

# **Artemisinin-based Combination Therapy in Zambia:** **From Policy Change to Implementation**

## *Authors:*

- Caesar Mudondo, Pharmaceutical Consultant, Unicare Pharmaceuticals, Lusaka, Zambia
- Pascalina Chanda, Operations Research Officer, National Malaria Control Centre, Lusaka, Zambia
- Micky Ndhlovu, Lecturer, Chainama Hills College of Health Sciences, Lusaka, Zambia
- Pauline Wamulume, Communications Specialist, National Malaria Control Centre, Lusaka, Zambia

<b><u>TABLE OF CONTENTS:</u></b>	<b>page</b>
<b>ACKNOWLEDGEMENTS</b>	3
<b>1. INTRODUCTION</b>	3
1.1 Background	3
1.2. Structure of the health delivery system in Zambia	5
<b>2. POLICY CHANGE</b>	5
2.1. WHO Guidance on Treatment Policy Change	6
2.2. Zambia Policy Change Process	7
<b>3. POLICY OPTIONS</b>	7
3.1. Uncomplicated malaria	7
3.2. Complicated and severe malaria	11
3.3. Malaria in pregnancy	11
3.4. Chemoprophylaxis	11
3.5. Policy Process	12
<b>4. IMPLEMENTATION OF NEW POLICY</b>	13
4.1. Implementation strategy	13
4.2. Implementation Plan	15
4.3. Policy implementation	20
<u>4.3.1. Phase I</u>	20
<u>4.3.2. Phase II</u>	25
<u>4.3.3. Phase III</u>	31
<b>5. CONCLUSIONS</b>	37
5.1. Achievements	37
5.2. Failures	37
5.3. Key recommendations	38
<b>6. REFERENCES</b>	40

## **ACKNOWLEDGEMENTS**

The authors are grateful to the following without whose support the paper would have been difficult to complete:

- 1) Dr. Naawa Sipilanyambe for allowing the authors access to data available at NMCC
- 2) Messrs Kapelwa, Nkunika and Moonga of NMCC for their input on the aspects relating to laboratory diagnosis
- 3) Marthe Everarde and Richard Laing of WHO for reviewing the initial draft and their valuable recommendations
- 4) Mr. B. Chita of CBoH for providing useful comments on economic aspects
- 5) Department of Meteorology, Lusaka, Zambia for providing data on climatic conditions in Zambia

## **1. INTRODUCTION**

### **1.1 Background**

Zambia is a southern African country with a population of 10.6 million people. The country is subdivided into 9 provincial regions and a total of 72 administrative districts. The climate is mostly warm with hot season temperatures reaching up to 30°C and cold season temperatures of about 10°C. The rainy season runs from October to April and the rest are dry months<sup>1</sup>. The health system in Zambia is largely government-financed with a few privately owned facilities<sup>2</sup>. In addition, substantial numbers of patients receive treatment through the private sector. There is however no readily available data on the actual figures on the utilisation of both the formal and informal private sector.

Malaria in Zambia is a disease of major public health significance. It is responsible for approximately 50,000 deaths and over 4 million clinical cases in the public sector annually<sup>3</sup>. It is endemic in all the nine provinces with levels of endemicity ranging

from holo- to hyper- endemic, depending on the climatic and geographical characteristics of the area<sup>4</sup>. There is some variation in the transmission rate from one season to another and from one geographical setting to another. The peak transmission season coincides with the onset of high rainfall. However, no part of Zambia at any time of the year can be considered to be free from malaria.

The predominant parasite is *Plasmodium falciparum*, the most deadly form of malaria particularly for young children, adults who are infrequently exposed and pregnant women<sup>5</sup>. The species accounts for 95% of the malaria cases and is the most fatal of the four human plasmids<sup>6</sup>. The vector species present in the country are mostly the *Anopheles gambiae* complex and *Anopheles funestus* complex<sup>7</sup>. These mosquitoes are known to be efficient at transmitting the malaria parasites in the population.

Public sector records show rising trends in malaria morbidity and mortality. From 1976 through the early 1990's, public sector Out Patient Department (OPD) visits rose from 122 to over 300 per 1000 population per year<sup>8,9</sup>. In addition, substantial numbers of patients receive treatment through the private sector. Health centre records show that one in every five Zambian children dies of malaria before the fifth birthday<sup>10</sup>.

Malaria accounts for about 40% of all under-5 deaths in the country<sup>8</sup>. For adults, malaria is the most common cause of health centre visits. It is the contributing cause of about 20% of all pregnancy-related deaths in Zambia<sup>9</sup>.

The National Health Strategic Plan aims at reducing malaria morbidity and mortality by half by 2005<sup>11</sup>. Zambia also ascribes to the goals of the Roll Back Malaria (RBM) and the Abuja declaration by implementing interventions that are effective in controlling and preventing malaria. The strategies being implemented include: improving malaria case management, integrated vector management (Insecticide Treated Mosquito Nets, Indoor Residual Spraying, Environmental Management, etc.), Advocacy/Information Education and Communication (IEC), Surveillance, Research and Monitoring and Evaluation. This integrated approach is hoped to be scaled up to levels which will positively affect indicators for malaria control<sup>12</sup>.

Chloroquine has been the first line drug for treating uncomplicated malaria in Zambia for well over four decades. Parasite resistance to chloroquine in Zambia was first

documented in 1982<sup>13</sup>. In 2002, drug efficacy studies showed treatment failures as high 54% in certain parts of the country<sup>14</sup>. Health centre and hospital admissions have risen from 11.4% in 1982 to 39% in 1999/2000<sup>8</sup>. Treatment failure rates with chloroquine rose from zero in 1980 to an average of about 40% (range 24-52%) in 1999/2000<sup>15</sup>. Although the rates varied from region to region, all regions recorded levels of not less than 10%<sup>15</sup>.

## **1.2. Structure of the health delivery system in Zambia**

Malaria is the leading public health problem in Zambia. It is managed at various levels of the healthcare system. In the public sector, which is administered by the Ministry of Health (MOH), the Central Board of Health (CBoH) is responsible for the management of the hospitals, clinics and health centres under this sector. Community Health Workers (CHW's), who are largely community volunteers who have a task of providing very basic health service in their communities (especially in areas far away from the health and where there is a critical trained personnel shortage) are supervised by health centre personnel. Drugs for all diseases in the public sector are supplied to patients free of charge. The private sector, which comprises mine hospitals, private hospitals and clinics, pharmacies and other retail outlets, is under the charge of either individuals or corporate bodies. Mission hospitals, which provide a substantial proportion of health services in the rural areas, are managed by religious organisations.

Pharmaceutical and other medical supplies required by the public sector are procured by the MOH but are stored and distributed by Medical Stores Limited (MSL).

It was acknowledged that the new policy could not be implemented successfully if it did not embrace all the sectors in the healthcare system.

This paper is written for the purpose of documenting the process of changing the malaria treatment policy as experienced by the Zambian authorities. It is hoped that this experience may be of value to other countries intending to revise their policies.

## **2. POLICY CHANGE**

The Ministry of Health of Zambia, as a consequence of the increasing levels of resistance, deemed it necessary to re-consider the role of chloroquine in the management of malaria. The National Malaria Control Centre (NMCC), a department

of the CBoH, which is the operational arm of the Zambian Roll Back Malaria (RBM) programme, was given the responsibility to move the process.

The NMCC appointed a committee (the Case Management Working Group) to seek consensus and formulate a recommended policy for adoption by the relevant authorities. Several consultative meetings involving key stakeholders and local and international experts were held between 2000 and February 2002 to decide on a malaria treatment policy for Zambia. The invaluable contribution by experts from the World Health Organisation (WHO) deserves special commendation.

The NMCC, in collaboration with local research institutions and financial support from WHO and USAID/ARCH has since 1995 embarked on systematic sentinel site assessment and monitoring of the efficacy of antimalarials. The studies have been conducted in 11 sentinel sites located in all the nine provinces of Zambia and are representative of the epidemiological regions of the country. The data from these studies were provided to the committee charged with the responsibility of reviewing the malaria treatment policy.

The committee considered the resistance data available, potential interventions and other factors such as the availability of resources to implement a new policy and the ability of the country to sustain a change in the policy. The consequences of not taking any action were also considered.

### **2.1. WHO Guidance on Treatment Policy Change**

The WHO has recommended the following in considering the suitability of a first line drug for a significant public health problem like malaria<sup>16</sup>:

Alert phase - period when treatment failure rate with the first line drug is 6-15%.

During this phase mechanisms for change should be set in motion

Action phase – Treatment failure rate of 16-25%. Implementation of change should be commenced

Change phase – Over 25%. Change should have been made

WHO recommends that an effective malaria treatment policy should aim to:

- Reduce morbidity

- Halt the progression of uncomplicated disease to severe and potentially fatal disease, and thereby reduce malaria mortality
- Reduce the impact of placental malaria infection and malaria-associated anaemia through chemoprophylaxis or preventive intermittent treatment
- Minimise the development of anti-malarial drug resistance

The recommendations by WHO provided a useful guide to the review committee in making recommendations for the policy change in Zambia.

## **2.2. Zambia Policy Change Process**

Data available indicated chloroquine treatment failure rates in Zambia averaging about 40%<sup>15</sup>. Although there was some apprehension about the adequacy of the data available it was acknowledged that the treatment failure rates had far exceeded the WHO recommended guidelines for effecting a change in policy and therefore there was a need for change.

The committee was guided by the above aims in deciding on the policy options. It was decided that the morbidity and mortality due to malaria merited a revision of the treatment policy. The policy should address treatment for uncomplicated malaria, complicated and severe malaria, chemoprophylaxis and the management of malaria during pregnancy.

## **3. POLICY OPTIONS**

### **3.1. Uncomplicated malaria**

The drug(s) recommended as first line treatment for uncomplicated malaria in Zambia where malaria is endemic and home management is common should have the following properties:

- Good efficacy and safety profile
- High degree of acceptability and ease of administration
- Capable of being used in special groups e.g. pregnant women and infants
- Cost-effectiveness
- Little or no reported resistance or cross-resistance
- Useful therapeutic life

Since resistance to chloroquine was deemed to be unacceptably high, chloroquine was ruled out as an option for the drugs to be considered. The following options were considered:

- **Amodiaquine.** This drug had been in use in Zambia up to the mid-80's when the indication for treating malaria was withdrawn due to concerns about hepatotoxicity and agranulocytosis<sup>17,18,19,20</sup>. These concerns were later found to be unfounded except in cases of prolonged use for prophylaxis. There is no resistance to amodiaquine reported to-date in Zambia. The WHO Expert Committee on Malaria at its nineteenth meeting concluded "amodiaquine could be used for treatment if the risk of infection outweighs the potential risk for adverse drug reactions"<sup>20</sup>. It was felt that a first line drug for treating uncomplicated malaria in Zambia is likely to be used, particularly at household level, several times a year. This frequency of use could be considered to be quite similar to prophylactic use. Further, amodiaquine is structurally closely related to chloroquine. The risk of cross-resistance therefore exists. For these reasons and also since it is a monotherapy amodiaquine was considered not to be a suitable first line drug for uncomplicated malaria.
- **Halofantrine.** The side effect profile of halofantrine was considered not good enough for a first line drug for malaria in Zambia, especially that there is substantial unsupervised use<sup>20</sup>.
- **Mefloquine.** Like halofantrine the side effect profile of mefloquine was considered not suitable for a first line drug for uncomplicated malaria<sup>20</sup>.
- **Sulfadoxine-pyrimethamine (SP).** At the time of taking the policy decision, drug efficacy studies indicated that SP was still an effective anti-malarial drug in Zambia<sup>15</sup>. SP has a good side effect profile and is easy to administer, being a single dose formulation<sup>20</sup>. Concern was raised about the absence of anti-pyretic and analgesic properties, as patient acceptability is reported to be adversely affected by this property. This problem would be addressed by recommending an appropriate dose of paracetamol or another suitable anti-pyretic and analgesic. Although SP appeared to meet most of the desired properties it was felt that, based on experiences elsewhere where it has been adopted as a first line drug, it would not provide a long enough

useful therapeutic life to justify the resources to be directed to the policy change. SP was, however, considered to be a good option for use in the Intermittent Presumptive Treatment (IPT) of pregnant women and as the first line drug in the interim period before the long-term first line drug is deployed. The interim period should be as short as possible.

- **Quinine.** Quinine is effective against malaria in Zambia and it is cost effective. However, as a first line drug for uncomplicated malaria it was not considered suitable because it has an unfavourable side effect profile and it is not easy to administer. Further, it has been proven to be effective for treating severe malaria. It was therefore felt that it would be better reserved for treatment of severe malaria and in situations where there was failure or contraindication with the first line drug.
- **Artemisinin and its derivatives.** This group of drugs has been in use in Zambia, largely in the private sector, for a few years. Efficacy studies indicate high efficacy rates. Apart from the high cost of the drugs they meet all the required properties of a first line drug for uncomplicated malaria. Their gametocytocidal property has the added benefit of reducing transmission. However, recent thinking in the treatment of malaria and indeed other infections like TB and HIV/AIDS favours the use of combination therapy as a means of prolonging the useful therapeutic life of important drugs. It was therefore considered that monotherapy using this group of drugs should be discouraged at the outset and instead consider a suitable artemisinin-based combination therapy (ACT).

The criteria adopted by the committee for selecting the ACT included:

- a) Therapeutic efficacy of the combination
- b) Safety of the combination, especially in the high risk populations
- c) Potential for widespread use at all levels of the healthcare system, including home management
- d) Potential for patient compliance
- e) Cost effectiveness
- f) Potential to delay or prevent development of resistance
- g) Availability of the ACT

Combinations containing chloroquine would be unsuitable for Zambia due to the existing resistance to chloroquine<sup>5</sup>. Both components of the combination should be efficacious. Some SP resistance, as pointed out earlier, has been reported in Zambia and in some neighbouring countries. SP would also be used as the first line drug where the new first line drug had not been deployed. For these reasons it was thought unwise to consider a combination containing SP as a partner drug.

**Artemether with lumefantrine** was chosen as the most suitable combination. Efficacy studies done in Zambia show that it is highly efficacious and it has a good safety and tolerance profile<sup>21</sup>.

The fixed-dose formulation available promotes patient compliance as opposed to the co-administered formulations currently available for the other ACT's. There is no reported parasite resistance to either of the partner drugs in the combination in Zambia. The impressive performance of the combination in Kwazulu-Natal where it was deployed in 2000 had a positive influence on the decision<sup>22</sup>. The high cost of the combination and the contraindications in children less than 10kg and pregnant women are drawbacks with this combination. To address the drawbacks alternative drugs were recommended for use in children less than 10kg and in pregnant women. It was understood that the contraindications were to be reviewed as more information on the safety of the combination in these categories became available. The cost was considered to be a problem which had to be faced as it was important to recommend a drug which was expected to significantly impact on the disease burden rather than opt for a cheaper but less effective one.

The six-dose regimen, to be taken over three days, was chosen in preference to the four-dose regimen over two days. This was to ensure adequate treatment for non-immune populations (visitors, immunocompromised persons, young children etc) who are most vulnerable to malaria.

The recommended drug for children less than 10kg was SP and quinine for pregnant women. This recommendation would be reviewed as soon as more safety data was available on the use of artemether –lumefantrine in these population groups.

### **3.2. Complicated and severe malaria**

Quinine has been used for treating malaria in Zambia for several decades. It has been shown to be still effective in the treatment of severe malaria. It has a reasonable safety profile, if administered by trained personnel. The committee therefore recommended quinine as the drug of choice for treating severe malaria in all population groups

### **3.3. Malaria in pregnancy**

#### **IPT**

Malaria can be particularly dangerous to the woman and foetus during pregnancy<sup>23</sup>. It is suspected that a significant proportion of women attending antenatal clinic in Zambia carry some level of parasitaemia, even when asymptomatic. It was considered necessary to protect pregnant women from the serious effects of malaria by introducing IPT.

SP has been shown to be effective when given for this purpose to pregnant women in the second and third trimesters. It was decided to choose SP for IPT.

HIV/AIDS prevalence in levels in women attending antenatal clinics in Zambia is 19.1%<sup>24</sup>. Studies done in Kenya indicate that a three-dose IPT regimen is more effective than a two-dose regimen in pregnant women who are immunocompromised<sup>25</sup>. In order to provide adequate protection to all women, including those who are immunocompromised, the three-dose regimen was opted for. Most pregnant women (81% in 2000) in Zambia attend antenatal clinic at least once. Giving IPT during pregnancy is considered to be likely to provide protection to the majority of pregnant women in the country.

#### **Treatment**

Artemether-lumefantrine is currently not recommended for use during pregnancy<sup>26</sup>. SP is also contraindicated during the first trimester. Quinine was therefore chosen as the first line drug for uncomplicated malaria during the first trimester. SP was chosen as the first line drug for uncomplicated malaria during the second and third trimester.

### **3.4. Chemoprophylaxis**

Chemoprophylaxis is not recommended for indigenous Zambians normally resident in the country. This is to avoid compromising their semi-immune status against malaria. However, in indigenous populations who are immunocompromised chemoprophylaxis may be of benefit. The policy does not recommend specific chemo prophylactic

agents, on the advice of WHO. Visitors from different countries are advised to take a variety of agents for chemoprophylaxis. In case of a problem contrary advice given locally could result in litigation. However, chemoprophylaxis using a drug which is recommended for treatment of malaria is not encouraged.

### **3.5. Policy Process**

The committee's recommendations were presented to the Zambia National Formulary Committee (ZNFC) for endorsement. Once the recommendations were endorsed by the ZNFC the recommended drugs would be included on the Essential Drug List (EDL) and Zambia National Formulary (ZNF) and all the treatment guidelines in use in Zambia would be amended to reflect the recommended regimens. Consequently changes have accordingly been made to the EDL, Standard Treatment Guidelines and the Integrated Guidelines for Frontline Health Workers. Changes to the ZNF and other guidelines will be made when the documents are due for revision.

Normally, once the ZNFC endorses the changes these are then expected to be effected by the health facilities. However, malaria being such an important public health problem, endorsement by the government was considered to be necessary. The recommended policy was therefore submitted, through the Central Board of Health (CBoH), to the Zambian government for endorsement. A new policy was finally adopted in November 2002.

The policy statement is as follows:

#### **Uncomplicated malaria**

##### **1. First line treatment:**

- a). Artemether-lumefantrine, an artemisinin- based combination therapy, except for children weighing below 10kg and during pregnancy.
- b). Sulphadoxine-pyrimethamine for children below 10kg (until more information on the efficacy and safety of artemether-lumefantrine in this age group becomes available)

##### **2. Second line treatment:**

- a.) Quinine would be used in cases of failure to the first line drug in all age groups

### **Severe malaria**

Quinine is the drug of choice for the management of severe malaria for all age groups and all categories of patients

### **Malaria in Pregnancy**

#### **1). Uncomplicated malaria**

##### a.) First line treatment

i) Quinine during the first trimester of pregnancy

ii). Sulphadoxine-pyrimethamine (SP) in the second and third trimester of pregnancy

##### b). Second line treatment

i). Quinine would be used in all cases of failure to sulphadoxine-pyrimethamine

#### **2). Severe malaria**

Quinine is first line drug for management of severe malaria at all stages of pregnancy

#### **3). Intermittent Presumptive Treatment (IPT)**

Sulphadoxine-pyrimethamine would be used for IPT during the second and third trimesters of pregnancy. A maximum of three adult doses would be given at least one month apart

## **4. IMPLEMENTATION OF NEW POLICY**

### **4.1. Implementation strategy**

A number of decisions had to be taken with regard to the implementation of the policy. These included deciding on whether to implement the policy selectively (i.e. only in areas where resistance levels exceeded a certain threshold or nationally regardless of levels of resistance) and whether the change should be made at the same time throughout the country or in phases (district by district or province by province). A multidisciplinary team of experts was sent to Kwazulu-Natal in South Africa to study the implementation of the malaria policy introduced there in 2000. The lessons learnt were expected to be useful in drawing up an implementation strategy for Zambia<sup>22</sup>. WHO also provided technical support in the development and finalisation

of the drug policy implementation strategic framework. A meeting was held in November 2002 with the representatives of the pharmaceutical industry and medical practice to discuss the possible impact of policy change on these vital sectors<sup>27</sup>. It was decided that the policy should be implemented nationally rather than regionally but that the deployment of the recommended first line drug be done in phases. The districts where artemether-lumefantrine would be deployed later would in the interim period use SP as the first line drug for treating uncomplicated malaria. All sectors of the healthcare system would be involved in the implementation programme. The rationale behind the decision was:

- a) All parts of the country had unacceptably high levels of parasite resistance to chloroquine and change was necessary for the whole country
- b) There is uncontrolled movement of populations from one part of the country to another, regional implementation would require considerable resources for surveillance to monitor such movements and trends in resistance patterns
- c) Unlike South Africa where provinces manage their health systems autonomously, in the Zambian system all resources (procurement, distribution etc) are provided centrally and so it would be difficult to implement the policy for such a key disease regionally
- d) Phased implementation would provide useful lessons before rolling out to the rest of the country.

An NMCC Drug Transition Team (DTT) based at and supervised by the NMCC, was established to act as a secretariat for the implementation of the policy. The team was made up of a malariologist, a pharmacist and supporting administrative staff. The DTT would be responsible for planning and supervising and monitoring implementation of the new policy. The operational costs of running the DTT were funded by United States Agency for International Development (USAID)/Applied Research for Child Health (ARCH)

The DTT identified the following as key elements for the successful implementation of the policy:

- Policy dissemination

- Health worker competence vis-à-vis implementing new malaria management protocols
- Drug supply logistics
- Identifying and mobilising resource needs
- Co-ordination and harmonisation of various activities and programmes
- Appropriate regulatory provisions
- Monitoring and evaluation

Technical working groups encompassing the different strategies for malaria control provided guidance on various arms of the implementation of the policy e.g. advocacy/ IEC , research, case management, IVM, drug supply management etc. These groups comprised members from different professional and occupational settings e.g. academia, research, industry, communications media etc.

#### **4.2. Implementation Plan<sup>28</sup>**

The DTT formulated an implementation plan. The plan addressed the following key aspects:

- Policy dissemination:** The policy had to be disseminated to both the general public and the health workers. An official press release from the MOH would be necessary. Health worker training packages should include a detailed section explaining the rationale and other relevant issues concerning the policy change. Health workers should be the government's major mouthpieces on the policy. Appropriate Information Education and Communication (IEC) materials had to be developed and distributed as widely as possible. Public education was recognised as an important tool to empower patients with the knowledge to make informed decisions when seeking treatment for malaria. Media such as drama, radio programmes etc. would be useful in this regard. and TV, print media etc. were noted as some of the key tools for disseminating the policy change.
- Improving health worker competence:** Appropriate training packages had to be developed. All health workers should be oriented on the policy. It was important to ensure that they were familiar with the treatment protocols for the new policy. Appropriate training programmes had to be developed and adequate resources allocated for the purpose. Suitable facilitators had to be

identified and orientation provided to the facilitators. Treatment guidelines incorporating the new policy recommendation had to be developed and distributed.

c) **Drug supply logistics:** This was one of the most demanding of the challenges. It involved dealing with the following:

- **Commodity (drug) quantification:** Accurate estimates of needs had to be determined. This had to be done for all the recommended anti-malarials, including the requirements of SP for use in IPT. Quantification was done for artemether-lumefantrine, quinine tablets and injectable and SP. Quantification of artemether-lumefantrine was particularly challenging because of the weight-specific presentations in which it is supplied and deciding on the best method of quantification. The available past consumption data could not be relied upon because it related to chloroquine which had varying but significantly high treatment failure rates and may not have been accurate in any case, judging from the chloroquine stocks carried over by health facilities at the time of policy change. Estimates had to take into account the phased deployment of drugs and the variations in morbidity between the selected districts.
- **Procurement:** The procurement of quinine and SP was to be done using the normal channels. Artemether-lumefantrine is currently available from one source, Novartis. WHO has negotiated a special price of the Novartis brand, Coartem<sup>®</sup> for public sector use. WHO would procure on behalf of the Zambian government according to procedures laid down by WHO. Some of the conditions include; providing quarterly forecasts of requirements in weight-specific packs, providing a 16-week lead time for each order, full advance payment, timely clearance of consignments on receipt of goods, obtaining waivers on local taxes and duties where this applies and arranging for suitable storage facilities. The Global Fund TB, HIV/AIDS and Malaria (GFATM) were expected to fund the commodities. Orders had to be raised in good time to avoid bureaucratic delays. The delay in securing the Global Fund caused substantial delays in the

implementation of the policy since drugs were a very important factor in the process. Authority had to be obtained from the Zambia National Tender Board to waive the requirement to follow government tender procedures since the product was from a single source and WHO was the procurement agent. GFTAM requires quarterly forecasts to be submitted. This requirement makes it imperative for the user facilities to submit the returns timely otherwise the forecasts will be inaccurate. A two-year procurement forecast was submitted with the application for funding.

- **Storage:** WHO would clear the consignment on arrival in the country and MSL would collect and store until delivery up to district level. The district health office would be responsible for storage until delivery to the health office. Health centres should have adequate storage capacity for supplies to last a fixed, short period of time. The public sector presentation of Coartem<sup>®</sup> is quite bulky. This should be borne in mind when considering storage capacity.
- **Distribution:** Chloroquine and, later, SP were components of the health centre kits. Supplies of drugs to health centres were largely through drug kits containing pre-determined quantities of drugs and supplies essential for use at that level of care. Higher-level facilities were not supplied through kits. Distribution of Coartem<sup>®</sup> through the kit system was not going to be feasible, at least initially, for the following reasons:
  - i. The requirements of Coartem<sup>®</sup> varied widely from one district to another and health centre to health centre. The kit's content was standardised for the country.
  - ii. The effective maximum shelf life of Coartem<sup>®</sup> (considering the lead time and distribution logistics) at any health facility is unlikely to be more than 18 months. It is important to avoid large discrepancies between needs and supplies received; especially considering the cost of the drug
  - iii. Manufacturers of drug kits do not manufacture or supply Coartem<sup>®</sup>. They would have to obtain their supplies from

Novartis for incorporation into the kit. This could result in further delay.

- iv. More accurate estimates of needs of Coartem<sup>®</sup> at all levels have yet to be determined. Until then it would be advisable to adopt a more flexible approach to distribution- facilities should be able to easily shift supplies to where there is greater demand if need be.

A plan was made that Coartem<sup>®</sup> supplies would initially be allocated to the districts at the centre (CBoH), according to estimates, and MSL would deliver to the district health office. MSL routinely deliver supplies on a monthly basis. Allocation and delivery to the health centres would be done by the district health office. The district and provincial health offices would monitor monthly consumption by the health centres and move stocks accordingly. Further supplies would be made on order from the districts and be based on consumption. A database of consumption would be developed after six to twelve months of uninterrupted use. Higher-level facilities would initially be supplied with Coartem<sup>®</sup> by the district health office based on estimates done at the centre but subsequently they would be supplied on order. The system will be reviewed in due course to consider the feasibility of including Coartem<sup>®</sup> in the drug kits.

- **Fate of chloroquine:** It was established that there were substantial stocks of chloroquine in the health facilities. A decision had to be taken whether the stocks had to be withdrawn or allow the facilities to use up the stocks they had. It was decided, based on the estimated quantities being held by the facilities, that the latter option would hinder the smooth implementation of the new policy. The use of chloroquine had to be discontinued throughout the system at a certain agreed time and arrangements made to withdraw the chloroquine left over. WHO had identified a neighbouring country which was still using chloroquine and it was agreed that the Zambian government would donate these stocks to that country.

- **Supplies to other sectors:** The defence forces, mission hospitals, mine hospitals and the private sector provide a substantial proportion of the population with health services. Coartem<sup>®</sup>, at affordable prices, had to be made available to these key partners. The defence forces and the mission hospitals can obtain the public sector product at the same price as the MOH, according to the WHO and Novartis terms, since they are part of the public sector as long as authority is obtained from the MOH. Modalities had to be developed to facilitate access to Coartem<sup>®</sup> to the mine hospitals and private sector at a more affordable price if successful implementation was to be achieved. A key issue to be addressed is the prevention of pilferage from the public to the private sector facilities. Other issues to be considered include health worker competence, incentives for the traders, drug safety monitoring, distribution categorisation etc.
- d) **Regulatory Issues:** The policy change needed to have the endorsement of the ZNFC so that all the reference literature used in Zambia was standardised accordingly and also to include all the recommended products on the EDL and ZNF. Product licensing is a requirement for all drugs marketed in Zambia. The Pharmacy and Poisons Board is responsible for product licensing. Coartem<sup>®</sup> is available in six-dose and four-dose presentations. Since the six-dose presentation is the one recommended in Zambia it would not be desirable to have the four-dose presentation available on the Zambian market.

A first line drug for treating such an important public health problem as uncomplicated malaria in Zambia ought to be available as close to the home as possible, in line with the National Drug Policy. Like was the case with chloroquine, it should be available as a General Sale (GSL) commodity otherwise access will be severely limited. The product licence for Coartem<sup>®</sup> in Zambia lists it as a Prescription Only Medicine (POM)<sup>28</sup>. In 2003 the registration authorities were requested to reschedule artemether-lumefantrine and SP but appeared apprehensive about changing the distribution category in the absence of further safety information and a request for revision by the manufacturers. A decision on the issue is still pending.

A recommendation was made to the registration authorities to consider fast tracking applications for anti-malarials as more products are in the development process and there may be need to consider adopting their use as they become available on the market.

- e) **Pharmacovigilance:** The need for drug safety monitoring was recognised in view of the paucity of knowledge and experience in Zambia on some of the newer drugs being introduced for use on a wide scale. A protocol establishing a drug safety monitoring mechanism for this phase was developed. A reporting form was developed and adopted and distributed during training. Consequently some reports have been received through the NMCC. The flow of reporting is likely to increase once the Zambia Pharmacovigilance Centre becomes active.
- f) **Resource Mobilisation:** The need to mobilise adequate resources to ensure sustainability was recognised as a very key requirement of the plan. Resources were required for procurement of commodities, training, policy dissemination, managing the implementation process etc. Some key partners were identified including; WHO, UNICEF, DFID, USAID, JICA, World Bank, GFTAM etc.
- g) **Monitoring and Evaluation:** Studies to monitor the efficacy of all the recommended anti-malarial drugs and other drugs under consideration will need to be carried out on an on-going basis. The monitoring and evaluation of the impact of change is an important element of the implementation plan.

### **4.3. Policy implementation**

#### **4.3.1. Phase I**

The WHO offered the MOH supplies of Coartem<sup>®</sup> which had a maximum of six months shelf life. The packaging was in 16's rather than in 24's as would be the future supplies. The offer was accepted. The challenge for the DTT was to deploy these supplies in accordance with the implementation plan for the new policy. It was decided that the deployment of this consignment be considered the first phase of implementation so that the lessons learnt could be used in the subsequent phases. The implementation package included; training of health workers, distribution of commodities (all anti-malarial drugs recommended in the policy), distribution of updated Information, Education and Communication (IEC) materials, drug safety monitoring and improving health worker competence in drug supply management, in

view of the high cost of Coartem<sup>®</sup>. The deployment had to be effected without delay because of the short shelf life of the drugs available.

The following activities were completed during this first phase of implementation:

### **Selecting districts for first phase:**

Seven (7) districts were selected for this first phase. The criteria used were:

- High malaria incidence in the district
- Proximity (accessibility) of district to NMCC for ease of distribution of commodities, orientation logistics and monitoring of implementation
- Existence of structures for monitoring and evaluation (sentinel sites)

All logistical requirements for deployment (communicating with districts, orientation of facilitators for the workshops etc) were put in place.

### **Drug quantification:**

Quantification of drug needs for the selected districts was done using the morbidity method. Based on the quantification it was estimated that the supplies available would be sufficient to last six weeks for each district. All public health (CBoH-managed) facilities in the district would be supplied with Coartem<sup>®</sup>.

Although the reporting rate into the Health Management Information System (HMIS) is reported to be satisfactory and hence the data obtained likely to be reliable, it was decided to introduce a Coartem<sup>®</sup> Monthly Stock Return which the user facilities would complete and return to NMCC monthly. The purpose of these returns was to develop a database on Coartem<sup>®</sup> use in order to improve on the quantification of needs thereby minimising the chances of either over- or under-estimating. Provincial and district officials were advised to monitor consumption patterns and shift stocks from facility to facility or district to district according to needs.

### **Health worker orientation:**

A decision was taken not to supply Coartem<sup>®</sup> to any district before health worker orientation was provided. All health workers in any given district were invited to attend an orientation workshop to be held at a designated location within the selected districts. The programme was divided into two parts. The first day's workshop was

for the senior professional and management staff. The second day's workshop was for the frontline health workers.

The first day's programme included providing orientation on the new policy (i.e. rationale for change, policy statement etc), drug supply management issues pertaining to Coartem<sup>®</sup> and introduction of an adverse drug reaction reporting protocol.

The second day's programme contained the same topics but dwelt less on the drug supply management issues and included a component on the recommended drug regimens for all forms of malaria. Detailed recommendations for the treatment of uncomplicated and severe malaria in all population categories (children, adults and pregnant women) were provided.

Appropriate training manuals (facilitator's and participant's) and treatment guidelines for the purpose were developed and produced by the DTT. These were used for the workshops.

The training involved presentations by the facilitators and completion, in groups, of exercises on the various topics covered by the participants. There was time provided at the end of each presentation for discussion.

More than 300 health workers (including medical practitioners, pharmacists, nurses, clinical officers, environmental health technicians) received orientation in all the seven districts over a period of less than three weeks.

### **IEC material:**

Dosage charts for Coartem<sup>®</sup> were designed and produced for use during the orientation. The design was based on the chart supplied by the manufacturer but adapted to suit the local environment. The charts which were intended mainly for the health worker were in English but plans were made to translate into some of the local languages in due course. The charts were distributed during the orientation and comments solicited from participants on their suitability for use.

### **Drug (Coartem<sup>®</sup>) distribution:**

The teams of facilitators (eight in all) carried supplies of Coartem<sup>®</sup> allocated to each district. The district management was responsible for allocating quantities for each health facility in the district. The allocation was based on the knowledge of the district officials of the morbidity patterns in each catchment area. The NMCC transport

delivered the allocated supplies to the facilities. At the end of the workshop each health facility had supplies of Coartem<sup>®</sup>.

The other drugs were available through the normal procurement system. It had been established that there was no shortage of sulfadoxine-pyrimethamine and quinine at MSL.

The entire process, from receipt of supplies from WHO to deployment in the last district, took 23 calendar days.

Three of the districts were subsequently visited (one of them twice) for follow up in order to monitor progress.

Stocks of Coartem<sup>®</sup> ran out in all districts within three months. The districts moved on to SP when they ran out of Coartem<sup>®</sup>.

### **Key observations from Phase I deployment:**

- Health workers require more knowledge and information on the management of malaria for the successful implementation of the policy. The level of knowledge on these aspects was unsatisfactory. Many of the participants were not sufficiently conversant with the guidelines for managing malaria. Health worker and public perceptions on the safety and efficacy of some of the anti-malarial drugs in use (especially SP) needed correcting<sup>30</sup>. Some of the districts ran out of stock before the estimated six weeks
- Health worker and patient acceptability of Coartem<sup>®</sup> was high in all districts which reported back (five). In one district Coartem<sup>®</sup> was nicknamed “*TWATEMWA*” (meaning “we are happy” in the local dialect) by the community. In some districts, many patients were refusing to take chloroquine even before the official change of policy.
- Health workers appeared to be conversant with the Coartem<sup>®</sup> regimen during the follow up visits. This was in spite of having been supplied the 16-pack rather than the 24-pack formulation.
- There were no substantiated reports of treatment failures
- Through the established system fifteen Adverse Drug Reaction reports were received during the first three months of deployment. There were no serious adverse events reported. The reports consisted largely of effects

like nausea, headache, itching, nightmares, abdominal pains, most of which were similar to the symptoms of the disease. Acknowledgement of receipt of all reports was made. During follow up visits health workers always included a report on adverse drug reporting (the usual comment being “we did not observe or receive any complaints about side effects”).

- Four districts submitted Coartem<sup>®</sup> Stock Returns in the first three months. There were no problems encountered in obtaining the required data and completing the returns by the districts which complied. One district adopted a tallying system administered at the point of dispensing to generate the data. There was some lack of clarity by some centres on how to complete the data from the 6-pack onto the return which was designed for the 24-pack.
- There were substantial stocks of chloroquine tablets in bulk as well as in kits at health centres in all the districts.
- The number of patients actually treated during this phase is not available

#### **Lessons Learnt from Phase I deployment:**

- The training package developed for the first phase deployment did not fully meet the needs on the ground. There is need for more suitable training and reference materials to be developed and disseminated. The treatment guidelines should contain enough information on the diagnosis and management of malaria and antimalarial drugs to serve as a reference manual.
- It was not practical for the NMCC to do the distribution of anti-malarial drugs. It would be better done through the existing distribution system. However, the allocation of stocks of Coartem<sup>®</sup> per district should initially be as per quantification done by NMCC.
- The needs estimates were not accurate in all cases. There was therefore need for collecting data to establish a more reliable source of data for subsequent drug quantification. The monthly stock return would be an important tool for this purpose. Introduction of this tool would not cause problems for health facilities as illustrated by the districts which had started using the tool.

- The Coartem<sup>®</sup> dosage charts needed revision, as some of the information was not clear and rather confusing. Visually illustrating the dosage on Day 1 was particularly challenging
- There were no significant adverse events reported with the use of Coartem<sup>®</sup>. The adverse reactions reported included; itching, sweating, frontal headache, nightmares, general body pains, general malaise, abdominal pains and ringing ears. The health workers appeared to have realised the need for reporting adverse events even if they are not serious. Sensitisation of health workers on ADR reporting is therefore a feasible approach
- A detailed plan had to be drawn up for withdrawing chloroquine from the health centres. The plan involved the health centre staff discontinuing the use of chloroquine immediately and putting all the stock aside. The stock would be collected by MSL during the monthly cycle of deliveries to the districts.

#### **4.3.2. Phase II**

Phase II implementation was scheduled to commence after securing funding from the Global Fund for TB, HIV/AIDS and Malaria (GFTAM). This was earlier anticipated to have been achieved by July 2003. The Funds were released in August 2003.

WHO was then requested to fund the purchase of bridging supplies of Coartem<sup>®</sup> for the seven districts where Coartem<sup>®</sup> had been deployed in Phase I. An order for this purpose was placed with the suppliers in May 2003. The order was delivered and received about the same time as the supplies procured through the Global Fund in October 2003.

In preparation for Phase II implementation the following activities were done:

#### **Policy dissemination:**

A policy statement was issued in June 2003 by the Permanent Secretary of the Ministry of Health which was published in all the national daily newspapers and radio and television stations. The statement gave the detailed policy on the treatment of malaria, including the basic rationale for the change.

Communication was sent to the districts in Phase II implementation detailing key aspects of implementation; including the withdrawal of chloroquine from circulation, ordering of Coartem<sup>®</sup>, etc.

The development of appropriate IEC materials for dissemination was set in motion.

Presentations on the policy and recommended treatments were made to professional groupings of general practitioners, pharmacists and students of nursing, pharmacy and medicine.

Orientation workshops for health workers also had dissemination of policy as a major objective.

### **Selection of districts for second phase implementation:**

An additional twenty one (total twenty eight) districts were selected for this phase. The criteria used were:

- All provinces should have at least two districts using Coartem<sup>®</sup> during this phase
- Districts with high parasite resistance to SP, since SP would be the first line drug in the absence of Coartem<sup>®</sup>.
- Districts designated as sentinel sites would be introduced earlier than those that were not
- High malaria incidence

### **Needs quantification:**

Quantification of needs for all the recommended anti-malarial drugs (Coartem<sup>®</sup>, SP and quinine) was carried out. For Coartem<sup>®</sup> this was broken down to estimates per district for all the districts (28) involved in this phase.

The morbidity method was used, as there was no more reliable data that could be used at this stage. The monthly stock returns had not been applied for a long enough period and Coartem<sup>®</sup> use data from most of the districts was not available.

This quantification was used to provide a budget for drug costs to GFTAM for year I.

**Drug Efficacy studies:**

The NMCC, in collaboration with local institutions, conducted drug efficacy studies in 7 sites to determine the efficacy of the following drugs:

- Artemether-lumefantrine
- Artesunate with sulfadoxine-pyrimethamine
- Sulfadoxine-pyrimethamine

These studies are part of the sentinel site surveillance system for assessing and monitoring the therapeutic efficacy of antimalarials in line with the standardised WHO protocol using a 14-day and a 28-day follow-up period which the country has been conducting since 1995.

**Procurement:**

Although negotiations to secure funding had not been concluded procurement plans, including suggested delivery schedules were prepared and submitted to WHO, the procurement agency for Coartem<sup>®</sup>. The order for annual requirements was broken down into three deliveries. This was done considering that the estimates for Coartem<sup>®</sup> may not have been accurate and provision should be made to change the delivery plans as a truer consumption picture emerged after use for a few months. CBoH's procurement unit was alerted to the needs for the other anti-malarial drugs and requested to ensure that adequate supplies were always available.

**Health worker orientation:**

It was decided that since the policy change affected the whole country and there was an apparent information and knowledge gap among health workers, orientation should be provided to all health workers in the country regardless of the programme for Coartem<sup>®</sup> deployment. This would be done through a cascade approach. The centre (NMCC) would train trainers from the provincial and district levels and these trainers would in turn train health workers within the districts. It was envisaged that this process should be completed before the next high malaria transmission season commencing in November 2004.

The DTT would develop and produce the training materials for the purpose.

These would be based on WHO training modules suitably adapted to local

situations through a process of reviewing by local experts. The training would include the following topics:

- Malaria policy- rationale for change, policy statement and recommended drug regimens
- Drug management – Coartem<sup>®</sup> stock return and stressing the need for a Coartem<sup>®</sup> database
- Pharmacovigilance – need for drug safety monitoring and pharmacovigilance system in Zambia
- Symptoms and signs of malaria
- Diagnosis of malaria
- Management of malaria at the various levels of the healthcare system
- Health Education

Guidelines for the Diagnosis and Management of Malaria were developed but were not ready for distribution at the time of the workshops in August 2003. The Guidelines became available for distribution during August 2004.

Eight facilitators, including paediatricians, malariologist, pharmacologist, general practitioner and pharmacist were identified and given appropriate orientation and further reference materials. Suitable topics were assigned to the facilitators.

The nine provinces were grouped into three and provincial offices were invited to send suitably qualified persons to attend training of trainers (TOT) 2-day workshops at designated centres (3 centres). Funding was provided by the NMCC.

The workshops were very well attended (>300 participants) and participation was very active. 110 participants were subsequently selected as trainers who could train health workers at provincial and district levels. Participating districts were provided with training material (i.e. CD of the training manuals and reference materials but no guidelines) for use at the district level.

One district conducted a workshop for its health workers within a month of the TOT having taken place. District trainers were used for this training.

### **Storage and Distribution:**

Discussions were held between the DTT, CBoH and MSL to ensure the following:

- Adequate stocks of the other anti-malarials had been planned for and would be available when and where they were needed

- Distribution mechanisms in place would ensure the efficient distribution and availability of all anti-malarials. Of particular concern was an existing restriction on certain levels of facilities obtaining their supplies of drugs from MSL. Such restrictions had to be lifted.
- Communication channels were established between the key players to avoid delays in clearing consignments from the port of entry and storage at MSL
- There would be no delay in distributing stocks of Coartem<sup>®</sup> according to the distribution list once the consignment was received
- The smooth withdrawal of chloroquine stocks from the health centres

By the time the WHO funded “bridging” and the Global Fund procured supplies were received there was no delay in clearing and collection of the consignment and MSL promptly found adequate storage.

A distribution list for all the 28 districts based on centrally developed estimates was prepared by the NMCC and passed onto MSL for distribution.

Distribution of Coartem<sup>®</sup> by MSL as per list commenced in November 2003.

The withdrawal of chloroquine from the centres was to be done by MSL. The centres were instructed to keep aside all chloroquine stocks for collection when MSL made the regular monthly deliveries. The whole process was anticipated to take three months.

### **Supplies to other sectors:**

Meetings were held with representatives of the defence forces, mission hospitals and the mines to work out the mechanics of facilitating access of Coartem<sup>®</sup> and implementation of the new policy in the above institutions.

Meetings with the private sector representatives (pharmaceutical distributors, general practitioners and pharmaceutical society) were also held for the same purpose. The private sector representatives submitted a proposal on how they could positively participate in the implementation of the policy. Key issues to be resolved with the private sector included; access of Coartem<sup>®</sup> by the public at a more affordable price, preventing “leakage” of public sector supplies to the private sector, sustainability of arrangement.

**Regulatory Issues:**

Revisions accommodating the new recommendations were made to the Standard Treatment Guidelines, Integrated Technical Guidelines for Frontline Health Workers, Essential Drug List, IMCI Guidelines and Guidelines for the Diagnosis and Management of Malaria. Revised product monographs were developed for the Zambia National Formulary for use when the Formulary is revised. Recommendations for the necessary changes to the distribution categories as discussed earlier were submitted to the Pharmacy and Poisons Board.

**Compliance studies:**

A protocol for carrying out Coartem<sup>®</sup> compliance studies was developed by the operational research office at NMCC. A study was done in 5 districts<sup>31</sup>. The study demonstrated reasonably high (64%) patient compliance with Coartem<sup>®</sup>.

**Pharmacovigilance:**

The WHO organised a training course for participants from the southern African region in April 2003. Members of the DTT participated in this course. A protocol for establishing a pharmacovigilance system in Zambia was drawn up. The Zambia Pharmacovigilance Centre is being established at the Pharmacy and Poisons Board (the drug regulatory authority for Zambia). In the meantime some ADR reports have continued being received by NMCC.

By the end of 2003 phase II implementation was in full effect.

**Findings from Phase II implementation:**

- Although funds were transferred to the provincial and district offices for rolling out training only one district had achieved this by June 2004.
- Some districts had departed from the guidelines in their implementation of the policy implementation. For example some districts had reserved Coartem<sup>®</sup> for use in laboratory confirmed cases, some were only using it for selected groups of patients etc.
- Some facilities did not know how to order stocks of Coartem<sup>®</sup>. This necessitated pushing supplies to all districts in May 2004.

- Stock returns for Coartem<sup>®</sup> were not being submitted regularly so a reliable database for Coartem<sup>®</sup> consumption had still not been established by July 2004.
- DHMT's did not have a common understanding of the implementation of the policy
- A study to assess the management of fever in children by health workers done early 2004, identified health worker competence in the management of malaria as a weakness<sup>31</sup>.
- The withdrawal of chloroquine from the facilities took a lot longer than was anticipated. Reports of chloroquine being found in health worker kits were being received as late as October 2004.
- There appeared to be general acceptance of Coartem<sup>®</sup> by both the community and health workers in areas where it was deployed. As a result some districts where Coartem<sup>®</sup> had not yet been deployed were pushing to be included.
- An inventory done on the availability of laboratory diagnostic capacity showed that about two thirds of the health facilities in the country did not have such capacity.<sup>33</sup>
- Some district and tertiary hospitals in areas where Coartem<sup>®</sup> had been deployed were not following the new policy guidelines

### **4.3.3. Phase III**

Plans for Phase III implementation commenced in June 2004. A number of key decisions had to be made:

#### **Implementation date and modalities for rolling out:**

It was decided that the policy should be in full effect in all the 72 districts in the country by the beginning of the next transmission season (November 2004). By this time the drug distribution, training and other aspects of the roll out should have been done for all districts.

The rationale for the decision was:

- To ensure that the whole country was using an effective drug by the beginning of the transmission season
- The training and drug distribution should have been completed before the onset of the rains, usually around mid-November. Once the rains start some

parts of the country are inaccessible and the roll out could then only effectively take place after the rains in April or May 2005

- Enough lessons have been learnt for the roll out to the rest of the country to be done
- From the advocacy perspective the SADC Malaria Day can be used to launch the roll out to the rest of the country

A team comprising the NMCC programme manager, case management specialist, pharmaceutical consultant, IEC specialist, operations research officer and laboratory diagnostics experts was constituted to plan the roll out.

The team analysed the experiences learnt in all aspects of policy implementation to date and considered how to address the key issues identified for the roll out.

A plan to effect the roll out was then prepared. The key issues addressed included:

#### **Coartem<sup>®</sup> needs estimates:**

There was an urgent need to place an order for Coartem<sup>®</sup> to meet the requirements of the entire country in order for the supplies to be received in time for the roll out, considering the 16-weeks lead time.

Quantification was done based on morbidity data for 2003. However, experiences from districts already using Coartem<sup>®</sup> were considered in this exercise. For instance, one of the districts with very high morbidity for children, according to HMIS data, had reported that their allocation for the smallest dosage pack was over estimated. Consumption data was not used because there was not enough of it available to meaningfully assist in the process.

An order for requirements up to October 2005 was placed in June 2004. The order was divided into three delivery lots, with the first delivery expected in September 2004.

#### **Drug distribution:**

MSL was considered to be the most suitable agency to distribute drugs in the roll out. However, NMCC would provide the details of products to be distributed and the dates.

It was learnt that many district hospitals were not prepared to obtain their supplies of Coartem<sup>®</sup> from DHMTs, for various reasons. It was therefore decided that district and

tertiary hospitals would obtain their supplies independently of DHMTs. Estimates of needs for these facilities therefore had to be determined and a distribution list prepared. They would be requested to order their allocations direct from MSL.

### **Diagnosis of malaria:**

Discussions on whether only laboratory-confirmed malaria cases should be treated with Coartem<sup>®</sup> had been going on. It was decided that until such time that there was adequate laboratory and Rapid Diagnostic Testing (RDT) capacity in the country clinical diagnosis would suffice. Training of health workers would aim at improving the competence of health workers in this skill.

### **Training:**

Since the cascade training approach had not achieved the desired results it was decided to organise the training at the central level (NMCC) using a combination of facilitators from the NMCC and some of those trained as trainers the previous year. It was also decided to provide orientation on salient aspects of policy implementation to the managers at provincial and district health offices (i.e. PHO and DHMT) in order to ensure uniform understanding of the process. Orientation would also be provided to management and clinical personnel at district and tertiary hospitals in order to bring these institutions on board. Private sector practitioners (general practitioners and pharmacists) would also be oriented on the policy.

A module for training frontline health workers, addressing some of the areas of weakness identified in the study referred to earlier, and separate modules for each of the above practitioners were developed. The training included diagnosis and management of malaria, drug supply management, pharmacovigilance and policy. The training and orientation was done at provincial centres. At least one frontline health worker from every health facility in all 72 districts was expected to attend. Funding was provided from the Global Fund<sup>34</sup>.

### **Home management of malaria (HMM):**

It was recognised that not all cases of malaria were managed at health facilities. It was therefore considered important to address the question of how the management of malaria in the community can be improved. A workshop to build consensus on this issue was held in October 2004. It was agreed that competence and resources should

be developed for early recognition and prompt treatment of uncomplicated malaria using effective drugs, including Coartem<sup>®</sup> for this level of the healthcare system.

Appropriate protocols are now in the process of being developed.

A rapid assessment on the practices related to home management of malaria was planned and the tool has so far been developed to help collect data which will feed into the development of the strategy for implementing HMM. A technical working group has also been instituted to oversee the HMM strategy.

### **Role of private sector:**

The private sector provides an invaluable service in the Zambian healthcare system. Coartem<sup>®</sup>, and other artemisinin based combination therapies (ACT) are available in the private sector but at exorbitant prices. The need to consider making ACTs more readily accessible in the private sector was identified.

Discussions with hospitals run by copper mining companies on the Copperbelt are to be held to address this issue.

A pilot project to determine the feasibility of distributing subsidised Coartem<sup>®</sup> through the private (for-profit) sector is commencing in November 2004. This is being undertaken jointly by NMCC and Society for Family Health, a non-profit making, non-government organisation experienced in the distribution of condoms, contraceptives and insecticide-treated mosquito nets. The project is being funded by Novartis.

Another important objective with the private sector is to ensure that the use of chloroquine is discontinued. Orientation to private sector practitioners was provided during the training conducted in October to November 2004<sup>34</sup>.

### **Rapid Diagnostic Tests (RDTs):**

In view of the lack of laboratory diagnostic capacity in most of the health facilities in the country<sup>33</sup> it is considered that RDTs could play an important role in confirming the diagnosis of malaria, particularly where microscopy is not available.

Plans to undertake a pilot study to determine the feasibility of using RDTs in Zambia are advanced. It is anticipated that the study will commence during early 2005.

**IEC activities:**

Policy dissemination was thought to be a critical element in the successful implementation of the policy. A comprehensive programme of IEC activities has been developed. This programme includes providing orientation on the treatment policy to journalists from the various media channels operating in Zambia.

**Operational research and M&E:**

The need to undertake studies to identify operational obstacles, like compliance, drug efficacy and safety, cost effectiveness, product acceptability, disease management practices etc was recognised. Operational research would therefore be an important component of implementation.

The need for developing an M&E plan was identified. Indicators for this purpose had to be developed and an implementation plan effected. The main indicators included measurement of programme performance, drug supply, change in malaria morbidity and mortality and knowledge about malaria and policy at the different levels of the healthcare system.

A drug policy implementation-monitoring plan was developed by the operational research office. 6 sentinel districts received training on the use of this tool on 4<sup>th</sup> November 2004 and the tool will be implemented during early 2005. The tool focuses on the broad areas of malaria control and will feed into improving the malaria information system.

**Pregnancy Register:**

The restriction on the use of Coartem<sup>®</sup> during pregnancy is a major setback since pregnant women are particularly susceptible to serious disease. It is important to assess its safety in pregnancy.

Novartis, WHO, TDRC and NMCC have started a pregnancy register to document use and eventually assess the safety of Coartem<sup>®</sup> in pregnancy.

**Implementation:**

In order to ensure that health workers in all facilities were conversant with the guidelines for implementation and the public duly sensitised about the policy it was felt that the roll out activities should be harmonised.

Consequently the drug distribution and the various orientation activities were scheduled to take place in the different districts around the same time. The IEC programme would also kick off around that time. Some M&E activities, e.g. determination of baseline data would also be undertaken, while the others e.g. effects on morbidity and mortality due to malaria would be scheduled for later stages.

The distribution of drugs by MSL started according to a schedule prepared by NMCC in the second week of October 2004 and was completed in the first week of November 2004. District and tertiary level facilities were advised to order and collect their needs from MSL at dates when training and orientation were expected to be done in their respective districts. Stocks of Coartem<sup>®</sup> remaining from Phase II deployment were allocated for this purpose.

In September 2004 Novartis organised training for about 300 frontline health workers in the management of malaria. The challenge for the NMCC was to ensure that the course content was in harmony with the policy and implementation goals. Consequently, although most of the speakers were international, the course content was adapted to local treatment recommendations.

The training and orientation of managers, frontline health workers and district and tertiary facilities during the roll out was done between October and December 2004. The week's programme started with a 2 to 3 hour programme of orientation for managers, followed by a 2 to 3 hour programme for referral facilities and finally a 2-day training programme for frontline health workers in two groups of 60 participants each. During the training participants received individual and institutional copies of the Guidelines for the Diagnosis and Management of Malaria as well as Coartem<sup>®</sup> Monthly Stock Returns and ADR forms.

## **5. CONCLUSIONS**

### **5.1. Achievements**

Probably the biggest achievement is in getting the commitment by various stakeholders to accept the need to change the treatment policy and to implement the change.

The implementation process is a very challenging exercise which is progressing reasonably well. The change has now been accepted by most health workers, as can be demonstrated by the responses during the health worker training sessions. Initially there was quite a lot of apprehension about the change which was not evident during the training for the roll out.

In the areas where Coartem<sup>®</sup> has been in use for sometime the community and health workers appear to be pleased with the performance of the drug.

The policy implementation process has provided the programme with an opportunity to emphasise the need and ensure the availability of the other antimalarial drugs; SP and quinine.

The training and reference materials, like the treatment guidelines offered the health workers an essential resource which had been lacking. This view was expressed by many course participants.

The change has offered the country an opportunity to develop diagnostic capacity, not only for malaria but for other disease conditions.

The IEC activities will provide the public with vital knowledge about malaria and its management thereby assisting in decision-making on seeking treatment.

Since the start of the policy implementation programme a total of 1161 health workers, including managers, frontline health workers and private sector practitioners have been trained in aspects of disease management, policy implementation, pharmacovigilance and antimalarial drug supply management.

### **5.2. Failures**

Much still needs to be done in the following areas:

- The flow of returns for consumption of Coartem<sup>®</sup> has been erratic. It has therefore taken a lot longer to develop a database than had been planned. Estimation of needs, even as Phase III implementation started, was still not based on reliable data.

- The implementation of the policy was not satisfactory in all districts during Phase II. Follow up visits to some of the districts suggested that closer supervision from the centre might have resulted in better performance.
- IEC activities during Phase II were not as effective as required to satisfactorily sensitise the public on the policy
- The establishment of the pharmacovigilance system has taken an unacceptably long time
- Some health facilities experienced stock outs of some packs of Coartem<sup>®</sup> yet stocks of all packs were always available at MSL.
- The withdrawal of stocks of chloroquine from health facilities was not as satisfactory as anticipated. Some facilities still had stocks several months after the deadline.
- A survey of health facilities during Phase II showed that some health workers' skills in the diagnosis and management of malaria were still below acceptable standards.
- Funding for the implementation of the change is largely from the Global Fund. This is not healthy, as it does not guarantee sustainability. This is a question which keeps arising from the health workers. There is a need to develop a financial sustainability plan which is not totally dependent on the Global Fund.

### **5.3. Key recommendations**

- The process of adoption of a new policy should involve health workers at all levels of care. Managers of DHMTs, leaders of private sector professional organisations, regulatory authorities, opinion leaders at key hospitals etc should all be involved in the process from the beginning.
- The decision should be backed by ample evidence, preferably from local studies. The involvement of international experts, particularly from WHO, adds credibility to the process
- Quantification of Coartem<sup>®</sup> (or indeed ACTs, in general) is a critical and yet complex exercise. Substantial resources should be devoted to this element. Getting it wrong can jeopardise the success of the change.

- Health worker training assists in ensuring that malaria is being managed in accordance with guidelines. This is critical for planning needs of drugs and other resources as well evaluating performance.
- Implementation at CHW and private sector levels should be done about the same time as in the public sector to ensure compliance in all sectors.
- In deciding on issues like the role of RDTs or microscopy in the diagnosis of malaria, it is important to assess the capacity of the programme to implement the decisions. It is sometimes more prudent to defer decisions until the necessary capacity is developed.
- The efficient distribution of drugs is an important component which should be left to agencies which have the competence to carry out this task. NMCC, as an example, realised that the programme did not have the capacity to do this during Phase I.
- Resource mobilisation, even from the GFTAM, tends to be a long drawn out process. This should be initiated several months before the anticipated change
- Total commitment from the government to the change cushions the programme from undue political pressures which arise for various reasons
- Announcements and instructions to implementers on the implementation should be issued by the MOH or CBoH rather than the NMCP. The level of compliance is likely to be better using this channel.
- The completion of the policy change roll out should be announced by the Minister to give it the final endorsement

Finally, in Zambia like any other sub-saharan country experiencing high incidence of malaria and coupled with increase in parasite resistance to antimalarials, the use of ACTs is the best option. It is hoped that Zambia's experience will assist other countries hoping to take this route of change. The task is very challenging but given the number of deaths that can be prevented it is our view that it well worth the effort.

## 6. REFERENCES

1. Weather and Climate. Report. Department of Metriological Services. Ministry of Transport. Zambia
2. CBoH/MOH (2003) National Health Accounts Report.14-15
3. Health Management Information System (HMIS) 2003
4. Baseline survey 2000
5. NMCC (2000) National Malaria Situation Analysis. Zambia. 5
6. 1999, Malariometric survey, NMCC
7. Bransby-Williams 1976
8. NMCC (2000) National Malaria Situation Analysis. Zambia. 9-15
9. Health Statistics Bulletin, MOH/CBOH
10. HMIS Reports
11. Strategic Plan for Rolling Back Malaria in Zambia. 2001-2005. 27
12. RBM Strategic Framework for Zambia
13. NMCC. Malaria Situation Analysis
14. NMCC preliminary report 2002
15. NMCC (2000) National Malaria Situation Analysis. Zambia 25-29
16. WHO. 1999. Framework for developing, implementing and updating antimalarial drug policy in Africa. 29-31 Ref- WHO refs
17. WHO (2000). Severe falciparum malaria.
18. Transactions of the Royal Society of Tropical Medicine and Hygiene, 94, supplement 1. S1/39.
19. P.Olliaro et al. (1996). Systematic review of amodiaquine treatment in uncomplicated malaria. The Lancet:**348**:1196-1201
20. WHO/CDS/RBM/2001.33. The use of antimalarial drugs. Report of a WHO informal consultation. 47-50
21. Chanda P, Sikaala CH, Kapelwa W, Moonga H, Njunju E, Macdonald M, Thea D, Hamer DH, Sipilanyambe N. Assesment of the therapeutic efficacy of artemether-lumefantrine (Coartem(r)) and sulphadoxine-pyrimethamine (SP)-artesunate in Zambian children. 53rd Annual Meeting of the Society of Tropical Medicine and Hygiene. Miami, FL. Abstract 213
22. NMCC. Nov 2002. Kwazulu-Natal Familiarisation Tour. MOH/CBoH Report
23. Robert D Newman et al. (2003). Safety, efficacy and determinants of

- effectiveness of antimalarial drugs during pregnancy: Implications for prevention programmes in Plasmodium falciparum-endemic sub-Saharan Africa. *Tropical Medicine and International Health*. **8**, 488-506
24. ANC sentinel surveillance of HIV/Syphilis Trends in Zambia 1994-2002. 22. CBoH.
  25. Monica E. Parise et al. 1998. Efficacy of sulfadoxine-pyrimethamine for prevention of placental malaria in an area of Kenya with a high prevalence of malaria and Human Immunodeficiency Virus Infection. *Am. J. Trop. Med. Hyg.* **39(5)**, 813-822
  26. WHO/CDS/RBM/2001.33, 94-95
  27. NMCC. 2002. Report on national malaria treatment policy change meeting held on Wednesday 27 November 2002 at Chrismar Hotel-Lusaka. MOH/CBoH Report
  28. NMCC. 2003. Implementation plan of the revised antimalarial drug policy in Zambia. MOH/CBoH
  29. Product licence number 121/001. Pharmacy and Poisons Board.
  30. Patrick David Mwanza. Dec 2002. Rapid Assessment on acceptability and prescribing of sulphadoxine-pyrimethamine (SP or Fansidar) in Lusaka and Chipata districts
  31. Chanda P, Hazemba O, d'Allesandro U, Sipilanyambe N. 2004. Compliance with artemether-lumefantrine (Coartem<sup>®</sup>) for the treatment of uncomplicated Plasmodium falciparum malaria in Zambia. Abstract 943. American Society of Tropical Medicine and Hygiene 53<sup>rd</sup> Annual Meeting, 7<sup>th</sup> –11<sup>th</sup> November 2004, Miami, FL.
  32. Ref. M. Ndhlovu et al. 2004. Outpatient malaria case management study in Zambia. NMCC/MOH/CBoH
  33. NMCC (2004) Report on availability of Laboratory Diagnostic Capacity
  34. Report on the training of health workers on the management of malaria- October to November 2004