Roll Back Malaria Strategic Framework for Scaling up Effective Malaria Case Management - *1 March 2004 Draft 4*

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1 Introduction

1.1 Purpose of the strategic framework

The Roll Back Malaria partnership has set up a series of Working Groups to advise on how effective can be taken to scale. This strategic framework has been developed by the Roll Back Malaria Case Management Working Group to promote the scaling up of country and WHO technical strategies on malaria case management.

Effective case management is a fundamental element of malaria control and a key component of Roll Back Malaria strategy. Global and regional leaders have committed themselves to the following goals and targets:

Millennium Development Goals. By 2015:

Goal 4. Reduce child mortality
Target 5. Reduce by two-thirds, by 2015, the under-five mortality rate.

Goal 5. Improve maternal health
Target 6. Reduce by three-quarters, by 2015, the maternal mortality ratio.

Goal 6. Combat HIV/AIDS, malaria and other diseases
Target 8. Have halted by 2015 and begun to reverse the incidence of malaria and other major diseases.

Roll Back Malaria Goal. By 2010:
Halve the world's malaria burden

Abuja Target. By 2005:
At least 60% of those suffering from malaria / fever will have prompt access to and are able to use correct, affordable and appropriate treatment within 24 hours (adopted by African Heads of State at the African Summit on Roll Back Malaria in Abuja in 2000).

In malaria endemic countries of Africa it has been estimated that in 2000 there were nearly 3 billion fever episodes a year (1.5 billion in children and 1.4 billion in adults, Snow et al in prep). Thus to achieve the Abuja target would require 1. 8 billion effective treatments to be delivered each year.

There is a long way to go to achieve these targets due primarily to increasing antimalarial drug resistance and poor access to effective treatment (affordability, weak systems, lack of consensus or access to information on best practice). Efforts to improve malaria case management are often wasted as they do not focus on priorities nor address all the critical steps to ensure that cases are managed effectively.

This strategic framework aims to set out the necessary components to achieve the Abuja target and beyond as a guide to RBM partners (policy makers, implementers and supporting partners) on how to focus their resources and efforts and how to work together more effectively. It is not intended to be a detailed guideline or manual on case management policy and strategy. Many countries already have guidelines taking into account national strategies and circumstances. This framework can be used by countries as a tool to review their own guidelines and by

supporting partners to identify gaps where they can contribute. It focuses on ensuring effective case management reaches the majority of populations at risk rather than on management of individual cases.

2 Defining Effective Case Management

Goal of case management as a public health strategy
To maximise the reduction in mortality and morbidity (severity, duration of illness and adverse outcome) due to malaria disease by efficiently using available, appropriate antimalarial drugs and other resources.

Definition of effective case management
The administration of a complete, effective antimalarial treatment and provision of necessary supportive care to a person with malaria-like symptoms within 24 hours of the start of the symptoms, unless a diagnostic procedure has shown that the patient does not have malaria. This includes self-treatment, treatment of uncomplicated malaria and of severe malaria.

Effective management of malaria requires that the consumers and care-givers, seek, obtain, and use drugs appropriately. This is based on:

1. A timely decision to treat, based on clinical or parasitological diagnosis
2. Accessibility (availability, geographical access affordability and acceptability) of appropriate drugs (right drug at the right time, good quality, appropriate formulations)
3. Correct use of the drugs (dose, frequency, duration)
4. Follow-up to detect treatment failure and timely referral to appropriate care

Definition of malaria home care
Decisions and actions taken at home on recognition and treatment of suspected malaria.

Purpose of an antimalarial drug policy:
To ensure availability and appropriate use of safe, effective, good quality and affordable antimalarial drugs to those that need them and at the same time promote rational drug use which will minimise the development of antimalarial drug resistance (ref AFRO)

1. *To ensure rapid and long lasting clinical cure;*

2. *To reduce morbidity, including malaria related anaemia;*

3. *To prevent the progression of uncomplicated malaria into severe and potentially fatal disease;*

4. *To reduce the impact of placental malaria infection and maternal malaria associated anaemia through intermittent preventive therapy;*

5. *To minimise the chance and slow the rate of development of drug resistance.*

3 Learning from history

Before effective chemotherapy was introduced, morbidity and mortality from malaria was probably very high (high enough to favour survival of people with sickle cell disease and blood enzyme disorders protecting from malaria) (refs Weatherall, Maitland). For example India reported 75 million fevers a year. It has been estimated that 2% of malaria cases would die if untreated (White? Sudre et al. Int. J.Epidemiol. around 1992(?)). From the 1950s and 1960s until the early to mid-1980s chloroquine was widely available and fully effective. Did this limit the burden of disease from malaria? Access was initially mainly through formal health facilities (public, mission, private). Later, with great variability between countries, this was gradually supplemented by community-based services, informal private services and home treatment. The mortality increase, coinciding with emergence and spread of resistance in the 1980s (Trape), suggests that chloroquine treatment had previously helped to curb mortality. Even during the period of chloroquine sensitivity mortality was still high in many rural areas (Spencer, Greenwood), but low in some urban areas (Trape Brazzaville). Was the problem in rural areas mainly related to accessible at all times?

It is likely that the decreasing therapeutic effectiveness of chloroquine caused decreased confidence in public health facilities. This was compoundedby decreasing funds and structural adjustment in the public health services during this period. Cost-recovery schemes probably further enhanced the move of patients to the private formal and especially informal sector, where drugs and service could be obtained more efficiently.

While some countries in Southeast Asia systematically changed policy for first-line treatment as resistance increased, the early 1990s saw a period of great caution in Africa with prolonged use of ineffective drugs for fear of developing resistance to better ones. The tide is now turning with an acceptance that people should not be denied effective treatment where at all feasible, so strategies to make effective drugs available while limiting irrational use are being developed.

The greater choice of drugs and delivery systems in recent years has been used to develop and implement good treatment policies in some countries, but has led to confusion in other countries. This has slowed the introduction of effective treatment policies and practice, and has also provided opportunities for fake and substandard drugs.

As more countries have taken decisions to change their policy on drug choice, lessons are emerging on the impact of policy change. In several countries the decision to change has been followed by a delay in implementing the change, either through lack of adequate planning or through lack of true consensus on the choice made. In other countries, such as Cambodia, which has changed policy four times since 1993, observations have been made that even where policy is changed and good implementation steps are taken in the public sector, many people continue to choose inappropriate treatments in the private sector. More attention to treatment seeking behaviour change is needed (Sim) as well as enabling the private sector to offer appropriate treatment. In several countries the decision to change drug and provision of the drug have acted as a catalyst for working together more effectively than before to make the systems improvements necessary to benefit from the better drug. Examples are Mozambique's second line treatment of amodiaquine plus sulfadoxine-pyrimethamine (SP) in 1985, Malawi's first line treatment with SP in 1993, Cambodia's change to mefloquine plus artesunate in 2001, South Africa's introduction of Coartem and recently, similar processes in Rwanda, Uganda, Zanzibar, Zambia, Burundi and Senegal.

The range of drugs suitable for treatment is limited, and for particular high risk groups such as pregnant women, there are very few safe choices. There is, however, some increased interest in drug development with promising new drugs in the pipeline.

Lessons

- Effective, high quality drugs are essential
- These drugs must be widely available and affordable
- Lack of confidence in the public sector leads to greater use of alternative sources, so both the public and alternative sectors must offer quality services
- The widest coverage possible of effective case management is essential
- Implementation strategies should include effective communication to encourage patients, carers and providers to use recommended drugs appropriately
- Issues of adherence and provision of safe effective drugs for special groups, such as pregnant women, must be considered at the time of policy change.
- Policy change can be used as a catalyst for overhauling the whole system to achieve effective case management

4 Current Practice in Case Management

There are many examples of good practice in case management, but these are often not applied on an adequate scale. Some examples of efforts to scale up good practice are given in the Annex.

4.1 Obstacles to effective case management

- Many sufferers from malaria are not treated effectively, because they:
  1. recognise illness too late or seek treatment too late (inability to recognise signs and symptoms of severity of illness, perception that malaria is not a childhood killer/ serious disease, user fees, geographical inaccessibility of facilities, direct and indirect costs e.g time away from work,), perception of poor availability of drugs or quality of services.
  2. are treated too late or not at all (reasons: no drugs, drugs not affordable, facilities poorly functioning, importance not understood, misdiagnosis)
  3. use the wrong drug (are given the wrong drug by providers or take the wrong drug due to self-treatment)
  4. use drugs incorrectly (poor adherence due to lack of knowledge, inability to afford full treatment),
  5. poor communication and inadequate instructions from providers by providers/dispensers
  6. consume fake or ineffective drugs (weak regulatory environment)
  7. rely on private sector due to failings of public sector which is more difficult to control
  8. do not think the health system / treatment is working, when poor diagnosis means they are being treated for the wrong disease

- Parasite resistance to currently used antimalarial drugs
- Change of policy on first-line treatment is slow (inadequate evidence, no consensus on best options, aversion to change, lack of political will and vested interests)
- Few good treatment options and most are expensive
- Slow implementation of policy changes (weak systems or lack of political will to speed up implementation)
- International and national support for systems strengthening is inadequate and poorly coordinated and tends to be focused on components rather than the whole system

- No clear agreed on strategic framework to address financing and availability (supply) of future drug options
- Malaria sufferers have little influence over policy makers, as most are young children and many are from the poorest and remotest parts of society
- Gaps in evidence on the affordability, safety and effectiveness of recent options make optimal choices difficult.
- Serious gap in availability of promising drugs (such as currently artemisinin-based combinations) and capacity and motivation to fill this gap quickly
- Inadequate resistance monitoring systems
- Inadequate supply of good quality drug products even for existing treatments. WHO Prequalification Pilot Programme has approved only one supplier of one antimalarial drug.

5 Strategic Framework for implementation of strategies for effective malaria case management on a country-wide scale

5.1 A shared vision

There is universal timely utilisation (access and rational use) by those at risk of malaria of effective malaria treatment (an affordable, relatively safe, relatively simply administered, highly efficacious drug and functioning systems to deliver it, so that it is widely available in public and private sectors and in the community) through the following:

- Stakeholders have achieved consensus and clarity on strategy
- Countries have the capacity (access to information, political will, resources to implement policies) to make appropriate choices and to implement resulting policies
- A strong regulatory environment ensures quality products throughout private and public systems
- Strategies to minimise cost are operating (including wide availability in the private sector)
- Prevention programmes decrease the need for treatment
- Information is easily accessible to all who need it and regularly updated on the basis of new evidence
- Public awareness is translated into demand for appropriate treatment from private and public systems
- Policies encourage rational drug use
- Future promising drugs are always in the pipeline

In order to achieve this vision a range of actions can be taken by countries to improve policies (what to do) and strategies (how to do). The strategic framework attempts to organise these actions in such a way as to help countries to review their own status and identify priorities based on evidence and consensus on effective approaches. To this end a framework is presented, then policy issues and strategy issues are discussed. Some examples of successful approaches are included in the annex.

Figure 1. Strategic framework to achieve large-scale effective case management

Action	**Pathway to Survival (Components of effective treatment)**			
Response to illness	**Recognise illness ►►**	**Seek treatment (home, community ► or facility)**	**Diagnosis & treatment (public and private ►► sectors)**	**Ensure quality and equity of care ►► Improved health**
Policy	- Education (children, women, public – target most vulnerable)	- Equitable distribution of health facilities - Regulation and support of private providers - Policies addressing socioeconomic inequities - User charges assessed - Quality of care in health facilities improved	- Antimalarial treatment policy for all uses (1st & 2nd line, severe, pregnancy, children, treatment failure, malaria species): efficacy, safety, cost, quality, acceptability, access - Diagnosis policy - Regulatory policies - HRD policies - Financing policies Adherence to policy in private sector Policies to target most vulnerable	- Continuous cycle of policy review and update - Adjustment of policy based on evidence
Strategy	Communications	- Empowerment of women - Communications	- Institutional roles determined - Budgets developed - Commodity needs forecasted - Coordination of planning from district to national, malaria to health to finance	- Monitoring and evaluation undertaken
Implementation	- Reaching everybody (going to scale)	Understand and improve: - User decisions on whether to wait, where to go, how to pay, how to cover other activity. - User and provider decision on what to take and how to take it	Provider - Performance - Quality of service - Quality of drugs - Procurement & distribution User - Adherence - Understanding & acceptance - Payment	- Resistance / treatment failure monitoring - Quality of drugs and services monitoring - Referral - Treatment of children under 5 and pregnant women promoted
Evidence	- Local beliefs - Effectiveness of communications Behaviour change	- Treatment seeking behaviour - Equity in coverage across socio-economic groups Target groups seek early treatment	- Best drugs to treat disease - Best drugs to delay resistance - Provider & user behaviour - Effects of cost	- Resistance mapping over time Other evidence (health seeking behaviours, costs of failure etc) - Communication of results

5.2 Policies for effective case management

National policies need to address the following points:

5.2.1 Choice of drugs

The choice of drugs for treatment of malaria (first line, second line, different population groups - pregnant women, children, other ages, people in endemic areas, displaced people etc, severe, uncomplicated, complicated malaria, parasite present eg *vivax*, drugs for facility level and home level) is difficult. Each country needs to consider the evidence available locally and internationally to make its choices, and to have systems of continual review of these choices.

Current guidance from WHO is as follows:

1. A recent (August 2003) AFRO consultation recommended that countries should change first line treatment when the rate of clinical treatment failures is above 15% and parasitological failure above 25% at 14 days. Thus WHO recommends that all countries in Africa south of Sahara, still applying chloroquine monotherapy as first line treatment should, without delay, change to something more effective.
2. All 1st line treatment for falciparum malaria to be introduced from now should be combination treatment (WHO, 2001).
3. On the basis of the accumulating evidence the following options are considered acceptable:

Artemisinin-derivative Combination Therapies (ACTs):

1. Amodiaquine-artesunate
2. Artemether – lumefantrine (Coartem)

If there are barriers in a country to using ACT the following non artemisinin combination can be considered:

1. Amodiaquine/SP
2. possibly amodiaquine/Lapdap

Other combinations currently showing potential to be important include:

1. Lapdap-artesunate (Lapdap Plus)
2. Pyronaridine-artesunate
3. Piperaquine- dihydroartemisin

The data are currently insufficient for these last four combinations to be recommended by WHO. There is a good chance that some will be ready for registration by 2005. If one or more of the last 3 become available, this would increase the choice among co-formulated ACTs, and probably allow a lower price. Work is also progressing on co-formulation of artesunate-amodiaquine and artesunate-mefloquine. However, the latter is currently not recommended in areas with intense transmission because of the long half-life of mefloquine.

Combinations of SP with artesunate would not now be considered as a top choice, given the rapidly progressing resistance to SP in recent years.

5.2.2 Policy for home-based management of fever:

Delivery of prompt and adequate treatment for uncomplicated malaria at the community level is a key strategy to reduce the burden of malaria in sub-Saharan Africa, where treatment for uncomplicated malaria is rarely sought at health facilities and treatment provided at home is often inappropriate or delayed. To increase access to effective antimalarial treatment by the vast majority of the population, the strategy of home management of malaria (HMM) has been developed, which aims to improve the quality of treatment provided by caregivers at home through IEC and training, and by making pre-packaged drugs available at community level.

However, as first-line treatment policy for uncomplicated malaria changes as a result of spreading resistance to chloroquine, this raises particularly difficult issues. If Combination Therapy (CT) is considered the best option to use for first-line treatment of uncomplicated falciparum malaria in facilities, there are three main arguments for making it available also at home and community level:

1. there would be problems recommending or offering a less effective treatment to patients in the community or at home, who may delay seeking treatment in facilities on the basis that they have already taken recommended treatment.
2. if widespread use of monotherapy outside facilities includes use of drugs, which are components of the CT recommended for use in facilities or have similar modes of action, the added benefit of CT in delaying development of resistance may be reduced
3. if CT were offered in facilities but not at home, the messages to be delivered in communications strategies will be complicated, as strong marketing of CT will be necessary given the more complex dosing.

Countries already introducing CT have taken different approaches to this issue. Uganda has a systematic strategy of supply, training and communications for home-based management of fever with prepackaged, fixed dose chloroquine/sulfadoxine-pyrimethamine (CQ/SP) for children under 5 years. Zambia has opted for a phased approach introducing the treatment with lumefantrine-artemether (Coartem®) in facilities first. Zanzibar, which has a good network of health facilities, has chosen to restrict AQ/AS to public sector facilities. A phased approach allows patients to benefit soonest from access to CT, while strategies for home-based management are elaborated. [NOT SURE I FOLLOW THIS; PHASED WORKS BEST BECAUSE TRYING TO MOVE TOO QUICKLY WILL CREATE SUPPLY GAPS?]

5.2.3 Pricing

The substantially higher cost of combination therapy is probably the major reservation to adoption. CT must be competitive with alternatives and affordable to the poorest. As a clear public health measure subsidies could be justified, but would need to be sustained. Cost must be low in the private sector as well as the public sector if wide coverage is to be achieved.

It is recognized that initially the additional costs of CT will require external funding in most countries, although in the long term there are likely to be substantial cost savings enjoyed through more effective treatment of patients preventing development of severe disease. Strategies for financing of CT need to be addressed at both international and national level. They are discussed in 4.3.2.

5.2.4 Diagnosis

In areas of high transmission, confirmation of malaria diagnosis through microscopy or rapid diagnostic tests (RDTs) is rarely undertaken except for inpatients with severe malaria and patients failing to respond to treatment. This is partly owing to lack of resources and infrastructure and partly because many people with malaria parasites are asymptomatic, so patients with positive slides may have another cause of illness. With the introduction of much more expensive ACT, it will be more important to improve rational drug use through limiting overdiagnosis and treatment of patients without malaria, so the role of diagnostic tests needs to be considered further, at least in the longterm. The costs of the tests could be offset by the cost savings on drugs. This will have important implications for IMCI, where malaria treatment is currently indicated for all children under five with fever in countries of the region and several studies show that trying to increase specificity of diagnosis of malaria using clinical algorithms has unacceptable trade offs in sensitivity. The role of RDTs needs further definition.

About 25-30% (?) of the population of tropical Africa now lives in cities, where transmission is not intense. Many others live in areas with unstable malaria. For all these populations, the prevalence of asymptomatic parasitaemia in young children is generally below 50%, so that if the treatment is much more expensive than the test, there are still possible savings. In adults, the prevalence of asymptomatic parasitaemia is generally much lower, and there would be huge savings to be made by applying diagnostic tests for adults.

5.3 Implementation strategies

As well as best practice for management of individual cases there are a number of issues which need to be addressed at national and supranational level in order to achieve public health improvements by ensuring maximum access to effective case management. Implementation strategies need to be developed for the following:

5.3.1 Capacity Development (human and institutional)

Delivery of effective treatment depends on a chain of people each enabled to play his or her role. Although most countries and partners recognise the importance of human resource development (HRD), the investments are rarely proportional to the need, often focussing only on training. Recent increased investment in malaria provides opportunities to support more comprehensive HR strategies. If initiatives for scaling up and increased funding target commodities and systems without proportional investment in HR, it will put excessive pressure on overstretched health workers. Furthermore patient load will increase where facilities are well-equipped and supplied with good drugs. A further reason for paying more attention to HR strategies is the high and increasing attrition (from senior health professional to rural shopkeepers).

Part of the strategy for improving case management will be to develop, fund and implement a human resource strategy taking into account all the needs of effective case management. It would address:

- Skills development
    - *Integration, pre- and in-service training, efficiency measures, achieving appropriate skill mixes.*

- HR needs assessment for newer interventions, eg IPT, new drug policies, IPTi, home management
- Needs of different case management providers: private-for-profit, mission and NGO
- Institutional development
    - *Regulatory authorities and Quality Control, planning cells, training institutions, schools, community capacity, private sector associations, NGO Networks, infrastructure.*

5.3.2 Delivery Systems

The systems to ensure that good drugs reach those who need them, and are used effectively include the systems of care provision and the systems of pharmaceutical management. Care is provided from different sources: home, community, primary to tertiary health facility, private and public sector.

a) Management of Care Provision

Home management
As mentioned in section 5.2.2 the widespread use of home management including treatment with shop-bought drugs necessitates greater efforts to ensure this management is as good as possible, while continuing to strive to provide more effective public health services as close to home as possible. A few examples exist of attempts to improve the quality of home management (Uganda, Eritrea,), but there is still limited information for recommending best strategies for nationwide intervention. Some key lessons learnt so far are:

1. Improving home management through training community based distributors and providing prepackaged drugs can be very popular, so there is a challenge to ensure supply meets demand (Uganda), and this must be anticipated in planning.
2. Attrition rate of drug distributors (Uganda) or turnover of shopkeepers selling antimalarials (Tanzania) can be high. In Tanzania an approach of mass communication to shopkeepers and consumers may be more feasible than a training programme for shopkeepers. In Uganda a scheme of replacing distributors who leave is needed

[This one could go either here or below with private sector, but I suggest reserving the HM section for programs more focused on placing responsibility with the caregivers, i.e. traiing caregivers to do the right thing.]*To add*

Public sector facility-based case management

To add

Private sector case management
The formal and informal private sector is often the first contact for those seeking care for malaria. Unfortunately even in licensed and registered shops, shop attendants are poorly trained and unfamiliar with appropriate drugs, drug doses or regimens for malaria treatment. The private sector, particularly the informal drug sellers, are also often a major source of poor quality or fake drugs and they pose a major problem in many countries where they are, and will almost certainly continue to be, a major source of treatment for malaria. Governments are often reluctant or lack the means and appropriate approaches to work with the private sector to improve the quality of drugs and service. A few examples exist of programs designed to

improve the private sector management of malaria (Kenya, Tanzania, Nigeria), but much needs to be done to develop comprehensive approaches that involve situational analyses, advocacy and situation appropriate interventions to improve malaria management.

1. In Kenya training of shopkeepers was found to be feasible
2. In Tanzania, Kenya and Ghana, franchising has been used to improve shops
3. In Nigeria, a brief training and introduction of pre-packaged improved the drug sellers management of malaria in under-5s.

[I can add more later, but see first what others think this is on track.]

To add

b) Pharmaceutical Management

A systematic approach to pharmaceutical management will ensure that antimalarials for a complete course of malaria prevention or treatment are available and appropriately used according to an effective treatment strategy and timeline. It involves four basic functions: selection, procurement, distribution and use, each building on the others. At the centre of pharmaceutical management are management support systems which hold these functions together. All these rest on the policy and legal framework which establishes and supports the political commitment to essential pharmaceutical supply. Improving the supply and management of antimalarial drugs is achievable. Different countries are at different points in achieving effective drug management for malaria.

Selection

Selection is the process of establishing and using a limited list of antimalarials. It involves a review of malaria epidemiology, identification of the best clinical treatments for the various populations affected, and the generation of a list of antimalarials and supplies to ensure these standardised treatments. It is important to establish at which level of health care the various antimalarials will be available. Whether a country is drawing up its standard treatment guidelines or changing its policy , programme managers and/policy makers selecting first-line antimalarials need to realise that to achieve optimum implementation, a country not only needs an efficacious antimalarial, but also an effective one.

Guidelines for the criteria to be considered when selecting/changing first and second-line antimalarials have been discussed elsewhere (reference). Some considerations are listed below.

- *Analysis of evidence base for change (data from drug resistance studies)*
- *Consideration of up to date recommended options*
- *Review of lessons learned from similar countries*
- *Analysis of barriers to implementation of existing antimalarial drug policy*
- *Provision of options for special groups e.g infants and pregnant women*
- *Choice of individual drug/s and dosage forms*
- *Decision on which drugs will be available at each level of health care*
- *Approximation of financial burden for change*
- *Revision of Standard Treatment Guidelines and Essential Drug Lists*

Procurement

The goal of effective procurement of antimalarials is to purchase the most cost-effective antimalarials in the right quantities; select reliable suppliers of high-quality products; ensure

timely delivery and achieve the lowest possible cost for all the antimalarials procured. Some considerations for procurement are listed below:

- *Estimation of antimalarial drug needs*
- *Selection of procurement method*
- *Consideration of packaging options*
- *Consideration of dosages of pre-packaged drugs*
- *Management of tenders*
- *Establishment of appropriate contract terms*
- *Assurance of drug quality*
- *Determination of lead time for delivery*
- *Consideration of existing stocks/early planning for change*

Distribution

This ensures that antimalarial drugs are available in the quantities needed for all patients who need them whether through the public or private system. This includes clearing drugs through customs, transporting them, making timely deliveries to all public health facilities for treatment of patients, keeping records, maintaining adequate stock levels, and following appropriate storage procedures in all facilities. Communication of guidelines for distribution in the private sector is also important. The creation and implementation of a distribution plan is highly recommended. Some of the considerations for effective distribution are listed below:

- *Managing co-administered drugs*
- *Labelling of drugs to distinguish them eg SP for IPT*
- *System of distribution eg ANC for IPT*
- *Appropriate physical condition for storing antimalarial drugs*
- *Good record keeping*
- *Good recall systems for expired drugs*
- *Good stock control*

In cases where countries use combination therapy there is the need to ensure that, if co-formulated/pre-packaged antimalarials are not available, users co-administer drugs according to the CT treatment guidelines. Most importantly, methods to ensure that monotherapies are replaced with CTs in the public and private sector must be developed.

Use

This includes appropriate diagnosing, prescribing and dispensing antimalarials by public and private sector health providers as well as their proper consumption by patients. There is a need to ensure that antimalarials are used appropriately, safely and rationally according to standard treatment guidelines. Some considerations for rational use are listed below:

- *Accurate diagnosis*
- *Good prescription practices (correct antimalarial consistent with the STGs in the right dosage and duration)*
- *Revision and dissemination of STGs*
- *Good dispensing practices eg DOT for IPT*
- *Patient adherence to treatment (which in turn may be influenced by many factors)*

[SHOULD WE PRESENT/DISCUSS THAT PRESUMPTIVE TREATMENT OF CHILDREN UNDER 5 MAY BE AN APPROPRIATE STRATEGY IN HIGH ENDEMIC AREAS?]

Packaging of antimalarial drugs should be carefully considered, particularly when using ACTs; which are not co-formulated, as pre-packaging can improve adherence to the correct dose. Pre-packaging of different dosages for children also needs to be considered.

Management support

A variety of different management support systems are required at all organisational levels, from the national programme level down to where drugs are prescribed and dispensed. Some considerations include:

- *Establishment of well-organised management support systems*
- *Provision of proper financial management*
- *Setting up of proper management information systems* (*e.g. drug information systems,* pharmacovigilance)
- *Management of human resources*
- *Consideration for monitoring and evaluation*
- *Training and supervision*

Overall measures to overcome the drug management challenges should include full integration of malaria treatment into national health systems, improving access to effective drugs for treatment as close to the home as possible, and engaging the private sector.

Drug Quality

[SUGGEST THAT THIS SECTION BE TRANSFORMED INTO A SET OF BULLETED POINTS, SIMILAR TO THE OTHERS.]

The number of substandard and counterfeit antimalarial products circulating in developing countries is an issue of growing concern. Many countries do not have quality assurance programs to control medicines, either for imported products or those locally manufactured. Use of poor quality antimalarial drugs is a waste of limited financial resources and undermines public confidence in the national malaria program. Substandard products may lead to treatment failure. Poor quality drug products may also contribute to the emergence of resistance, as their use may result in low bioavailability or suboptimal dosing.

Drug quality starts with the raw materials, both active ingredients and excipients. Manufacturers of the raw materials and the finished products must meet internationally accepted standards for the drug substances and products and must produce using good manufacturing practices (GMP). For established drugs, such standards are publicly available in internationally recognized pharmacopoeal compendia. For new drugs, the innovator company must share their standards and analytical methods with the drug regulatory authority of the country where the drug will be marketed. This implies that the regulatory authority has the expertise required to evaluate the technical information provided by the drug company.

GMP compliance can be confirmed by sporadic site visits to the factories by trained GMP experts. The WHO Prequalification Pilot Project has found only one manufacturer of one artemisinin-combination anti-malarial product that it can approve. More manufacturers of reliable products may be the best way to keep the cost of medicines low. Considering the lack of manufacturers for good quality antimalarial drugs, RBM and other global initiatives should consider investing in technical assistance for manufacturers who are identified as “almost there” in terms of GMP compliance.

It is up to the drug regulatory authority of each country to register products for sale in that country. A good registration process will include a pre-marketing assessment of the product quality. Again, this means the regulatory authority must have staff trained in drug product evaluation. The WHO Prequalification Project attempts to do this assessment on behalf of

countries that may lack sufficient expertise within the government sector. Other international organizations may be able to provide a similar service. Drug product evaluation includes a technical review of the dossier and laboratory testing of samples from each lot intended for sale in the country.
The regulatory authority is also expected to license and routinely inspect pharmacies and other retail outlets where antimalarial drugs are sold or distributed. The inspection should confirm that the products are stored in a way that will maintain quality up to the expiry date printed on the label. The inspection should also verify that only registered or authorized products are accessible at each outlet. Many countries lack an adequate number of trained inspectors. It is recommended that investments be made in building up capacity within the public, private and/or nongovernmental sectors to assist with drug quality surveillance, particularly in peripheral areas where inspectors seldom visit. There are a number of simple, low-cost testing methods available that can be implemented outside a laboratory setting to provide an initial screening for drug identity and strength. Products that fail the initial screening tests should be tested more thoroughly by a reference laboratory to verify the quality problem, e.g., amount of active ingredient, contamination with toxic substances, failure to disintegrate or dissolve, etc. This can provide enough information for the regulatory authority to determine to do a product recall (which can be done much more easily if the drugs are registered) and/or a public awareness campaign warning people not to use the poor quality products..
In addition to monitoring drugs on the market for quality through product surveillance, many countries monitor adverse drug reactions through reports received from phyisicians, pharmacists and patients. Athough there are many causes of adverse reactions to drugs, e.g., interactions with other medicines being used, improper adherence, incorrect treatment prescribed; poor drug quality can be one reason for an adverse event.
It is a myth to say that nothing can be done to improve drug quality assurance because it is too costly or too technical for poor countries. There are low-technology, sustainable activities that can be undertaken for a modest investment. RBM Partners should include this investment in their scale-up strategies, enabling countries to build capacity for addressing malaria that will support every other disease initiative as well. Special efforts are neede to combat counterfeit drugs by strengthening import registration, monitoring distribution channels, control of smuggling and board trade. The option of setting up special antimalaria programme supply chains may not be feasible in most African settings.

5.3.3 Financing strategy

Lack of sustainable financing of newer more expensive antimalarials and the systems to deliver them has been one of the major bottlenecks to better case management on a large scale, but the international community is beginning to show more commitment, and national authorities are showing more confidence to plan on the basis of best practice. A well-considered financing strategy is key to longterm improvements in case management.

At **international level** the following elements of a financing strategy are being debated:

- Differential pricing for rich and poor markets
- Tax incentives to companies producing CT in their home countries
- Public sector investment in private sector research and development eg DFID funding lapdap development
- Global initiatives and financing / procurement facilities, for example addition of CT to the Global Drug Facility and drugs against tuberculosis or development of a Malaria Medicines Supplies Service
- Global funding (loans, grants), especially the World Bank and the Global Fund

- Subsidy strategies
- Reduction of price by bulk purchasing or pooled procurement among countries
- Implications of trips?
- Minimising cost of drug quality control by establishing sub regional centres to provide quality control services to groups of countries.

At **Country level** the following could be considered:
- Cost sharing /user fee policies for malaria treatment may need to be revisited
- Targeted subsidies for high risk groups
- Incorporation of the CT budget into broader health and development plans, including national health sector strategic plans and poverty reduction strategies
- Increased public sector spending on health/malaria
- Issues of pricing in the private sector need particular consideration
- Ensuring comprehensive budgeting in annual planning and funding proposals to include the necessary systems support to deliver antimalarials.
- Including necessary funding for adequate drug quality control in proposals to GFATM, World Bank, etc.

5.3.4 Communications strategy

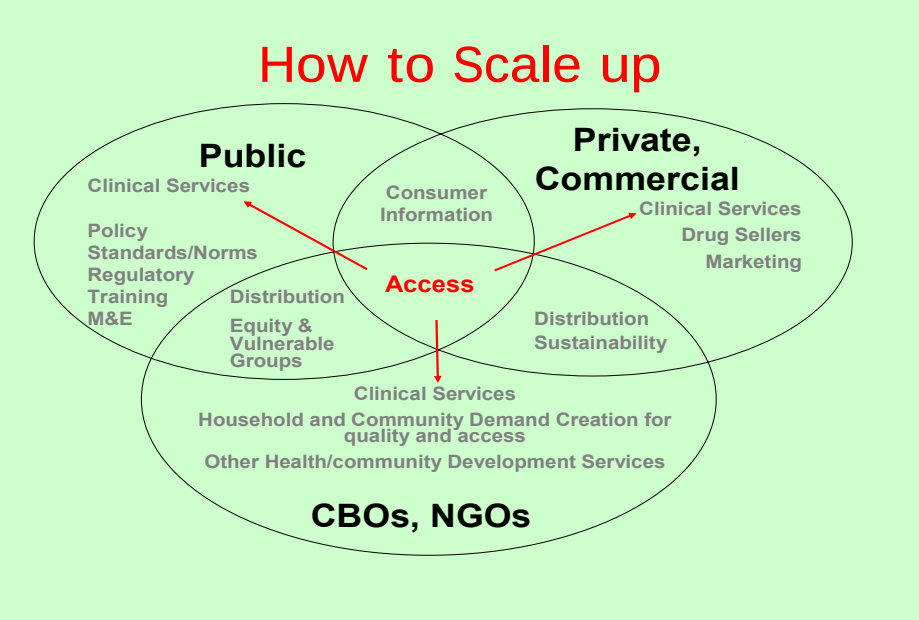
To add

5.3.5 Coordination strategy

In order to reach more people with effective case management it is essential to harness the resources of all current and potential providers. Some useful steps in developing a coordination strategy are:

1. Identification of areas of case management needing coordination:
    - During policy development
    - During planning to introduce new policies
    - During implementation of policies
2. An assessment of all the players in a country, their roles and how their contributions could be enabled and enhanced
3. A plan for collaboration and integration with other programmes, for example:
    - Improving case management through IMCI
    - Improving pharmaceutical management through EDP
    - Integration of PMTCT and ANC through Reproductive Health programmes is a good opportunity to strengthen health care delivery system
4. A strategy for engaging and improving quality of private sector providers (for profit and NGO)
5. A strategy for identifying, mapping and improving access of services to vulnerable, remote and underserved groups

The diagram below, which was borrowed and adapted from the ITN Strategic Framework, describes the roles and interactions and different groups, highlighting how they can work together to increase access to effective treatment:



5.3.6 Monitoring and evaluation

To add

5.3.7 Research

Current Evidence Gaps

1. Efficacy of different combinations in different regions
2. Safety especially lumefantrine-artemether and amodiaquine.
3. Absorption – There is evidence that absorption of Lumefantrine-artemether (Coartem®) by the patient is inadequate unless administered with fatty food. This is a serious concern, particularly as young children are unlikely to have access to food at the treatment facility and may have a reduced appetite due to the malaria.
4. Effects of incomplete dosing, best strategy for increasing adherence
5. Effects of incomplete cover. Do we lose two drugs more quickly?
6. Effects of resistance to one drug in combination
7. Drug choice in vulnerable groups e.g. pregnancy (both for treatment but also IPT)
8. Threshold resistance to SP at which IPT would no longer be effective
9. Safety of artemisinin derivatives and other drugs in pregnancy. The results of animal studies showing toxicity in pregnancy should not preclude the use of artemisinins for treatment in the second and third trimesters if there is no other effective alternative available. However, they should not be used in the first trimester unless the life of the mother is at stake.

10. How to manage treatment failures
11. How to incorporate private sector into strategy
12. Feasibility and acceptability of home management using new drugs/combination therapy
13. Strategies to scale up home management
14. IPT in infants

Evidence on user and provider perceptions and behaviour, optimum systems, finance and supply issues

To add

6 Strategic Framework for partner support to countries for large-scale effective malaria case management

6.1 Key strategic areas where partner support is needed:

The scale of the gap between adequate access to effective treatment and the current situation demands urgent large-scale and sustained support from partners to countries. The nature of support needs to reflect local experience and demands as well as global consensus.

What can Roll Back Malaria contribute by working as a partnership that support agencies could not achieve alone? The RBM Partnership Objectives defined by Roll Back Malaria are:

1. To improve coherence & co-ordination of technical & programmatic support to endemic countries
2. To support improved mobilisation and use of human and financial resources in endemic countries
3. To support enhanced service delivery in endemic countries
4. To support availability and use of reliable evidence on impact and outputs

These objectives can be used to develop partner plans in dialogue with country authorities.

Policy and strategy gaps	**International and Regional Partner Roles**	**Country and Intercountry Partner Roles**
Effective policies for case management	- Communicate strategic frameworks for implementation and scale up to guide countries - Synthesise information for countries on drug options - Develop strategy for improving drug quality - Develop strategic framework for "interim" treatment policy for home management - Develop strategies for NGO and commercial sector engagement	- Support policy development process - Facilitate transformation of policy to strategy and implementation - Update countries on drug information - Support dissemination of new guidelines/strategy
Capacity development (strengthening (human and institutional) strategies	- Ensure coordination of support beyond malaria control across health sector and beyond -	Technical support for capacity development
Delivery systems	Ensure availability of drugs: production levels, effective supply and distribution in country - Drug quality monitoring support - Support more efficient registration processes and strengthening national drug authorities	TA for drug regulation, procurement, distribution
Financing strategy	- Mobilise additional resources through advocacy. - Develop strategies to reduce ACT costs (eg pooled procurement) - Develop strategies for making best use of subsidies Develop strategies to increase incentives for	- Identify resource gaps - Support CCMs with GFATM proposals and implementation

	manufacturers to reduce cost	
Communications strategy	- Develop advocacy strategy for support of effective treatment, - Ensure research findings are broadly shared	- Support development of communication strategies for policy change, home management, rational drug use etc - Identify and share examples of best practice
Coordination strategy	- Develop strategic framework for coordinated support - Ensure inter- and intra-agency consistency and communication - Support coordinated technical assistance	- Ensure in-country partner coordination - Provide coordinated technical assistance - Build capacity of consultant pool skills for improving treatment
Monitoring and evaluation	- Global tracking and partner coordination - Shared drug efficacy database - Ensure data collection includes operational indicators as well as drug efficacy	Technical support to monitoring resistance, drug quality and quality of care
Research	Ensure coherent research agenda informed by countries and production of timely findings Ensure pipeline of new drugs Research on products for home care	Technical support for country level research

6.2 Priority actions by partners to scale up effective case management

Recommendations to the RBM partnership for urgent action

1. Accelerate availability of co-formulated ACTs which are registerable fulfilling ICH and GMP criteria, cheaper and simpler to use than the ones currently available and likely to be recommended by WHO by supporting, and monitoring the work of MMV and TDR and other entities involved in R&D
2. Accelerate pre-qualification of currently recommended co-packaged combinations, which are recommended by WHO and request WHO to publish specifications for blister-packed SP and amodiaquine
3. Set up forecasting and support countries to work together on procurement to lower prices and increase supply security
4. Support and promote price subsidies of ACTs through GFATM and other mechanisms, so that price is not an obstacle to the implementation of ACTs as 1st line antimalarial drug policy at least to the extent it is provided through public health systems
5. Support all countries in tropical Africa, which still use chloroquine as first line treatment to change **as soon as possible** without awaiting further results of chloroquine efficacy testing to a **combination treatment** in accordance with WHO recommendations (AFRO drug policy meeting 2003, WHO combination treatment consultation,2001).
4.1 Support countries to develop policies, which address not only public health facilities, but also private sector and home and community-based treatment, in countries where a significant proportion of malaria cases are treated outside public health services
5. Work together at country level to implement and monitor new drug policies and old ones, which are effective (issues to deal with in implementation and monitoring are covered above)

a.
b. Identify role of diagnosis in different epidemiological and operational settings
c. Work out

Action over the longer term

- Develop multilevel communication strategy to involve international, regional and country level decision makers including those at risk of malaria. This should include a strong, coherent global communication strategy to address the enormous threat of fake and counterfeit antimalarials
- Organise and coordinate support to systems strengthening, capacity development and policy making process
- Identify best practices for engaging informal private sector in particular for ensuring that this sector plays a positive role in relation to the goal of good quality home management
- Implement multi-faceted fast-track research to fill key evidence gaps delaying deployment of potentially good drugs (socioeconomic, policy, operational and systems research to be undertaken simultaneously with drug testing)
- Create enabling environment for developing new drugs and adequate supply of raw materials
- Pay particular attention to treatment strategy for home management
- Develop strategic approaches to improve quality of drugs and regulatory capacity
- Develop a clear strategy for addressing overdiagnosis and treatment to contain costs and limit excess distribution. This must address diagnosis strategy and the role of IMCI.

Annex. Examples of good practice

(Task force to expand to brief description and key lessons) ?merge with history section

- Delivery of home management – public sector
  - Uganda – home management prepackaging, general community agents *Fred Kato*
  - Eritrea – home management *Wilson*
- Delivery of home management – private sector
  - Kenya – shopkeepers Franco
- Rational Drug Use
  - Malawi – limiting registered products *Jack*
- Financing
  - Tanzania- $10million for malaria in SWAp
- Drug management
  - Tanzania – Pharmacy board to implement with the help of MSH Quality Assurance Programme rapid screening of imported drugs at points of entry in Dar es Salaam and along the Kenyan border. A tiered programme has been instituted to screen the quality of selected key drugs and suspicious products entering and on the market using standardized inspection and TLC techniques and pilot product quality testing programmes for developing and monitoring ports of entry along with post-marketing surveillance in selected areas of the Lake, Northern and Coastal Zones
  - Zambia – Good procurement practice, quantification
  - Senegal – collaboration among MOH, National Drug Quality Control Lab and University of Dakar to conduct drug quality surveillance
  - Cambodia – sentinel surveillance sites conduct screening for drug quality
- Capacity development
  - Ghana – contracting out training / education
- Targeting vulnerable groups
  - Cambodia – remote populations use dipsticks and suppositories, nationwide prepackaged CT through GF support using social marketing, agreed by partners *Allan*
  - Mali – Treatment outreach by relais from health centres *Massambou*