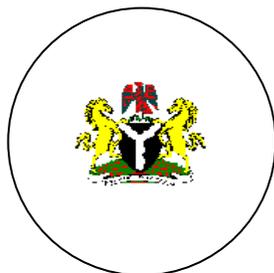# FEDERAL REPUBLIC OF NIGERIA

NATIONAL ANTIMALARIAL TREATMENT POLICY

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

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Foreword

There are over 100 million people at risk of malaria every year in Nigeria and indeed it is estimated that about 50% of the adult population in Nigeria experience at least one episode yearly while the under five children have up to 2 - 4 attacks of malaria annually. The yearly economic loss due to malaria in Nigeria has been put at 132 Billion Naira due to costs of treatment ad transport to source of treatment, loss of man-hours, absenteeism from schools and other indirect costs. Thus malaria imposes a heavy cost not only on a country's income, but also on its rate of economic growth and invariably on its level of economic development.

At the African Summit on Roll Back Malaria, the Heads of Government and International Agencies signed the Abuja declaration committing themselves to the Abuja target, one of which stipulates that concerted efforts would be made to ensure that by the end of 2005 at least 60% of those at risk of malaria should have access to good quality, affordable and efficacious antimalaria drugs. The spread and intensification of antimalarial drug resistance is one of the greatest challenges facing effective malaria control in the world today. This has been identified as a potent hindrance to the achievement of the set targets aimed at halving the malaria burden by 2010. The efficacy of the most affordable antimalarial drugs has declined remarkably in the last 15-20 years, and new drug development is not keeping pace.

To ensure that this trend does not abort the laudable targets set during the Abuja Summit, my ministry has put in place effective machineries in form of sentinel sites and networks to monitor parasite resistance to antimalarial drugs and use the output to inform treatment policy. Accordingly, this first updating of the antimalaria drug policy since the advent of the Roll Back Malaria Initiative has come as a very vital step in the fight against the recalcitrant disease.

I, therefore call on all major stakeholders to adopt this policy and be involved in scaling up effective case management at all levels, including at the home, community and the health facilities within the Country.

I wish to acknowledge the support of the Roll Back Malaria partners in Nigeria who have worked concertedly to bring this to fruition.

It is my hope and desire that this document would serve as a guide to all players working to ensure that all at risk of malaria have access to appropriate antimalaria drugs within 24 hours of the onset of symptoms.

We are at the brink of making history, and only a little concerted and consistent effort is needed to make us succeed.

Prof. Eyitayo Lambo
Honourable Minister of Health

Acknowledgement

The development of the National Antimalaria treatment Policy is a major leap towards the scaling up of effective case management in the Country.

During this crucial process of drug policy review, many stakeholders expressed their interest and showed commitment to ensure the completion of this important national exercise. The Federal Ministry of Health, Federal Republic of Nigeria, hereby specially acknowledges the contributions of the various organizations and their staff towards the successful development and production of this articulate document.

Many thanks to the team of experts from the Roll Back Malaria Partnership in Nigeria viz World Health Organization, United States Agency for International Development, UNICEF Department for International Development, Society for Family Health, ENHANSE, etc.

Many individuals have also worked tirelessly to ensure the timely production of this document and these represent Research Groups, Professional Groups, Government Departments and the Private sector, especially the Pharmaceutical Manufacturing Group of Manufacturers Association of Nigeria. We appreciate your efforts and furthermore hope that in the spirit of true partnership, we shall all contribute to the implementation of effective case management of malaria in Nigeria.

1. INTRODUCTION

This National antimalarial treatment policy describes our goal with respect to the treatment of malaria and the strategy by which the goal is to be achieved.

1.1 GOAL OF ANTIMALARIAL TREATMENT

The primary goal of treatment in malaria is to cure the patient of the infection and thereby reduce morbidity and mortality. A second purpose is to encourage rational drug use to prevent or delay the development of antimalarial drug resistance.

Malaria is an eminently preventable, treatable and curable infection. Drugs and other interventions for its prevention and treatment are widely available. Many of these are easy to apply and are affordable and accessible. There is therefore, no justification for this country to continue to suffer under the severe disease and economic burden brought upon it by malaria.

In order to reduce steadily and ultimately remove completely, the burden of malaria on our people, we need to know more about what has made the disease persist at such a high level in our population. New remedies need to be developed and deployed in the fight against malaria to replace older ones with waning efficacy. Perhaps, more importantly, we need to develop more effective use of existing remedies.

This treatment policy therefore aims to:
• reduce morbidity,
• halt the progression of uncomplicated disease into severe and potentially fatal   disease, and thereby reduce malaria mortality,
• reduce the impact of placental malaria infection and maternal malaria-associated anaemia through intermittent preventive treatment,
• minimize the development of antimalarial drug resistance.

1.2 POLICY STRATEGY

The strategy for the implementation of the national malarial treatment policy is that of Roll Back Malaria (RBM). This strategy seeks to establish a social movement in which the local communities, public and private sectors, all tiers of government and non-governmental development agencies etc come together in a partnership and network to implement malaria control interventions. Roll Back Malaria is a global initiative that has set specific deadlines for the attainment of explicitly defined milestones. One of these is the reduction of malaria burden everywhere by 50% by the year 2010.

The RBM intervention strategy has four key elements:

i. Patients with malaria should have access to appropriate and adequate treatment within 24 hours of the onset of symptoms

ii. Pregnant women particularly in their 1st and 2nd pregnancies should have access to effective antimalarial prophylaxis and treatment

iii. Insecticide treated nets and other materials should be available and accessible to persons at risk of malaria particularly pregnant women and children under 5 years of age.

iv. Epidemics of malaria should be recognised and steps initiated for their containment within one week of their onset.

It is obvious that achieving the goal of this policy would require the availability of appropriate antimalarial drugs and their proper management, including storage and rational use. This means that proper financial provisions should be made at all levels for the regular availability of these drugs at costs that the people can afford. The consumers and providers have to be properly educated on malaria and its treatment and an effective monitoring and evaluation system set up to ensure that objectives are being properly pursued.

Finally, malaria is a moving target. New understandings of old problem would be needed and new problems requiring clarification will arise. These call for continued strategic as well as operational research. All these issues are addressed in this policy.

2.1 MALARIA SITUATION IN NIGERIA

2.1.1 Background

Malaria is the commonest cause of hospital attendance in all age groups in all parts of Nigeria. It is also one of the four commonest causes of childhood mortality in the country, the other three being acute respiratory infection (pneumonia), diarrhoea and measles. It is estimated that 50% of the population has at least one episode of malaria each year while children under 5 have on the average of 2 – 4 attacks in a year. Malaria has severe negative effects on maternal health and birth outcomes. It causes maternal anaemia, increases miscarriage and low birth weight.

P. falciparum is the most predominant parasite specie accounting for about 98% of malaria cases in the country. *P. malariae* usually occurs as a mixed infection with *P. falciparum*. *Anopheles gambiae* is the main vector of malaria in Nigeria, but An. *funestus* and *An. arabiensis* are also commonly encountered. *An. melas* is found in the coastal areas.

Malaria is characterized by a stable, perennial, transmission in all parts of the country. Transmission is higher in the wet season than in the dry season. This seasonal difference is more striking in the northern part of the country.

2.1.2 Economic Burden

Malaria impedes human development and is both a cause and consequence of under development. Every year, the nation loses over N132 billion from cost of treatment and absenteeism from work, schools and farms.

2.1.3 Malaria Control – historical perspectives

However, within the last five years, advocacy, political awareness and commitment to malaria control has continued to improve. In 1996, Nigeria developed its first National Malaria Control Policy. A yearly Plan of Action was developed for 1997 and 1998 and a three-year Plan of Action was also developed for 1999 – 2001. Malaria Control units in the States were revitalized or reestablished and awareness to funding malaria activities was created. The highest advocacy between 1996 and 1998 was the celebration of the National Social Mobilization Day when the Malaria Control logo was launched by the then Minster of Health, Rear Admiral Jubril Ayinla.

The National Technical Committee was resuscitated in 1998. The National Malaria Control Committee is a body consisting of National, State and some LGA malaria programme managers and officials, as well as representatives from the private sector and international agencies. The committee meets at the end of each year and is responsible for reviewing the activities of the previous year and planning those of the next year.

Between 1997 – 1998 Training of Trainers activities were carried out on management of severe and uncomplicated malaria. The trainings were held nationally and in the zones. It was hoped that these trainings would produce a core of trainers skilled in monitoring and evaluation.

2.1.4 Roll Back Malaria in Nigeria

RBM is an initiative to improve malaria control in the context of health sector reform. It was initiated in 1998 through a joint partnership of WHO, UNICEF, UNDP and the World Bank. RBM consists of two phases - the inception phase and the implementation phase. After the Consensus Building Meeting for countries in West Africa in March 1999, Nigeria started the RBM inception phase.

Sensitization and advocacy on RBM at the highest level started with letters to all Commissioners of Health in the States and FCT, Abuja. Ministerial press briefing was held to enlighten the public about the importance of RBM and the need for all stake-holders and partners to embrace the new approach to malaria control. Workshops were held for executives of media houses to inform them adequately on RBM and its technicalities.

Nigeria drew attention of the world to problems of malaria control in Africa by hosting and co-financing the African Heads of State Summit on RBM in April 2000. Forty-four of the fifty malaria-affected countries in Africa attended the summit. Nineteen country delegations were led by the Heads of State while the remaining delegations were led by senior government officials. The Summit was also attended by the senior officials from each of the four founding agencies (WHO, UNICEF, World Bank & UNDP) and other development partners.

The Summit concluded with the signing of the Abuja Declaration and Plan of Action. By signing the Declaration, African leaders rededicated themselves to the principles and targets of the Harare Declaration of 1997 and gave commitment to intensify efforts to halve the malaria mortality in Africa by the year 2010 through implementing strategies and actions of Roll Back Malaria.

In line with RBM approach and Abuja Declaration the following activities have been carried out to complete the inception process in Nigeria.

➢ Consensus building meeting nationally and in all the six geopolitical zones. A three year National Plan of Action which also contained the States Plan of Action was developed.
➢ Partnerships have been developed with stakeholders (private and public sectors) and NGOs and International developmental agencies (WHO, UNICEF, DFID USAID, etc.)
➢ Deskwork analysis of the malaria situation was completed
➢ Malarial situation survey was carried out to assess the actual situation of malaria in the country to fill the gap created from the deskwork
➢ A National strategic plan was developed to guide implementation from 2001 to 2005
➢ A round table partners / stakeholder meeting was held to
  - brief the partners on the findings of the survey and National Plan of Action developed from it.
  - deliberate on modalities of funding the National, State and
    LGA Plan of Action

The implementation of RBM has started with Federal Ministry of Health, States and LGAs carrying out some activities as in the Plan of Action.

2.1.5   Malaria Situation Analysis*

➢ The perception of the cause of malaria is poor and very few people in the community link mosquito to malaria.

➢ 80% of malaria cases are inadequately managed at community level by the facility and home based caregivers.

➢ 96% of caregivers initiated actions within 24 hours but only 15% of their actions are appropriate due to inadequate dosage.

➢ 60% of mothers had no knowledge of the current management of convulsions. Only 5% referred such cases to hospital while most either go to traditional healers or use traditional home made concoctions

➢ Improper use of parenteral antimalarials

➢ Only 5% of antimalarial drugs are produced in Nigeria

➢ 85% of health facilities surveyed in rural areas had stock-out. None had prepackaged drugs.

➢ 51% of mothers obtain drugs from Patent Medicine Vendors, 89% of the drugs were found to be substandard and 43% of syrups unsatisfactory.

➢ Non-availability of treatment guidelines in sampled health facilities.

➢ Poor laboratory support in diagnosis of malaria.

➢ 40% of patients with severe malaria die due to poor quality care.

➢ Treatment of malaria illnesses accounted for 46% of the curative health care cost incurred by households with a mean of ₦330.00 per month.

➢ Reporting of malaria is poor in the country.

* Malaria Situation analysis- FMOH 2000

2.2 ANTIMALARIAL DRUG SITUATION IN NIGERIA

Malaria remains a major public health problem in Nigeria. Although several strategies are presently available for the control of the disease, one strategy that has been consistently used in the last three and a half centuries is chemotherapy. Malaria control in Nigeria is based primarily on early recognition and prompt and appropriate treatment. However, the armamentarium of drugs available for malaria case management and the prospect for the discovery of new molecules is limited.

2.2.1 Antimalarial Drug Resistance

The development of resistance, defined as the 'ability of a parasite strain to multiply or to survive in the presence of concentrations of a drug that would normally destroy parasites of the same species or prevent their multiplication' has threatened the continuing usefulness of the presently available antimalarial drugs. Resistance to Chloroquine has spread rapidly through South America, Southeast Asia to East Africa and eventually to all endemic countries of the continent. A similar process has happened to Sulfadoxine–Pyrimethamine (SP) except that resistance to the drug in Africa is low in West Africa, and is beginning to increase in East African countries where Sulfadoxine–Pyrimethamine (SP) has replaced Chloroquine as the first line antimalarial drug. There is an urgent need to preserve and prolong the usefulness of the presently available antimalarial drugs.

The important consequences of drug resistance are: an increase in morbidity and mortality, delay in initial therapeutic response and, an increasing cost to the community. These consequences need to be urgently addressed in Nigeria.

The results of the drug efficacy trials carried out in the six geo-political regions of the Country in 2002 and 2004 are shown in Table 1. WHO guidelines advise policy review when adequate clinical and parasitological response hits the 75% mark. The result of the 2002 Efficacy Studies indicated that Chloroquine and SP were no longer adequate for national first line use. The need to move from monotherapy to more effective combination therapy was recognized. As a result, further efficacy trials were conducted in 2004 by Federal Ministry of Health on two suitable Artemisinin based combination therapy. Both combination therapies were found to be highly efficacious and thus suitable for use in the treatment of uncomplicated malaria.

Table: Therapeutic Efficacy of Anti-malarial Drugs in Nigeria
(Adequate Clinical and Parasitological Response ACPR)

	Zones	Chloroquine*	Sulphadoxine/Pyrimethamine*	Artemether/Lumefantrine**	Artesunate/Amodia
1	SE	3.7%	14.9%	100%	100%
2	SS	9.1%	8.5%	87%	82.5%
3	NC	53.2%	82.7%	100%	96%
4	NW	77.3%	94.2%	100%	100%
5	SW	40.9%	75.6%	-	-
6	NE	50.8%	64.8%	-	-

* 2002 Drug Efficacy Study   ** 2004 Drug Efficacy Study

In general, sensitivity of the parasite in-vivo to amodiaquine, halofantrine, mefloquine and other artemisinin derivatives has been known to be very good (>90% cure rate on day 14). Primary reduced sensitivity in-vitro of P. falciparum to mefloquine and to artemisinin has been reported in up to 10 - 15%

of isolates obtained from southwest Nigeria but as previously indicated above, response <u>in-vivo</u> to these drugs is excellent.

Resistance to pyrimethamine has long existed in Nigeria (since the late 1950s). There is no convincing evidence that the drug has potent prophylactic efficacy in pregnancy. However, pyrimethamine in combination with sulphadoxine has been demonstrated to have markedly improved efficacy. It is generally assumed that daily proguanil is effective prophylactically, but there is no hard data to support this. Certainly, carefully designed clinical studies are required to address the issue of antimalarial chemoprophylaxis in vulnerable groups such as sickle cell anemia patients.

3. ESSENTIAL ANTIMALARIAL DRUGS

3.1 Definition

Essential antimalarial drugs are those drugs that meet the needs of appropriate antimalarial treatment in the vast majority of the people. They should therefore be available at all times, in adequate amounts and appropriate dosage forms and should be affordable to the people.

3.2 Criteria for Selection

The criteria for selection of essential antimalarial drugs should be the same as for the selection of essential drugs in general. They are as follows:

➢ The drugs should satisfy the antimalarial treatment needs of the vast majority of the people at all levels of health care.

➢ They should be drugs for which there is sufficient evidence of efficacy and safety from local and global controlled clinical studies and from experience in general use.

➢ The preferred dosage forms should be those which have reasonable shelf-life and are able to withstand adverse environmental conditions unavoidable in our distribution chain. For example, tablets and capsules are more stable under our prevailing ambient temperatures and humidity than mixtures, syrups and elixirs. Preferably, therefore, paediatric doses should be achieved from the use of either paediatric tablet strengths or scored tablets of standard tablet strengths

➢ They should be registered for wide distribution in the country.

➢ They should be drugs for which quality certification can be readily obtained from local institutions, from the country of origin or through the auspices of the World Health Organisation.

➢ They should be drugs that can either be manufactured locally using locally produced or imported raw materials or that can be imported in bulk cheaply.

➢ Drugs with known serious side effects but with acceptable risk/benefit ratio considering the severity of the situations in which they are to be used (e.g. quinine) have been included in the expectation that their procurement, storage, distribution and use would be subject to the strict technical and ethical control associated with such drugs.

3.3 The list of Essential Antimalarial Drugs

This list is necessarily short since the number of programmatically effective antimalarial drugs globally is quite small. The list is presented under the subheadings of (a) Current Drugs for uncomplicated malaria, (b) Current Drugs for severe malaria, (c) Other Drugs for multi-resistant malaria, (d) Older drugs for treatment of uncomplicated malaria, (e) Adjunctive Drugs,

3.3.1 Current Drugs for Treatment of uncomplicated malaria
Current drugs for treatment of uncomplicated malaria are Artemisinin based combination therapies. This combination takes advantage of the rapid blood schizontocidal action of the artemisinins and the long duration of action of the partner compound to effect rapid cure with low level of recrudescence. The use

of two or more drugs together in therapy has been found beneficial in clinical medicine, the best-known examples being in tuberculosis, leprosy and some bacterial infections. It has been argued that with the limited number of antimalarial drugs available and the growing resistance of the parasites to these drugs, better responses to drug treatment and a significant slowing down of the rate of development of resistance can be achieved by combining antimalarial drugs. The most widely advocated combinations are those in which the artemisinin compounds are combined with a longer acting antimalarial. These drugs include:

Drugs*	Dosage form	Strength
+Artemether+ Lumefantrine	Tablet	20mg artemether + 120mg lumefantrine per tablet

*Use of the different components of these drugs as monotherapy is not recommended

3.3.1b other Artemisinin based combination available

Amodiaquine – Artesunate	Tablet	Amodiaquine 10mg/kg and Artesunate 4 mg/kg
Artesunate- mefloquine	Tablet	Artesunate 4 mg/kg/ Mefloquine 15- 25mg/kg

These ACTs may not be currently deployed for programmatic use for the following reasons:

- They are not available as co-formulation and it may result in poor compliance with using combination treatment.

- With the existing level of Chloroquine resistance in the country, it is anticipated that resistance to amodiaquine will rapidly emerge when deployed on a large scale. This has been the pattern elsewhere. Studies in Nigeria as of 2002 showed that sensitivity to Amodiaquine in Bayelsa is about 90%..

- Mefloquine is associated with a number of undesirable side effects.

3.3.3 Other drugs available for treatment of malaria
These drugs are available as mono-therapy in Nigeria and have been used in the management of malaria. The use of monotherapy is no longer recommended.

Drugs	Dosage form	Strength
Amodiaquine	Tablet	200mg (153.1mg base)
Halofantrine		250mg (233 mg base)
Dihydroartemisinin (and other artemisinin derivatives)	Tablets	20, 60 or 80mg

3.3.4 Current Drugs for severe malaria
Severe malaria is a medical emergency and requires parenteral treatment. The current drugs for the management of severe malaria are as shown in the table:

Drugs	Dosage form	Strength
Quinine	Injection	300mg/ml in 2 ml ampoule
Artemether	Injection	80mg / ml in 1 ml ampoule
Artesunate	Injection	60 mg /1 ml vial

Artesunate*	Suppository	50mg suppository

*Suppositories of Artesunate can be used _only_ as pre-referral treatment

3.3.4b Follow-on treatment for severe malaria

Once a patient with severe malaria can take orally, following initial administration of parenteral antimalarial, change to the first line antimalarial and give a full course.

3.3.4 Older drugs for treatment of uncomplicated malaria,

These are drugs that were previously used on wide programmatic basis for the management of uncomplicated malaria. The efficacy levels of these drugs have been undermined by the parasite resistance trend observed.

These drugs include:

S/N	Drug	Comments
1	Sulphadoxine Pyrimethamine	Not recommended for treatment of malaria. Reserved for intermittent preventive treatment (IPT) in pregnancy
2	Chloroquine	Inadequate efficacy and therefore no longer recommended

3.3.5 Adjunctive Drugs

Adjunctive therapies used in the management of malaria for the relief of symptoms and complications. These are mentioned as appropriate in the Treatment Guidelines

3.4   Updating the list of antimalarial drugs

The antimalarial drug list should be a dynamic list. The drugs included should be reviewed for efficacy and safety (pharmacovigilance) regularly to determine their continued usefulness in malaria therapy. At the same time new drugs are becoming available in the country and those that are found to be useful should be added to the list.

A network for surveillance of the susceptibility of malaria parasite to drugs has been set up in the country. Sentinel sites have been identified, and should be strengthened to generate reports on the performance of specific drugs in the treatment of malaria. These reports should be reviewed regularly by the malaria control authorities.

4. RATIONAL USE OF ANTIMALARIAL DRUGS

Rational use of antimalarial drugs refers to appropriate use of antimalarials for the right indications and at the correct/adequate dosages. Antimalarial drugs will be needed for treatment of uncomplicated malaria, severe malaria and chemoprophylaxis for groups at risk. The appropriate use of antimalarial drug is determined by the goal of treatment and the person responsible for taking the primary decision on use of the drug either at home or at the different health care levels.

4.1 Disease management at the home

The effectiveness of home treatment will depend upon early diagnosis, prompt, appropriate treatment, and proper health education about malaria. Early commencement of appropriate treatment will ensure better outcome and prevent the progression to severe malaria. An antimalarial drug to be used at home must be safe, effective, affordable, easy to administer and preferably in single dosage packs.

4.1.1 Diagnosis of malaria in the home

Diagnosis in the home will depend on recognition of symptoms and signs such as fever, vomiting and loss of appetite. Even where there are other main symptoms like cough and diarrhoea, malaria should still be treated in addition to any other care given in the home.

Caregivers should be taught to recognise signs of severe malaria for which they must immediately bring a child to the nearest health facility.

4.1.2 Home treatment of malaria

Use Artemisinin based combination therapy (ACTs) for malaria
Age specific pre-packed artemisinin based combination drugs artemether+lumefantrine and an alternative Artesunate-amodiaquine is recommended for home treatment of malaria in accordance with the dosage schedule indicated below. Drugs are to be taken every day for 3 days.

4.2 Disease Management in Health Facilities: Level I, Level II and Level III

4.2.1 Level I: Primary Health Care Centres, Dispensaries and Health Posts: the Village Health Workers (VHW), Junior Community Health Extension Workers (JCHEW) or trained Patent Medicine Vendors (PMV) belong to this level. There is no laboratory facility at this level.

Malaria diagnosis is based on symptoms using the IMCI classification. The health worker should be able to recognize the general danger signs, give pre-referral treatment and promptly refer patients with severe febrile disease.

In addition to the treatment of malaria indicated above under home management, a health worker at this level is able to give artemisinin based combination therapy for uncomplicated cases. The health worker is also able to give artesunate suppositories for pre-referral treatment.

4.2.2 Level II: General Hospitals, certain categories of Private Hospitals staffed by Medical Officers, Community Health Officers or Nurses.

At this level, there may or may not be a laboratory. It is however desirable that a laboratory diagnosis of malaria be established when possible. Detailed history, physical examination and laboratory tests would be employed in the diagnosis of malaria in order to exclude other possible conditions, treatment failure and complications. For those without formal medical training, the IMCI algorithm would still be employed.

Management capabilities would include using alternative antimalarials for failure of response to first drug, providing urgent treatment for severe malaria or other severe febrile illnesses. Health workers at this level MUST however refer the following category of patients with severe malaria. These are patients:

- who are unconscious and not responding to treatment
- with uncontrollable convulsions
- who have severe pallor (except if blood transfusion facility is available)
- with renal failure

4.2.3 Level III: Specialist, Teaching and some categories of Private Hospitals.

Three categories of patients may be anticipated at this level. These are patients presenting for the first time, those visiting for follow-up of the same illness and those referred from other levels that have failed to respond to therapy or have severe complications.

Management of malaria at this level would focus on confirming diagnosis, giving the most effective treatment (including use of appropriate antimalarial drugs where necessary), providing intensive care for patients with severe complications and laboratory monitoring. Therefore, this level must be appropriately staffed and well equipped with needed drugs and laboratory supplies.

4.3   Referral

The referral system starts from the caregiver at home who should visit the nearest health facility as soon as there is no perceivable response. In general, health providers and health workers at all levels should be able to recognise their limitations and make early referrals.

Referral should be a two way process whereby the health worker at the higher health facility should also endeavour to give a feed back to the lower level health facility on the outcome of the patient's management.
 ;

4.4   Chemoprophylaxis

Malaria prophylaxis is generally not necessary in persons living in a malarious area because it may lower ones resistance to the disease. Prophylaxis should however be used in sickle cell anaemia and in non-immune visitors because of risk for severe disease, but it is not 100% protective. Intermittent preventive treatment of malaria in pregnancy is recommended for all pregnant women.

4.4.1   Children and Adults with Sickle Cell Anaemia

Individuals, both children and adults, with sickle cell anaemia are widely recognised to be at increased risk of sickle cell crisis from malaria infections. It is recommended that children with known sickle cell anaemia be given chemoprophylaxis. The most common prophylactic agent is proguanil. The recommended dose is 100mg daily for children or 200mg for adults.

4.4.2   Chemoprophylaxis of Non-Immune Visitors / Residents

Non-immune visitors to areas of malaria transmission are considered to be at high risk of malaria infection. In addition to the provision of information concerning effective measures to reduce human mosquito contact, non-immune visitors to Nigeria should also be given chemoprophylaxis. It is currently recommended that several options, including mefloquine, doxycyclin, Atovaquone-proguanil be used as

chemoprophylaxis for non–immune travelers to all areas of Nigeria. Doses should be taken prior to arrival in Nigeria and continued during the stay in Nigeria and following departure from Nigeria. In spite of this, if the patient develops fever, a full dose of an appropriate antimalarial should be taken by the patient, and the patient should go to the nearest hospital.

Non-immunes who have commenced mefloquine from their home countries should continue its use in Nigeria.

4.5   Pregnancy:

Intermittent Preventive Therapy (IPT) with sulfadoxine / pyrimethamine has been used and shown to be effective in parts of Africa for several years. This is an evidence-based approach and is hereby recommended.

Dosage: One full treatment dose during the 2nd and 3rd trimesters. The last dose should be given not later than one month before the expected date of delivery. *Sulphadoxine-Pyrimethamine must not be used in the first trimester of pregnancy.*

Uncomplicated malaria:
Recommended options:
1.   Quinine is considered safe in pregnancy and can be used in all trimesters
2.   Artemisinin based combinations are considered safe in the second and third trimesters. Therefore Artemether-Lumefantrine can be used in the second and third trimesters.
However, in the first trimester arteminisin based combinations can be used where there are no suitable alternatives.

5. PROPERTIES OF ANTIMALARIAL DRUGS IN CURRENT USE IN NIGERIA

The salient pharmacological properties of the antimalarial drugs currently in use in Nigeria are shown in tabular form below.

Except for chloroquine and quinine, the pharmacokinetics and the pharmacodynamic properties of many of the drugs have not been studied in-depth in the indigenous population. It is essential that these be done.

Properties of antimalarial drugs in current use in Nigeria

1. Artemisinn derivatives	Schizotocidal		
i) Dihydro-artemisinin	Prevent gametocytogenesis by effect on ring and early (stage I – III) gametocyte stages	10mg / kg twice on 1st day then 10mg / kg daily for 4-6 days	• **Route: Oral, intra-rectal***
ii) Artemisinin	•	10mg / kg twice on 1st day then 10mg / kg daily for4-6 days	• **Route: Oral**
iii) Artesunate	•	2mg / kg twice daily on 1st day then 2mg / kg daily for 4 – 6 days	• **Route: Oral, Parenteral, (iv), intrarectal**
iv) Artemether		2mg / kg twice daily on 1st day then 2mg / kg daily for 4 – 6 days	• **Route: Parenteral,**
			• **Absorption: oral very rapid, but may be incomplete.** • **Artemisinin is five times less potent than dihydroartemisinin, artesunate or artemether** • **Artesunate and artemether are metabolised to dihydroartemisinin** • **Half life very short** **Artemisinin – 2 h** **Artesunate – 2 min** **Artemether – 3-6 h** **Dihydroartemisinin – 48min** • **Safe in pregnancy** • **Adverse effect: very few: fever, reduced reticulocyte count without anaemia, neurotoxicity at high doses in animals but not in man** • **Should be used in combination with other slower acting antimalarial drugs for mutual protection**
2. Quinine	Schizontocidal	10mg/kg 8–12 hourly for 5 – 7 days	• Route: Oral, parenteral (im, iv not subcutaneously) • Peak plasma concentration 1-3h • Not concentrated in red cells • Plasma protein binding 75 – 85% • Wide tissue distribution • Plasma half life 9 – 12h • Metabolised to 3- and 2- hydoxyquinine and other polar metabolites • Clearance: hepatic 80% renal 20% • Has antipyretic effect • Safe in pregnancy (when used judiciously) • Adverse effect: GIT disturbances, tinnitus, vertigo, dizzines, hypoglycaemia Use: in severe malaria

Drug	Mode of action	Dose	Disposition/Properties

Drug	Mode of action	Dose	Disposition
3. Halofantrine	Schizontocidal	500mg 6 hourly for 3 doses (adults) 8mg / kg 6 hourly for 3 doses (children)	• Route: Oral • Absorption may be erratic • Absorption increases with fatty meals • Metabolised to the active metabolite desbutylhalofantrine (DHF) • Half life: 3 – 5 d, DHF 4 - 8d • Not for use in pregnancy • Adverse effect: GIT disturbances, cardiotoxicity, pruritus • Use: in uncomplicated drug-resistant malaria
4. Chloroquine	Schizontocidal Gametocytocidal against immature gametocytes of P. falciparum, and mature forms of other species	25mg / kg base over 3 days	• Route: oral, parenteral • Absorption: rapid • Peak plasma concentration in 1 - 3h after oral administration • Concentrated in rbc, granulocytes and platelets • Plasma protein binding 55% • Wide tissue distribution • Half life of elimination: 6 - 10 days • Metabolised to desethyl and bisdesethyl chloroquine • Clearance: 51% renal, 45% hepatic • Has antipyretic and anti-inflammatory effect • Safe in pregnancy Adverse effects: nausea, abdominal pain, headache, dizziness, postural hypotension, pruritus, retinopathy on prolonged use. • Contraindication: severe Chloroquine-induced pruritus

5. S–P (Sulphadoxine- or sulfalene-Pyrimethamine	Schizontocidal
	
	Sporontocidal (in animal models)
		25mg / kg of the sulfonamides
		1.25mg / kg of Pyrimethamine
			• Route: oral, parenteral
			• Peak plasma concentration in 2- 6h
			• Not concentrated in red cells
			• Components have high protein binding
			  Sulphadoxine 88%
			  Pyrimethamine 93%
			• Wide tissue distribution
			• Half life: Sulphadoxine 9-10 days,
			                Pyrimethamine 3-4 days
			• Has no antipyretic effect
			• Safe in 2nd and 3rd trimesters of pregnancy
			• Adverse effects: minor skin rash, exceptionally severe e. g. Stevens Johnson syndrome, toxic epidermal necrosis (TEN), haemoltyic anaemia
			• Use: in uncomplicated malaria

6. Mefloquine	Schizontocidal	15mg / kg single dose	• Route: Oral • Absorption: rapid but may be dose-limited • Peak plasma concentration 2 – 4h • 98% plasma protein bound • Not concentrated in red cells • Wide tissue distribution • Metabolised to carboxylmefloquine • Clearance: mainly hepatic • Half life of elimination 16 – 33 days • Safe in pregnancy • Adverse effects: GIT disturbances, self limiting neuropsychiatric symptoms: seizures, psychosis, encephalopathy • Use: in uncomplicated drug-resistant malaria
7. Amodiaquine	Schizontocidal	25mg / kg base over 3 days	• Route: oral • Rapidly converted to desethyl amodiaquine which is active • Desethylamodiaquine is concentrated in red cells • Wide tissue distribution Half life of 10h following IV administration • Half life of desethyl amodiaquine 18 – 20h • Has antipyretic and anti-inflamatory effect • No information on use in pregnancy • Adverse effect: similar to Chloroquine, but may also cause hepatitis, leucopenia, agranulocytosis on prolonged use Indication: uncomplicated chloroquine sensitive or resistant malaria

Drug	Mode of action	Dose	Disposition
8. Proguanil	Schizontocidal Sporontocidal	For prophylaxis 100mg daily in children 200 mg daily in adults	• Route: Oral • Peak plasma concentration 2 – 4h • Concentrated in red cells • Metabolized to cycloguanil • Half life 11 – 20 h • Safe in pregnancy

* Doses do not apply to suppository formulations, which may vary between 10 – 40 mg / kg, e. g. Artesunate suppository 1600 mg total dose over 3 days or 1200 – 1600 mg over 60 h

6. MANAGEMENT OF ANTIMALARIAL DRUG SUPPLY

Malaria control in Nigeria is anchored primarily on early diagnosis and prompt effective treatment of cases. Successful implementation of the malaria treatment policy would depend upon the availability, accessibility and affordability of the antimalarial drugs needed at all levels of the health care system. In effect, there should be a regular supply of the drugs at all health care facilities and the people using them should be able to afford them. A reliable antimalarial drug supply system should therefore be set up. Beginning from procurement (through national manufacture or importation) through storage to the ultimate distribution to the end users.

6.1   PROCUREMENT
Central purchase at the Federal or State level should really not be necessary. At the transition period of ACTs use in Nigeria, well coordinated bulk purchasing will be necessary through appropriate authorities. Decentralization of activities should be paramount in the supply chain and the private sector should play a prominent role in this process.

Antimalarial drug supply to the country can be through local manufacture and /or importation. Private sector should be encouraged to manufacture antimalaria drugs. Some antimalarials are already being manufactured in Nigeria albeit from the bulk product rather than the basic raw materials. These companies should be encouraged and assisted to invest in the primary manufacture of ACTs, Sulfadoxine Pyrimethamine and Amodiaquine in the country.

Government, whether State or Federal should help in encouraging adequate and equitable supply of antimalarial drugs of good quality and low cost, for example in making regulations and enforcing them.

6.2   PACKAGING
Packaging of the antimalarial drugs is also important in ensuring adequate treatment. With the present system in which many antimalarials are packaged in single tablet units of 10, 100, 1000 or more units, patients all too often buy only the number of tablets they can afford at a given time. This practice frequently leads to under treatment since the number of tablets bought may be less than the effective therapeutic dosage.

One way to avoid this problem is to distribute the antimalarial drugs as single treatment dosage packs. Age related differences in dosage can be taken care of by having different packs for different age groups. The private sector drug manufacturers in the Roll Back Malarial partnership will be relied upon to work on and produce these packs.

6.3   STORAGE
Antimalarial drugs will be stored as far peripherally as possible in the supply chain. Storage conditions should therefore be met at every storage point to ensure the shelf life of the drugs.

Appropriate facilities should be provided at each storage point (for example State central medical stores, hospital, clinic and community stores) to ensure that the drugs are kept at as near optimum condition as possible. Appropriate measures should be taken to ensure antimalarials are adequately protected during transportation.

Overstocking should be avoided just as much as understocking so as not to over stretch storage facilities. It should be realised that in the spirit of Roll Back Malaria wherein home treatment of malaria is to be encouraged, antimalarial drugs should be kept in small

quantities at home. Home caregivers should be properly educated on the correct way of keeping these drugs in the home.

6.4   DISTRIBUTION

The test of the effectiveness of the antimalarial drug supply chain is how available and accessible the drug is to the end user. This has to do with the distribution strategies employed. It is now recognised that health managers of the level I health care facilities should have direct access to a reliable source of supply and not depend on supplies from a distant store be it State or National. In this way, the local government level health facility can stock and restock their supplies as required. They should have sufficient financial authority to incur expenditure.

As much as possible the informal private sector should be allowed to participate in drug distribution at the peripheral level. Thus the community represented by CBOs, NGOs, CORPs and patent medicine vendors, should be trained and allowed, subject to regular supervision, to handle antimalarial drugs where the licensed pharmacists do not operate.

6.5   COST

Price must not be a barrier to access to life-saving antimalarial drugs. The cost of antimalarial drugs to the user should be as low as possible. Cost which is unaffordable to the poor rural dwellers on whom the burden of malaria is heaviest will frustrate effort to control the disease.

Ideally, malaria treatment should be free in the public sector. If, for any reason, treatment cannot be free, then it should be subsidized to a level at which cost will not be a disincentive to the seeking of prompt and adequate treatment of malaria. At the national level, tariffs and taxes on locally manufactured and imported antimalarial drugs should either be waived altogether or reduced substantially. This will contribute to bringing down the treatment costs to affordable levels.

7. INFORMATION, EDUCATION AND COMMUNICATION (IEC)/BCC

The ultimate aim of IEC is to ensure that individuals, families, communities and health workers are taking preventive measures to prevent disease, improve on their recognition of malaria and use of antimalarial drugs rationally. Concerted efforts should be put in place to facilitate a smooth transition into the use of ACTs. Intensive BCC and capacity development should be directed towards consumers and all cadres of health providers through under listed means:

7.1   Approach:

The key components of the IEC/BCC strategy for malaria control will include:

- Advocacy: Malaria is a major public health concern, which will require a concerted effort in order to control it. Thus, advocacy would be necessary at different levels to influence policies and obtain support for malaria control from partners.

- Involvement of partners: these will include all tiers of government, non-governmental development agencies, civil societies, private sectors and individual communities.

- Development of key messages: Messages on transmission of malaria, use of insecticide treated nets, diagnosis of malaria, home treatment of malaria, recognition of danger signs and referral will be developed. These messages should be disseminated through the most effective means of communication in relation to the target audience. Options include

posters, pamphlets, mass media (electronic/print), special announcement in places of worship etc.

- Monitoring and evaluation of IEC efforts: This is important in order to evaluate effectiveness. There is a great need to evaluate IEC messages to get feedback from the community on the impact of the IEC.

- Applied research: This will be conducted focusing on areas where gaps in information exist.

7.2   Key strategies

    (i)   A baseline survey to determine the knowledge, attitude, beliefs and practices on malaria control activities should be conducted

    (ii)   Review and update the existing guidelines for malaria control for different levels and target groups

    (iii)   Design and produce appropriate messages to reach pregnant women, caregivers of under 5 year old children, health workers, community leaders, drug vendors, pharmacists etc.

    (iv)   Production and distribution of IEC materials

    (v)   Train health providers/workers at all health care levels on skills for community mobilization and use of IEC messages

    (vi)   Training on the cause, recognition, treatment and prevention of malaria should be extended to pregnant women, caregivers, heads of household, religious and opinion leaders and school children.

    (vii)   Produce and distribute IEC materials to target groups nationwide

    (viii) Formulate IEC work plans in all communities or wards

    (ix)   Holding of meetings and community IEC activities using traditional/local channels

8   MONITORING AND EVALUATION

Monitoring and evaluation of antimalarial treatment policy is needed for the policy to remain applicable to the evolution of the malaria situation. This will usually involve the following processes

(i)   Monitoring the therapeutic efficacy of the recommended treatments

- ▸ This involves the precise determination of the proportion of treatment failures in a given patient population through simplified *in vivo* testing based on a minimum number of post-treatment checks and simple clinical assessment.

- ▸ This can be done using the modified WHO procedure manual for therapeutic efficacy testing of antimalarial drugs for level II or III health facilities.

(ii)   Assessment of compliance to determine;

- ▸ the influence of patient compliance on treatment effectiveness, and determine implications for treatment policy

- ▸ the influence of prescriber compliance on treatment effectiveness (i.e. quality of disease management in and outside the health services)

(iii)   Routine monitoring of treated cases

(iv)   Assessment of the pattern of antimalarial drug use patterns to determine:

- ▸ the extent of and reason for drug use within and outside the formal health sector; and

- ▸ the sources of the drugs, types and formulations available, distribution patterns, comparative costs, legislation on over the counter drugs and pharmaceutical advertising.

(v)   Assessment of drug tolerance and adverse drug reactions (pharmacovigilance) to determine:

- ▸ the type and frequency of drug effects which influence absorption, and therapeutic efficacy of the drugs (i.e. vomiting, diarrhoea)

- ▸ the type and frequency of drug effects which compromise correct disease management (i.e. health seeking behaviour, acceptability, compliance)

- ▸ the type and frequency of serious drug effects which are life threatening

- ▸ the type and relative importance of risk factors associated with drug effects, including concomitant medication, drug dosage, age, medical history, drug accumulation.

  This may be done through the sentinel sites and surveys.

(vi)   Monitoring the sensitivity of malaria parasites to antimalarial drugs *in vitro*. The objectives would include:

- ▸ longitudinal follow-up of drug susceptibility of the parasites where changes are introduced compared with those where such changes are not implemented

- ▸ monitoring the pattern of cross resistance

- ▸ the establishment of baseline data on the response to a new antimalarial drug, even before its deployment for treatment

vii   Monitoring including post-marketing surveillance to assure the quality of antimalarial drugs being used in the country, in collaboration with relevant stakeholders.

viii   Supportive supervision with appropriate feedback mechanism should be instituted and strengthened in collaboration with relevant Agencies such as National Primary Health Care Development Agency (NPHCDA).

Monitoring and evaluation should be built into all intervention activities and should be considered and approved at the same time that the activities are being approved. Funds for monitoring and evaluation implementation as well as for the training of the monitoring and evaluation personnel should be made available as needed,

Process evaluation should commence as early as possible in each work plan year and outcome should be evaluated annually if possible. Process and outcome indicators should be developed at the same time that the work plan is being prepared and should be described in the work plan.

9.   RESEARCH

The antimalarial treatment policy of a country should be supported by well focused coordinated research and development strategies if it is to succeed in reducing morbidity and mortality and reducing cost of treatment to the community. The research in every instance must be need driven.

Government, other national organization and international agencies should support the funding of research. Research focus should include:-

 (i)   basic medical sciences research including those geared toward the discovery of new molecules, if possible, or new uses for old drugs or tools.

 (ii)   vaccine development

(iii)   operational research which seeks to maximize drug use and minimize or delay development of resistance in the parasite.

(iv)   periodic clinical efficacy and safety evaluation of existing antimalarial drugs and of new candidate drugs or tools.

 (v)   evaluation of genetic, and other determinants of response to the currently available antimalarial drugs.

(vi)   antimalarial drug utilisation studies including pharmacoepidemiology and pharmacoeconomics of antimalarials.

(vii)   operational research in health seeking behaviuor, household decision making process and home management of malaria, use and acceptability of mosquito nets, quality of care at health facilities, role of patent medicine vendors in the community and drug distribution channel in the community.

(viii)   use of chemoprophylaxis especially in pregnancy

(ix)   other studies designed to reduce transmission in the country including resistance of vector to currently available insecticides.

 (x)   evaluation of the role of traditional medicine and herbal drugs in malaria control

In Nigeria, research efforts have been centered mainly on studies designed to evaluate efficacy and safety of antimalarial drugs, and even then on a low scale.

There is need to invest in other areas of research listed above.

10   FINANCE

For the objectives of the National Antimalarial Treatment Policy to be attained there should be appropriate and adequate deployment of funds to malaria control. Funds would be needed to facilitate implementation of preventive measures, drug availability / distribution at all levels, capacity building, and improved referral from one health care level to another. There will also be a need to provide funds for monitoring /evaluation of all aspects of malaria control, social mobilization and operational research.

10.1   Sources of fund

Funding for malaria control would be by the Federal, State and Local governments. Appropriate percentage of the health budget based on the malaria burden and malaria related needs shall be allocated and released by all tiers of government for malaria control.

Others sources of funds include international and local non-governmental development agencies/organizations, communities and philanthropic individuals.

10.2   Resource Mobilization

Resource mobilization should be carried out and sustained through:
- Increase in budgetary allocation to health by Governments at all levels envisaging the 15% set out by Abuja Declaration
- Effective Public/Private collaboration – special appeal should be made to corporate organizations to make specific contributions to their respective communities.
- Community involvement even during planning stages till execution and monitoring of use of funds
- Organizations operating within specific communities

CONCLUSION

This document has been put together as a consensus document for all stakeholders and is subject to review as the malaria situation need arises.

GLOSSARY

1	ACPR	-	Adequate Clinical and Parasitological Response
2	ACT	-	Artemisinin based Combination Therapy
3	An.	-	Anopheles
4	BCC	-	Behaviour Change Communication
5	CBO	-	Community Based Organization
6	CHEW	-	Community Health Extension Worker
7	CORPs	-	Community Oriented Resource Persons
8	FCT	-	Federal Capital Territory
9	GIT	-	Gastro-Intestinal Tract
10	IEC	-	Information Education and Communication
11	IMCI	-	Integrated management of Childhood Illnesses
12	IPT	-	Intermittent Preventive Treatment
13	JCHEW	-	Junior Community Health Extension Workers
14	LGA	-	Local Government Area
15	NC	-	North Central
16	NDHS	-	National Demographic and Health Survey
17	NE	-	North East
18	NGO	-	Non-Governmental Organization
19	NW	-	North West
20	PMV	-	Patent Medicine Vendor
21	RBM	-	Roll Back Malaria
22	SE	-	South East
23	SP	-	Sulphadoxine Pyrimethamine
24	SS	-	South South
25	SW	-	South West
26	TEN	-	Toxic Epidermal Necrosis
27	UNDP	-	United Nations Development Programme
28	UNICEF	-	United Nations Children's Fund
29	USAID	-	United States Agency for International Development
30	VHW	-	Voluntary Health Worker
31	WHO	-	World Health Organization