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Framework for Developing, Implementing and Updating National Antimalaria Treatment Policy:

A Guide for Country Malaria Control Programmes

World Health Organization
Regional Office for Africa
Brazzaville

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FOREWORD

There are 550 million people at risk of malaria in Africa today. The majority of these live in areas of stable transmission. Every year, some 270&480 million cases occur resulting in about one million deaths, most of whom are children below five years of age. The economic loss due to malaria was estimated at US$ 12 billion in 2000. 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. In order to save lives and contribute to poverty alleviation, the African Regional Committee in August 2000 adopted a Framework for the Implementation of Roll Back Malaria (RBM) (Resolution AFR.RC50.12). RBM in the African Region builds on the Accelerated Implementation of Malaria Control, the Regional Strategy for Malaria Control and the African Initiative for Malaria Control (AIM) in the 21st century.

The spread and intensification of antimalarial drug resistance is one of the greatest challenges facing effective malaria control in the world today. 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. Therefore, it is necessary to find a way of ensuring access to effective and affordable antimalarial drugs while minimizing the rate of evolution of resistance. In the African Region, the phenomenon of drug resistance, first observed in East Africa in 1979, is now spreading to other sub-regions. WHO/AFRO has taken the following actions to tackle the issue: (i) developed a standard in-vivo protocol for antimalarial drug therapeutic efficacy testing for use by countries, (ii) supported countries to build capacity for monitoring drug resistance, (iii) developed a framework for developing, implementing and updating national antimalarial treatment policies to guide countries faced with this problem.

This document aims at guiding countries on how to review their existing antimalarial drug policies. This framework document is a response to requests from countries and other interested parties who wanted to know when to change first-line drugs for treatment of uncomplicated malaria in the face of antimalarial drug resistance. The decision on when to change antimalarial treatment policy will depend on many factors, including drug efficacy, drug profile, drug availability and cost, health delivery systems and provider and consumer preferences.

This framework is based mainly on experiences from some countries in Eastern and Southern Africa where resistance to chloroquine is high and the drug is no longer used as first-line treatment of uncomplicated malaria. It is targeted at policy-makers, programme managers, researchers, cooperating partners, nongovernmental organizations and others involved in malaria control. The lessons learned from this part of the region have enabled WHO/AFRO to develop this framework so that other countries facing this problem in the future could rapidly review, update and implement effective treatment policies. Member States are therefore urged to think through the process.

Dr Ebrahim M. Samba
Regional Director

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EXECUTIVE SUMMARY

There are 550 million people at risk of malaria in Africa today. The majority of these live in areas of stable transmission. Every year, some 270&480 million cases occur resulting in about one million deaths, most of whom are children below five years of age. The economic loss due to malaria was estimated at US$ 12 billion in 2000. 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. The situation is worsened by the appearance and spread of chloroquine resistant *Plasmodium falciparum* which was first documented in East Africa in 1979. It is therefore essential that countries be guided on how to review existing antimalarial treatment policies.

The essential components for developing, implementing, evaluating and updating a national antimalarial drug policy include: (i) a clear analysis of the technical, social and economic issues related to malaria control and antimalarial drug resistance, the magnitude of malaria resistance, potential interventions and the consequences of action or inaction; (ii) analysis of the potential environment for decision making; (iii) consensus building and selection of options among policy-makers, researchers, control staff and other relevant stakeholders and (iv) a supervisory body to oversee the development, implementation and revision of the policy. The process of change itself requires a number of ingredients. Most important among these is the signal for change. This signal comes in the form of increased morbidity and mortality associated with malaria; consumer and provider dissatisfaction with current antimalarial drug policy; evidence from therapeutic efficacy tests indicating that any of the drugs currently used for therapy may be ineffective in the treatment of malaria; and evidence from new drugs, strategies and approaches indicating that the currently implemented approaches may not be the best. One of the indicators for change will be a high level of treatment failure of the currently used antimalarial drug. In order to have a systematic and common approach to this dynamic process of change of antimalarial drug policy and to counteract the likewise dynamic process of the development and spread of antimalarial drug resistant, levels of treatment failure have been used to classify the process. A detailed description of the classification is provided in this document.

Since the process of drug resistance development is dynamic and evolves with time, it offers the opportunity for monitoring and timely planning of change. Consequently, the process of developing, implementing and evaluating a national antimalarial drug policy is also dynamic, and the activities to be implemented are based on the rate of development of drug resistance. Monitoring the effectiveness of an established drug policy is a necessary component of the activities in the process leading to policy change which has to be dynamic and include all partners and stakeholders.

This document, which is based on experiences from countries that have gone through the process of change, is meant to provide countries with guidance on how to develop, implement, evaluate and make the necessary changes that will ensure that the objectives of an antimalarial treatment policy are being met.

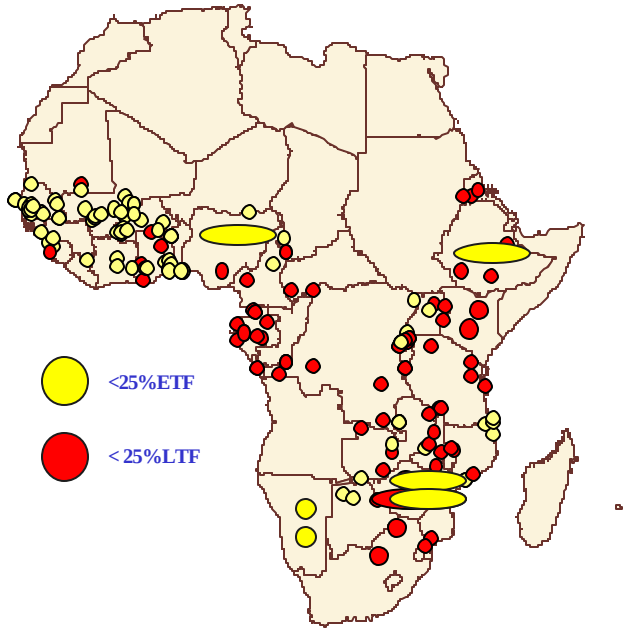
1. INTRODUCTION

1.1 Background

Every year there are about 270&480 million cases of malaria resulting in about one million deaths, mainly in Africa and especially in children under the age of five years (1). The economic loss due to malaria in Africa in 1989 was estimated at US$ 800 million, and by 2000 this had risen to US$ 12 billion, an enormous constraint on already poor countries (2).

The burden of malaria disease has been worsened by the appearance of chloroquine resistant *Plasmodium falciparum* which was first documented in East Africa in 1979 (3). Since then, there have been reports of chloroquine resistance in most countries in Africa; high resistance in the east, moderate resistance in central and southern Africa and low resistance in west Africa (Figure 1). In addition, resistance to sulfadoxine-pyrimethamine (SP) is increasing in Africa. Evidence is growing to show the relationship between increased resistance to first-line antimalarial therapy and increased morbidity and mortality (4,5,6). Resistance has also been implicatedn in the increasing frequency and severity of epidemics.

Figure 1: **In-vivo chloroquine resistance in the African Region: 1995–2001**



ETF: Early treatment failure
LTF: Late treatment failure

In some countries in Africa, chloroquine resistance remains low; in these countries, an antimalarial drug policy which includes chloroquine as first-line therapy for uncomplicated malaria is indicated. These countries should consider how to extend as long as possible the utility of chloroquine by ensuring appropriate *use* of the drug. The sensitivity to chloroquine and alternatives should be monitored in order to measure the trend in antimalarial drug resistance and ensure that the recommended therapy is efficacious.

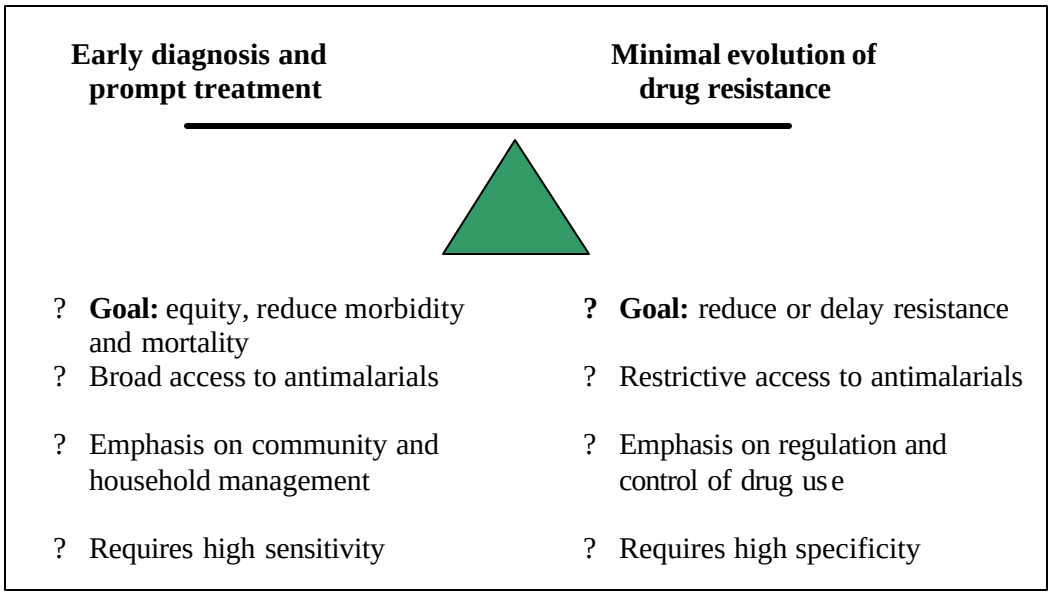
In areas with evidence of increasing chloroquine resistance, only a few countries have opted to change the first-line antimalarial drug from chloroquine to an alternative. Section 2.5 examines the decision making process and looks at some of the reasons why change in policy has not occurred.

1.2 Rationale and Approaches to Antimalarial Drug Policy

The development of resistance to antimalarial drugs has prompted countries in Africa to develop this document which is designed to support malaria control programmes as well as formulate, implement and update their recommendations for antimalarial drug availability and use. In addition, various issues have stimulated development of a drug policy framework. Case management is one of the key components of the regional strategy for malaria control. It requires the provision of prompt, cost effective and safe treatment of malaria disease for different clinical settings. There are few antimalarials that are suitable for widespread use in public health settings. In addition, the development of new antimalarials is an expensive, slow and difficult process. It is necessary to develop a way of ensuring access to effective antimalarial drugs yet at the same time minimize the evolution of resistance, due mainly to the widespread availability and misuse of antimalarial drugs (Figure 2).

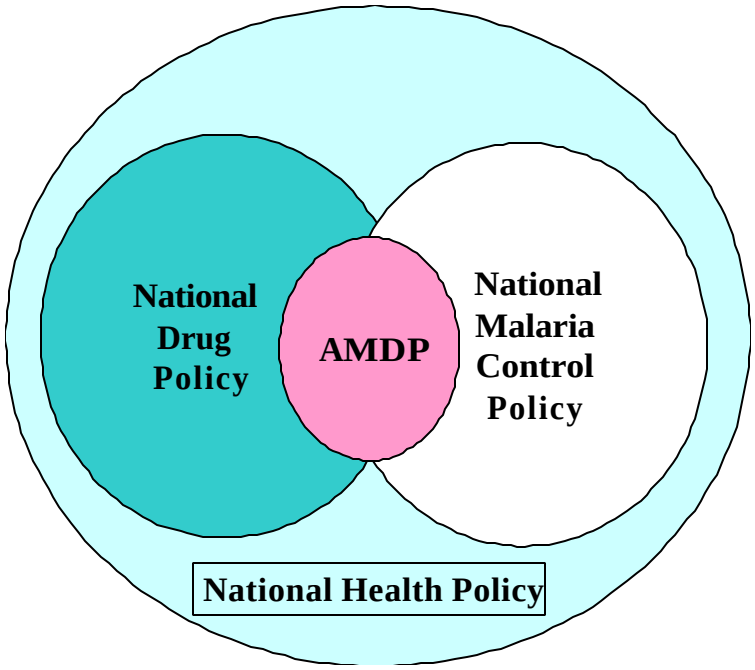
Therefore, an approach should encourage rational drug use of currently available antimalarial drugs in order to avoid exerting unnecessary selection by the parasite to develop drug resistance and to ensure long-term utility of the drug. At the same time, these antimalarial drugs should be available to people who need them, through early detection and prompt treatment to reduce the morbidity and mortality associated with malaria.

Figure 2: **Balancing early diagnosis and prompt treatment with drug resistance**



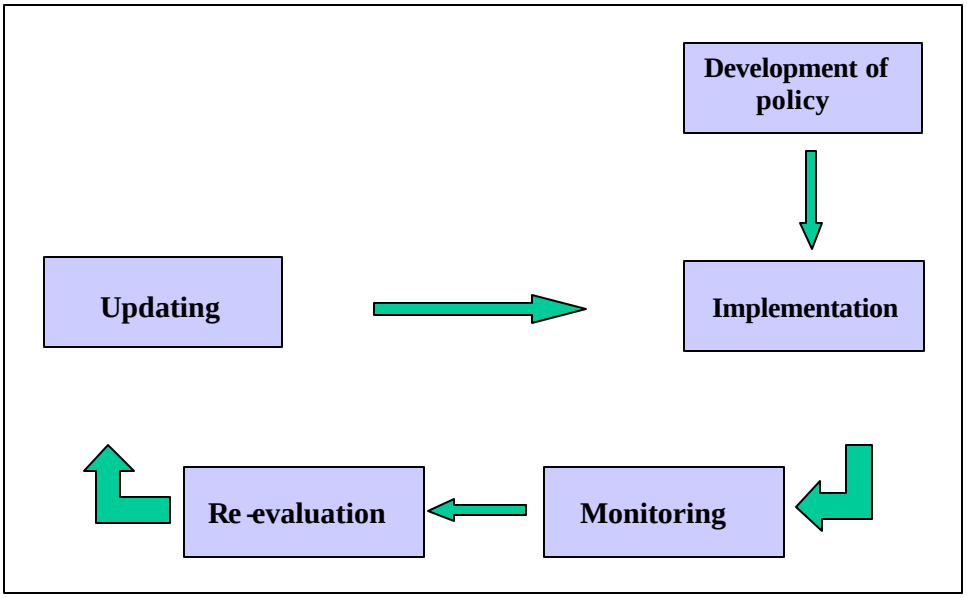
Countries will benefit by having an antimalarial drug policy which is a set of recommendations and regulations concerning the availability and rational use of antimalarial drugs in a country (7). Given the importance of the issue of antimalarial drug use, the antimalarial drug policy (AMDP) should be give prominence within and supported by the National Drug policy (NDP) and National Malaria Control Policy (NMCP) (Figure 3). The NMCP and the NDP) should be in line with the overall National Health Policy. An antimalarial treatment policy, development of health systems and new advances in science should assist countries in providing a prompt response to malaria disease in a dynamic world of antimalarial drug resistance.

Figure 3: **Interacting policies**



The stages of an antimalarial drug policy can be viewed as a cycle (Figure 4) that requires constant appraisal. The initial step is to develop a rational country-specific antimalarial drug policy based on information required for developing an antimalarial drug policy (Section 2.2). The AMDP is designed to ensure the purpose and objectives of the policy (Section 1.3). Once developed, the policy should be implemented. Steps for implementation are outlined in Section 3. Monitoring of the antimalarial treatment policy (Section 4) can provide information on whether the policy is appropriate or whether it needs review (Section 2.3). If updating is considered necessary, information will be collected and collated to assist with the revision of the antimalarial treatment policy (Section 2.2).

Figure 4: **Stages of antimalarial drug policy**



A critical starting point for developing or updating antimalarial drug policy will be the assessment of the status of antimalarial drug efficacy. Collection of data using a standardized method will allow decision-makers to compare information, assess the trends over time and space, and share this information with neighbouring countries.

Apart from data on therapeutic efficacy, the Ministry of Health needs reliable information on provider and consumer perceptions and behaviour which may indicate whether existing policy or recommendations are rational; such information could also ensure implementation of new policies. Information on costs, including administrative and logistical, and cost effectiveness analysis of alternatives would strengthen the process. The Ministry of Health should encourage and support the collection of locally generated information from the country's Health Management Information System (HMIS**)** and operational research projects conducted by experts, the whole process being designed to build local capacity in updating antimalarial drug policy. This information will provide a strong technical basis upon which to advocate and build consensus among key stakeholders. The initial process of defining the research agenda should include the decision-makers and implementors; their participation will make all the actors responsible for utilizing the data in the decision-making process.

A mechanism for consensus building and advocacy for antimalarial drug policy should be put in place. The mechanism, be it a steering committee or a task force, should be composed of representatives of all stakeholders (i.e. policy- and decision-makers; health financiers; producers, providers and distributors of drugs; researchers; epidemiologists; social scientists; economists; consumers) and other partners involved in health, both in the public and private sector.

Since 1993, antimalarial drug policies have been re-evaluated in Malawi, Kenya, Tanzania, Botswana, Ethiopia and some parts of South Africa. These countries are at different stages of re-evaluation and updating. They have different contexts and have used different approaches to revise policy or guidelines, and these reflect differences in human and financial resources, health systems, malaria epidemiology, level of resistance and programme goals. Therefore, a framework for updating antimalarial drug policies has to take into account the dynamic and variable situation of each country. However, certain issues recur from one country to another, and these may serve as guidelines by which each individual country may work out a process that most readily facilitates the updating of antimalarial drug policy and treatment guidelines within local contexts.

1.3 Goal and Objectives of an Antimalarial Drug Policy

The goal of an antimalarial drug policy is to efficiently use available antimalarial drugs and other resources to maximize the reduction in mortality and morbidity (severity, duration of illness and adverse outcome) due to malaria disease. The main purpose of a rational antimalarial drug policy is to ensure availability of safe, effective, quality and affordable antimalarial drugs to those who need them and at the same time promote rational drug use which will minimize the development of drug resistance.

Box 1: The objectives of an antimalarial drug policy are to:

- ensure rapid and long-lasting clinical cure;
- reduce morbidity, including malaria-related anaemia;
- prevent the progression of uncomplicated malaria into severe and potentially fatal disease;
- reduce the impact of placental malaria infection and maternal malaria-associated anaemia through chemoprophylaxis or intermittent therapy;
- minimize the chance and rate of development of drug resistance.

1.3.1 Ensure rapid and long-lasting clinical cure

The Global and Regional Strategy for Malaria places emphasis on cure of the clinical illness rather than removal of all the parasites. Effective therapy, therefore, will provide rapid clinical relief from malaria and prevent recurrence of illness for a long period of time. The length of this period of relief from illness will depend on the local epidemiology of malaria and the immunity of the individual as well as other factors.

In areas with intense transmission, this period of clinical relief may be relatively short compared to areas of low transmission or seasonal transmission as re-infection may occur. In areas of intense transmission, reappearance of the infection (recrudescence) may be difficult to distinguish from re-infection. Other factors which influence the clinical response and duration of clinical cure include compliance with therapy and drug characteristics, including quality of drugs.

1.3.2 Reduce morbidity, including malaria-related anaemia

In addition to clinical episodes of malaria, there is the morbidity and mortality associated with incomplete parasitological cure, anaemia and chronic ill-health. Studies have shown that incomplete parasitological cure can lead to severe anaemia and rapid return of clinical illness. Anaemia, secondary to chronic parasitaemia, may lead to other problems: schooling of children, productivity of adults and serious consequences for pregnant women. In order to reduce these consequences, the antimalarial drug should effectively clear the parasitaemia and maintain the parasite-free period for as long as possible. However, in areas of high transmission, it is particularly difficult to prevent re-infection by the use of antimalarials.

1.3.3 Prevent the progression of uncomplicated malaria into severe and potentially fatal disease

Emergence of chloroquine resistance has been accompanied by an increase in severe disease (including severe anaemia) and mortality, as demonstrated by several studies from the region (5,6,8).

1.3.4 Reduce the impact of placental malaria infection and maternal malaria-associated anaemia through chemoprophylaxis or intermittent therapy

In areas of stable malaria, pregnant women, especially during the first and second pregnancies, have an increased susceptibility to malaria, malaria-related anaemia and having low-birth-weight babies. This in turn increases the risk of morbidity and mortality in the pregnant woman and newborn. In areas of unstable malaria, the pregnant woman has little or no immunity, and malaria infection is associated with severe disease and high risk of maternal and perinatal mortality. This document does not address this aspect of antimalarial drug policy.

1.3.5 Minimize the chance and rate of development of drug resistance

The evolution of drug resistance is not fully understood. It appears that increased drug pressure is one of the leading contributors to drug resistance; as increasing amounts of a drug are used, the likelihood that parasites will be exposed to inadequate drug levels increases. The likelihood of resistance is related to parasite factors (including the intensity of transmission), human factors (such as widespread use or misuse of the antimalarial drug) and drug factors (such as the half-life and quality of the drug). More thought is being applied to reducing the evolution of resistance through more accurate diagnosis of malaria and appropriate use of drugs. Studies have suggested that by reducing the intensity of malaria transmission, there will be a reduction in the rate of development and the level of resistance.

2. DEVELOPING OR UPDATING ANTIMALARIAL DRUG POLICY

It is important to note that an antimalarial drug policy is established in order to accomplish certain goals and objectives. If the purposes for which the policy was established are not met or are only partially met, then there is need to review the policy environment in order to ensure achievement of the intended purposes.

2.1 Essential Components

The essential components for developing, evaluating and updating a national antimalarial drug policy include:

(a) a clear analysis of the technical, social and economic issues related to malaria control and antimalarial drug resistance, the magnitude of resistance, potential interventions and the consequences of action or inaction;

(b) analysis of the potential environment for decision making;

(c) consensus building and selection of options among policy-makers, researchers, control staff and other relevant stakeholders (e.g. donors, private providers, industry and user representatives);

(d) a supervisory body to oversee the development, implementation and revision of policy.

2.2. Necessary Information

In order to develop or revise the antimalarial drug policy, comprehensive country-specific information is required from multiple, global sources. In order to define which effective, affordable drug can be provided safely to satisfy the health care needs of the majority of the population, information is required on epidemiological situation, available alternative drugs, human behaviour, cost and cost-effectiveness, and health system capacity.

2.2.1 Assessment of the epidemiological situation

Understanding the prevalence of malaria, stability of disease, species of parasites and pattern of drug efficacy is essential to providing information to the policy maker in order to develop an appropriately targeted policy based on availability of resources and infrastructure. Information is available from the Health Management Information System (HMIS), surveillance, research and malaria risk analysis such as Malaria Risk in Africa project (MARA).

2.2.2 Assessment of available alternative drugs

The WHO criteria for essential drugs are:

(a) relevance to the pattern of disease;

(b) proven efficacy and safety;

(c) evidence of performance in a variety of settings;

(d) adequate quality (conformity to quality standards);

(e) favourable cost benefit ratio in terms of total treatment cost;

(f) preference for well-known drugs with good pharmacological properties and possibilities for local manufacture;

(g) single component active ingredients.

Although most of the criteria remain relevant to antimalarial drugs, a few other specific characteristics also need consideration (9) (see Box 2).

Box 2: Drug characteristics

- Efficacy of current first-line drug
- Efficacy of alternative drugs
- Cost
- Quality
- Cross-resistance
- Drug interactions
- Side-effects
- Contraindications
- Special groups (e.g. pregnant)
- Useful therapeutic life
- Reputation
- Acceptability, compliance, dosage regimen

A standardized method for monitoring drug efficacy has been developed by WHO (7). Various factors related to the efficacy of antimalarials should be taken into account when developing or revising an antimalarial drug policy. For example, the level of clinical failure with a particular drug is an important determining factor in the process of developing or revising an antimalarial drug policy. In addition to the recommended first-line drugs, the efficacy of alternative drugs should be assessed so that information is available on alternatives if the first-line drug is inadequate. Tests should be conducted throughout the country in order to provide an indication of the geographical pattern of resistance. Efficacy studies should be carried out at regular intervals (18 months to two years) to provide a longitudinal perspective of the problem. All drugs tested should be of prescribed and recommended quality.

The additional cost associated with the use of more expensive drugs should be shared between governments and households. It is estimated that consumers pay 80% of the cost of drugs in Africa. Cost of drugs is an important determinant for both policy-makers and consumers. This is because the additional cost of the drug will place additional burden on the already-stretched national health budget and may influence the choice of therapy.

Drug quality should be considered at all stages of the drug management cycle, including selection. Poor quality of the selected drug will hinder the success of the drug in providing a clinical cure; it will also affect the reputation of the drug and undermine the drug policy. Selected drugs should be those that are produced using appropriate manufacturing practices. Quality control of drugs in Africa is hindered by the limited capacity of the national quality assurance mechanisms, including quality control laboratories, and the unofficial parallel marketing of poor quality drugs. The establishment of a process for quality assurance of compounds to be used in a country therefore becomes an important issue. This is to prevent substandard drugs from compromising those used by the population in the public and private sectors.

Some antimalarial drugs currently available are chemically related. Cross-resistance becomes important when the compound to be introduced has similar properties as a drug to which parasites are resistant. For example, amodiaquine and chloroquine are both 4-aminoquinolines and differ only with respect to side chains. These structural similarities mean that the drug receptors and metabolism are similar, making cross resistance to both drugs relatively easy to achieve. In other words, the degree of resistance to chloroquine will affect the development of resistance to amodiaquine, and the widespread use of sulfadoxine-pyrimethamine (SP) will affect the utility of other sulfa drugs such as chlorproguanil-dapsone. Likewise, the use of cotrimoxazole for pneumonia may affect the use of SP for malaria.

Drug side-effects may be mild, moderate or severe. Mild adverse effects, such as itching (with chloroquine), abdominal pain (with amodiaquine) and skin rash (with sulfadoxine-pyrimethamine), may influence compliance and drug choice. The risk of severe adverse effects such as Stevens-Johnson syndrome (particularly with sulfadoxine-pyrimethamine), agranulocytosis and hepatic dysfunction (with amodiaquine) must be considered when deciding policy. Information is needed from research and ongoing experience with the drugs used in practice. The value of national adverse reaction databases cannot be over-emphasized for their long-term utility, especially with respect to drug use and registration.

Although not well understood, some drugs given concurrently or sequentially can produce undesired effects. For example, folate supplementation can inhibit the action of SP, increasing the likelihood of treatment failure. In making a choice of a new

drug or drug combinations, complementarity and potential synergistic effects must be taken into consideration. This is an area where focussed research may be undertaken to provide required information if the presence or absence of such effects have not been determined before. Some drug interactions may be fatal, such as the potential cardiotoxicity of quinine, mefloquine and halofantrine when given at close intervals.

Pregnancy is a contraindication for many drugs, including some antimalarials. The risk to mother and foetus should always be carefully weighed against the risk of malaria. If necessary, a different drug or strategy may be necessary for use in pregnancy. Some drugs are contraindicated in children (such as tetracycline in those aged under eight years). There may be occasions when high-risk groups such as non-immune refugees will need a different first-line drug from that recommended in the national policy. This will require additional discussions between policy-makers and the providers of health care in these situations.

There is a high level of HIV infection in some malarious areas. The full effects of HIV/AIDS on the administration of antimalarial drugs are not yet known. Preliminary data show that HIV infected patients tend to have more side-effects from treatment with sulfadoxine than patients without HIV. Special attention to generate useful information for this group will be necessary when introducing SP as a first-line drug. At present, the experience of Malawi is that there has been no increase in skin reactions in the general population following introduction of SP as first-line treatment for uncomplicated malaria.

The expected duration of time that a drug will remain effective depends on factors related to the deployment and characteristics of the drug. That is, the potential number of people who take the drug, amount of drug consumed, recommended use of the drug (prophylaxis versus treatment), compliance and pharmacokinetics (short or long half-lives) will influence the development of resistance to the drug. More information is needed in order to derive strategies such as combination therapy (Box 3) for reducing the development of antimalarial drug resistance. In addition, it is recommended that certain drugs be reserved for limited use so as to protect their utility (e.g. use of artemisinin derivatives in Africa). This should be ensured at the time of registration.

Box 3: Monotherapy and combination therapy

Combination therapy is a well known therapeutic principle in antimicrobial treatment; it is used to slow down the development of resistance of microbial pathogens. The basic rationale is that the chances of resistance appearing under the use of two drugs is a product of the rate of the appearance of resistance to each of the two compounds separately, especially when the sites of action of the two drugs differ. This observation is now being used in the design of new combination therapy strategies for the treatment of malaria. The challenges to the use of combination therapy are:

- determining whether combination therapy will slow down the development of resistance in areas of high transmission;
- overcoming the operational hurdles of implementation;
- community-based malaria, IMCI and reproductive health programmes;
- risk/benefit ratio compared to monotherapy.

2.2.3 Studies related to human behaviour

The analysis of health seeking behaviour is essential to ensuring the development and implementation of a rational drug policy and that the purpose of the treatment policy is attained. Consumer choice of therapy and compliance will be influenced by a number of factors, including disease, health system and provider action.

Critical information is required about classification and severity of illness, quality and convenience of health services, advice and care available from the community, family decision-maker in health matters, economic barriers to seeking care and alternative treatments, relative prices of different drugs and therapies, availability and access to drugs, and drug preferences (commoditization, indigenization, reputation of effectiveness and quality). In addition, provider actions are diverse and influenced by many factors, including classification of illness, knowledge and understanding of national treatment policy, availability of training and guidelines, pharmaceutical industry drug promotion strategies, accessibility to consumers, competition among providers (private and public), ownership of health care facilities, financial incentives and regulations governing drug use. Adequate information about these factors and improved understanding of people's perceptions of illness and treatment will assist in the development and implementation of rational drug policy.

National programmes should therefore be able to describe the way users and providers perceive and respond to malaria and what influences their choice of treatment, where it is sought or provided and the factors that affect compliance with alternative treatments. Optimizing provider and consumer behaviour will increase compliance, promote the likelihood of clinical cure and limit the development of drug resistance. Three main factors related to human behaviour and the development of antimalarial drug policy are acceptability, affordability and accessibility. Consumer and provider acceptability of an antimalarial drug policy is one of the determinants of compliance with treatment. If a country is considering a change of policy, it is important to understand the opinions, preferences and beliefs of patients and providers regarding alternative drugs. This will help determine whether additional strategies are needed. Increased acceptability will result in better compliance, improved clinical response and deterred evolution of drug resistance.

The true perceived drug profile and the reputation of the drug will influence acceptability. An important aspect of drug profile is dosage regimen which should be simple to understand, similar to existing practice and easy to follow. Because chloroquine and amodiaquine have identical dosage regimens, the change from chloroquine to amodiaquine should create relatively little confusion regarding dosage. Long half-life drugs, such as SP, are dispensed as a single dose which can improve compliance. Methods should therefore be explored when developing new drugs or approaches (e.g. combination therapy) to simplify the dosage regimen. Other key aspects of drug profile include commoditization, indigenization and side-effects. The latter may deter completion of the full course or future use of the drug.

The perceived drug profile will be influenced by the speed of clinical response, antipyretic effects and relative lack of side-effects. These factors may affect compliance in one or two ways. The apparent positive clinical response may instil user confidence in the drug and lead to improved compliance. However, it may also lead to complacency: the perceived clinical cure may cause the user to neglect completing a full course of therapy. Methods should be developed to encourage completion of therapy despite apparent clinical cure. Choice of drug by all decision-makers (policy-makers, dispensers or consumers) will be influenced by the reputation of that drug. Reputation of a drug may be based on previous use in the country, experiences in other countries, research and various sources of communication (see Box 4).

Box 4: Acceptability of SP in Malawi

In Malawi, following the change of antimalarial drug policy in 1993 from chloroquine to sulfadoxine-pyrimethamine, there were problems with acceptability of the new first-line drug. SP did not appear to provide an immediate clinical response due to the lack of antipyretic quality. Also, the change in dosage regimen from 3-day chloroquine to a single dose SP caused confusion.

Small but focussed operational research projects on acceptability are important before and after drug policy change in order to guide the development of appropriate health messages and training.

Consumers often bear the main costs of drugs, and this may determine adherence to drug policy. If the consumer perceives the drug cost to be higher than the value derived, then compliance will be compromised. Sufficient value to the consumer of paying for and complying with a total treatment course is essential to ensure rational drug use and limit the future consequences of antimalarial drug resistance.

Accessibility refers to the percentage of the population that can reach appropriate health services by local means of transport in no more than one hour. These services also need to provide appropriate quality drugs. The system of drug procurement, distribution and scheduling determines the availability of quality drugs within the public sector. Drugs may be available from other outlets in the private sector which may be less susceptible to methods of control and regulation. There still remains a gap between suppliers and those who need the drugs, especially the rural poor, women and children. Their access to drugs is limited by geographical and financial access to health services, systems of supply and affordability of available drugs.

2.2.4 Cost and cost-effectiveness analysis of alternative therapies

There are scarce financial resources available for clinical care in Africa. Hence, it is essential to determine, through cost analysis (including analysis of existing available resources), the budget implications of changing antimalarial drug policy. It is also important to determine the financial feasibility of implementing such change. In addition, cost-effectiveness analysis (CEA) is useful. CEA compares the costs of interventions (in terms of the value of resources used) and their benefits (in terms of health outcomes). It is a tool to provide policy-makers with information on how to maximize health gains from a given budget.

CEA is not simple and is often difficult to determine and quantify. It will be dependent on many variables, such as the useful therapeutic life (UTL) of the replacement drug and the degree of mortality and morbidity associated with the level of resistance. CEA is not possible in all districts and countries, and information from more generic models may be used to show possible implications in different settings. Some useful sources of information regarding the economics of antimalarial drug policy do exist (10, 11, 12, 13, 14, 15).

2.2.5 Assessment of health systems capacity

The antimalarial drug policy will be dependent on the existing systems to ensure access to quality essential drugs and health care. Various national strategies exist to finance, distribute and dispense safe, effective, quality drugs to those who need them. These may be functions of either the private or public sector. It should be recognized that in many countries, health care is sought through the formal and informal private sector and from traditional healers. An assessment of the potential role of government to ensure quality service through the private sector should be conducted. This may include improved regulation, control of drug stocks, training, recognition of non-formal providers and better public awareness of the implications of using poor quality health care provision.

Health sector reforms have been introduced in many African countries. The aim is to improve the quality, coverage, effectiveness and sustainability of health services. Some countries have decentralized health services and drug management to district level. District-level finances and human capacity to manage and account for drug supply should be included in overall assessment. Community drug schemes have been developed to encourage availability of affordable essential drugs at community level. These too should be analysed to ensure their function and to promote equitable access. The strategies for ensuring availability of the drugs at user level will require careful analysis. Potential benefits of alternatives such as the *push system* or *indent system* should be considered.

The health system requires sufficient political support and financial, managerial and technical resources to effectively implement policy. The critical areas for analysis should include the following *systems*:

- Management and organization
- Human resources
- Drug supply
- Supervision
- Transport

- Communications
- Equipment and supplies
- Referral
- Financing
- Health information.

The assessment of these systems requires a lot of human and financial resources. Therefore, it is advisable to use results from assessments that have already been carried out or to support an assessment with a broader scope than malaria. Such an assessment could include specific questions considered necessary for analysis of health system capacity to implement antimalarial drug policy.

2.3 Conditions that Signal the Need for Re-evaluation

If an antimalarial drug policy is developed with a clear set of objectives and these are not being met, then there is a need to re-evaluate the policy. During the re-evaluation, different options must be explored as it may be necessary to investigate alternatives other than changing the recommendations for first-line antimalarial drug. This will include strategies to improve the provision and use of first-line drug as well as improved diagnosis. Some specific conditions that signal the need for re-evaluation of antimalarial drug policy are discussed below.

2.3.1 Increased malaria-associated morbidity and mortality

Data from health facilities and the HMIS can be used to indicate failure of the existing policy. An increase in re-visits to health facilities after the first-line drug has been correctly prescribed and administered, increase in admissions due to anaemia or severe malaria, or increase in crude mortality and malaria-related deaths observed from routine HMIS surveillance are indicators for re-evaluation of policy.

Routine collection of disease information should be strengthened, and data originating from HMIS should be carefully analysed and used recognizing the limitations. Most of the existing routine disease surveillance systems do not measure the impact of malaria, nor do they evaluate current programmes or policies related to malaria.

The data collected should be those necessary for action, and approaches should be devised to improve the acceptability and reliability of data as well as the specificity and sensitivity of the system. The data should be relevant and should be promptly disseminated to all those responsible for taking action as well as those responsible for generating the data. WHO is promoting a strategy to strengthen the surveillance system

through an integrated approach: *Integrated Disease Surveillance in the African Region* (AFR/RC48/48) (see Box 5).

Hospital-derived data may help to indicate the relationship between increase in drug resistance and malaria-related morbidity and mortality. In West Africa, it was observed that as the level of chloroquine resistance increased in Ibadan, cerebral malaria became more common (5). Greenberg et al (4) used hospital data to show an increase in proportional malaria admissions and proportional malaria mortality associated with the evolution of chloroquine resistance in former Zaire. Examples from Tanzania, Malawi and Kenya suggest that levels of drug resistance correlate well with malaria-related mortality.

Box 5: Integrated disease surveillance (IDS)

The IDS strategy developed with the overall guiding principles of flexibility, usefulness, simplicity and integration of all synergistic surveillance actions. It is a district-centred and outcome-oriented strategy which focuses on linkage of data to public health action at all levels. It promotes national ownership, decentralized decision-making and action at all levels.

2.3.2 Consumer and provider dissatisfaction with current policy

Consumer and provider satisfaction with existing recommendations for antimalarial drugs may be adversely influenced by many factors, including:

(a) decrease in efficacy of antimalarial drugs in current use;
(b) cost, indigenization, commoditization and availability of recommended drug;
(c) introduction of new drugs and the publicity and information surrounding them.

Analysis of behaviour and recognition of reasons for dissatisfaction with currently recommended treatment will assist decision-makers to recognize whether the existing policy is rational or whether the policy needs to be updated.

2.3.3 Evidence from therapeutic efficacy tests

WHO has prepared a standardized protocol, *Therapeutic Efficacy Tests for Uncomplicated Malaria in Areas of Intense Transmission* (7), for assessment of therapeutic efficacy of antimalarial drugs; it focuses on the clinical efficacy of the drug rather than the previously recommended parasitological data. A simplified version of the protocol is also available: *A Practical Handbook for Antimalarial Drug Therapeutic Efficacy Testing for District Health Workers* (9).

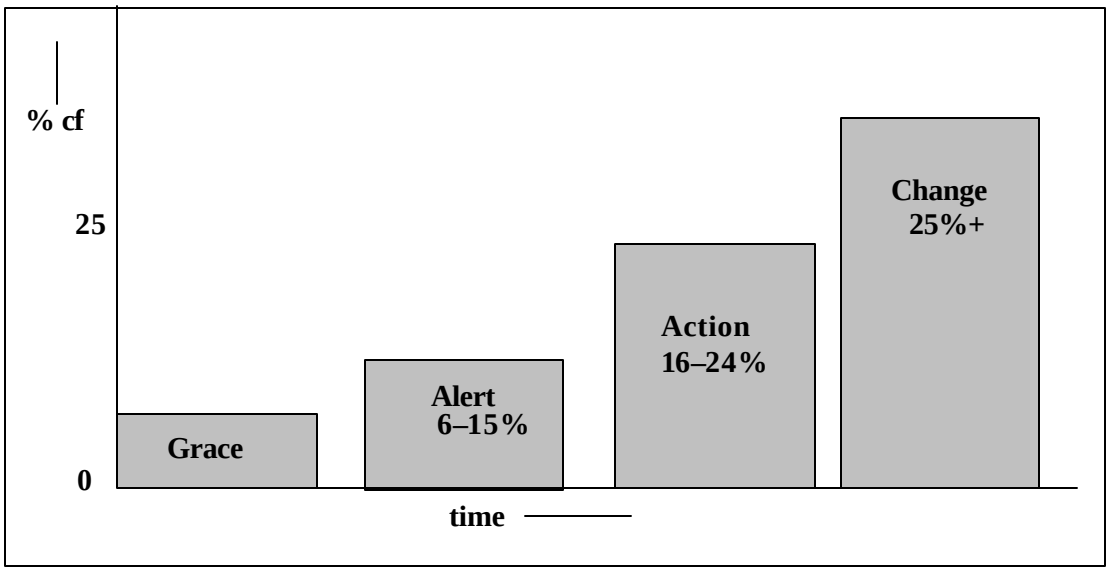
Since 1995, WHO has been building capacity in therapeutic efficacy tests of antimalarial drugs using these standardized guidelines. Data have been generated from 30 ministries of health in Africa and have been collated in a database in the WHO Regional Office for Africa (AFRO). Further development of networks and use of protocol will assist in the dissemination of standardized data from neighbouring countries in order to review national antimalarial drug policies. The database will provide information on resistance trends in Africa.

There is no fixed point of the proportion of clinical failures to the currently used first-line antimalarial beyond which change is necessary. The decision will be country-based, and the speed of change will depend on several complementing factors and conditions: the level and geographical distribution of clinical failure rate, the effect of failure rate on morbidity and mortality as well as the availability of acceptable, affordable and effective alternative drugs. A workshop to devise a Framework for Antimalarial Drug Policies in Africa held in Harare in May 1999 proposed that dynamic change could be analysed according to the rate of clinical failure (Figure 5). This may provide the reference points for different levels of action and may change depending on the useful therapeutic life and cost of the alternative antimalarial drug.

Countries will have to identify their situation as regards the antimalarial drug treatment failure rates. The situation can be classified as *grace period, alert period, action period* and *period of change*. At all stages, policy makers should be informed as to the relevance of available information.

The grace period is when drug efficacy is 95% and above. In other words, it is the early period of the introduction of an antimalarial when levels of drug resistance are low and drug failure rate is less than or equal to 5%. During this period, countries have time for building consensus, conducting a wide range of research studies of the epidemiological, social, cultural, parasitological situation and health systems analysis, without urgency. This period should establish reliable mechanisms for data collection and analysis. Quality baseline data and the trends of drug efficacy should be determined.

Figure 5: **Stages of analysis and update of antimalarial drug policy based on clinical failure rate (% cf) of first-line therapy**



In the alert period, when the treatment failure rates are between 6 and 15%, mechanisms for the process of change should be set and discussions on the rate of change of drug efficacy to the first-line drug initiated. The discussions should include forecast of when to expect intolerable rates and when to implement change. Relevant information should be collected and provided for the discussions, and there should be sensitization on the expected adverse effects of increased drug resistance. Assessment of the available options should be undertaken, and relevant strategies for meeting the challenges should be developed in anticipation of a worsening situation. This will ensure that there are no unnecessary delays in the proc ess at the time when action for change is required.

During the action period, the treatment failure rate range is 16&24%. At this stage, action for change should take place based on the strategies already set. Important information will include countrywide ascertainment of the level and consequence of treatment failure as reflected by severity of disease and mortality, available alternatives, cost and cost-effectiveness of alternatives and channels of distribution. It will provide for a timely plan for intervention such that at the time when parasitic resistance to the first-line drug is intolerable, updating and impleme nting the policy can be instituted in the shortest period possible. Such timely intervention will minimize the unnecessary suffering and loss of life that could happen due to delays in change of policy.

When the rate of treatment failure has reached 25% or above, consensus for change must be reached so that change is made within the shortest period possible. There may be no fixed point of change as it will depend on many factors. The levels stated here are arbitrary and are meant to sensitize countries on the need for continuous monitoring and consensus building in the process leading to change. One area for further research should be to define what proportion of clinical failures as measured using antimalarial drug efficacy monitoring is responsible for significant malaria-related mortality.

In view of the lack of haematological response associated with early and late treatment failures the WHO *Therapeutic Efficacy Tests for Uncomplicated Malaria in Areas of Intense Transmission* (7) recommends that haemoglobin should be measured. The failure to produce an effective haematological response should also be considered when updating antimalarial drug policy. Several recent studies have demonstrated the relationship between increasing levels of resistance to antimalarial drugs and anaemia. This makes it important for investigators to regularly monitor the levels of anaemia in their subjects during efficacy tests. This may prove to be an important, additional data source.

Since decisions will be influenced by the results of the drug efficacy studies, the representativeness of the choice of sites and population for drug efficacy monitoring is very important. Currently, drug efficacy tests are conducted on the most vulnerable group, which in areas of stable malaria includes children below the age of five years with clinical illness. This group provides information on the efficacy of the drug in those with little natural immunity and at greatest risk of treatment failure. It does not therefore translate to adults with developed immunity, who may be able to use a sub-optimally effective drug in conjunction with their own immunity to combat disease. Similarly, pregnant women may have a different therapeutic response from children and other adults.

Significant heterogeneity in the therapeutic response to first-line antimalarial drugs may exist in different geographical localities and regions of a country. Treatment policies in Africa have already attempted to differentiate between localities with varying drug resistance. In Botswana, for example, selected districts changed first-line antimalarial treatment from chloroquine to SP before a national decision was made a few years later. Such decisions depend on whether countries are able to implement different drug policies for different regions and whether the health system can deliver the drug successfully to end users. As the available drugs become more expensive or less safe, dual policies for vulnerable and less vulnerable groups may need to be considered.

2.3.4 Evidence from new drugs, strategies and approaches

The increase in malaria-associated morbidity and mortality, consumer and provider dissatisfaction with current antimalarial drug policy and evidence from therapeutic efficacy tests explain why there is a need for new solutions. In addition, new knowledge from research (biological and social science) and practice is constantly leading to new ideas and technologies. There are new drugs being developed, and strategies define better ways of using available drugs and minimizing development of resistance. There are new approaches for delivering health care.

Despite limited drug industry investments (due to the prospect of limited commercial returns), new drugs have been developed which are considered more effective, safer and more affordable than existing drugs. In order to ensure further resources for developing antimalarial drugs, a new partnership, called Medicines for Malaria Venture, between international organizations (including WHO and World Bank) and the pharmaceutical industry has been established.

In the development of new drugs, appropriate parallel thinking should focus on maximizing the utility of the drug and recognizing how the drug is used. Once a new drug is developed, a further challenge is how to introduce it into policy. If the newly developed drug is demonstrated as superior to the existing recommended drugs, the investment in changing policy (including the attitudes and beliefs of consumers and providers) should be balanced against the relative benefit of the new drug. This too applies to new strategies. The strategy needs to be demonstrated as having a comparative advantage (theoretically and practically) over the existing approach and valued by those involved in decision making. But even then, the complex process of decision making does not lend itself to immediate change.

2.4 Standardization and Validation of Results

Requirements for standardization and validation are discussed below. They consider the process of data collection as well as quality of data.

Standardization of the methods and processes of data collection within a country is necessary for consistency and interpretation of data. Utilization of the same method to assess efficacy of a drug has the advantage of allowing a country to have a long-term scientific perspective of the evolution of resistance to a particular drug and possibly the rate of change of resistance to the drug. Standard methods for measuring the efficacy of antimalarials have been developed by WHO and are being used within the region. This will enable easy data comparison within a country and between countries. A database of results from drug efficacy monitoring has been developed in AFRO, with assistance from partners, to facilitate international information exchange and comparisons.

While it is important that standard methods should be used for measuring efficacy, it is equally important to validate data that are being collected for the purpose of evaluating an antimalarial drug policy. Two levels of validation are suggested. The first is internal validation involving national experts within the country. In order to ensure that similar standards are kept in the region, the WHO is proposing a process of external validation by a network of experts. In addition to the validation of data, there should be validation of methods, interpretation, statistics and the entire process involved in data collection and analysis.

A process of supervision has to be in place in any routine programme in order to ensure that standards are met during the process of implementation. In order to facilitate the process of supervision of data collection, WHO is developing tools that would accompany the current tools for data collection. Supervision and monitoring will be standardized from one site to the other, and between countries. Data from such supervisory visits will be utilized to improve the current tools for monitoring drug efficacy.

Collection of additional information (e.g. related to social science) to assist with policy development may not need to be standardized, yet methods should be applied that ensure the quality and validity of the data. Some tools have been developed and are awaiting publication.

2.5 Decision-making

Decision-making is a complex and dynamic process involving many agendas and interests (Box 6). There is need for clear recognition of the problem of drug resistance and understanding of the options available. These should be articulated to decision makers who create the political will for policy-making.

It is essential that those involved with the control of malaria provide a clear technical appraisal of the existing situation of malaria control, the implication of resistance to the disease burden and the socioeconomic status of the country, community, household and individual. Options should be based on best evidence.

Box 6: Requirements for decision-making

- sufficient evidence to define and develop consensus on the local problem and best solution (there is a need for comprehensive scientific research, including drug efficacy studies, that is representative of the local population, social science and health systems research);
- communication between researchers (national and international), national programmes and implementers;
- information gathered from monitoring and evaluation of existing national policy and policies of neighbouring countries;
- problems and solutions articulated clearly to decision makers, focussing on consequential morbidity, mortality, economic implications and available options;
- analysis of priorities, interests and agenda of the decision-makers and other stakeholders.

Decisions will be made or not made depending upon the political climate. An analysis of the stakeholders should identify the relative potential *influence* of the stakeholders and the *importance* of the policy change to each of them. This should also identify barriers to decision-making, areas of agreement and contention, and how to capture the interest of policy-makers in the issue of antimalarial drug policy. Lessons learned from countries that have gone through the process appear in Annex 1.

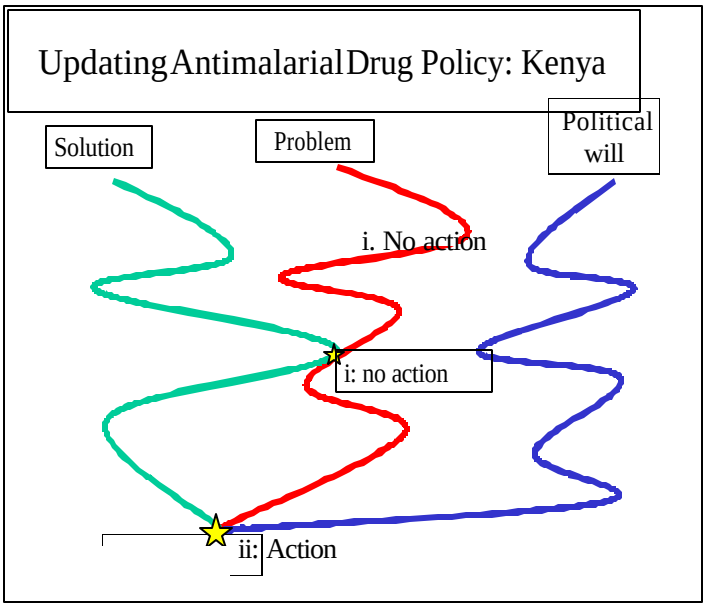
This process of political analysis will also form an initial step in the development of consensus between decision-makers and implementers. The malaria programme should devise a good strategy for dissemination of targeted information, creating a two-way process, in order to achieve consensus and trigger appropriate action. Scenario development is one way to analyse the options and decide which is considered most appropriate. The process of consensus should include consultation and negotiation with policy-makers, Ministry of Health officials at the level of implementation, such as programme managers and other control people, educators from both the Ministry of Health and Ministry of Education, other health professionals, private providers, industry, donors and the community.

The importance of ensuring appropriate political support for a technical argument is emphasized using a model of the multiple streams and policy-making to examine two country examples. A problem may exist without a clear solution being

identified and hence no action can be taken to address it. Even if the solution to the problem is identified (problem stream and solution stream approximate), there is a need to clearly define the problem to the decision-makers and provide an appealing solution in order to achieve political will for change. When all three streams (problem, solution and political will) are similar, then appropriate action is taken.

An example is Kenya (Figure 6). In 1995, researchers suggested that the problem of chloroquine resistance had risen to a level that signalled a change in first-line therapy. A solution was proposed to change to an alternative drug (point i). However, the problem and solution were not articulated well enough to the appropriate decision-makers in order to advocate the change. Only when the problem and solution were recognized as important by the decision-makers was the policy updated (point ii).

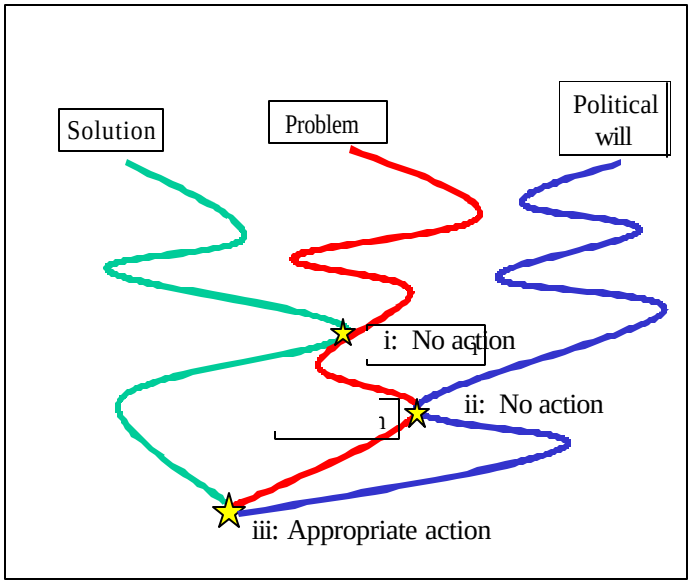
Figure 6: **Multiple streams and the updating of antimalarial drug policy in Kenya**



Another more complex example is that of Tanzania (Figure 7). In December 1997, the research community urged for a change in policy based on the significant evidence of resistance to chloroquine. The proposed solution was sulfadoxine-pyrimethamine (SP) (point i). However, at the time (point ii), there was no political will

for change. Over recent years, however, there has been a development in the political recognition of the implications of chloroquine resistance (point iii). There is now stronger political will for change. However, Tanzania, is now facing another difficulty, in that the solution is now less well defined. There is evidence that resistance is developing to the alternatives, and use of SP may lead to a reduced utility of future alternatives such as chlorproguanil-dapsone. Despite the difficult choice, a best solution based on best available evidence, recognizing the best and worst case scenarios is being developed in Tanzania. Methods are also necessary to understand the political environment in order to maintain the appropriate level of political will.

Figure 7: **Multiple streams and the updating of antimalarial drug policy in Tanzania**



3. IMPLEMENTING ANTIMALARIAL DRUG POLICY

Policy formulation and implementation form a continuous interactive loop (see Figure 4), requiring a constant process of advocacy, research and demonstration. The process of implementation requires careful planning and understanding of the contextual situation, the possible opportunities and constraints. The following section will provide steps for implementation, sharing experiences from Malawi and Kenya, two countries that have implemented a change in antimalarial drug policy.

The implementation of a revised antimalarial drug policy requires a framework

of political commitment, planning, mobilization of resources, coordination with donors, a regular budget and a sustainable programme.

Planning is an important component of all steps of implementation. The planning process should ensure inclusion of all key players and stakeholders. Planning should recognize all the stages of implementation: preparatory, transitional and maintenance. Each phase should have clear time lines, potential achievements within the phases and evaluation of contributions from those involved, recognizing their strengths and possible areas for collaboration. Planning should identify strategies which are appropriate within the context of the existing health delivery systems to maximize the use of available human and financial resources. Planned supervision, monitoring and evaluation should measure and encourage a rational approach.

The required steps recognized for implementing a revised policy appear in Box 7 and are discussed below. They were developed at a workshop in Mangochi, Malawi (1996).

Box 7: Steps in implementing an antimalarial drug policy

- Establish a multisectoral coordinating body for implementation
- Mobilize resources
- Regulatory control
- Develop and distribute guidelines
- Train health care workers
- Ensure adequate supplies of all necessary drugs to all levels
- Create public awareness and acceptance of the policy
- Define the responsibilities of health care at each level
- Monitoring and evaluation of the policy
- Quality control and continuous quality improvement
- Post implementation surveillance

3.1 Establish a Multisectoral Coordinating Body for Implementation

In some countries there already exists a multisectoral coordinating body for malaria control. In these cases, the coordinating body can assist the malaria control unit to bring together appropriate stakeholders in the policy decision to discuss antimalarial drug policy formulation, implementation and updating. If such a body does not exist, a

multisectoral coordinating body should be created and maintained. A possible list of participants is given in Box 8. This list is not exhaustive, and countries should draw up their own list to suit the local preferences and context.

Box 8: Participants suggested for a multisectoral coordinating body

Ministry of Health

- **$** Malaria control programme
- **$** Pharmacy unit of the Ministry of Health
- **$** Essential drugs programme
- **$** Health education unit of the Ministry of Health
- **$** Integrated Management of Childhood Illnesses unit
- **$** Medical Services Department of the Ministry of Health
- **$** Roll Back Malaria National Committee
- **$** Planning department of the Ministry of Health
- **$** Medical schools and other health training institutions

Health sector

- **$** Pharmaceutical companies
- **$** Private practitioners
- **$** Research institutions
- **$** NGOs, including other major health providers
- **$** Collaborating partners in health, including multilateral and bilateral organizations

Other sectors

- **$** Ministry of Finance
- **$** Parliamentarians
- **$** Consumer organizations/individual consumers
- **$** Local media

3.2 Mobilization of Resources

Before implementing the new policy it is essential to recognize sources of sustainable funding. Box 9 contains a few possible options for funding the implementation of the policy.

Box 9: Sources of funding

- $ Ministry of Finance
- $ Ministry of Health
- $ Developmental assistance partners
- $ Community and household resources
- $ Decentralized resources (provincial or district budgets)
- $ Private sector resources for marketing and training
- $ Drug companies
- $ Non governmental organizations
- $ Internal and external research resources

3.3 Regulatory Control

The Ministry of Health should ensure appropriate regulatory control. This should include:

- Drug control (quality, security, storage, import restrictions, manufacturing regulations)
- Registration
- Prescription regulations
- Regulations related to procurement, distribution, pricing, taxation and scheduling of drugs (levels at which the drug can be dispensed).

The level of use of the antimalarial drug should be carefully analysed, recognizing the need for access to safe effective drugs by those who need them. Efforts should be made to restrict the use solely to those who need them.

A strategy should be developed to bring about necessary regulatory and legislative changes to support the policy. In certain circumstances, relevant parliamentary legislation may need to be amended to support the new policy implementation. A pharmaceutical inspectorate should ensure compliance with the laws and regulations regarding importation, distribution, storage and dispensing.

Quality of the antimalarial drugs not produced in the country (imported) should be assured by centres for quality assurance of the pharmaceuticals, although simple tests can be undertaken by national laboratories and institutes. The centres for quality assurance are set up to support regulatory authorities to deliver high standard quality drugs. However, few countries in Africa are able to provide the adequate human and

financial resources to sustain such an approach. WHO has provided input to strengthen four national laboratories to support countries in the Region. Box 10 provides the addresses of the four Regional Drug Quality Control Laboratories (RDQCLs). In addition, the Centre for Quality Assurance of Medicines (CENQAM), Potchefstroon, South Africa, is a WHO Collaborating Centre for the Quality Assurance of Medicines. Countries can request the service of these laboratories for assessing drug quality and validating their own standard of quality assurance of drug testing.

Box 10: Regional Drug Quality Control Laboratories (RDQCLs)

- Zimbabwe Regional Drug Control Laboratory, Harare, Zimbabwe
- National Laboratory of Public Health, Niamey, Niger
- National Laboratory for Quality Control of Medicines, Yaounde, Cameroon
- Ghana Standards Board Sub Regional Drug Quality Control Laboratory, Accra, Ghana

3.4 Develop and Distribute Guidelines

Treatment guidelines and formulary manuals should be created and formatted to suit the different levels of health care with the help of many interested partners, including the health education unit, researchers (including social scientists), technical agencies, private sector, implementers, senior health care workers, pharmacists, other technical programmes and approaches (such as IMCI, PHC, Reproductive Health). The recommendations should be fully integrated into existing programmes and approaches. Appropriately tailored training (see Section 3.5 below) should accompany distribution, preferably integrated with existing channels of health care training.

Other existing methods of information dissemination, such as those used by the Essential Drugs Programme, should be utilized to inform health care workers of the change in policy. For example, in Kenya an update of the clinical guidelines has come at an opportune time as the new policy can be incorporated into the guidelines. Other sources of information dissemination may include handbooks, posters and wall charts. In some countries, drug bulletins can provide up-to-date information for health care workers. Professional associations, such as private practitioners associations, are another useful channel of information dissemination.

The guidelines should clearly articulate the recommended dosage regimens, preferably for weight and age. These recommendations should be based on best available evidence on efficacy and toxicity.

3.5 Training of Health Care Workers

Refresher courses for health care workers should accompany the dissemination of the new information allowing the health care workers to fully comprehend the change. All providers of health care and dispensers of drugs should be targeted: pre-service and in-service trainees, employees in the public and private sector, shopkeepers, drug vendors and traditional healers.

The level of health worker to which information will be targeted will depend on the scheduling of the drugs and the levels at which the different drugs can be dispensed. As with the guidelines, the tools used should be modified to suit the audience to be trained. Partners already involved in training should be requested to assist with the process. It should be integrated into ongoing and established in-service training programmes. For example, approaches such as IMCI should be involved in the policy dialogue in order to ensure consistency of information and beneficiary training expertise and structures. The IMCI approach also recognizes the importance of access to essential drugs and optimal use of such drugs. As an essential component of the IMCI consultation, providers are trained to improve consumer compliance with dispensed drugs. Training of other health providers, such as shopkeepers in Kenya, has been shown to improve the use of drugs by consumers.

As available drugs become more expensive and have more side effects, methods to improve diagnosis by clinical and laboratory techniques should be devised. Based on the cost and predictive value of such tools, programme guidelines should state where and when to use them and how best to incorporate them into routine practice.

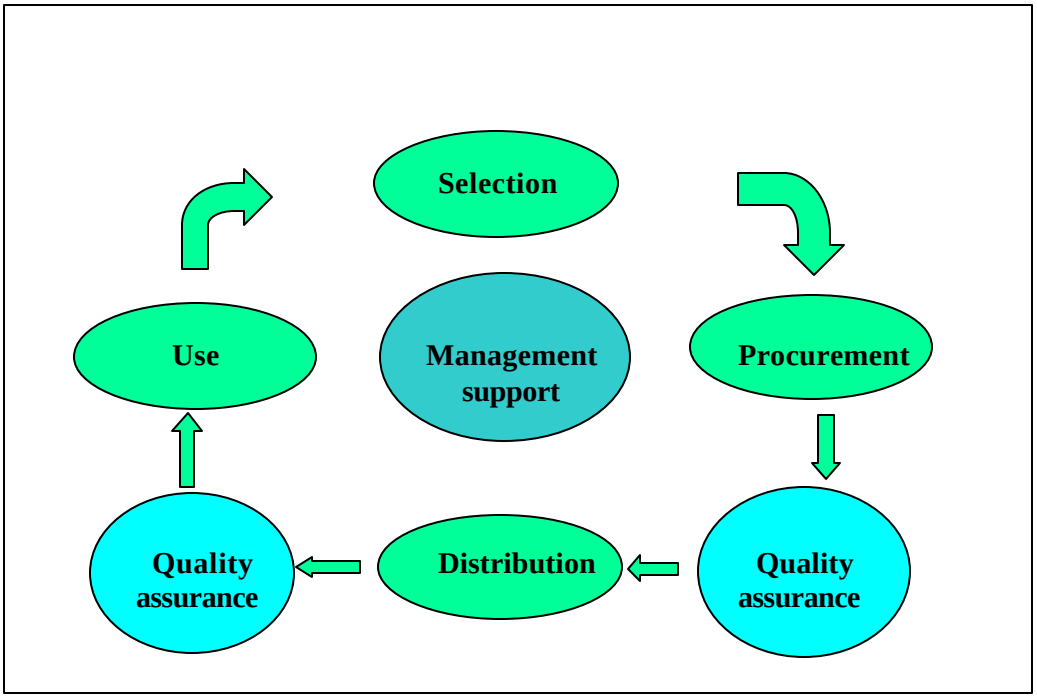
3.6 Ensure Adequate Supplies of All Necessary Drugs to All Levels

Ensuring adequate supplies requires an effective method of national procurement and distribution. The initial step will be to quantify the drug need. Simple methods should be developed to estimate drug need using routine data or other methods. Availability of drugs should be maintained and monitored through supervision. Ideally, the antimalarial drug policy will be an integral part of the National Drug Policy and hence the availability of antimalarials will be part of the comprehensive procurement and distribution of essential drugs. In some countries, such as Tanzania, the content of drug kits is determined for a defined period of time. Therefore, the responsible body for defining the content of the kits should be informed of any policy change well in advance of the implementation of the policy, as it will take at least 18 months to change the content of the drug kits. Methods should also be developed on how to deal with the stock of antimalarial drugs previously recommended. This should involve planning of how to maintain an adequate stock of

the original drug until such time that it has been agreed to change and there is sufficient quantities of replacement drug.

Roll Back Malaria has set up a technical working group to address issues of access and quality of antimalarials. The drug management cycle is given in Figure 8.

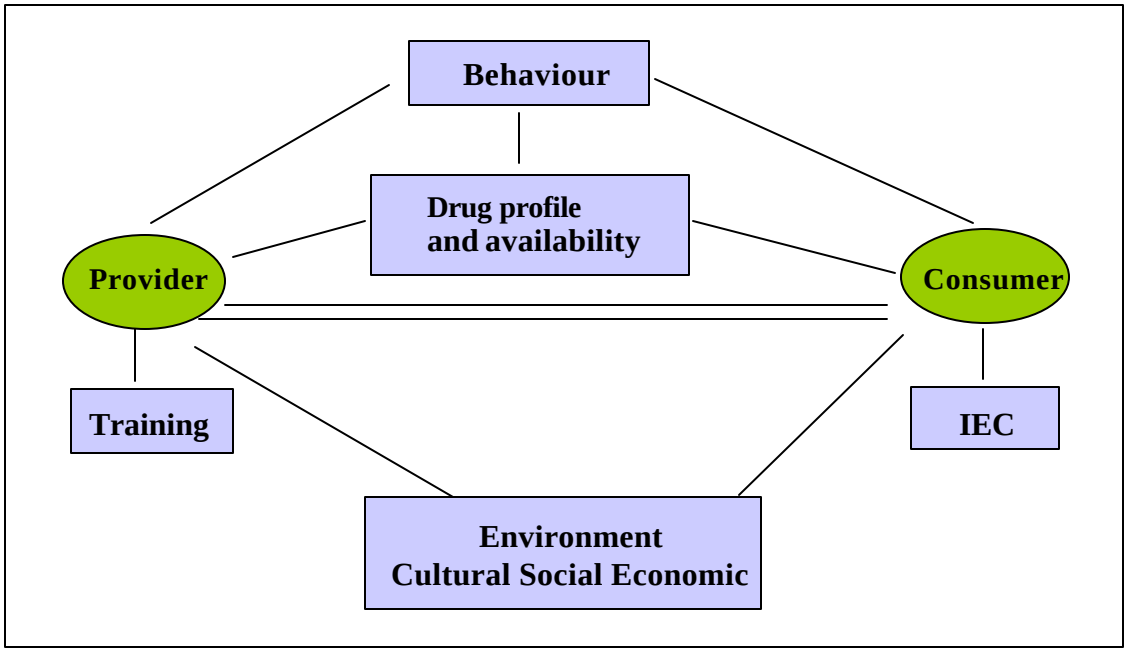
Figure 8: **Drug management cycle**



3.7 Create Public Awareness and Acceptance of the Policy

It should be recognized that illness classification is dynamic and responsive to new ideas (16). Clear information, education and communication (IEC) messages can be developed and transmitted to the public through various channels. The use of eminent public and political figures and high profile launches provide support. The private sector can be involved through social marketing and other channels (Figure 9). Existing channels of community communication should be used such as religious organizations, NGOs, community leaders and other social structures. The messages should promote appropriate use of antimalarials through clear, concise and culturally appropriate messages. Research continues about the benefits of prepackaging of antimalarials to improve patient compliance and use.

Figure 9: **Factors influencing health seeking behaviour and use of drugs**



3.8 Define the Responsibilities of Health Care at Each Level

The different structures of health care within different countries will dictate the responsibility at each level of care. This will require an assessment of the capacity at that level, existing health systems and available resources.

4. MONITORING AND EVALUATION OF DRUG POLICY

There is a need to maintain a method of continued monitoring of the efficacy of the present therapy and alternatives, preferably at the sites used for initial testing. There should be monitoring of the availability, acceptability and affordability of effective drugs to the consumer. Through methods of social research, ranging from focus groups to interviews, consumers use of antimalarial drug therapy, health seeking behaviour, incentives for making their choice of therapy and compliance with recommendations can be elicited. The provider's opinion and adherence to the policy and quality of care should also be followed up.

Appropriate surveillance systems should be devised for monitoring adverse drug reactions (ADR). Such a system will address the issue that adverse effects and tolerance of the drug may compromise disease management by altering the provider and

consumer confidence and compliance. In addition, the proportion of severe and life threatening events may influence whether the drug is appropriate for first-line therapy.

The impact of the change needs to be assessed using appropriate indicators in order to assist national policy-makers to review the policy and for countries within the region to assess the value of changing antimalarial drug policy. In addition, indicators for assessing the cost of not changing policy at an appropriate time should be developed in order to influence change.

5. CONCLUSIONS

The process of drug resistance development is dynamic and evolves with time, offering the opportunity for monitoring and timely planning for change. Consequently, the process of developing, implementing and evaluating a national antimalarial drug policy is also dynamic, and activities undertaken in this process are based on the rate of development of drug resistance. Monitoring the effectiveness of an established drug policy is therefore a necessary component of the process leading to policy change, which has to be dynamic and inclusive of all partners and stakeholders. If an appropriate and functional monitoring system is put in place, it should be possible to avoid emergency situations and indecision which can be costly in terms of unnecessary suffering, inadequate treatment, added financial burden, visits, admissions and deaths.

Routine surveillance systems will have to incorporate clear ways of detecting the increase in drug resistance, and maintenance of national and regional drug monitoring systems are essential to complement these activities.

Minimum essential criteria for change must be established in order to provide for quick informed action. The level of resistance, purchasing and distribution costs of drugs as well as efficacy and safety can be considered as essential and minimum information to convince policy-makers. In the selection and supply of appropriate antimalarials, cost of drugs will be critical as those who need the drugs (such as rural children and pregnant women) cannot afford the high cost of new drugs. Innovative public and private collaboration will be needed to ensure wider, equitable and sustainable distribution of new antimalarials.

A national malaria control strategy requires national and district health systems to operate well, and human and financial resources are required to face the challenge posed by drug resistance. Regular consultations between policy- and decision-makers, malaria control people, national essential drug programme people and suppliers, researchers and the donor community will be needed and must be clearly stipulated in the national plans. Timeliness of decisions at national and district level are critical to implement change without undue delays which will be costly in terms of preventable deaths.

REFERENCES

1. WHO (2000). Roll Back Malaria in the African Region: A framework for implementation. WHO/AFRO AFR/RC50/12.

2. Sachs J (2000). Economic analyses indicate that the burden of malaria is great. Paper presented at the African Summit on Roll Back Malaria, Abuja, Nigeria.

3. Fogh S, Jepsen S & Effersoe P (1979). Chloroquine resistant *Plasmodium falciparum* malaria in Kenya. **Transactions of the Royal Society of Tropical Medicine and Hygiene 73: 228&229**.

4. Greenberg AE, Ntumbanzondo M, Ntula N, Mawa L, Howel J & Davachi F (1989). Hospital-based surveillance of malaria-related paediatric morbidity and mortality in Kinshasa, Zaire. **Bulletin of the World Health Organization 67: 189&196**.

5. Sowunmi A, Walker O, & Salako LA (1993). Cerebral malaria in non-paediatric subjects resident in southwestern Nigeria. **African Journal of Medical Sciences 22: 49&53**.

6. Trape JF, Pison G, Preziosi MP, Enel C, Desgrees du Lou A, Delaunay V, Samb B, Lagarde E, Molez JF, & Simondou F (1998). Impact of chloroquine resistance on malaria mortality. **C R Acad Sci III 321: 689&697.**

7. WHO (1994). Strategies d'utilisation des antipaludiques: Besoins de donnes, traitement du paludisme non complique et prise en charge du paludisme pendant la grosses. Rapport d'une consultation informelle. **WHO/MAL/94.1070.**

8. Bloland PB, Lackritz EM, Kazembe PN, Were JB, Steketee R & Campbell CC (1993). Beyond chloroquine: implications of drug resistance for evaluation of malaria therapy efficacy and treatment policy in Africa. **Journal of Infectious Diseases 167: 932&937.**

9. WHO/AFRO (1999). A Practical Handbook for Antimalarial Drug Therapeutic Efficacy Testing for the District Health Worker.

10. Foster S & Phillips M (1998). Economics and its contribution to the fight against malaria. **Annals of Tropical Medicine and Parasitology 92: 391&398**.

11. Sudre P, Breman PF, McFarland D & Koplan JP (1992). Treatment of chloroquine-resistant malaria in African children: a cost-effectiveness analysis. **International Journal of Epidemiology 21: 146&154.**

12. Schapira A, Beales PF & Halloran ME (1993). Living with drug-resistance. **Parasitology Today 9: 168&174.**

13. Goodman C, Coleman P & Mills A (1999). Using cost-effectiveness analysis as a tool for informing malaria drug policy. **London School of Hygiene and Tropical Medicine.**

14. Goodman C, Coleman P & Mills A. Cost-effectiveness of malaria control in sub-Saharan Africa. **Lancet (in press).**

15. Phillips M & Phillips-Howard PA (1996). Economic implications of resistance to antimalarial drugs. **Pharmacoeconomics 10: 225&238.**

16. Williams HA, Kachur SP, Nalwamba NC, Hightower A, Simoonga C & Mphande PC (1999). A community perspective on the efficacy of malaria treatment options for children in Lundazi district, Zambia. **Tropical Medicine and International Health 4: 641&652.**

ANNEX 1

NEW EMPHASES IN MALARIA DRUG POLICY

1. MALAWI

Malawi initiated review of national antimalarial drug policy in 1990 with a series of drug efficacy studies in various parts of the country. A decision to change was made based on the evidence from efficacy studies, consumer and provider dissatisfaction, and capacity to change. In 1993, change was officially launched where sulfadoxine-pyrimethamine (SP) replaced chloroquine as the first-line drug for treatment of uncomplicated malaria.

Lessons learned are as follows:

(a) time-frame from taking the decision to implementing updated policy was about 12 months;

(b) advocacy, public campaigns, development and distribution of treatment guidelines were done in advance of public pronouncement of change;

(c) mechanisms for sustained procurement of SP and withdrawal of chloroquine were put in place;

(d) acceptability of SP as a new first-line drug for malaria by clients (particularly adults) and health workers was a problem in the early stages as SP did not appear to provide immediate relief to signs and symptoms of the disease;

(e) despite review of legislation and regulations on chloroquine, limited stocks of the drug are still available in shops;

(f) monitoring and evaluation of policy was not very well conceptualized at the time of change. As a result, lessons learned have not been properly documented. Although there has been continued monitoring of efficacy of present therapy at sentinel sites, appropriate surveillance systems for adverse reactions, compliance on use by providers and clients, and impact of policy change on mortality and morbidity do not seem to have been properly instituted.

Annex 1

2. KENYA

Updating of antimalarial drug policy in Kenya started in 1995 when the research community suggested that the problem of chloroquine resistance had risen to a level that signalled a change in first-line therapy. This was mainly based on results from antimalarial drug efficacy studies done in some parts of the country. A solution was proposed to change to an alternative drug. However, the problem and solution were not articulated well enough to the appropriate decision-makers in order to advocate the change. Only when the problem and solution were recognized as important by all stakeholders and decision-makers was the policy reviewed in 1997, changing the first-line drug from chloroquine to SP.

The lessons learned are:

(a) review of drug policy is not the domain of researchers alone; other stakeholders need to be identified and involved in the decision-making process;

(b) scientific information needs to be packaged in a manner that is easily understood by policy-makers so as to enhance decision-making;

(c) clear analysis of who the decision-makers are, and what their priorities, interests and agendas are is crucial;

(d) research and not practice should drive policy;

(e) mechanisms for monitoring and evaluating policy change are not well documented.

3. TANZANIA

In 1997, researchers in Tanzania urged for change in policy based on significant evidence of resistance to chloroquine. The proposed solution was SP. However, at that point in time there was no political will for change. Over two years later, there was a growing political recognition of the implications of chloroquine resistance. By 1999, there was stronger will to change the first-line drug. However, Tanzania by then was already facing another difficulty in that the proposed solution was no longer robust or useful as resistance to SP was increasingly reported. In August 1999, a national consensus meeting made a decision based on available evidence and recognizing the best and worst case scenarios. It was decided to replace chloroquine with SP.

Annex 1

The lessons learned are:

(a) methods are necessary to understand the political environment in order to maintain the appropriate level of political will;

(b) the longer it takes to make a decision, the more likely that the proposed solution may no longer be valid or useful;

(c) regular dialogue and consultation among researchers, clinicians and policy-makers facilitates decision-making.