUCTION

Malaria remain a major public health problem in Nigeria; children under the age of five and pregnant women are still the most affected. More than 60% outpatient visits in Nigeria are due to malaria. The disease has impacted negatively on the economy with about 132 billion Naira lost to the disease as cost of treatment and loss in man-hours.

The launching of the Roll Back Malaria initiative in April 25, 2000 and the commitment of all African leaders to fight the disease which kills over one million children and pregnant women every year was commendable.

One of the key strategies to control malaria is effective case management. Unfortunately, this has received a major setback in the past years because of the high level of resistance to the first and second line antimalarial medicines; Chloroquine and Sulphadoxine-Pyrimethamine.

In 2005, the National Malaria Treatment Policy was reviewed during which the Artemisinin based Combination Therapies were introduced. These medicines are presently the most efficacious antimalarial treatment available. The therapeutic efficacy study in 2004 and a repeat test in 2009 has continuously demonstrated high efficacy of these artemisinin combinations. In addition, the Federal Ministry of Health is aware of the development of new potent combinations that are also highly effective and may deploy some of these as pilots in selected sites.

Until recently, in areas of high malaria transmission such as Nigeria, malaria treatment has been based mainly on clinical diagnosis which was presumptive, because malaria was considered one of the commonest causes of fever.

With the deployment of several other control interventions such as Long Lasting Insecticidal Nets (LLIN) and Indoor Residual Spraying (IRS),

Intermittent Preventive Treatment (IPT) etc, there has been emerging evidences of decline in the incidence of malaria in some regions. These have further been corroborated by the reduced rate of parasitaemia in the recently concluded Drug Therapeutic Efficacy Test in the six epidemiological settings in the country.

With the availability of new tools such as parasite-based rapid diagnostic kits, which compliments the standard microscopy, it is imperative to provide targeted treatment and, accurate estimation of true malaria cases. However, in cases where parasitological confirmation is not available, highly vulnerable groups (including children under five years and those suspected with severe malaria) can be treated on a clinical basis.

This guideline has been produced to provide information on the use of some antimalarial medicines approved for use in Nigeria to reflect the changes that have been incorporated into the reviewed National Antimalarial Treatment Policy.

1.1 OVERVIEW OF THE GUIDELINES FOR DIAGNOSIS AND TREATMENT OF MALARIA

1.1.1 Objectives

The objectives of this document are to provide guidelines for:

- the diagnosis of malaria using rapid diagnostic tests (RDTs) and microscopy
- treatment of uncomplicated malaria
- management of severe malaria
- chemoprophylaxis and preventive treatment of malaria

1.1.2 Target audience:

- Health care providers at all levels

1.2 HEALTH CARE LEVELS AND THEIR ROLES IN MALARIA MANAGEMENT

Community based Care

Informal health care providers in the communities are Role Model Care Givers (RMC) and the Patent Medicine Vendors (PMVs). These are trained to recognize basic symptoms of uncomplicated malaria and treat them.

Management of malaria at health facilities occur at three levels:

Level I

This includes such facilities as the Primary Health Care Clinics, Dispensaries and Health posts and is expected to be available in all the political wards and communities in the country. The cadre of staff found in this level include Nurses, Community Health Officers, Community Health Extension Workers, Pharmacy technicians etc. These are trained to provide comprehensive management for uncomplicated malaria and also

initiate appropriate treatment before referring suspected cases of severe malaria to higher facilities. Occasionally, there may be medical officers and pharmacists and trained microscopist at this level of health care delivery. The main form of diagnosis is the use of Rapid Diagnostic Test kits.

Level II

This level consists of Comprehensive health centres, Cottage hospitals, General hospitals and some private hospitals. At this level, there is capacity to carry out microscopy and other basic laboratory services and also to treat severe malaria in addition to providing in-patient care. Each LGA is expected to have at least one of these.

The cadre of staff found at this level are medical officers, pharmacists, medical laboratory scientists, nurses, Community Health Officers etc. Parasite based confirmation with microscopy shall be used to confirm suspected cases of malaria; however RDTs may be used at this level as appropriate.

Level III

This represents the highest level of medical care in the country. The facilities include Teachinghospitals, Specialist hospitals, Federal Medical centres. Some General and private hospitals belong to this category. At least, one of these categories is found in each state of the Federation and provide specialized health care services. The cadres of health workers found here include specialists in various health disciplines.

Parasite based confirmation with microscopy shall be used to confirm all cases with febrile illnesses; however RDTs may be used at this level as appropriate.

1.3 EPIDEMIOLOGY AND CLINICAL DISEASE

Malaria is an infectious disease caused by the parasite of the genus *Plasmodium,* transmitted mostly by the bite of an infected female

anopheles mosquito. There are four identified species of the parasite causing human malaria, namely, *Plasmodium falciparum, P. vivax, P. ovale and P. malariae*. In Nigeria, the species most responsible for the severe form of the disease that leads to death is *P. falciparum*. P*. vivax* does not occur in indigenous Nigerians.

Malaria transmission is stable in Nigeria. Children under the age of five, pregnant women and non-immune visitors from non-endemic areas are particularly more susceptible than the general population.

Based on clinical and laboratory profiles, malaria can be classified as uncomplicated or severe. Patients with malaria can die when the disease is not appropriately classified. Failure to recognize severe malaria may be fatal.

a. **Uncomplicated malaria**:
This is symptomatic malaria that has no vital organ dysfunction or life threatening manifestations.

b. **Severe malaria**:

This is when there is *P. falciparum* asexual parasitaemia and no other confirmed cause of their symptoms with the presence of life threatening clinical or laboratory features.

2.0 HISTORY

A complete history should include:

- General information such as age, place of residence and recent history of travel within or outside the country.
- Enquiry about the following symptoms:-
  * Fever
  * Chills (feeling cold) and rigors (shaking of the body)
  * Headache
  * Joint weakness or tiredness

- Also ask for the symptoms of other common childhood diseases
  * Cough or respiratory distress
  * Diarrhoea
  * Ear pain and skin rashes in the last three months.

3.0 DIAGNOSIS OF MALARIA

Malaria can be diagnosed based on clinical and laboratory evaluations.

3.1 Clinical diagnosis

The signs and symptoms of malaria are non-specific. However, clinical suspicion is based on fever or history of fever in the last 24 hrs and/or the presence of anaemia. It is important to note that clinical diagnosis alone may result in over-diagnosis of malaria; hence, parasitological confirmation is strongly recommended.

Clinical signs may include amongst other symptoms:

- Raised body temperature ≥ 37.5°C.
- Enlarged spleen or liver, especially in children.
- Pallor (children/pregnant women)
- Exclude signs of severe disease.

3.2 Parasitological Diagnosis

The changing epidemiology of malaria due to scale up of interventions and the introduction of ACTs have increased the urgency of improving the specificity of malaria diagnosis. Parasitological diagnosis has the following advantages:

- Improved patient care in parasite-positive patients;
- Identification of parasite-negative patients in whom another diagnosis must be sought;
- Prevention of unnecessary use of antimalarials, reducing

frequency of adverse effects, especially in those who do not need the medicines, and drug pressure selecting for resistant parasites;
- Improved malaria case detection and reporting;
- Confirmation of treatment failures

Parasitological confirmation is recommended in all suspected cases of malaria. However, in areas of high transmission such as Nigeria, children under five years can still be treated on clinical basis where parasitological confirmation is not feasible. This is also applicable in cases of suspected severe malaria.

Prompt and accurate diagnosis is part of effective disease management. High sensitivity of malaria diagnosis is important to identify those positive cases in all settings. High specificity is vital to identify negative cases, which can reduce unnecessary treatment with antimalarial medicines and improve differential diagnosis of febrile illness.

The two methods in routine use for parasitological diagnosis are ***Light Microscopy*** and ***Rapid Diagnostic Tests*** (RDTs). The latter detect parasite-specific antigens or enzymes and some have a certain ability to differentiate species. Deployment of microscopy and RDTs must be accompanied by quality assurance.
Other tests outside the routine clinical setting such as ***Polymerase Chain Reaction*** (PCR)-based techniques are used for parasite diagnosis under special circumstances in tertiary institutions and research (for instance resistance testing)

Antimalarial treatment should be limited to test positive cases. The negative cases should be reassessed for other common causes of fever. The benefit of parasitological diagnosis depends entirely on health-care providers adhering to the results in managing the patient. However, the severity of the disease justifies the use of antimalarial medicines in test negative cases, considering the possible small risk of false negative tests.

The risk of false negative microscopy is higher if the patient has received a recent dose of an artemisinin derivative.

The results of parasitological diagnosis should be available within a short time (less than two hours) of the patient presenting.

3.2.1 Microscopy:

Microscopy is the standard method for parasitological diagnosis of malaria. This is done by examining a stained thick or thin blood smear for the presence of malaria parasites.
Thick films are recommended for parasite detection and quantification and can be used to monitor response to treatment. Thin films are recommended for species identification.

Microscopic examination of stained blood films by a highly skilled microscopist has a sensitivity range of 86-98% with a lower sensitivity in detecting low parasitaemias (≤ 320/µl). Various factors such as the stage of the malaria infection and previous medication may reduce parasitaemia below the detectable threshold and necessitate repeat examination.

3.2.2 Malaria Rapid Diagnostic Tests (RDTs)

Malaria Rapid Diagnostic Tests (RDTs) is a device which detects specific antigens (proteins) produced by malaria parasites. The RDT signifies presence of the antigens by colour change on nitrocellulose strip (test strip)
They provide a useful guide to the presence of clinically significant malaria infection. They complement microscopy based diagnosis where such services are not available. However, RDTs should not replace microscopy as the sole means of malaria diagnosis.

The general management of a malaria patient should base treatment decisions not only on results but also other clinical parameters. In case of uncomplicated malaria, the rationale of treatment for a MP slide/RDT negative should be clearly defined by the managing clinician.

Like all laboratory procedures the accuracy of an MP slide /RDT is dependent on the care and expertise with which it is prepared and interpreted.
Quality assured Histidine Rich Protein 11 (HRP 2) based RDT is the recommended for the diagnosis of malaria in all age groups. Most RDTs have a sensitivity of 95% at parasite densities of 200/µl of blood.

The sensitivity of malaria RDTs is determined by the:

- Species of parasite
- Number of parasites present in the blood
- Condition of the RDT
- Correctness of technique used to perform the test.
- Correctness of interpretation by the reader
- Parasite viability and variation in production of antigen by the parasite.

3.3 The Choice between Rapid Diagnostic Tests (RDTs) and Microscopy

The choice between RDTs and microscopy depends on local circumstances, including the skills available, patient case-load, epidemiology of malaria and the possible use of microscopy for the diagnosis of other diseases. Where the case-load of fever patients is high, microscopy is likely to be less expensive than RDTs, but may be less operationally feasible. Microscopy has further advantages in that it can be used for speciation and quantification of parasites, and to assess response to antimalarial treatment. Microscopy can also be used in the identification of other causes of fever.
However, a major drawback of light microscopy is its requirement for well-trained, skilled staff and, usually, an energy source to power the microscope. In many areas, malaria patients are treated outside of the formal health services, e.g. in the community, in the home or by private providers; microscopy is generally not feasible in many such circumstances, but RDTs may be possible.

Although RDTs for detection of parasite antigen are generally more expensive, their deployment may be considerably cost effective in many of these settings. The sensitivities and specificities of RDTs are variable, and their vulnerability to high temperatures and humidity is an important constraint. Despite these concerns, RDTs make it possible to expand the use of confirmatory diagnosis

In the diagnosis of severe malaria cases, microscopy is a preferred option; it not only provides the diagnosis of malaria, but it is useful in assessing other important parameters in a severely ill patient. In situations where an RDT has been used to confirm malaria, this allows for a rapid institution of antimalarial treatment, however, where possible a microscopic examination is recommended to enhance the overall management of the patient.

Summary Box 1: Diagnosis of Malaria 4.0

- Prompt parasitological confirmation by microscopy or RDT is recommended in all patients suspected of Malaria before treatment is initiated.
- Treatment solely on the basis of clinical suspicion should only be considered when a parasitological diagnosis is not accessible

TREATMENT OF UNCOMPLICATED MALARIA

4.1 Treatment Objective:

The objective of treating uncomplicated malaria is to cure the infection as rapidly as possible. Prompt treatment will prevent both progressions to severe disease and the additional morbidity associated with treatment failure. Cure of the infection means eradication from the body of the parasite that caused the disease. Additional objectives are to prevent transmission, and the emergence and spread of resistance to antimalarial medicines.

4.2 Artemisinin based Combination Therapies

The treatment of choice for uncomplicated malaria is Artemisinin Based Combination Therapy (ACT). ACTs are combination medicines consisting of an artemisinin derivative and another effective long acting schizonticidal antimalarial medicine.

4.3 Recommended treatments

The recommended ACTs for treatment of uncomplicated malaria in Nigeria are Artemether-Lumefantrine and Artesunate-Amodiaquine. The 2009 Drug Therapeutic Efficacy Tests carried out on these medicines in the country have confirmed that they remain efficacious.

Artemether-Lumefantrine

It is available as co-formulated. Each tablet contains 20mg artemether and 120mg lumefantrine.

There are 4 different packet sizes (see table below); some children packs containing six and twelve tablets come in dispersible tablet form.

Dosage regimen

Weight	Number of tables/dose
5 - < 15kg	1 tab twice daily X 3days
15 - >25kg	2 tabs twice daily x 3days
25 - <35kg	3 tabs twice daily x 3days
>35kg	4 tabs twice daily x 3days

It is important to emphasize that the **6 doses** must be taken by the patient. The first two doses should be taken between 8 to 12 hours apart. Absorption of the medicine is enhanced by fatty meals.

Artesunate-Amodiaquine

It is available as co-formulated and co-packaged. The co-formulated medicines are however preferred.

National recommended Artesunate and Amodiaquine combination

Medicines	Dosage form	Presentation
Artesunate - Amodiaquine	Tablet	Co-formulated

Dosage regimen for co-formulated Artesunate-Amodiaquine

Weight/Age	Tables strength	Dosage regimen
4.5kg - <9kg 2months - 11months	25mg/67.5mg	1 tab once daily for three days
>9kg - <18kg >1 year - 5 years	50mg/135mg	1 tab once daily for three days
18kg - >36kg >6 years - 13 years	100mg/270mg	1 tab once daily for three days
36kg and above 14 years and above	100mg/270mg	1 tab once daily for three days

If the patient shows evidence of inadequate response (persistence of fever, parasitaemia or deterioration in clinical condition), do the following:

- Evaluate the patient and review diagnosis
- Exclude sub optimal dosing or inadequate intake
- Investigate further

In the absence of clinical improvement and persistence of positive parasitaemia, despite adequate treatment, quinine should be used. (Please see below for the dosage regimen of quinine).

Monotherapy with any artemisinin derivatives and other antimalarial medicines are not recommended in the treatment of uncomplicated malaria. It should be noted that Sulphadoxine-Pyrimethamine is not a combination therapy and should not be used as such. In Nigeria, the use of Sulphadoxine-Pyrimethamine is restricted to pregnant women as Intermittent Preventive Treatment.

4.4 Practical issues in Management of Uncomplicated Malaria

- ***Antipyretic measures***
  If temperature is > 38.5°C, give Paracetamol 10 - 15 mg/kg in children or 500-1000 mg in adults every 6 8 hours or when necessary or advice

to tepid sponge (wipe the body with towel soaked in lukewarm water) and avoid over=clothing.

- ***Persistent Vomiting***
  If a patient vomits the medicine within 30 minutes, repeat the dose. If this is vomited again and the vomiting becomes persistent, the patient should be considered as having severe malaria and managed accordingly.
- ***Febrile Seizures***
  If a patient has a seizure and does not recover within 30 minutes from that seizure, it should be considered as severe malaria.

5.0 TREATMENT OF UNCOMPLICATED MALARIA IN SPECIAL GROUPS

5.1 Children less than 5kg

Malaria in children less than 5kg can be serious and may progress to severe disease with increased risk of dying if not treated promptly. Artemisinin derivatives are safe and well tolerated by young children. ACTs can be used for the treatment of uncomplicated malaria in infants and young children but attention must be given to accurate dosing and the providers must ensure that the administered dose is retained. Oral quinine 10mg base /kg every 8 hours for 7 days and other supportive therapy can also be used for treatment.

5.2 Pregnant women and Lactating mothers

Falciparum malaria in pregnancy carries a high mortality for the foetus and increased morbidity for the pregnant woman. Quinine is safe for the treatment of malaria in all trimesters of pregnancy. In the second and third trimester ACTs can be used. However there should be proper monitoring and documentation in all cases.

In the first trimester the safety of the ACTs has not been ascertained for a categorical recommendation on their use. However, should be used if it is

the only effective antimalarial medicine available.
Lactating mothers should also be treated with recommended ACTS.

6.0 COMMUNITY MANAGEMENT OF MALARIA

One of the strategies introduced to improve access and rapidly scale up malaria diagnosis and treatment is the introduction of community management of malaria. Role Model Caregivers and Private Medicine Vendors (PMVs) in remote communities where access is difficult are identified and trained to recognize basic symptoms of uncomplicated malaria in children less than five years, carry out diagnosis where feasible with malaria Rapid Diagnostic Test and initiate appropriate treatment. They also recognize symptoms of severe malaria and support the referral process.

Recommended medicines for the treatment of malaria at community level is as recommended for the treatment of uncomplicated malaria.

Key Messages for Oral Medicines at Home

- Tablets are preferred as oral medication
- Determine the appropriate medicine and dosage according to weight and age
- Tell the patient or the caregiver the reason for giving the medicine
- Demonstrate how to take or give the correct dose
- Watch the patient taking the medicine
- Explain that the treatment course must be completed even when the patient feels well
- Advise them on when to return
- Check that the patient or caregiver has understood the instructions before leaving the clinic

Follow up

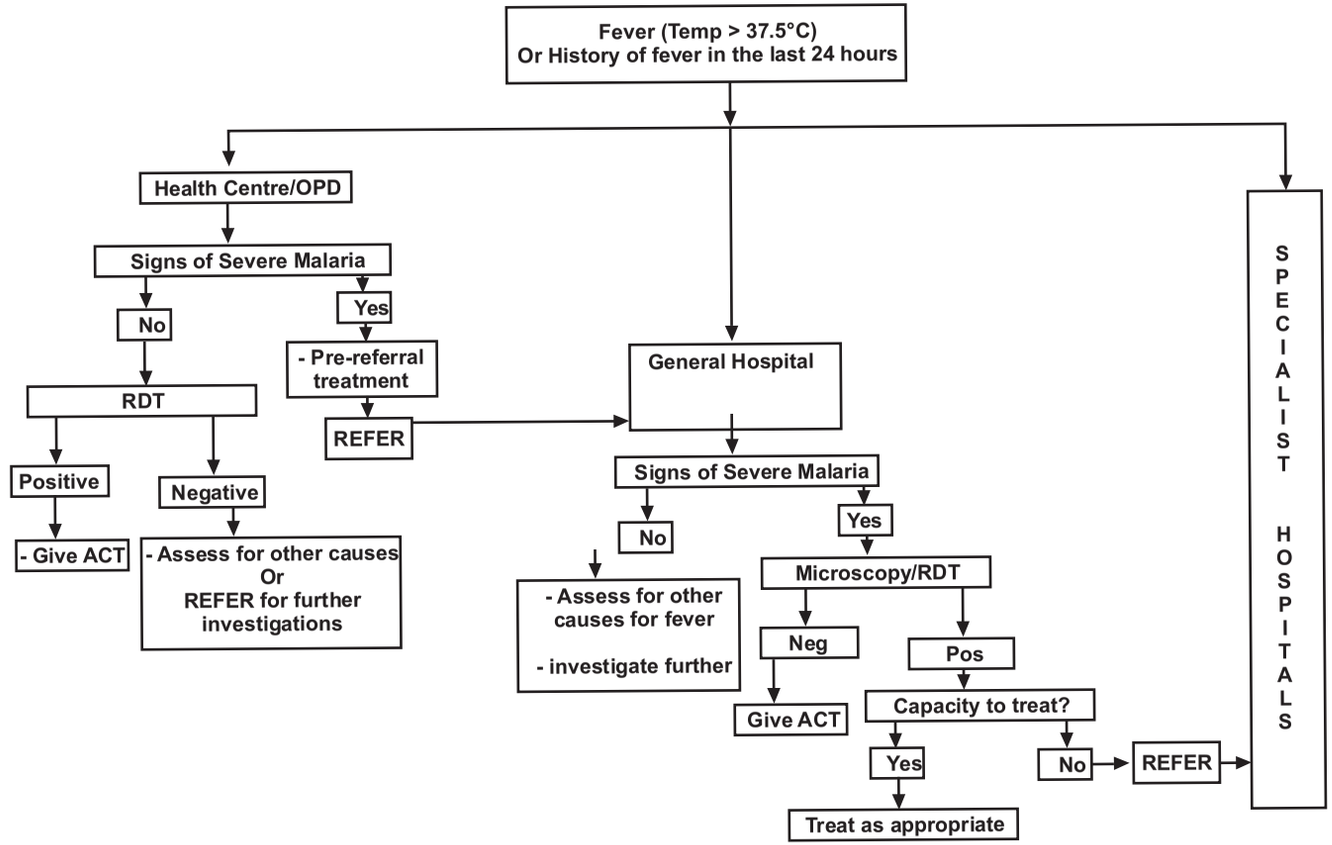
- Counsel the patient to return immediately;

* if condition gets worse or develops symptoms of severe disease,
* if fever persists for two days after commencement of treatment
- When patient returns,
* Check that the treatment regimen was complied with,
* Do a complete assessment to exclude any other possible cause of the fever,
* Repeat or do blood smear for malaria parasites and
* Refer or manage as necessary

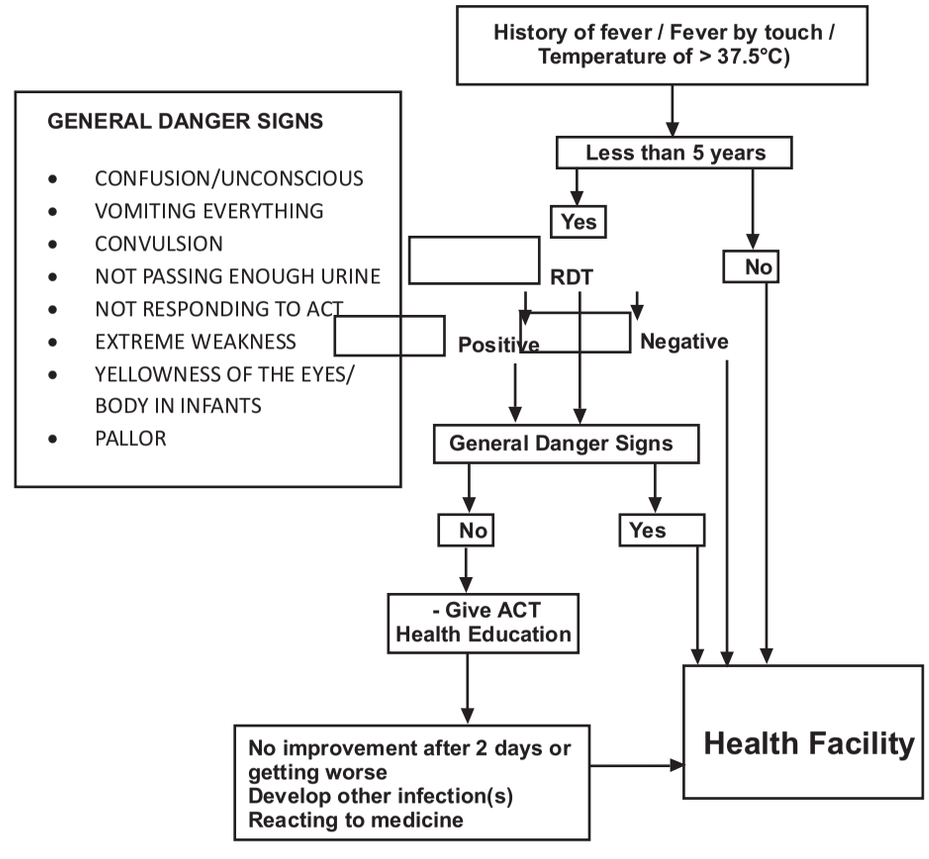
Summary Box 2: Treatment of uncomplicated malaria

- Parasitological confirmation of diagnosis is recommended in all age groups.
- Artemisinin Combination Therapy (ACT) is the recommended medicines for the treatment of uncomplicated Malaria.
- Artemether-Lumefantrine (AL) and Artesunate-Amodiaquine (AA) are the recommended ACTs for programmatic use in Nigeria.
- The use of monotherapies is not recommended

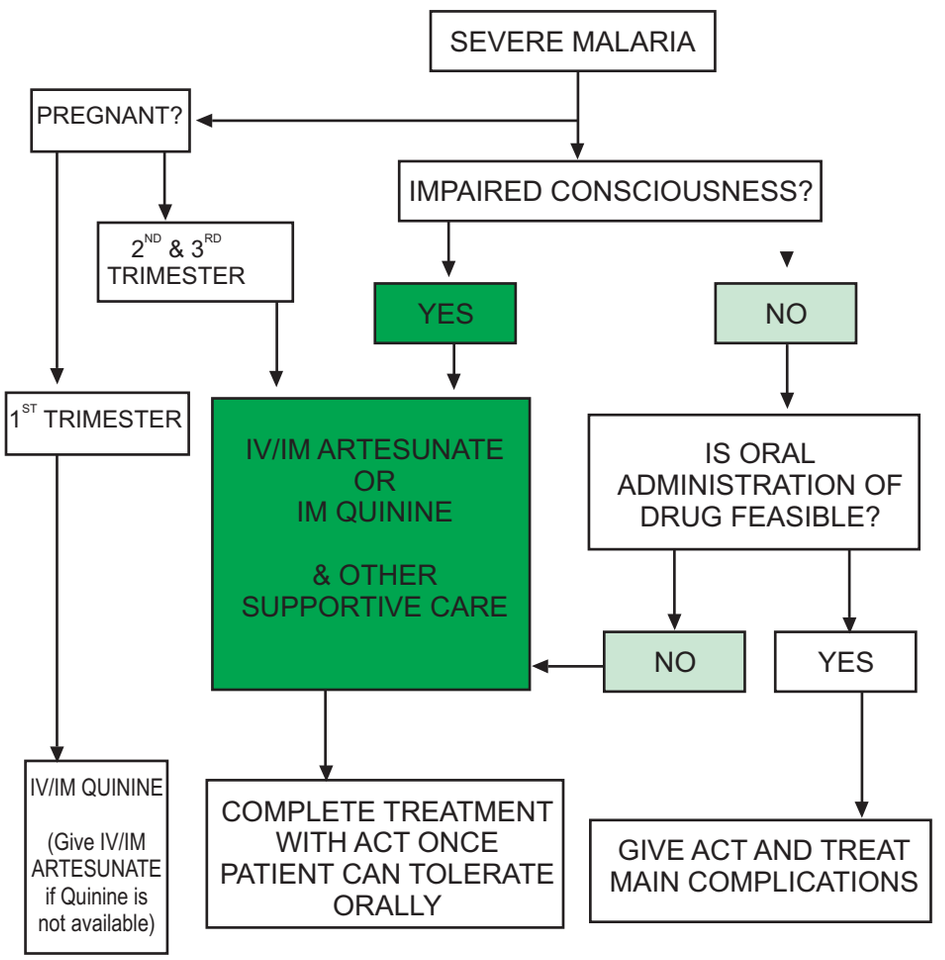
ALGORITHM FOR FACILITY BASED MANAGEMENT OF MALARIA AT DIFFERENT LEVELS OF HEALTH CARE IN NIGERIA



ALGORITHM FOR COMMUNITY TREATMENT OF MALARIA



ALGORITHM FOR MANAGEMENT OF SEVERE MALARIA



7.0 ASSESSMENT AND MANAGEMENT OF SEVERE MALARIA

Management of severe malaria should be carried out in secondary facilities with adequate facilities to manage complications or at specialist facility.

7.1 Definition

A patient has severe malaria when there is *P. falciparum* asexual parasitaemia and no other confirmed cause of their symptoms, in the presence of one or more of the following clinical or laboratory features:

Clinical Manifestations or laboratory findings	Frequency [a]	
	Children	Adults
• Prostration *(i.e. Generalized weakness or inability to sit, stand or walk without support)*	+++	+++
• Impaired consciousness *(confusion or drowsiness or coma)*	+++	++
• Respiratory distress *(difficulty in breathing, fast deep breath)*	+++	+
• Multiple convulsions *(>2 generalized seizures in 24 hrs with regaining of consciousness)*	+++	+
• Severe anaemia *(Hb <5g/dl)*	+++	+
• Circulatory collapse *(shock)*	+	+
• Hypoglycaemia *(Less than 40mg or 2.2 mmol/l)*		
• Pulmonary oedema *(respiratory distress/radiology)*	+/-	+
• Abnormal bleeding *(disseminated intravascular coagulopathy)*	+/-	+
• Jaundice *(yellow discoloration of the eyes)*	+	+++
• Haemoglobinuria *(Coca-cola coloured urine)*	+/-	+
• Hyperparasitaemia [b]	++	+
• Renal failure *(Urine output of less than 400 ml in 24 hours or <12ml/kg per 24 hours in children and a serum creatinine of more Than 265 µ mol/l (> 3.0 mg/dl), failing to improve after rehydration)*	+/-	++

[A] on a scale from + to +++; +/- indicates infrequent occurrence.

[b] *Density of asexual forms of P. falciparum in the peripheral smear exceeding 5% of erythrocytes (more than 250,000 parasites per µl at normal red cell counts)*

7.2 Explanatory notes on the features of severe malaria

a. Anaemia

Anaemia occurs as a result of destruction of parasitized red blood cell by the spleen, TNF mediated depression of erythropoiesis and immune mediated haemolysis.

b. Cerebral Malaria:

For a diagnosis of cerebral malaria, the following criteria should be met:

i. *Deep, unarousable coma*: Motor response to noxious stimuli is non-localising or absent. However management should be instituted once there is an altered consciousness.

Ii. *Exclusion of other encephalopathies*:

Iii. *Confirmation of P. falciparum infection*:

c. Abnormal neurological manifestations:

Convulsions may be as a result of very high temperature, hypoglycaemia, hypoxaemia, severe anaemia or the effect of herbal concoction.

d. Hypoglycaemia:

This may occur as a result of decreased intake, increased glucose utilization; antimalarial mediated reduction, glycogen depletion or impaired gluconeogenesis.

e. Acidosis:

This is due to elevated levels of lactic acid which results from tissue anaerobic glycolysis, particularly in skeletal muscles.

f. Breathing difficulties:

Patients with severe malaria may present with difficulty in breathing as a result of any of the following:

- Heart failure resulting from severe anaemia.
- Pulmonary oedema (following administration of excessive fluids) usually there is frothing from the mouth and marked respiratory distress.
- Acidosis causes deep and rapid respiration.
- Aspiration

g. **Renal Failure:**

Renal failure develops due to low blood pressure as a result of dehydration or shock.

H. **Haemoglobinuria:**

This occurs as a result of excessive breakdown of red blood cells by parasites or drugs like sulphonamides and primaquine, especially in G6PD deficiency patients.

7.3 Who are the people at risk for severe malaria?

- Children < 5 years
- Pregnant women
- People returning or coming to Nigeria after living in malaria free areas
- People who have had splenectomy

7.4 History

In addition to the general history taken in patient with uncomplicated malaria you should ask about the following

In all patients *ask about*:-

- ***Extreme weakness*** (Prostration): inability to eat and drink or do anything without support. **Progressive weakness should immediately alert you that the patient may be developing**

- **Severe malaria**.

- ***Abnormal behaviour or altered consciousness:*** ask relatives to tell you any observed changes in the patients' behaviour since the illness started or when the unresponsiveness started.
- ***Convulsions:*** ask about the number of episodes, part of the body involved, previous history and time onset of last episode. Focal or multiple convulsions over a period of 24 hours is indicative of severe disease.
- ***Drowsiness*** or deteriorating level of consciousness.
- ***Time of last drink or food*** since the onset of the illness.
- ***Fast breathing*** which may occur due to pulmonary oedema or acidosis.
- ***Reduced urinary output*** (time patient last passed urine).
- ***Colour of urine:*** whether dark or coca-cola coloured (this may suggest excessive breakdown of red blood cells or dehydration).
- ***Pregnancy***: in adult females.

Ask history to exclude other severe diseases

- ***Drug History:*** Ask about antimalarial drugs, salicylates and herbal concoctions that may influence treatment or cause some of the symptoms.
- ***Previous illnesses:*** Ask about any history of recent febrile illness and treatment which may suggest treatment failure or relapse (consider typhoid, malaria and other infections).

7.5 Physical Examination:

In the physical examination you should aim at

- Assessing for the presence of signs of severe malaria.
- Identifying other possible causes of disease.

a. Central Nervous System

Assess the level of consciousness using an objective scale such as the

AVPU scale, Glasgow coma scale or the Blantyre coma scale:
The AVPU scale is as show below

A = alertness (is the patient alert)
V = response to voice command (does the patient respond to his name)
P = response to pain (does the patient feel pain or cry if a child)
U = unresponsive. (Patient does not respond at all)

b. Respiratory System

* Check for respiratory distress (fast, deep or laboured breathing)
* Listen to the chest for rales or other added sounds.

C. Cardiovascular

* Examine the rate, rhythm and volume of the pulse.
* Cold extremities or poor capillary refill at the tips of the fingers *(delay for >3 seconds).*
* Check blood pressure

d. ***Abdomen***

* Feel for the spleen and the liver

7.6 Differential Diagnosis:

- Meningitis- Patient may have a stiff neck.
- Encephalopathy- Repeated convulsions or deep coma.
- Diabetes Mellitus- Patient may be dehydrated, acidotic or in coma.
- Septicaemia- Usually very ill and toxic with warm extremities.
- Epilepsy- Usually no temperature and will have history of convulsions before.
- Acute renal failure from other causes- usually associated with reduced or no urine output
- Viral hemorrhagic fevers- usually associated with jaundice and bleeding tendency

7.7 Laboratory Investigations:

Laboratory investigation in aimed at confirming diagnosis, assess severity of

disease and exclude other possible causes of severe disease.
Recommended tests include:

* Blood smear for malaria parasites
* Haematocrit (PCV)/Haemoglobin
* Blood sugar level
* Lumbar puncture in unconscious patients.
* Urinalysis for:-
  Sugar (to exclude diabetes)
  Proteins (exclude pregnancy-induced hypertension)

Notes about Diagnosis of Severe malaria:

- High index of suspicion in patients with fever and any of the features discussed above.
- Absence of fever does not exclude a diagnosis of severe malaria.
- Microscopic diagnosis should not delay antimalarial treatment if there is a clinical suspicion of severe malaria, with-holding treatment may be fatal.
- Patients' progress should be monitored and management changed as deemed necessary.

7.8 Treatment

Severe malaria is a medical emergency requiring in-patient care. Deaths from severe malaria can result either from direct effect of the disease or the complications. The provider should attend to the immediate threats to life first.

7.8.1 Life threatening emergencies

Coma or unconscious patient

- Ensure airway is patent; gentle suction of nostrils and the oro-pharynx.
- Make sure the patient is breathing.
- Nurse the patient lying on the side or with the head sideways.
- Insert a naso-gastric tube (NGT).
- Establish an intravenous line. It will be necessary for giving drugs and fluids.
- Correct hypoglycaemia:

  Children: 0.5 ml/kg of 50% dextrose diluted to 10-15%.

  Adults: 25 ml of 50%dextrose.

  -Where intravenous access is not possible, give dextrose or any sugar solution through the naso-gastric tube.

Convulsions

- Ensure patent airway and that the patient is breathing.
- Correct hypoglycaemia or control temperature.
- In children give rectal diazepam 0.5 mg/kg or IM paraldehyde 0.1 ml/kg. If convulsions continue, give IM phenobarbitone 10-15 mg/kg.
- In adults give 10 mg diazepam IV.

Severe dehydration or shock

- Give 20-30 ml/kg of normal saline and reassess the patient within 30 minutes to decide on the next fluid requirement according to

the degree of dehydration.

- After correction of the fluid deficit it is important to reduce the maintenance fluid to two thirds of the required volume when the patient is well hydrated.

Severe Anaemia

- Give urgent blood transfusion to patients with ***severe pallor/anaemia*** in heart failure. **The blood must be screened to ensure that it is HIV, Hepatitis B and C negative.**
- Use packed cells (10 ml/kg in children) or whole blood (plus frusemide).
- Where blood is not available, give pre-referral treatment and **refer urgently** to a health facility with blood transfusion services.

7.8.2 Specific Antimalarial Treatment

Treatment Objectives

The primary objective of antimalarial treatment in severe malaria is to prevent the patient from dying. The secondary objectives are prevention of disabilities and recrudescence. The antimalaria

medicines recommended for the treatment of severe malaria in Nigeria is Intravenous or intramuscular Artesunate. Where this is not readily available, intravenous or intramuscular quinine, intramuscular artemether can be used as alternative.

i. **Artesunate**

Recommended Dosages:

Give 2.4 mg/kg body weight IV or IM stat, repeat after 12 hours and 24 hours, then once daily for 6 days. However once patient regains consciousness and can take orally, discontinue parenteral therapy and commence full course of recommended ACT.

ii. **Quinine**

It is administered by either IV or IM route, depending on the availability of infusion facilities.
Recommended dosage:
Intravenous quinine

Children:
Give 20 mg/kg of Quinine dihydrochloride **salt** as loading dose diluted in 10 ml/kg of 4.3% dextrose in 0.18% saline or 5% dextrose over a period of 4 hours. Then 12 hours after the start of the loading dose, give 10 mg **salt** /kg infusion over 4 hours every 8 hours until when patient is able to take orally. Change to quinine tablets 10 mg/kg 8 hourly to complete a total of 7 days treatment OR give a full course of recommended ACT.

Adults:
Quinine dihydrochloride 20 mg/kg of **salt** to a maximum of 1.2gm (loading dose) diluted in 10 ml/kg isotonic fluid by intravenous infusion over 4 hours then, 8 hours after the start of the loading dose, give 10 mg/kg **salt** to a maximum of 600 mg over 4 hours every 8hours patient is able to take orally.
Then give a full dose of recommended ACT.

NOTE:
- If intravenous quinine is required for over 48 hours, reduce the dose to 5-7mg/kg to avoid toxicity. A practical way of doing this is to reduce the dosing frequency to every 12 hours
- If there is a history of prior administration of quinine or mefloquine in appropriate doses in the last 24 hours do not use loading dose.

Intramuscular Quinine:
Where intravenous access is not possible give quinine dihydrochloride intramuscularly at a dosage of 20 mg/kg **salt** (loading dose), diluted to 60mg/ml, and continue with a maintenance dose of 10mg/kg 8hourly until patient is able to take orally.

Thereafter change to oral quinine at 10 mg/kg 8 hourly to complete a 7-day treatment OR give a full dose of recommended ACT.
Quinine comes in highly concentrated salt (2ml ampoule containing 600mg quinine dihydrochloride). It is recommended that quinine be diluted to 60 - 100mg/ml before administering intramuscularly.
To achieve 60mg/ml concentration, add 4mls of sterile water to **1ml of quinine salt** to make up to 5mls.

NOTE: Intramuscular injections should be given with sterile precautions into the anterior or lateral thigh, NOT THE GLUTEAL REGION.

Quinine in pregnancy:
Quinine is administered as 10mg/kg body weight orally to a maximum dose of 600mg 8 hourly, for 7 days.

Quinine is safe in pregnancy and it does not cause abortion or premature delivery when given in normal therapeutic dose, rather it is the malaria that causes these complications.

Treatment of severe malaria in pregnancy

First Trimester:
Current body of evidence is not conclusive on the safety of artemisinin derivatives in the first trimester. However, the risk of death from severe malaria far outweighs the potential risk of artesunate to the foetus, therefore parenteral Artesunate can be used for treating severe malaria during pregnancy. The use of Quinine is safe during the first trimester of pregnancy.

Second and Third trimesters:
The treatment of severe malaria in these periods of pregnancy is as recommended for all adults.

7.8.3 Supportive Treatment

High temperature

- Give paracetamol (rectal) if temperature is >38.5 ° C, in children, also tepid sponge (wipe the body with towel soaked in lukewarm water), avoid over -clothing.

Pulmonary oedema

- Prop up the patient at an angle of 45 degrees, give oxygen and frusemide 2-4 mg/kg IV, stop intravenous fluids and exclude other causes of pulmonary oedema. .

Renal failure

- Give fluids if patient is dehydrated 20 ml/kg of normal saline and challenge with frusemide 1-2 mg/kg.
- Pass a urinary catheter to monitor urinary output.
- If patient does not pass urine within the next 24 hours refer for peritoneal or haemodialysis.
- Exclude pre-renal causes

Profuse bleeding

- Transfuse with screened fresh whole blood, give pre-referral treatment and refer urgently.

Other possible treatments:-

- 1

➢ If meningitis is suspected, and cannot be immediately excluded by a lumbar puncture, appropriate antibiotics should be given.

- Other severe diseases should be treated accordingly.

7.8.4 Treatments not recommended:

The following drugs have no role in the treatment of severe malaria.

- Corticosteroids and other anti-inflammatory agents
- Agents used for cerebral oedema e.g. Urea

- Adrenaline
- Heparin

8.0 NURSING AND QUALITY OF CARE

Severe malaria is a serious condition and the clinicians and nurses should closely monitor patients. Therefore nursing care should include all the following:-

1. **Monitor vital signs**
    1. Pulse
    2. Temperature
    3. Respiratory rate
    4. Blood pressure

These should be monitored at least every 6 hours but may be more frequent at the initial stages.

2. **Monitor input and output**

    A strict 24-hour input / output chart should be kept in all patients with severe malaria. Examine regularly for signs of dehydration or fluid overload.

3. **Monitoring unconscious patient**

    Unconscious or comatose patients need close monitoring of all vital signs more regularly to assess their progress. Monitor the level of consciousness at least every 6 hours. Patients should be turned in bed regularly to avoid bedsores.

4. **Drug chart**

    A drug chart where all drugs given are recorded should be kept and should include dose given, time given and number of times a day.

5. **Pregnant women**

    They should be monitored closely ensuring the well being of the

foetus and preventing the development of maternal hypoglycaemia. Watch out for signs of severe anaemia and pulmonary oedema.

Laboratory monitoring

5. **Monitor the parasitaemia**
   Do blood smears daily. If high after 2-3 days, review adequacy of the medicine dosages.

7. **Monitor blood glucose**
   Do blood glucose level or maintain with dextrose containing infusion

8. **Monitor Haemoglobin/haematocrit**

Assessment of recovery

When the patient recovers, assess for possible residual problems of the disease or treatment.

- Assess the ability of the patient to do what he/she was able to do before the illness.
- Assess vision and hearing by asking whether they can see or hear; for children use objects or noisy rattles respectively.
- Organize for follow up of the patient.
- Management of residual disability might require a multi-disciplinary approach.

9.0 PRE-REFERRAL TREATMENT

The risk of death for severe malaria is greatest in the first 24 hours. To survive, a patient with severe illness must get access rapidly to a health facility where parenteral treatment and other supportive care can be given safely and as appropriate. The affected patient may die on the way to hospital or be admitted with advanced disease and complications. It is

recommended that the patients be treated with one of the following recommended pre referral treatment. .

Intramuscular pre- referral treatment

- Artesunate 2.4mg/kg stat
- Quinine dihydrochloride at a dosage of 10 mg/kg salt diluted to 60mg/ml intramuscularly at the anterolateral aspect of the thigh given at divided sites.

Artesunate suppositories

The appropriate single dose of Artesunate suppositories should be administered rectally as soon as the presumptive diagnosis of malaria is made. In the event that an Artesunate suppository is expelled from the rectum within 30 minutes of insertion, a second suppository should be inserted and, especially in young children, the buttocks should be held together, or taped together, for 10 minutes to ensure retention of the rectal dose of artesunate

Adults: One or more Artesunate Suppositories inserted in rectum as indicated in Table below. Dose should be given once and followed as soon as possible by definitive therapy for malaria.

Intra-rectal pre-referral treatment

Intra-rectal artemether at the dose of 10-40mg/kg body weight and intra-rectal quinine at 12mg/kg body weight can also be used as alternative based on availability. These should be administered with a syringe without the needle

Dosage regimen for Artesunate suppositories in children

Weight (kg)	**Age**	**Artesunate**	**Dosage regimen** (Single Dose)
<10	<12months	50mg	One 50mg Suppository
10 - 19	1yr - 5yr months	100 mg	One 100 mg Suppository
20 -29	6 - <10years	200 mg	Two 100 mg Suppositoies
30 - 39	10 - 13 years	300 mg	Three 100 mg Suppositories
> 40	>13 years	400 mg	Four 100 mg Suppository

Summary Box 3: Management of Severe Malaria

- *Severe malaria is a medical emergency. Full doses of parenteral antimalarial treatment should be commenced without delay with an effective antimalaria first available after rapid clinical assessment and confirmation of diagnosis.*
- *Artesunate 2.4mg/kg IV or IM given at time 0, 12 and 24 hours, then once daily is the recommended treatment.*
- *Quinine is an acceptable alternative if parenteral artesunate is not available. Quinine 20mg salt/kg IV or divided IM injection, then 10mg/kg every 8hrs, infusion rate should not exceed 5mg salt/kg per hour.*
- *IM artemether 3.2mg/kg given on admission, then 1.6mg/kg per day should be used if none of the alternatives are available as its absorption may be erratic.*
- *Give parenteral antimalarial medicines in the treatment of severe malaria for a minimum of 24hours, once started (irrespective of the patient's ability to tolerate oral medications earlier) and thereafter complete treatment by giving a complete course of ACT.*

10.0 PREVENTIVE TREAMENTS AND CHEMOPROPHYLAXIS

10.1 Intermittent Preventive Treatment

Pregnant women have higher risk of malaria than same women before pregnancy and other non-pregnant females and adults. The high prevalence of malaria during pregnancy has been associated with pregnancy-associated immune changes and the extensive proliferation of the parasites within the placenta.

In high transmission areas such as Nigeria, malaria is usually asymptomatic during pregnancy. The use of Intermittent Preventive

Treatment (IPT) with *Sulphadoxine-Pyrimethamine* has been shown to be effective in preventing several malaria related complications during pregnancy. IPT is given as a one-dose of a full course treatment after *Quickening* as Directly Observed Therapy (DOT) and the second dose is given not earlier than one month after the first dose. A single dose is **three tablets of SP** each containing **Sulphadoxine (500 mg) + Pyrimethamine (25 mg).**

Pregnant women who are HIV positive and are on *Co-trimoxazole* chemoprophylaxis, should not receive IPT. This is because of their increased risk to the adverse effects of the *Sulphonamides*. Encourage them to use other preventive measures such as regular use of Long Lasting Insecticide Nets (LLINs).

10.2 Malaria Chemoprophylaxis

Malaria chemoprophylaxis is not recommended for individuals living in areas of intense transmission, however, people with sickle cell anaemia and non immune visitors are expected to be on regular chemoprophylaxis. There is however no effective antimalarial presently available for long term chemoprophylaxis. Until such becomes available, these risk group should be targeted with other preventive interventions e.g. ITNs and also ensuring that they have ready access to effective case management.

10.3 Non immune Visitors

The recommended chemoprophylaxis for non immune visitors will be as available in the visitor's country of origin. The following options are recommended for use in Nigeria; Mefloquine, and atovaquone-proguanil. Doses should be taken prior to arrival in Nigeria and continued during the stay and following departure from the country.

Mefloquine

5mg base per kg weekly, giving an adult dose of 250mg of base per week. It should be started 2-3 weeks prior to arrival and two to three weeks after departure.

Atovaquone-Proguanil

Exist as a fixed dose combination. Commence 1-2 days before travel and continue throughout the stay and 7 days after return.

Age	Dosage
11 - 21kg	Paediatric preparation (25mg/ 62.5mg) daily
21 - 31kg	2 tablets daily
31 - 40kg	3 tablets daily
Adult and children over 40kg	Adult preparation 1 tablet (100/ 250mg) daily

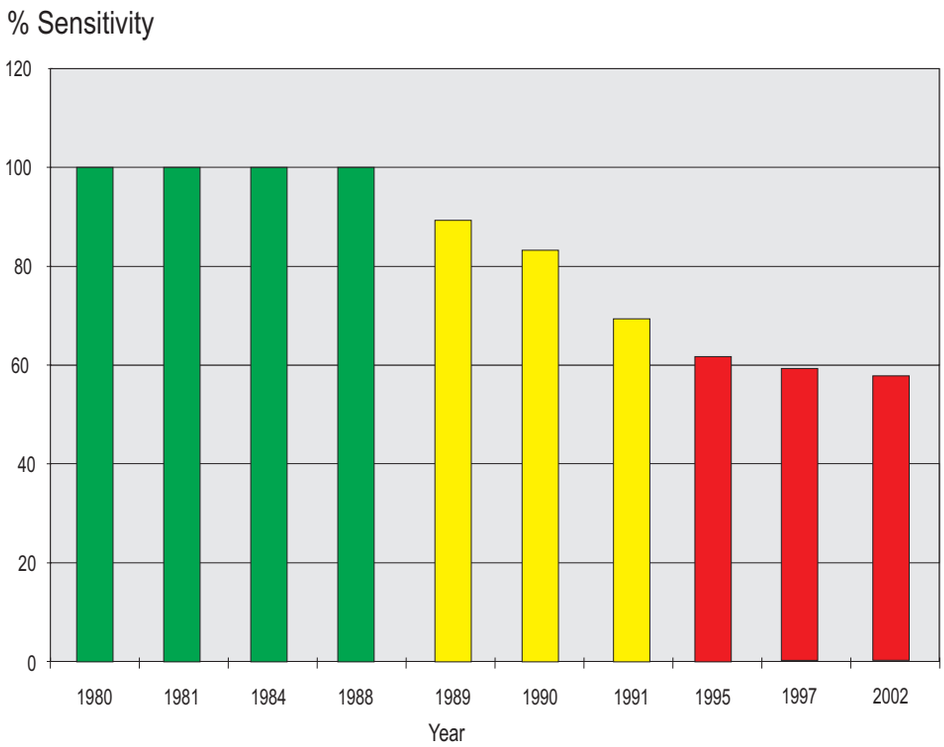
11.0 ANTIMALARIAL DRUG RESISTANCE

Antimalarial drug resistance is defined as the ability of a parasite strain to survive and/or multiply despite the proper administration and absorption of an antimalarial medicines in the dose normally recommended.

It has resulted in a global resurgence of malaria and it is a major threat to malaria control. Widespread and indiscriminate use of antimalarial drugs places a strong selective pressure on malaria parasites to evolve mechanisms of resistance. Prevention of antimalarial drug resistance is one of the main goals of these antimalarial treatment recommendations. Resistance can be prevented by combining antimalarial medicines with different mechanisms of action, and ensuring very high cure rates through full adherence to correct dose regimens.

11.1 Antimalarial drug resistance in Nigeria

Appreciable resistance of *P. falciparum* has developed against monotherapeutic agents previously used in Nigeria, such as chloroquine and Sulphadoxine Pyrimethamine. This is summarized below.



Chloroquine efficacy estimated at various drug therapeutic testing sites in Nigeria between 1980 and 2002 showing the decline in malaria parasite sensitivity to chloroquine

{***Source:*** *National Drug therapeutic Efficacy Trials (DTET)*}

It should be noted that anti-malarial medicines resistance is not necessarily the same as malaria treatment failure, which is defined as the

failure to clear malaria parasitemia and/or resolve clinical symptoms despite the administration of antimalaria medicines. While drug resistance may lead to treatment failure, not all treatment failures are caused by drug resistance. Other causes of treatment failure are

- Incorrect dosing
- Problems of treatment compliance
- Poor drug quality
- Interactions with other drugs
- Compromised drug absorption
- Mis-diagnosis of the patient

11.2 Impact of resistance

The impact of antimalarial drug resistance is insidious initially. The initial symptoms of the infection resolve and the patient is better for weeks. When symptoms recur, usually more than two weeks later, anaemia has worsened, and there is a greater probability of carrying gametocytes (which in turn carry the resistance genes) and transmitting malaria. But the patient and the doctor or dispenser may interpret this as a newly acquired infection. At this stage unless drug trials are conducted, resistance may be unrecognised.

As resistance worsens the interval between primary infection and recrudescence shortens, until eventually the symptoms fail to resolve. At this stage mortality begins to rise. Antimalarial medicine resistance accounts for our failure to control malaria in many areas of the tropical world and the consequent increasing global mortality. But resistance can be prevented, or its onset slowed considerably with judicial use of the limited number of effective drugs currently available to treat malaria.

12.0 BRIEFS ON PHARMACOLOGY OF ANTIMALARIAL DRUGS

Chloroquine

Chloroquine resistance is now widespread globally. It is no longer

recommended either alone or as a combination partner for the treatment of uncomplicated falciparum malaria.

Amodiaquine

Amodiaquine is a Mannich base 4 amino-quinoline that interferes with parasite heam detoxification. It is more effective than chloroquine in both chloroquine sensitive and P.f*alciparum* infections. However, there is cross-resistance between chloroquine and amodiaquine.

It is available as tablets containing 200mg of amodiaquine base as the hydrochloride and as 153.1 mg base as chlorohydrate. It is readily absorbed in the GIT and rapidly converted in the liver to the active metabolite, desethylamodiaquine. Desethylamodiaquine is responsible for all the antimalaria effect. Adverse effect of amodiaquine includes pruritis and when used for prophylaxis it causes agranulocytosis. Amodiaquine is recommended as a partner drug in artemisinin based combination therapy.

Sulphadoxine-Pyrimethamine

Sulphadoxine is a slowly eliminated Sulphonamide. It is used in a fixed dose combination of 20 parts Sulphadoxine with 1 part Pyrimethamine given orally or intramuscularly. It is available as tablet containing 500mg Sulphadoxine and 25mg Pyrimethamine, and in ampoules containing similar concentration of the 2 components for intramuscular use.

The medicine is no longer recommended for the treatment of malaria in Nigeria. However, it has been proven to be effective for use for Intermittent Preventive Treatment during pregnancy.

Sulphadoxine is readily absorbed from the GIT. It is widely distributed in body tissues and fluids and crosses the placental into foetal circulation. It is also readily detectable in breast milk. It is excreted predominantly as the unchanged drug.

Adverse effect includes nausea vomiting and diarrhoea. Hypersensitivity reaction may occur as well as photosensitivity and a variety of dermatological adverse reaction. It may also cause a crystaluria and interstitial nephritis. Pyrimethamine is a di-amino pyrimidine that is also used in the treatment of toxoplasmosis and pneumocystic carini pneumonia. Like sulphadoxine, it is rapidly absorbed from the GIT. Prolonged administration may cause depression of haematopoiesis due to interference with folate metabolism

Quinine

It is an alkaloid derived from the bark of cinchona tree. It is an isomer of quinidine. Like other structurally related drugs, it is effective against matured trophozoites of P.falciparum matured sexual forms of *P.falciparum, vivax* and *malariae*. It is available as both tablets and injectable solutions. It is rapidly and almost absorbed from the GIT and also after IM in severe malaria. It is widely distributed throughout the body tissues, and fluids including CSF and, breast milk. Toxicity includes mild form of tinnitus, impaired high tuned hearing, headache, nausea, dizziness, vomiting, abdominal pain, diarrhoea and vertigo.

Hypersensitivity reaction may also occur. Intravascular haemolysis that may progress to life threatening haemolytic uremic syndrome can also occur. Thrombocytopeania and haemolytic anaemia. Other adverse effect includes cardiac rhythm disturbances, hypotension and hypoglycaemia

Artemisinin and its derivatives

Artemisinin and its derivatives, artemether, dihydro-artemisinin, artesunate and artemotil are sesquiterpenelactones. These drugs are potent and rapidly acting blood schizonticides active against all plasmodium species. These medicines kill all stages of young rings to schizonts and young gametocytes.

Artemisinin itself is now less frequently used compared to its derivatives; dihydro-artemisinin, artemether, artesunate and artemotil. It is

converted to dihydro-artemisinin.

Artesunate is a sodium salt of the hemisuccinate ester of artemisinin. It is soluble in water but has poor stability in aqueous solution at neutral or acidic pH. In the injectable form, artesuric acid is drawn up in sodium bicarbonate to form sodium artesunate immediately before injection. It is available as tablet, ampoules for IM or IV, rectal capsules, and as co-formulation with amodiaquine. It is rapidly absorbed after oral, rectal and IM administration and is almost entirely converted to dihydro-artemisinin, the active metabolite. It is rapidly eliminated from the body.

Artemether is methyl ether of dihydro-artemisinin. It is more lipid soluble than artemisinin or artesunate. It can be given as an oil based intramuscular injection or orally, and as co-formulation with lumefantrine. Absorption after oral administration is rapid. After IM administration, absorption is variable particularly after administration in children with poor peripheral perfusion. It is metabolized to dihydro-artemisinin, the active metabolite.

In general, artemisinin and its related derivatives are well tolerated. These drugs in general are less toxic than other currently available antimalarial medicines. Mild GIT disturbances, dizziness, elevated liver enzymes and minor ECG abnormalities and reticulo-cytopaenias have been reported after the use of these drugs. Potentially, serious adverse effects are related to Type I hypersensitivity reactions. Neurotoxicity has been reported in experimental animals and largely has not been found in humans. Currently, clinical resistance has not been reported to this class of antimalaria.

Lumefantrine is an aryl amino alcohol. It is structurally related to halofantrine. It is highly effective against P.falciparum. It is available as oral preparation as co-formulation with artemether. Following oral administration, bioavailability is variable but can be improved by co

administration with fatty foods. Toxicity includes nausea, abdominal discomfort, headache and dizziness. It does not significantly prolong the ECG Q-T interval

ANNEXURES

ANNEX 1

QUALITY ASSURANCE FOR MALARIA DIAGNOSIS WITH MICROSCOPY

The quality assurance (QA) of a malaria laboratory or diagnostic programme is a system designed to continuously and systematically improve the efficiency, cost-effectiveness and accuracy of test results. It is critical that QA ensure:

- the clinical teams have full confidence in the laboratory results
- the diagnostic results are of benefit to the patient and the community.

These demands can only be met through a commitment to QA that ensures the microscopic services are staffed by competent and motivated staff supported by both effective training and supervision and a logistics system that provides an adequate and continual supply of quality reagents and essential equipment which are maintained in working order.

The principles and concepts of QA for microscopic diagnosis of malaria are similar to those for microscopic diagnosis of other communicable diseases, such as other protozoan diseases, tuberculosis and helminth infections. This provides a potential for the integration of laboratory services where it is feasible and cost-effective.

ANNEX 2 SUMMARY OF CHECK-LIST FOR INTERNAL QUALITY ASSURANCE FOR MALARIA MICROSCOPY

Category	Check List Questions	Yes	No
Laboratory Design	There is sufficient working surface for each member of the laboratory staff.		
	The electric microscope(s) are not located directly in front of a window but face a blank wall.		
	The laboratory has access to a clean water supply.		
	There is hand washing facilities.		
	There is good ambient lighting at all times (including cloudy weather).		
	There is an adequate electrical supply for the microscope(s).		
	There is adequate storage space for reagents, equipment, and storage of slides.		
	There is a safe waste management system.		
	Laboratory chairs and/or stools are suitable for microscopy.		
Quality of the Microscope	The microscope(s) is binocular and electrically powered.		
	The microscope lamp(s) has sufficient power to provide good illumination at **small** aperture settings.		
	The light source can be centred.		

Category	Check List Questions	Yes	No
	The microscope(s) have Plan C x 100 objectives.		
	Blood smears are able to be brought into sharp focus x 100 oil immersion magnification.		
	The stage movement mechanism is precise and stable.		
Microscope Slides	Microscope slides are clean.		
	Microscope slides are not oily to the touch.		
	Microscope slides do not have scratches or surface aberrations.		
	Microscope slides do not give a blue background colouration (microscopically at x100) after staining.		
	Microscope slides do not have fungal contamination.		
	Slides are protected against fungal contamination (in high humidity settings).		
Methanol	Methanol is AR grade.		
	Methanol is supplied to the laboratory is in the original sealed container as supplied by the manufacturer, and is not repackaged by the supplier.		
	Methanol is not oily (test place some methanol on the fingers, it should not be sticky).		

Category	Check List Questions	Yes	No
	There is no deformation or blistering of red blood cells in the thin blood film (this is caused by poor quality methanol).		
	The methanol used for slide fixing is stored in moisture-proof containers.		
Giemsa Stain	Only stain prepared from high quality Giemsa powder is used.		
	Commercial Giemsa stain is supplied to the laboratory in the original sealed.		
	The stain is within the manufacturer's expiry date.		
	The laboratory has a Stain QC Register recording the batch number and expiry date of supplies received the QC results on each batch (staining time, staining quality, and optimal pH of use) and any problems encountered.		
	Stock stain is stored in a dark glass bottle tightly sealed.		
	Stock stain is not stored in direct sunlight or near a heat source.		
	The stock stain used by the laboratory was prepared less than two years ago.		
	Stained blood films do not contain stain precipitate.		
Diluted Giemsa stain	Stock stain is always diluted in buffer to the correct pH.		

Category	Check List Questions	Yes	No
	The diluted stain contains no stain precipitate.		
	The surface of the diluted stain does not have an oily appearance. For horizontal slide staining (using a staining rack) this is best observed after the stain has been added to the slides. This effect can be caused by poor quality methanol used to prepare Giemsa stain from powder.		
	Diluted stain is always discarded within 15 minutes of preparation.		
Thick blood films	>95% of thick films have the correct thickness. It should be just possible to read newsprint through the thick film while it is still wet.		
	There is flaking in the centre of the smear (a hole in the centre of the thick film) in <2% of the thick films.		
	100% of the thick films are correctly stained.		
	None of the thick films contain stain precipitate contamination.		
	There a protocol for the preparation of thick films of the correct thickness from patients with severe anaemia.		
	Slide warmers may be used with caution in high humidity settings.		
Thin blood films	>95% of the thin films have a smooth semi-circular tail.		

Category	Check List Questions	Yes	No
	In >95% of the thin films the red cells are just touching and not overlapping in approximately 20%30% of the film (the reading area).		
	No thin films have water damage (retractile artefacts inside the red cells).		
	Thin films are fixed immediately after drying.		
Staining	The laboratory has a pH meter that reads to 2 decimal places.		
	The pH meter is calibrated with calibration buffers according to manufacturer's directions.		
	pH adjusted buffer always used to prepare diluted Giemsa.		
	The pH of the buffer is calibrated for each batch of Giemsa.		
	Slides are always washed in water of the same pH as the buffer used for Giemsa dilution.		
	The diluted Giemsa is always prepared in a clean measuring cylinder.		
	There is an absolute rule that the diluted Giemsa stain is discarded in <15 minutes after preparation.		
	The trophozoite chromatin stains red to “rusty red”.		
	The trophozoite cytoplasm stains blue to strong blue.		

Category	Check List Questions	Yes	No
	The thick film background is stained light pink to grey.		
	The thick film background is stained light pink to grey.		
	The red cells in the thin film are stained pink.		
	The nuclear lobes of the polymorphs are stained significantly darker than the cytoplasm.		
	Slides are always washed from the thin film end.		
	All slides are washed gently by a technique that “floats”' the stain off with minimal without disturbing the thick film.		
	Laboratory staff who perform staining have protective clothing to protect their personal clothing.		
Counting	The laboratory reports the actual number of trophozoites when required against 500 (200) WBC.		
Slide Reading Times	All laboratory staff who report malaria examination results read a minimum of 10 thick blood films each month.		
	Laboratory staff always read a minimum of 100 fields before reporting a film as negative.		

Category	Check List Questions	Yes	No
	There is no pressure on microscopists to read slides more quickly than the standard reading time (such as end of day, “urgent cases”).		
	Is there a laboratory protocol that ensures that microscopists do not continuously read malaria slides for more than 3 hours without a 30 minute break?		
Species identification	Thin films are available for species identification where a mixed infection is suspected or species identification is unclear on the thick film.		

ANNEX 3 QUALITY CONTROL IN LABORATORY DIAGNOSIS OF MALARIA

The main focus of QC is on reproducibility (precision) of results. The programme is used within the laboratory for checking its own performance. Quality control (QC) is the responsibility of the laboratory chief but all laboratory personnel must be involved.

Standard operating procedures (SOPs) need to be developed, depending on the type of analyses carried out at each level of the health services so that tests can be performed in an acceptable standard way. The SOPs should state clearly the minimum QC for each method or test. By standardizing test procedures, it allows easier clinical and epidemiological interpretation of the results. Troubleshooting guides for equipment, reagents and methods would be useful additions to the more isolate laboratories where "instant" help is not available.

With such a multitude of steps involved in processing of a specimen, errors can occur at any stage. Laboratory management needs to be aware where errors can happen to reduce the possibility of their occurrence. Therefore, all stages from the preparation through to the examination must be monitored. Below quality controls issues will focus on microscopy and rapid tests. The general points are equally pertinent for all techniques.

ANNEX 4 BLOOD SMEARS FOR MICROSCOPY

Blood smears-preparation and staining

Blood should be taken from a finger prick, when possible. Blood collected in anticoagulant causes morphological changes to the parasite if left too long before examination. Anticoagulant also causes thick smears not to stick well onto the slide.

The specimen should be clearly labelled and be accompanied with

correctly completed form (clinical request or field). A thick film exposed to alcohol or placed in a hot oven to "quickly" dry the blood renders the film unreadable as the erythrocytes cannot dehaemoglobinize. If blood films in high temperature environments are not stained within a couple of days, the films suffer auto fixation.

Smears stored in humid and hot conditions facilitate the growth of fungus and bacteria. Similarly, dusty conditions cause the formation of deposits making the smear unreadable or the deposits might be confused for parasites leading to a false result. Smears, both stained and unstained must be protected from the voracious appetites of cockroaches, flies and ants and should where possible be stored in slide boxes.

The smears need to be well stained to facilitate the reading and if using Giemsa, species determination and accurate parasite counts. A stain can either be commercial or house made. It is imperative that each batch be checked by comparing batches of new staining solution with the old on the same group of thick and thin films. House made stain is not necessarily reliable and requires high quality reagents. Standardized forms must be draw up that indicate the stain, the lot number, the producer and the dilutions used to determine concentration and staining time and the result.
Dilution/buffer solutions also need to be controlled. With Giemsa stain often used, well water is the normal choice of diluents as the supply of reagents to the periphery is poor. Unfiltered stain and metallic scum of the staining solution leaves as precipitate on the thick film which are often confused with parasites. Working solution should be prepared daily to avoid de-naturation and even changed during the day depending on the workload.

Maintenance of a microscope is very important. It is an expensive piece of equipment that in poor condition cannot aid the microscopist to read the slide. Humid atmosphere can cause the growth of fungus especially on the

lens. Other problems are the bad alignment of the microscope, immersion oil not wiped from the objective and condenser leaving a coating.
Other materials to monitor are the slides and lancets, lancets should be sterile and preferably single use and slide should be without oily residue.

Recommended procedure notes

- Make a thick and a thin film on a clean microscope slide
- Stain with Giemsa method (See box below)
- Examine under a high power objective starting with thick and then thin films. The thick film is used to establish the presence of malaria parasites, while the thin film is for parasite speciation
- Report type of parasite(s) seen, developmental stage and parasite count as parasite/200WBCs or parasite/µl blood
- Ensure you always use relevant standard operating procedure (SOPs) in all processes
- If blood slide is negative, it is recommended that further investigations for the cause of disease including repeating blood slide after 24 hours should be carried out. If the repeat slide is positive, treat accordingly.

Rapid Staining Method

1. *Fix the thin film by dabbing it with a pad of cotton wool dampened with methanol or by briefly dipping the film into methanol.*
2. *Avoid contact between the thick film and methanol, as methanol and its vapours quickly fix the thick film, and make it not to stain well.*
3. *Using a test tube or a small container to hold the prepared stain, make up a 10% solution of Giemsa in the buffered water by mixing three drops of Giemsa from the stock solution, using the Pasteur pipette, with 1 ml of buffered water. Each slide needs approximately 3 ml of stain to cover it.*

4. Depending on whether you are using a staining tray, plate or rack, place the slides to be stained face down on the curved staining tray or face upwards on the plate or rack tray until each slide is covered with stain, or gently pour the stain onto the slides lying face upwards on the plate or rack.
5. Stain the films for 810 min. Experience with the stain you are using will help you to decide the exact time needed for good staining.
6. Gently wash the stain from the slide by adding drops of clean water. Do not pour the stain directly off the slides, or the metallic-green surface scum will stick to the film, spoiling it for microscopy.
7. When the stain has been washed away, place the slides in the drying rack, film side downwards, to drain and dry. Ensure that thick films do not scrape the edge of the rack.

Malaria Parasite Density Determination

This is a practical method of reasonable and acceptable accuracy. The number of parasites per microlitre of blood in a thick film is counted in relation to a standard number of leukocytes (8000). Although there are variations in the number of leukocytes between healthy individuals and even greater variations between individuals in ill health, this standard allows for reasonable comparisons.

Step 1

(a) In routine practice, using a x100 oil immersion objective and an eyepiece with a field number of 18, parasite quantitation is performed against 200 or 500 WBCs.
(b) If, after counting 200 WBC, 100 or more parasites are found, record the results in terms of number of parasites/200 WBC.
(c) If less than 100 parasites are found after counting 200 WBCs, parasite

quantification should be continued until 500 WBCs are counted. All parasites in the final field are counted even if the count exceeds 500 WBCs.

Step 2

To determine parasite density, the parasite count is adjusted against the true WCC where available. If unavailable, the common practice is to assume a WCC of 8000/µl. In each case, the number of parasites relative to the leukocyte count can be converted to

parasites per microlitre of blood by the simple mathematical formula:

$$\frac{\text{Number of parasites} \times 8{,}000}{\text{Number of leukocytes}} = \text{parasites per microlitre}$$

In effect, this means that if 200 leukocytes are counted, the number of parasites is multiplied by 40 and if 500 leukocytes are counted the number of parasites is multiplied by 16.

Note: It is normal practice to count all the species present and to count and record separately the gametocytes of P. falciparum and the asexual parasites. This is particularly important when monitoring the response to schizontocidal drugs, which would not be expected to have any effects on the gametocytes.

Re-examination of Blood Slides

Cross- checking in malaria diagnosis is part of supervision activities and involves the re examination of a proportion of positive and negatives slides from each laboratory. Cross checking of slides provides the supervisor with information about the accuracy of the examination by scientist and criteria for improvement if required. An idea about the quality of the preparation can also be ascertained.

Measurement of quality

Assessment can be made on three different areas.

These areas are;

- Positive and negative readings
- Intensity of infection
- Species identification

Intensity of infection

Before now, only positive and negative results have been discussed. The results from the majority of routine malaria diagnosis tests have been given in a semi-quantitative fashion (plus system) but in epidemiological studies, parasite density is always applied. The frequency of agreement and disagreement between laboratories can be calculated by using kappa statistics.

For semi-quantitative results, which are subjective, a two- step grading of positive could suffice those slides that have parasites in every field and those that have less than one parasite per field. This would certainly be sufficient to determine those failing to detect low parasitaemia from those failing to detect parasites at all.

Species identification

Misdiagnosis of the species can be addressed. This is particularly important where there is high degree of chloroquine resistance of both P. falciparum and *P. vivax*. The type of species determined the treatment that is given. In Nigeria, where over 90% of single infections are due to *P. falciparum*, non- recognition of the other species would cause mis-readings of about 10% of the slides, which is a considerable proportion of error.

ANNEX 5: ISSUES WITH RDTS IN THE FIELD

- Detects antigen, not parasites
- Parasite load is not quantified
- HRP-2 RDTs could remain positive even after the patient has taken ACTs and the antigen could remain in the blood for over 2 weeks

- Occasionally, test could be negative in the presence of parasites
- Degraded by excessive heat and may not function properly
- Limited shelf life (18 24 months)

Accuracy is dependent on following the prescribed procedures:

Appropriate Storage of RDTs

- Determine a cool place in your facility for RDTs storage. Storage temperature must never go beyond 35°C
- Keep RDTs in a cool place where drugs are stored
- Do not expose RDTs to direct sunlight
- Do not keep RDTs in a car parked in the sun (temperature may sometimes rise beyond what RDTs can tolerate)
- Open a pack only when you are ready to use them

Just before and RDT is done

- Be ready to use the results to inform treatment
- Check that the RDT has not expired
- Read the instructions in order to do it well
- Put on latex gloves

Materials required before doing an RDT

An RDT kit contains the following:

- alcohol swab
- sterile lancet
- a blood transfer device
- Buffer solution

The following items must also be available:

- Watch or clock to use as a timer
- Marker to write patients' data on RDT
- Sharp container(s) for used lancets & blood transfer device
- Waste bin for used alcohol swabs, cotton wool, gloves etc

Recommended Procedure notes

Note: It is pertinent to follow specific instructions on various RDT types before use.

1. *Wear your latex gloves*
2. *Open an RDT cassette and write the name of the patient and date.*
3. *Swab patient's fourth finger (the left hand of a right handed person) with methylated spirit and allow to dry (this will ensure that the patient's blood collects and not spread around the finger).*
4. *Take an unused lancet and prick the tip of the swabbed finger and discard lancet in the sharps quickly (do not re-cap the lancet).*
5. *Get the blood transfer device and collect the recommended volume of blood*
6. *Dispense the blood in the well (allow the transfer device to touch the pad in the well before releasing the content so that the blood collected is deposited fully insufficient blood can give a false result).*
7. *Dispose transfer immediately (do not leave on your table)*
8. *Put the recommended drops of buffer in the buffer well (ensure that the buffer container faces the well vertically, a little above the RDT cassette do not allow buffer to spill on the side of the well)*
9. *Note the time immediately by writing the start time on the cassette. Also indicate the stop time by adding the recommended time for the test. For example, if you were to read the test result after 15 minutes, add 15 minutes to the start time to get the stop time.*
10. *Interpret the result at the recommended time and not after as this could give you a false result.*

ANNEX 6: PHARMACOVIGILANCE

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse drug reactions or any other drug related problems such as drug abuse and misuse, medication errors, lack of efficacy and counterfeits.

An Adverse Drug Reaction (ADR) is a response to a medicine which is noxious (harmful) and unintended, and occurs at doses normally used in man for prophylaxis (prevention), diagnosis or therapy (treatment) of disease or the modification of physiological function

The recent medicine mishap in Nigeria has increased the need to ensure the quality, **safety** and efficacy and the rational use of deployed medicines hence it is mandatory for all levels of care to be involved in Pharmacovigilance.

In all suspected cases of an adverse drug reaction, the Pharmacovigilance form from NAFDAC should be completed at all levels of care. It is necessary to complete all section of the adverse drug reaction form.

Completed ADR forms should be sent to the following:

- The National Pharmacovigilance Centre (NPC) NAFDAC
- Plot 2032 Olusegun Obansanjo Way, Wuse Zone 7, Abuja
- Through NAFDAC offices in the 36 states & FCT
- Reports can also be scanned & emailed to npcadr@nafdac.gov.ng
- By Telephone: 08086899571 or 07098211221

Pharmacovigilance form

NATIONAL PHARMACOVIGILANCE CENTRE (NPC) NIGERIA

National Agency for food and Drug Administration & Control (NAFDAC), Headquarters Office
Plot 2032 Olusegun Obasanjo Way
Wuse Zone 7 Abuja

FORM FOR REPORTING OF SUSPECTED ADVERSE DRUG REACTIONS

IN STRICT CONFIDENCE

Tel: 08086899571 or Fax: 09-5241108

1. * PATIENT'S DETAILS

Full Name or Initials: _____ Patient Record No: _____

AGE/DATE OF BIRTH: _____ SEX: M ☐ F ☐ WEIGHT (kg): _____

HOSPITAL /Treatment Centre: _____

2. * ADVERSE DRUG REACTION (ADR)

A DESCRIPTION

DATE Reaction Started	DATE Reaction Stopped

C. OUTCOME OF REACTION

TICK AS APPROPRIATE

☐ Recovered fully ☐ Recovered with disability (Specify) _____

☐ Congenital Abnormality (Specify) _____ ☐ Life Threatening (Specify) _____

☐ Death ☐ Others (Specify) _____

B. **Was Patient Admitted Due to ADR** Yes ☐ No ☐

If Already Hospitalized, Was it Prolonged Due to ADR Yes ☐ No ☐

Duration of Admission (days) _____

Treatment of Reaction: _____

3. * SUSPECTED DRUG (Including Biologicals Traditional/Herbal Medicines & Cosmetics)

A. DRUG DETAILS (State name and other details if available / Attach product label / Sample (if available)

Brand Name: _____ Generic Name: _____ Batch No: _____

NAFDAC No: _____ Expiry Date: _____

Name & Address of Manufacturer: _____

B. Indications for Use	Dosage	Route of Administration	Date Started	Date Stopped

4. * CONCOMITANT MEDICINES (All medicines taken within the last 3months including herbal and self medication)

Brand or Generic Name	Dosage	Route	Date Started	Date Stopped	Reason for Use

5. * SOURCE OF REPORT:

Name of Reporter: _____

Address: _____

Profession: _____

Signature: _____ Tel No/E-mail: _____

*** MANDATORY FIELDS**