Operational Challenges of Implementing Multiple First-Line Therapies for Malaria in Endemic Countries

Rima Shretta

June 2008

Center for Pharmaceutical Management
Management Sciences for Health
4301 N. Fairfax Drive, Suite 400
Arlington, VA 22203 USA
Phone: 703.524.6575
Fax: 703.524.7898

This report is made possible by the Resources for the Future under contract number MSH 1931.2008 ANTMW.

Recommended Citation

Shretta, Rima. 2008. *Operational Challenges of Implementing Multiple First-Line Therapies for Malaria in Endemic Countries*. Arlington, VA: Management Sciences for Health.

Center for Pharmaceutical Management
Management Sciences for Health
4301 North Fairfax Drive, Suite 400
Arlington, VA 22203 USA
Telephone: 703.524.6575
Fax: 703.524.7898

CONTENTS

ACRONYMS

ACT	artemisinin-based combination treatment
AL	artemether-lumefantrine
AQ	amodiaquine
AMFm	Affordable Medicines Facility for malaria
AS	artesunate
BCC	behavior change communication
EML	essential medicines list
GFATM	Global Fund to Fight AIDS, Tuberculosis and Malaria
IEC	information, education, and communication
IMCI	Integrated Management of Childhood Illnesses
M&E	monitoring and evaluation
MFT	multiple first-line therapies
MoH	Ministry of Health
MSH	Management Sciences for Health
QA	quality assurance
RBM	Roll Back Malaria [Partnership]
RDT	rapid diagnostic tests
SP	sulfadoxine-pyrimethamine
STG	standard treatment guidelines
USAID	U.S. Agency for International Development
USD	U.S. dollar
WHO	World Health Organization

ACKNOWLEDGMENTS

A special thank you to David Lee for initial discussions, conceptualizing the framework, and reviewing the final paper.

Thanks to Gladys Tetteh for reviewing the initial framework for implementation as well as attending and presenting this preliminary framework at a meeting organized by Resources for the Future at the Kruger National Park, South Africa, in April 2008.

Thanks also to Jane Briggs and Niranjan Konduri for their review.

Thanks to the following MSH staff and consultant in the field for providing information on current practice regarding ACT implementation in the field.

Angola	Malick Diara
DRC	Gabriel Bukasa
Ghana	Gladys Tetteh
Kenya	Gladys Tetteh
Liberia	Lloyd Matowe
Madagascar	Kathy Webb
Malawi	Cynthia Kamtengeni
Mali	Thidiane Ndoye
Nigeria	Kate Adegoke
Rwanda	Willy Kabuya
Senegal	Thidiane Ndoye
Southern Sudan	Robert Azairwe
Uganda	Loi Gwoyita
Zambia	Oliver Hazemba

Thanks also to the CPM editorial department.

BACKGROUND

> The purpose of an antimalarial drug policy is to ensure availability 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 minimize the development of antimalarial drug resistance (WHO 2001).

Parasite resistance to antimalarial medicines has social, political, and economic consequences at the global, regional, and country levels. As a response to increasing levels of resistance to antimalarial medicines, the World Health Organization (WHO) recommends that all countries experiencing resistance to conventional monotherapies, such as chloroquine, amodiaquine, or sulfadoxine–pyrimethamine (SP), should use combination therapies, preferably artemisinin-based combination therapies (ACTs) for the treatment of *Plasmodium falciparum* malaria. Evidence from Western Thailand has indicated low levels of treatment failures with ACTs in children (WHO 2007). Although ACTs are currently not widely available in Africa, there are growing concerns that as more people with malaria gain access to them, resistance to ACTs could soon spread rapidly (White 2008).

These concerns have given rise to increased dialogue at the global level on mechanisms to delay the emergence of parasite resistance and preserve the effectiveness of ACTs. Among the strategies that have been discussed is the use of multiple first-line therapies (MFT). Smith et al. (2008) and Boni et al. (2008) use theoretical models to show that deploying more than one first-line co-formulated malaria medicine (instead of a single co-formulation for everyone) in a population could have significant benefits in fighting drug resistance by slowing the fixation of resistant strains and retarding selection pressure to the partner drugs used in artemisinin combinations. Similar strategies have been used for slowing down antimicrobial and insecticidal resistance (Bonhoeffer et al. 1997; Laxminarayan et al. 2002; Smith et al. 2006; Davey et al. 2007).

Malaria endemic countries have traditionally relied on the use of a single first-line therapy for the treatment of uncomplicated malaria. Changes in first-line medicine policies have occurred when parasite resistance to these single therapies have crossed a certain threshold, rendering them ineffective. MFT for malaria has occurred in endemic countries mainly by default because of a combination "natural experiments," as well as private market dynamics and public sector policy whereby different health care delivery sectors, programs or organizations have adopted and implemented different treatment guidelines or policies and may not be following the national first-line treatment as established by the countries' Malaria Control Programs and Ministries of Health (MoH).

MFT have the potential to decrease mortality and morbidity while maximizing the useful therapeutic life of ACTs by delaying the development of drug resistance. However, the effectiveness and success of any strategy will also depend on the financial and operational viability of the intervention. The potential operational challenges and cost implications of

systematically adopting and scaling up implementation of a potential MFT strategy in endemic countries are largely unknown. Nevertheless, sources of financing of antimalarials already include the Global Fund to Fight AIDS, Tuberculosis, and Malaria (GFATM); UNITAID; the President's Malaria Initiative; and the World Bank Booster Program. The arrival of new global strategies such as the Affordable Medicines Facility for Malaria (AMFm) may potentially enhance the effort to scale up MFT for malaria.

Objectives

This report proposes to—

- Present a framework for discussing the appropriate adoption, introduction, and implementation of MFT for malaria
- Identify and address key challenges to adoption and implementation of MFT and proposes key principles to facilitate appropriate and timely adoption and implementation
- Suggest mechanisms for a way forward on the challenges
- Discuss the effect of new global strategies on introducing MFT

This framework may be applied in a country context to evaluate the actual process and potential in-country barriers and costs.

Target Audience

The paper is aimed at members of the malaria community including program managers interested in adopting and implementing MFT for malaria control at the global and country level.

Methodology

The methodology used to develop this framework was a review of published literature on MFT and the experience of the authors and staff from Management Science for Health's (MSH) Strengthening Pharmaceutical Systems in providing technical assistance to countries in the policy change process and in implementing first-line therapies for malaria. This paper builds on previous MSH experience supporting similar framework development for ACT implementation (RPM Plus 2005), zinc for acute diarrhea (Zinc Task Force 2006), and tuberculosis retooling (Stop TB Partnership 2007).

The initial framework for adoption and implementation of MFT was presented at a meeting organized by RFF in April 2008 during which the evidence of the effectiveness of MFT, the viability of its implementation as well as the various MFT options were discussed. The

framework was revised and the report was elaborated as a result of the discussions at the meeting.

Structure

The introduction outlines the working definition of MFT, potential MFT options, the effect of new global strategies particularly the importance of the AMFm, and key challenges in adopting, introducing, and implementing MFT with suggestions for actions that may facilitate the process. The second section, Adoption and Policy Change to MFT at the Global and Country Level, discusses the factors affecting adoption and changing to an MFT policy at the country level. The third section, Introduction and Implementation of MFT Policies at the Country Level, presents the framework for MFT policies at the country level. The final section provides a discussion of the way forward.

Table 1 lays out the framework for adoption, introduction, and implementation of MFT with a summary of the key actions and issues to consider.

Annex 1 includes the current first-line recommendations and observed practices for the treatment of uncomplicated malaria in select African countries. An illustrative generic timeline for the framework for adoption, introduction, and implementation is presented in Annex 2.

Public and Private Sector Definitions

The following definitions have been used when alluding to the public and private sectors—

- Public sector is comprised of the government entities that provide health services (Ministry of Health, Ministry of Defense, etc.).

- Private sector includes the following (USAID/DELIVER, 2008)—
  - Service Providers
    - Social marketing organizations
    - Nongovernmental (NGO)/faith-based (FBO) service providers and/or associations
    - Private doctor/nurse/midwife providers and/or associations
    - Private pharmacists and associations
    - Commercial (for-profit) shops and boutiques including private pharmacies
    - Traditional medicine providers

  - Supply system functions
    - In-country distribution and transportation, either as functions outsourced by government (or parastatal) or NGO, FBO, or commercial pharmaceutical distributors
    - Commercial manufacturing (multinational, regional, country)
    - Procurement: as a function outsourced by government
    - Quality assurance

- Demand creation/advocacy
  - NGOs
  - Grass roots/civil society
  - Social marketing
  - Commercial

- Health financing
  - Health insurance/HMOs/third party

Public services may be provided by the following when private sector firms have an MOU with the government and are funded by the government to provide such services—

- Public sector organizations,
- FBOs and other not-for-profit organizations
- Private-for-profit firms/clinics

In most of the countries, the private-for-profit sector implements a variety of treatments depending on availability, affordability, and preference of the patients and providers. Although, this current situation may be considered multiple first-line therapy, this paper considers MFT to be an explicitly recommended policy. In this case, the "natural" and haphazard individual prescriber's decision/selection may not necessarily be desired, unless it is explicitly defined to be one of the components of the policy.

INTRODUCTION OF MULTIPLE FIRST-LINE THERAPIES

Definition and Rationale for Multiple First-Line Therapies Policy

MFT is defined as a malaria medicine policy in which two or more therapies are made available to the same or adjacent populations and patients and clinicians can choose which therapy to use (Boni et al. 2008). A parasite's offspring that arises in a population where one ACT is used must be reasonably likely to encounter the unfavorable selection environment where another ACT is used. Furthermore, when using two or more medicines in equal amounts, the rate each medicine is used is cut to a half or a third of total use, thus reducing the overall selection pressure for resistance to that medicine. Boni (personal communication, July 4, 2008) clarifies that models demonstrate that there is no upper limit for the number of antimalarials that constitute an MFT, provided more types of products are used with independent modes of action.

The theoretical success of MFT is dependent on a population-wide distribution of medicine use independent of implementation. Smith et al (2008) and Boni et al (2008) evaluated the use of different first-line therapies in equal and unequal amounts in the host population to arrive at their conclusions. However, in order to achieve diversity of medicine use, implementation will need to achieve a particular pattern/distribution of drug use. Implementation is addressed only tangentially in the studies above. Both Smith et al (2008) and Boni et al (2008) arrive at their conclusions using general multiple unspecified hypothetical antimalarial medicines and the clinical benefits and costs of using multiple first line ACTs have not yet been established. Future work will demonstrate and quantify this.

While an MFT strategy can have non-ACT components, the current WHO recommendation for first-line treatments is ACT. Therefore, until the efficacy of other treatments has been established (Boni 2008), this paper defines multiple first-line therapies for malaria as a heterogeneous policy with two or more ACTs for the treatment of malaria infection deployed in the same or heterogeneous populations resulting in a diversity of medicine use in the population. Currently, only two effective ACT products are recommended for high transmission areas (artemether/lumefantrine [AL] and artesunate/amodiaquine [AS/AQ]).

Possible MFT Treatment Options

The following options of MFT have been considered by its proponents and have been discussed by Boni et al (2008); Smith et al (2008) demonstrating good clinical outcomes as well as by participants at the meeting organized at the Kruger National Park, South Africa, in April 2008.

- ***Option A*:** One first-line treatment in the public sector and a different one in the private sector.

  Rationale: Good clinical outcomes demonstrated. Little incremental cost with implementation in the public sector because the status quo is maintained. Furthermore, most countries in Africa currently already different antimalarials in the public, not -for-

profit and commercial private sectors therefore the investment in behavior change will be lower.

Challenge: Achieving the desired degree of private-for-profit sector adherence to the recommended therapies may be difficult.

- ***Option B:*** Different first-line drugs for children and adults implemented in the public and private sectors.

  Rationale: Good clinical outcomes demonstrated. Easier implementation as pediatric and adult markets are already partitioned.

  Challenge: Achieving the desired degree of private-for-profit and public sector adherence to the recommended therapies may be difficult.

- ***Option C:*** Different first-line drugs for children and adults implemented only in the public sector and the private sector left to its own accord. The MFT sector policy can be set depending on what is observed as being implemented in the private-for-profit sector.

  Rationale: Implementing MFT in the public sector will be simpler as they are already used to prescribing treatment according to a set STG. This will ensures at least two treatments being used at the same time in almost equal amounts. In this option, we accept that it will be difficult to control what is given in the private sector and therefore this sector is left to its own accord.

  Challenge: Several options will be used in the private sector—little change from current situation in terms of availability of choices, but may not achieve the desired proportion of use of the various first-line therapies.

- ***Option D:*** Different first-line treatments by random assignment (e.g., birth dates, days of the week).

  Rationale: Little decision making for provider and less training on criteria for selection required.

  Challenge: Lack of reliable systems for random assignment and difficulties in monitoring. Furthermore, there may be clinical, biological, and ethical issues stemming from the choices under this option that have not been studied.

- ***Option E:*** Do nothing. Multiple first-line therapies exist on some level in most countries.

  Rationale: No cost associated with this.

  Challenge: No coordinated approach for implementation, and there is potential of compromising the efficacy of ACTs due to uncontrolled used in the private-for-profit sector.

Boni (2008) considered options A, B, C, D, and E. An additional strategy evaluated was rotation or cycling. This involves use of one antimalarial for first-line treatment for a specified period of time and then changing to another before resistance to the first develops. Although, this has successfully been historically used to slow down the development of antimicrobial and insecticide resistance for example, in the treatment of head lice, it does not entail using multiple treatments simultaneously and therefore is not classified as MFT. This strategy was eliminated due to worse clinical and drug resistance outcomes than the MFT options described above.

Option E maintains the status quo and does not fall within the definition of a *coordinated approach*, so was eliminated.

Therefore, the two main options evaluated under this framework were Options A and B.

In all the options above, it must be noted that control of the private-for-profit sector will be challenging. Furthermore, regardless of an MFT policy, monotherapies will need to be removed.

Adoption, Introduction, and Implementation of MFT

The decision to adopt MFT will be triggered by evidence of resistance to the existing single first-line therapy policy or greater efficacy of the proposed MFT strategy. The challenge is that there is little hard and direct evidence or parameter estimates of the efficacy of MFT compared with current recommended strategy. Historical changes in first line treatment policies for malaria have all occurred as a result of need due to clinical failures to the currently used antimalarial. The key driver for MFT is the interest in slowing the emergence of resistance. The type of evidence that is likely to be accepted as appropriate will need to be evaluated as well as the cost-benefit of "proactively" switching from current recommendations to MFT. MFT proponents will need to build consensus among both global and country policy makers and other stakeholders to adopt it formally, in whatever form, before any planning for implementation can take place. Furthermore, donors and funders need to be convinced that this is better than the single first-line treatment policy so that they can support country decisions. In addition, a presentation of MFT will require an elaboration of the specific combinations which may be considered appropriate for use as part of this strategy.
The following are factors that are taken into account when assessing benefits and risks of switching to another treatment policy, in addition to what is considered as appropriate evidence of benefit.

- Resistance to change

- Acceptability of the new treatments; this will be crucial for MFT whereby a negative perception of one of the products recommended as part of MFT may raise potential ethical and equity concerns and thereby comprise adoption

- Weak legal and regulatory frameworks and capacity

- Inadequate capacity for diagnosis particularly as biological diagnosis may be advocated
- Inadequate capacity for differentiating which treatment to be given according to the policy recommendation
- Inadequate capacity to manage pharmaceutical supply that includes more first-line therapies
- Inadequate infrastructure, equipment and support services
- Human resource constraints
- Lack of leadership; insufficient capacity to manage the change
- Financial constraints (for procurement of MFT as well as the cost of supportive actions needed to institute the change)

Adapted from: WHO. 2007. *New technologies for tuberculosis control: A framework for their adoption, introduction and implementation*. Geneva: WHO.

Facilitating Appropriate Adoption, Introduction, and Implementation

Engaging Key Stakeholders

Identifying key stakeholders and keeping them updated and informed about changes can facilitate the adoption and implementation process. Box 1 outlines potential stakeholders that need to be involved; however, this list will have to be adapted to each country context. It will be essential to engage the private sector, particularly as the MFT will be implemented in both the public and private sectors. In addition, antimalarial manufacturers need to be informed and involved to avoid potential resistance because of market losses for their products. Involving professional organizations and bodies such as national pharmaceutical societies may help engage the private sector.

Box 1. Illustrative List of Stakeholders

This list should be tailored to the specific context in each country.

Ministry of Health
- National Malaria Control Program
- Pharmacy and Essential Drugs Department
    - Drugs and Therapeutics Committee
- Health Education Department
- Provincial and District Health Officers
- Director of Reproductive Health
- Director, IMCI Program

Ministry of Finance
- Director of Health budgets

Private Sector
- Manufacturers of antimalarials and diagnostic products
- Importers and wholesalers
- Private hospitals and pharmacies
- Drug shops

Research Departments and Institutions
- Department of Epidemiology
- Pharmacy Department

Professional Organizations

Nongovernmental Organizations (including mission hospitals)

Consumers
- Patient and caretakers
- Consumer advocacy groups

Source: Adapted from MSH/RPM Plus (2006)

Appropriate Budgeting, Financing, and Resource Mobilization

Potential financing sources need to be addressed during policy change discussions because of potential significant costs associated with procuring the new treatment and needing time-limited investment of additional resources—including resources for developing and printing clinical guidelines and behavior change communication (BCC) materials, plus costs for training and other activities described further on. These costs need to be budgeted for at the planning stage. Although any incremental cost for the purchase of the ACTs as MFT components will be simple to define, the costs for the transition process including the costs for changing the standard treatment guidelines, training of providers in the new strategy and policy as well as communication to patients and caretakers will vary significantly with country context. Mulligan et al. (2001) calculated the transition process to ACTs in Tanzania to cost 813,734 U.S. dollars (USD). It is expected that these costs will be significantly higher for adoption and implementation of MFT because of private sector involvement. In addition, considerable

resources will be required for coordination, training, expanding health system capacity to implement the policy, and implementation monitoring by the regulatory body.

Currently, procurement of antimalarials is financed through a combination of Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM), UNITAID, President's Malaria Initiative, the World Bank Booster Program, other donors and national level resources, However, under these current financing mechanisms, coordinated implementation and availability of ACTs has occurred mainly through the public sector in a fairly controlled manner with the government as the predominant entity involved in implementation. As MFT may potentially be funded by existing and new funding sources, acceptability and consensus building among these donors will need to occur.

Under all the above financing mechanisms, ACTs currently make up only 20 percent of the total treatments taken for malaria and these are provided almost entirely by the public sector and not-for-profit clinics. In the for-profit private sector, where 60–80 percent of patients directly access treatment for malaria (in pharmacies and other retail medicines outlets, e.g., chemical seller shops), ACTs make up only 5 percent of the total market (AMFm, 2007).

The Affordable Medicines Facility for malaria (AMFm) is a proposed new global initiative that may enhance access to and use of ACTs, particularly in the private-for-profit sector. For example, Uganda has 15 private-for-profit sector importers, 50 wholesalers, 2,500 pharmacies, and 8,000 general retailers. ACTs scale up with a portion of the eligible buyers in Uganda under AMFm is likely to have a huge impact.

Affordable Medicines Facility for Malaria (AMFm)

Created as a response to the National Academies Institute of Medicine 2004 report *Saving Lives, Buying Time*, the AMFm was set up by the Roll Back Malaria (RBM) Partnership as a financing mechanism for ACTs. The objective of the AMFm is to ensure that people suffering from malaria have access to inexpensive, effective malaria treatment in the form of ACTs and to delay the development of drug resistance to artemisinins. The AMFm will promote the use of effective antimalarials and drive out ineffective medicines from the market by reducing prices of ACTs to an affordable level through price negotiations and a high-level buyer subsidy through co-payments to manufacturers. In addition, the AMFm will ensure that the reduced price benefits those suffering from malaria by introducing in-country supporting interventions. It is expected that prices of ACTs will be reduced to 0.20-0.50 USD making them comparable to prices of chloroquine and sulfadoxine-pyrimethanmine (SP) still circulating on the market despite public sector adoption of ACTs.

While AMFm has not been officially launched, there has been widespread political support for its introduction. Assuming that donor support for it is forthcoming, AMFm's arrival[1] may offer potential significant opportunities in the effort to scale up ACTs and MFT for malaria. Firstly, both strategies include a delay of drug resistance as an objective, In addition, increasing

[1] The GFATM Board is expected to make a decision with regard to hosting the subsidy in November 2008. Mechanisms to implement this intervention will begin soon after Board approval.

availability and affordability of ACTs has the potential to facilitate uptake of the multiple treatments required in MFT. However, the AMFm design is based on a free market approach whereby eligible buyers may purchase any of the subsidized products and distribute them in the country. This is likely to be contradictory to a policy that promotes a limited number of recommended options. If a MFT policy is to be adopted, discussions will need to begin early with the AMFm to ensure that coordinated approaches are developed and that the AMFm does not compete with a potential MFT strategy but is rather a mechanism to facilitate and finance it. The design of AMFm needs to include a variety of subsidized ACTs subsidized to a greater or lesser extent to ensure that they are all used widely in order to promote the MFT strategy and to avert potential resistance development to one ACT.

It may be beneficial to introduce both AMFm and the MFT concept to countries at the same time to avoid "intervention fatigue" and the perception of "yet another international recommendation." Furthermore, coordination and collaboration should begin as soon as possible while the implementation design mechanisms are being developed and continue to ensure that the mechanisms for supportive interventions that are currently being discussed within the context of the AMFm support MFT. The same eligibility criteria for buyers in the private sector may be used and the MFT approach can take advantage of any advances in forecasting that are made by AMFm.

Regardless of the MFT option selected, the ACTs that will be used in the private-for-profit sector as part of the MFT policy needs to be affordable. The introduction of the AMFm offers the opportunity for providing funding for supporting interventions associated with successful roll out of a potential new strategy which may be leveraged for MFT if coordinated appropriately.

Critical Questions on MFT

Facilitating Adoption, Introduction, and Implementation of a New Policy

- How will each ACT used in MFT be financed?

- Where will additional resources be obtained for supportive interventions for the transition and implementation process (e.g., changing standard treatment guidelines [STGs], training, monitoring)?

Facilitating Adoption, Introduction, and Implementation of MFT

Are the ACTs recommended for use in the private-for-profit market as part of MFT affordable? How will equity issues be addressed?

How will funding for MFT be coordinated with AMFm and other funding sources?

AMFm Related to Adoption, Introduction, and Implementation of MFT

- Will AMFm be subsidizing a variety of ACTs?

Advance Planning and Coordination

Experience has shown that there is a significant lag between the time a policy is endorsed at the global level and its implementation at the country level. Policy analysis, consensus building, and decision making all take considerable amounts of time. At the country level, the technical and operational challenges assessment needs to be mapped out and any weaknesses addressed. Furthermore, planning for any operational research or external technical assistance needs to be started early. Planning and coordination is key to any policy success and even more crucial with MFT which will require coordinated approaches with the private-for-profit sector including developing mechanisms and lines of accountability—a division with which there is little experience and documented success. In addition, planning and coordination with AMFm will be essential while approaches for implementation of this potential new strategy are being discussed and developed.

The following written plans are crucial to a successful rollout of any new policy and will certainly apply to MFT (adapted from Shretta 2007)—

- An implementation plan that describes each step, timelines for each step, roles, and responsibilities for all the stakeholders in the public, not -for-profit and commercial private sector, and budgets needed at each stage. This should also contain how coordination with the two sectors and with the other global initiatives will occur.

- A procurement plan that outlines each stage of the procurement process in the public, not -for-profit and commercial private sectors and the roles and responsibilities of all stakeholders in the procurement process in both sectors.

- A distribution plan that lays out the steps and describe the roles and responsibilities of the various partners involved in distribution. The plan should list the quantities to be distributed to different districts by sector and/or type of facility.

- A training plan for the public, not -for-profit and commercial private sectors that includes clear timelines for activities. A training strategy to introduce new STGs should be planned to coincide with the product's arrival in the country.

- A monitoring and evaluation (M&E) plan that measures the success of the policy implementation. This should outline targets and milestones, and list activities, roles and responsibilities, data needs and sources, and supervisory plans and schedules.

Operational Research

Prior to decision-making on MFT policy adoption there will be a need to gather local data to support the analysis of benefits, risks, costs, and capacity for implementation. Operational research will be needed to assess and design the MFT program and its implementation including the suitable MFT option depending on the country context and the particular ACT products recommended. The willingness of stakeholders in country to change to a new approach on the

basis of a potential societal benefit without an urgent need will need to be assessed. Such assessments, pilot projects, and phased implementation may facilitate organizational and operational adjustments for scale-up.

ADOPTION AND POLICY CHANGE TO MFT AT THE GLOBAL AND COUNTRY LEVEL

The policy change process for first-line therapies for malaria in endemic countries generally takes between 12 and 18 months (WHO/AFRO 2003). However, unless appropriate mechanisms have been put in place early in the process, it has taken as long as 10 years in some countries (Shretta et al. 2000, Williams et al. 2004). Similarly, a change in first-line treatment to MFT will require presenting appropriate data and evidence of the added value of MFT to key policy and decision makers at the global and country levels.

Garnering global and country level acceptance to change to a new strategy without an urgent need as perceived by unacceptable levels of drug resistance to current therapies is likely to be challenging and time-consuming. Furthermore, an MFT policy is almost contrary to the essential medicines approach adopted in the 1970s. This approach was based on a limited list of products (essential medicines lists) to avoid wastage, to promote rational medicine by training providers on a limited list of products, and to facilitate ease of implementation in the public sector. Adoption of MFT will require refocusing the objective of antimalarial treatment to encompass drug resistance.

A decision will need to be made on details of the policy. Will the policy require that only the two ACTs recommended as MFT be on the market and the rest phased out? Although the public sector is accustomed to having limited options of medicines, this may be challenging for the private-for-profit sector. While control of the private-for-profit sector may not be desirable, monitoring is needed to ensure that a significant proportion of the population is actually adhering to the recommendations.

Although global and country level adoption processes are separate, the components are essentially the same. Consensus building for policy change should begin at the country level soon after the global level discussions have begun. Although it is likely that some countries may decide to proceed with adoption and implementation without waiting for global recommendations, to garner widespread acceptance of an MFT approach, a policy change to MFT will need global technical acceptance and endorsement by a normative and standard setting body such as WHO.

The essential components for change to a MFT policy include—

- Analysis of needs and evidence for change including the risks and benefits of MFT
- Analysis and appraisal of the first-line therapy options available for the policy both in terms of the design of the MFT as well as the product options recommended in the strategy
- Stakeholder participation in developing recommendations and policies, consensus building, advocacy for change, and decision making

- Analysis of the health system environment and capacity to adopt, introduce, and implement MFT

- Development and endorsement of the new recommendations and policies and their dissemination

Adapted from: WHO. 2007. *New technologies for tuberculosis control: A framework for their adoption, introduction and implementation.* Geneva: WHO.

Needs Analysis and Evidence for Change

The adoption of MFT will require an appropriate evidence base to support a positive decision to formally adopt a MFT policy both and the global and national levels and is likely to be triggered by evidence of resistance to the existing single first-line therapy policy or greater efficacy of the proposed MFT strategy. While these processes are generic and apply to any change in first line treatment, as discussed earlier this step is likely to be even more challenging in the adoption of MFT due to the little hard and direct evidence of the efficacy of MFT compared with current recommended strategy. While Smith et al. (2008) argue that the international recommendation to adopt ACTs as first-line therapy was made under a similar context of uncertainty, this historic need to change was based on rapidly increasing levels of resistance to the monotherapies that were being used in addition to international pressure and availability of funding for the procurement of ACTs. In the absence of resistance to ACTs, the desire to slow the emergence of parasite resistance may not be sufficient. International consensus building will require agreement on the type of evidence that will support a decision to adopt a MFT policy. Such evidence may include data on resistance and treatment failure to existing treatment options, comparative cost effectiveness, or potential savings and societal benefits accrued from costs associated with having to change first-line treatment recommendations approximately every five years. Therefore, generating the desired information and compiling the evidence must start as early as possible.

Analysis and Appraisal of Options Available for the MFT Policy

Analysis and appraisal of specific first-line treatments for MFT policy needs to be carried out irrespective of which MFT option is selected. The MFT policy treatment options should be equally efficacious and perceived to be so. Any inequity in perception of one product over another is likely to raise serious ethical concerns of restricting products to particular proportions of the population and may be a significant barrier to the adoption of the MFT strategy.

A clear definition of the products that are recommended as part of MFT as well as simple criteria of allocating one combination to one part of the population versus the other must be clearly presented to facilitate policy adoption (and subsequent introduction and implementation).

In addition, the characteristics of the proposed MFT may influence their acceptability to patients and providers, and these factors must be taken into consideration in determining the best choice within a programmatic context. These properties include—

- Efficacy and perception of efficacy
- Cost and cost effectiveness
- Quality
- Side effects
- Use in special groups
- Adherence and dosage regimen

Stakeholder Participation

Stakeholder participation is required for development of recommendations and policies, consensus building, advocacy for change, and decision making. Early stakeholder analysis will identify those who will be key contributors of political, financial, operational and/or technical assistance support. Key global stakeholders include WHO; the RBM Partnership; GFATM, World Bank, philanthropic and bilateral donors and other funding agencies; research institutions; community advocacy groups; and others. At the country level, these stakeholders range from departments within the MoH to manufacturers, not-for-profit and commercial private providers, consumer advocacy groups, and patients and caretakers (see Box 1; page 5). Key stakeholders will need to begin consensus building and planning together early with evaluating and presenting the consequences of doing nothing.

Both options A and B will require considerable sensitization and consensus building among key stakeholders including manufacturers and private-for-profit sector providers carrying large increases in cost compared to adoption and implementation of single first-line therapy policies.

Development and Endorsement of MFT Policies and Its Wide Dissemination

Available evidence must be shared at global and country levels. In order to garner acceptance of an MFT approach, a policy change to MFT will first need acceptance at the international level as well as endorsement by WHO. In addition, buy-in and pledge for support of the proposed MFT strategy by other global stakeholders (RBM Partnership, United Nations Children's Fund, World Bank, GFATM, U.S. Agency for International Development, Bill & Melinda Gates Foundation, UNITAID, President's Malaria Initiative, etc.) will be essential. Dissemination and endorsement of the policy of the policy to the regional and country levels needs to occur. At the country level, a technical update by WHO is likely to facilitate the acceptance necessary to institute the change. Appropriate bodies/committees to oversee the development and implementation of the new policy may need to be created. For both options, A and B, private sector providers should be included in any committees that are created.

For both options A and B, where only selected products are recommended, there may be challenges to adoption and acceptance by local antimalarial medicines manufacturers that

currently supply the private-for-profit sector market because their products may not be recommended for use in the country's MFT policy and therefore they may lose their market. In addition, private-for-profit providers may be unwilling to restrict sales of other antimalarials which may carry higher profit margins. While increased competition carries public health benefits, private-for-profit sector providers may be unwilling to participate unless an incentive structure is put in place.

Analysis of the Health System Environment and Capacity to Adopt, Introduce, and Implement MFT

The capacity of the health system for implementing the policy needs to be analyzed in the context of the country in question. A country with a high utilization of an untrained private-for-profit sector will be less likely to be successful with option B which requires different products for the population less than five years of age and over five years. For option A, retaining the currently recommended ACT in the public sector will facilitate acceptance in this sector.

Both options A and B will require a higher level of regulation of the private-for-profit sector than conventional policies. In particular, option B will require monitoring and regulating prescribing and dispensing of private-for-profit providers to ensure that the appropriate combination is being used. A lack of capacity of the regulatory body to carry out these extended functions will affect the success of the policy.

Critical Questions

Adoption of a New Policy

- Is there a documented or perceived need for a more effective treatment policy, because of resistance or treatment failures?
- What is the type and level of evidence needed for decision making?
- Who are the key stakeholders and decision makers?
- Has there been consensus building and advocacy for change among appropriate stakeholders?
- What is the process for policy change in the country?
- How will the new policy be endorsed and disseminated?
- What is the capacity of the health system to manage change and successfully implement the policy?

Adoption of MFT

- Will evidence from theoretical models be sufficient for decision making?

- How will the private sector be engaged?
- What is the capacity of the health system to manage change and successfully implement MFT?
- Which MFT strategy should be recommended (according to what is feasible for implementation)?
- Which products will be recommended as part of the MFT strategy?
- How can coordination with AMF occur?

AMFm related to adoption of MFT

- Which products will be subsidized through AMFm?

Issues to Clarify before Adopting MFT

Before an MFT policy is adopted, several fundamental questions will need to be answered—

- A clear working definition for MFT needs to be developed including which particular treatment and how many first-line therapies will be recommended under the policy, which products are currently recommended and which target populations the recommendations apply to.
- In addition, in most of the countries, the private-for-profit sector implements a variety of treatments depending on availability, affordability, and preference of the patients and providers. Although, this current situation may be considered multiple first-line therapy, in the context of this paper where MFT is defined as an explicitly recommended policy, the "natural" and haphazard individual prescriber's decision/selection may not necessarily be desired, unless it is explicitly defined to be one of the components of the policy. For example, a specific ACT is recommended for the public and the not-for-profit private sector, while the choice of a different ACT is left to the private for-profit sector, to be influenced through the AMFm mechanism on commercial private sector suppliers. In either case, a decision must be made on how much private sector control is needed to achieve the required objectives. Although private-for-profit sector control or monitoring may not be desired and indeed may present significant challenges, some degree of regulatory monitoring may be necessary in order to achieve the desired degree of private sector adherence.
- A decision must be made on what should be done with the stocks of ACTs and other antimalarials that are not part of the potential MFT strategy. Does the policy require that only the two ACTs recommended as MFT be on the market and the rest phased out? One option would be to use the AMFm which would drive usage towards the lower cost

therapies/products (AMFm-subsidized) and thereby force non-recommended products out of the market.

In addition, as AMFm is likely to be a potential funding source for MFT, a level of advocacy with AMFm must begin early to ensure that a range of ACTs are considered for subsidy to facilitate the adoption of an MFT strategy.

INTRODUCTION AND IMPLEMENTATION OF MFT POLICIES AT THE COUNTRY LEVEL

Nearly all countries in Africa have adopted some ACT as first-line policy but implementation has been variable in the public, not-for-profit and private-for-profit sectors; some countries have not had sufficient funds to purchase enough for all public sector facilities, and national treatment policies may not have been properly extended to the private-for-profit sector. Countries would therefore fall on a continuum of implementation of an ACT policy which may affect their ability to implement a policy requiring MFT.

Most treatment seeking for malaria in sub-Saharan African occurs in the private-for-profit sector. However, this sector has thus far been relatively unregulated and implementing interventions such as MFT may require some capacity building of the regulatory body and behavior change of private providers. Furthermore, policies such as MFT may be contrary to the free market models by which the private-for-profit sector traditionally tends to function. In most malaria endemic countries in Africa, the antimalarial markets follow either strictly private sector or strictly public sector distribution, with few examples of mixed models. These traditional frameworks will need to be changed, particularly if an integrated procurement and distribution system for ACTs is used. Mechanisms for accountability in private-for-profit sector will also need to be developed. A decision will need to be made on how much control and regulation of the private-for-profit sector is desirable in order to achieve the necessary level of adherence without influencing its being able to provide wider access and without disrupting the market.

Introducing and implementing MFT requires countries to coordinate activities to prepare for effective implementation. This includes a combination of technical and operational considerations as well as mechanisms for monitoring and evaluating the process. Technical considerations include product registration; regulation; developing or updating treatment guidelines, essential medicines lists, and recording and reporting forms; dissemination of guidelines and training of health workers and providers and information, education, and communication (IEC). Operational considerations include the management of the medicines currently in use that will be replaced by MFT; management of the new medicines supply; addressing availability in public and private-for-profit sectors; development of a phase-in or roll-out plan; quantification and demand forecasting; procurement, distribution, and inventory management; and ensuring quality of products and services and their safety. While all the above processes will be necessary for any policy change, MFT present greater challenges in some areas due to the implementation of more than one product for the same disease. These are discussed in detail in the following sections.

The implementation process also encompasses the steps needed to operationalize the policy, including a system to monitor and evaluate the progress of these activities and their impact on malaria control. This framework focuses on the key components needed during the policy change and transition phase of the new policy as illustrated in Box 2. The framework addresses these components as they might affect the policy implementation under the two MFT options; one first-line treatment in the public and not for profit private sector and a different one in the

private-for-profit sector and different first-line drugs for children and adults implemented in the public and private (for profit and not-for profit) sectors.

Framework for Mapping Change from Single First-Line Treatment to MFT

Box 2. Key Components in Framework for Implementation of the MFT Policy

1. **Technical considerations**
   - Revision of Drug Regulation
   - Development/Review of the Essential Medicines List (EML), STGs, and/or other relevant guideline document ,and BCC materials for malaria
     - Dissemination of the revised STGs and/or other relevant guideline document and BCC materials
     - Training and supervision of health workers consistent with the new guidelines
     - IEC targeting the community
2. **Operational considerations**
   - Management of stock of antimalarials currently in use
     - Development of a phase-out plan
   - Management of ACT supply
     - Forecasting of demand and quantification
     - Procurement
     - Distribution
     - Inventory management
   - Review of quality assurance mechanisms
     - Pharmacovigilance
     - Product quality surveillance

Source: Adapted from MSH/RPM Plus (2005). *Changing Malaria Treatment Policy to Artemisinin-Based Combinations: An Implementation Guide.*

Revision of Drug Regulation

If therapies different than those that are currently in circulation are selected as MFT, they must be authorized for sale on the market (if not done already). In most countries, this will involve a drug registration process. Information on the different requirements for registration for any new ACTs must be obtained early enough to allow an adequate planning and lead time in the process.

Regulatory changes may include changes in drug scheduling[2] to ensure the availability of the new first-line ACTs at peripheral public and private-not-for-profit and for-profit health facilities, such as pharmacies, clinics, and dispensaries (in the public sector) and over-the-counter shops or chemical sellers in the private sector.

Alternative strategies, such as rescheduling of the antimalarials to prescription-only medicines to reduce the demand for the previous antimalarial product over time should be considered. Such

[2] This is the legal status of a medicine (e.g., prescription-only medicine, over-the-counter medicine).

legislative changes can take up to six months or more, depending on the country context. Furthermore, regulatory or legislative changes that allow only certain combinations to be sold in the public, not for profit and for-profit private sectors may be needed, such as deregistering all but the two (or more) MFT products recommended for first-line treatment of malaria. It may also be necessary to prevent procurement and importation of ACTs that are not recommended as part of the potential MFT strategy.

By nature, MFT are likely to require some investment in strengthening the medicines regulatory authority to monitor and regulate prescribing and dispensing in accordance with the policy. In particular, option B will be more challenging and costly to implement and will require monitoring and regulating private providers' prescribing and dispensing of to ensure that the appropriate combinations is being used to some degree of diversity in order to achieve the desired effect.

MFT can work with commercial private markets if these private markets are offering multiple ACT products at prices that lead to all the medicines being purchased and used. However, current commercial private market dynamics dictate the predominant use of particular therapies. The AMFm therefore needs to ensure inclusion of a variety of subsidized ACTs to ensure that they are all used widely.

The AMFm strategy intends to "crowd out" monotherapies and other unwanted antimalarials by increasing availability of the ACTs and coordination will be essential. Furthermore, the regulatory status of the MFT and the ACTs purchased through AMFm must be the same to avoid confusion. However, the AMFm currently favors a free market approach where buyers will be free to purchase "eligible" ACTs with the aim that several ACTs will be on the market at the same time and may serve to increase competition among manufacturers and drive prices down.

Any contradictions between the two interventions will need to be discussed and harmonized, and complementary approaches developed to avoid countries favoring one intervention over the other.

Critical Questions

Regulations and New Policies

- Are the new product/s registered?
- What regulatory changes are required to allow access in the commercial private sector?
- What regulatory or legislative changes are needed for phasing out of other products that are not recommended?
- What is the regulatory capacity and how can this be strengthened to facilitate the new policy?

Regulation and MFT

- What regulatory changes will be needed to facilitate implementation of MFT?
- What regulatory changes will be needed to allow access in the commerical private sector?
- How can regulatory conditions for MFT and AMFm be harmonized?

Review, Harmonization, Dissemination of Guidelines and Medicines Lists

If the first-line treatment is being changed in the public sector, the malaria sections of the STGs and EML, Integrated Management of Childhood Illnesses (IMCI), and other guidelines or documents recommending first-line treatments for malaria will need to be revised or addendums published. In addition, guidelines for the commercial private sector will need to be developed and disseminated. This may be challenging because of the heterogeneous nature of private sector providers including informal sellers and itinerant vendors.

In all the above documents, the time needed to complete the documents and print, publish, and disseminate them to the public and not-for-profit and for-profit private sectors must be planned for. This process can take between three and six months, and must include disseminating the guidelines to the respective providers in all sectors.

Revision of guidelines is a costly exercise and needs to be taken into consideration when selecting the MFT option. Furthermore, publishing and disseminating separate guidelines for the public, private not-for profit, and for-profit sectors as may be required for implementing option A is likely to be expensive.

Critical Questions

Review, Harmonization, Dissemination of Guidelines and Medicines Lists for a New Policy

- Which guidelines and lists need to be developed or revised?
- Who will the guidelines be disseminated to and how?

Review, Harmonization, Dissemination of Guidelines and Medicines Lists for MFT

- Will there be different guideline for the public, private-for-profit and private-not-for-profit sectors (depending on the choice of the MFT design)?

- How will dissemination to the private-for-profit sector occur?

Review and Dissemination of BCC Materials and Targeted IEC

Changing policy, particularly when it affects strategies and therapies unfamiliar to providers and patients, requires considerable planning for behavior change strategies and human capacity building at all levels. These activities should be coordinated with training to ensure that the same messages are being communicated to all. This is critical for MFT.

A major barrier to MFT may be the potential negative perceptions on equity raising critical ethical issues if all the therapies recommended under MFT are not considered equal. IEC messages should include information on the new policy, the rationale for the choice of MFT, and reassurance on the effectiveness of each of the ACTs that are recommended under the MFT policy.

Critical Questions

Communication and New Policies

- What should the content of the communication messages be?

Communication and MFT

- Is there a need for different IEC messages and BCC in the public, private-for-profit and private-not-for-profit sectors?

- What are the perceptions to the various ACTs and their related patient and provider acceptability?

- How will communication strategy be launched and coordinated with implementation of AMFm?

Updating Health Workers' Training and Supervision

Health workers and all private sector providers will need to be sensitized and trained on the potential new MFT strategy and guidelines (in the public sector, a refresher training may be needed if training has already previously carried out and the public sector recommendation has not changed). Work will need to be done with pre-service training institutions to incorporate revisions to antimalarial treatment in their curricula. Similar changes need to be made to IMCI and other in-service training curricula used in the country. Training/sensitization activities of health workers must be timed shortly before any new first-line antimalarial is available at the health facility level or private outlet to ensure adherence to the policy and rational use.

Training of private sector providers can be done together with the public sector for option B where the policy for children under the age of five and adults is the same in the respective sectors. In general, regardless of which option is chosen, training of private-for-profit providers is likely to be challenging and costly due to several reasons—

- Traditionally, targeted implementation of new (and existing) policies has been focused mainly on the public sector. Adopting an MFT strategy which includes a coordinated implementation in the private sector will need a different training strategy that incorporates these providers.

- It is unlikely that there are current lists of existing private-for-profit providers and new lists will need to be made

- There may be large numbers of small drug sellers and itinerant vendors, including all of them will be challenging and expensive

- The level of training of the providers will vary from fully trained medical doctors and pharmacists to those with little or no training and therefore training packages may need to be adapted to take this into account

Critical Questions

Training in a new policy

- Has a training strategy and plan been developed?
- Who will carry out the training?
- Who will be trained?

Training for MFT

- Will training for the public and private sectors be done together?

- Will the informal private-for-profit sector be included?

- Will different training curricula need to be developed for different levels of the system and educational background?

- How will the effectiveness of the training be monitored?

Phasing Out the Old and Phasing in the New

Provisions for phasing out the previous medicine must be made during the planning phase to avoid wastage when the new policy is implemented if the products recommended under the MFT are different from what were being used before. This will ensure only the recommended

treatment is available and to ensure removal of monotherapies. Regulatory options to facilitate phasing-out have been discussed above.

As part of the phase-out plan, accurate estimates of the current first-line treatments in stock and in the pipeline must be compiled, and future procurements should be adjusted to ensure that when the switch to the new medicine is made, there is not a large stock of the previous medicine in the system. Clearly, these actions will need to occur for any policy change regardless of whether the change involves the adoption of MFT.

A decision must be made on what should be done with the stocks of ACTs and other antimalarials that are not part of the potential MFT strategy. Does the policy require that only the two ACTs recommended as MFT be on the market and the rest phased out? One option would be to allow the non-recommended stocks to be consumed first or, alternatively, remove them from the system by passing them onto the next highest level of facility. However, recall in both the public and private sectors will probably be challenging.

For option A, if no change in the public sector first-line treatment is required, this step will not be necessary. Obtaining pipeline data from the private-for-profit sector will be next to impossible. However, it may be prudent to assume that the private-for-profit sector will not have large pipelines of other ACTs in stock due to their cost and small market share.

The new policy can be implemented either through a phased implementation or through an immediate nationwide and sector-wide rollout. The decision on which method to use has implications for the components listed in this framework. A nationwide and system-wide implementation plan involves rolling out the new policy in the entire country at the same time. A phased implementation can be done in two ways; geographically by selecting some areas for earlier implementation or system-based by selecting some parts of the health system for earlier implementation, e.g., fist select public health services, private faith-based and other not-for-profit clinics, then private health services).

Critical Questions

Phasing Out Old Policy and Phasing in New

- Will implementation be phased or nationwide?
- Is there a plan for phasing old medicines out? How will this be done?

Phasing Out Non-Recommended Medicines and Phasing in MFT

- Is the intention to phase out all medicines not recommended as MFT?

Forecasting Demand and Quantification

Forecasting for ACTs is currently a challenge due to a lack of data on actual demand. Quantification and forecasting for the components of MFT are likely to present even greater

challenges. The unavailability of morbidity data, particularly segmented by age groups, has made it difficult to accurately forecast for ACTs that are presented in the public sector in three to four different packages (by age or weight). The private-for-profit sector ACT market is even more daunting. In both sectors, there is no systematic collecting and assembling of accurate data on morbidity or consumption of currently used ACTs; also, treatment seeking in the private-for-profit sector is influenced by a variety of factors including medicine availability. In the absence of certain dosage packages, providers in several countries have been known to either split larger packages or to combine smaller packages to treat an older child or adult. In countries where some consumption tracking is done, this confuses the picture as data may indicate that four children were treated when, in fact, one adult was treated. This has led several countries such as Malawi to consider procuring only the smallest pack of artemether/lumefantrine (AL) where providers can issue one, two, three, or four of these packages according to the age group. Option B is therefore likely to have greater challenges in forecasting than option A because of the need to quantify for a different treatment in the population under age five and over age five in each of the public and private sectors.

A phased implementation has the advantage of allowing data to be collected that would improve estimates of health facilities' uptake of the new policy, thus enhancing the estimates of the potential demand before the nationwide implementation.

In all cases, the method of diagnosis will also influence the demand for ACTs. Implementing a policy of rapid diagnostic tests (RDTs) in the private-for-profit sector, for example, would greatly reduce the need for treatment.

Forecasting is a key element of the AMFm rollout and a potential MFT strategy can take advantage of the data obtained for the AMFm. Forecasts for all procurement efforts including the AMFm must be harmonized and coordinated. Strengthening forecasting capacity, particularly in the private-for-profit sector, will need to be emphasized.

Critical Questions

Forecasting for a New Policy

- What is the target population?
- What data is available for forecasting?
- Is human capacity building needed?
- Are RDTs being recommended to be used in conjunction with the ACTs?

Forecasting for MFT

- What is the additional target population?

- Is there data on the potential proportions that will be treated with each product as recommended in the MFT strategy?

- Is human capacity building needed in the private-for-profit sector (if included in the strategy)? How will this be done?

AMFm Forecasting

- Has forecasting been done by AMFm?
- How can this data be leveraged for MFT?

Procurement

A procurement plan incorporating MFT that considers the distribution strategy in both the public and private sectors must be developed. This procurement plan must also include information on the procurement method to be used and how coordination with other procurement mechanism for ACTs will occur. Irrespective of the procurement method selected, systems need to be put in place to ensure that the products procured are of appropriate quality. Depending on the source of funding countries and procurement agencies or institutions will need to adhere to the procurement requirements of the particular donor. If procurement for the public, for-profit and not-for-profit private sectors is done separately, these requirements may be different.

For both options, a decision will need to be made on how procurement will occur, who will conduct it, and whether procurement in the public and private sectors will be coordinated. There may be resistance by the private-for-profit sector to have a coordinated procurement or a single or limited supplier due to reduced control, reduced competition, and potentially, reduced profits. Often, actual procurement and financing of the procurement occur in different departments by different stakeholders. There is a need to coordinate activities to ensure synchronization between the financing activities and the requirements of the procurement cycle.

For option B where the same ACTs are used for the two age groups, coordinated procurement may be feasible, more cost-effective, and facilitate quality monitoring. However, it may be beneficial to have different packaging for the public and private sectors to enable monitoring and movement between the two sectors.

The choice of supplier will be influenced by whether pre-packaged or co-formulated ACTs are desired. Additionally, there must be a system in place for monitoring supplier performance and for resolving any problems identified as a result of this monitoring.

Coordination of procurement with the AMFm will be essential to avoid duplication and wastage.

Critical Questions

New Procurement Recommendation

- Who will carry out the procurement?
- Who will monitor suppliers?

Procurement of MFT

- Who will carry out the procurement for the private-for-profit sector?
- Will procurement be coordinated between the two sectors?
- Will different packaging for the public and private-for-profit sectors be needed and included in the tender documents?
- Should the same eligible buyers for subsidized products through AMFm be used for procurement for MFT

AMFm

- Who are the eligible buyers for the subsidized ACTs through AMFm?

Distribution

The detailed steps in the distribution of antimalarials will differ from country to country and whether the distribution channels for the public and private sectors will be independent or coordinated. This will depend on how the public and private distribution systems are currently organized, and whether or not a central medical store plays a role in the public sector's distribution system. The short shelf life of the ACTs (12–24 months) makes it imperative that distribution systems function effectively to avoid medicine loss due to expiry.

The distribution plan should outline who will carry out the distribution, where the goods will be stored at intermediate levels, and the quantities to be supplied. Distribution will need to be coordinated with training providers.

The private sector tends to have its own distribution system which will likely continue to be used to implement MFT. However, distribution for two separate products for children and adults (option B) is likely to be more challenging. In both the public and private sectors, under option B, the shortage of one product will likely lead to the dispensing of the other, thereby compromising the potential MFT strategy. Furthermore, option B may require larger storage areas for two different products each with potentially four packages. This will be challenging in the public and private sectors. In addition, as ACTs require storage in cool conditions, scaling up ACTs in the private-for-profit sector will need attention to the quality and capacity of storage.

Critical Questions

Distribution under a New Policy

- Who will carry out the distribution?
- Is there adequate storage capacity? How will this be addressed?

Distribution for MFT

- Who will carry out the distribution in the private sectors?
- Will distribution be coordinated between the two sectors?

AMFm

- Who will be carrying out the subsidized ACT distribution through AMFm?

Inventory Management

Inventory management measures may need to be assessed and upgraded, or established if they do not already exist. This will be particularly challenging in the private-for-profit sector. To implement option B, this will be essential to accurately capture data on consumption for future forecasting.
Mechanisms will be needed to ensure that records are kept and updated regularly and that physical checks are regularly performed. This will be more challenging in the private-for-profit sector as mechanisms to conduct supervision do not exist.

Provisions must be made to prevent diversion of medicines from the public facilities to the private-for-profit sector. One mechanism for monitoring is to have different packaging for the public and private sectors.

Critical Questions

Inventory Management under a New Policy

- Are there adequate systems for inventory management?
- Do they need to be updated?
- Who will do this and how?

Inventory Management for MFT

- What systems exist for inventory management in the private-for-profit sector?
- Do these systems need to be updated? How will this be done?

Revision of Quality Assurance Mechanisms

The main quality assurance issues are related to continued product efficacy (drug resistance monitoring), product safety (pharmacovigilance), product quality at registration and/or procurement, and post-marketing surveillance systems. With scale up of ACTs in the private-for-profit sector through MFT and AMFm, these will be essential.

The efficacy of the MFT will need to continue to be monitored. Mechanisms must be in place for surveillance of adverse events associated with the use of the ACTs.[3] This will be challenging in the private sector under both options. Depending on the source of funding, quality criteria for procured medicines will have to be adhered to. While all these mechanisms will need to occur regardless of an MFT policy, adoption of MFT will require active monitoring of all the products recommended as part of this strategy. The AMFm plans to issue a list of "eligible" products which comply with a minimum set of quality standards. If the AMFm is to be used as a potential source of funding harmonization with these criteria will need to occur.

Critical Questions

Quality Assurance Mechanisms under New Policies

- Is there a system for monitoring product quality? Does this need to be strengthened?
- Is there a system for post-marketing surveillance? How can this be strengthened?
- Is there a system for monitoring adverse drug reactions? How can this be strengthened
- Is there a system for monitoring drug resistance and clinical failures?

Quality Assurance Mechanisms for MFT

- Are all the multiple products recommended in the MFT policy being monitored for quality, effectiveness, and adverse drug reactions?

- How are data from the private-for-profit sector being collected and findings disseminated?

AMFm

- What is the list of "eligible" products which comply with a minimum set of quality standards?

Monitoring and Evaluation

Planning for monitoring and evaluation (M&E) of the new potential MFT strategy needs to be done early and integrated throughout the implementation process, so that data generated from monitoring can be used to guide any changes. Indicators to monitor the policy change process must be developed. Monitoring will be more challenging in the private-for-profit sector under both options, but particularly challenging under option B, and mechanisms for obtaining and using the data will need to be developed.

[3] The artemisinins are currently not recommended for use in the first trimester of pregnancy. It is likely that they will, however, be given to a cohort of the pregnant population unaware of their pregnancy. A system should be in place to detect adverse effects that may arise in the course of using the ACTs.

Professional associations and the sector may be included to facilitate the public-private partnership.

Indicators for MFT should be harmonized with the AMFm.

Critical Questions

Monitoring of new policies

- Have M&E indicators for the policy been developed?
- Who will carry out the monitoring? How will monitoring take place?

Monitoring of MFT

- What level of monitoring is needed to ensure the desired level of adherence to the policy in the private-for-profit sector is occurring?

- Who will carry out the monitoring in the private sectors? How will monitoring take place?

- What minimum set of indicators can be reasonably collected?

AMFm

- Which M&E indicators have been developed by the AMFm?

Table 1 summarizes the issues to consider when initiating an MFT policy at each step of the adoption, introduction, and implementation process. It outlines potential challenges that may be encountered in the process, the potential effect of the subsidy under AMFm, and suggests steps for a way forward.

Table 1. Framework for Mapping Change to MFT

Element	Key Actions	Issues to Consider	Potential Challenges and Cost Implications	Potential Effect of the Subsidy	Strategy for Way Forward
Planning and Coordination	• Stakeholders' Identification and determination of their importance at the various stages, their roles and responsibilities, and how they should be engaged (stakeholder analysis). • Identification of transition committee composition or, if using an existing mechanism, determination of which existing committee or group should carry out this process. • Establishment of working groups or task forces and their respective membership within the committee. • Develop written implementation plans with clear timelines and roles and responsibilities.	***Option A (public/private)*** Need to involve private-for-profit sector (often not included in existing committees). Strategy for implementation in private sector is different from public. Need to decide how closely implementation in the private sector will be controlled. ***Option B (children/adults)*** Same committee to oversee implementation in children and adults.	Increased cost and time to include larger group of stakeholders at planning stage. Higher cost to disseminate planning materials and plans to private-for-profit sector.	Challenges in coordination of approaches and planning.	Same groups should be involved in implementation of both and similar strategies for MFT and AMFm should be implemented to avoid conflict or competition between the two strategies. Written plans should include introduction of AMFm. Important to have consistent messages.

Element	Key Actions	Issues to Consider	Potential Challenges and Cost Implications	Potential Effect of the Subsidy	Strategy for Way Forward
Financing	Development/review of budget for transition to and implementation of MFT and mobilize resources— • Identification of potential national-level and other resources • Development of strategy for accessing funds • Development/review proposals for GFATM or other donors and funding agencies • Using AMFm as a source of funding	Who will pay for MFT? Need to determine who will pay for costs of implementing in the private sector. Need to develop budget for implementation and monitoring in private sector. Include financing for delivery.	Getting resources for private sector implementation may be more challenging.	Patients and providers likely to use subsidized ACT over other ACTs in MFT strategy.	MFT should use subsidized ACTs to avoid affordability issues.
	Evaluation of cost-sharing and exemption mechanisms and development of methods for improving equity	Only applicable if there is a cost-sharing strategy. Ensure option for private sector is affordable.	Potential for negative perceptions on equity if both treatments not considered equal.	Potential confusion if not appropriately coordinated and aligned. Ethical and equity considerations of one portion of the MFT being subsidized	Implement mechanisms to improve affordability in the private sector. Coordinate with AMFm in private sector
	Development/review of financial accountability mechanisms	Depending how funding for AMFm will flow, mechanisms for accountability may need to be developed.	Private sector accountability more challenging.	Different accountability mechanisms for various strategies may lead to confusion.	Consider developing or reviewing financial accountability mechanisms for both sectors.
POLICY ADOPTION					

Element	Key Actions	Issues to Consider	Potential Challenges and Cost Implications	Potential Effect of the Subsidy	Strategy for Way Forward
Policy Change	Analysis and presentation of evidence for change to MTF policy	Need rationale and country-generated evidence for advocating for change to MFT policy. Might be better and save time to call switch to MFT a change in guidelines as opposed to a policy change so that the change process is quicker and easier to implement.	***Both: Potential*** Increased cost of presentation to the private sector. ***Option A (public/private)*** Private sector already practicing some form of MFT principle and while this will facilitate acceptance, the need for a coordinated approach may not be acceptable. Increased cost of presentation to the private sector. ***Option B (children/adults)*** Challenges of obtaining evidence from trials/resistance monitoring in particular age groups.	MFT will be yet another international recommendation. Evidence should be presented and coordinated with AMFm and any other global, regional, and country initiatives impacting on the private sector in particular (e.g., health insurance schemes).	Operational research or pilot projects in private sector to asses actual ACT use Engage key stakeholders from private sector. Present operational research results to private sector. Liaise with AMFm and other initiatives to ensure uniformity of message. Consider coordinated of adoption of strategies.

Element	Key Actions	Issues to Consider	Potential Challenges and Cost Implications	Potential Effect of the Subsidy	Strategy for Way Forward
	Analysis and appraisal of the MFT medicines available and selection	***Option A (public/private)*** Need rationale and evidence base for selection criteria of which ACT for private versus public. Perception of efficacy of both must be same with rationale for option of public versus private. ***Option B (children/adults)*** Need rationale and evidence base for criteria for selection of which ACT for child versus adult. Perception of efficacy of both must be same with rationale for option of child versus adult. Clear criteria of selection for child versus adult must be presented. A different medicine may be recommended for children weighing less than 5 kilograms (at 1 year) due to safety issues with AL.	***Option A (public/private)*** Potential resistance to policy and choice of therapy especially in private sector. Resistance to change if one option considered better than the other Private sector unlikely to adopt just one particular ACT. If demand for public sector ACT exists, it is likely to be found in private sector also. ***Option B (children/adults)*** Resistance to change if one option considered better than the other. Challenge in justifying choice for each age group.	AMFm considering having several ACTs available at same time in a market. MFT strategy advocating for particular ACTs to specific populations may be contradictory.	Choice of ACT for private sector under both options should be coordinated with AMFm for optimal introduction and implementation. Need to present evidence to public and private sectors.

Element	Key Actions	Issues to Consider	Potential Challenges and Cost Implications	Potential Effect of the Subsidy	Strategy for Way Forward
	Development of appropriate bodies/committees to oversee process of policy change	For both options, need to involve private sector in decision making and monitoring. For Option B, same committee should monitor implementation in children and adults.	For both options, difficulty of committees to ensure adherence in private sector without appropriate authority. Cost of monitoring in private sector higher.	Having different stakeholders for both policies may create conflict and/or coordination problems.	Same committees for policy change should be involved in implementation. Committees for MFT and AMFm should overlap.
	Analysis of the health systems capacity for implementing the policy	***Option A (public/private)*** Private sector implementation independent-monitoring may be an issue. Self monitoring may be used but checks are still needed. ***Option B (children/adults)*** Need to consider training for implementation and options for monitoring adherence especially in private sector.	***Option A (public/private)*** Private sector likely not to restrict product. ***Option B (children/adults)*** Higher costs associated with training, different STG, monitoring. Implementing dual policies in the public sector raises some complications. Difficult to ensure adherence and follow up to particular treatments used for children under and over age five in the private sector. Patients likely to pressure providers for alternative medicines.	If option for AMFm different from MFT, there may be challenge.	Align with AMFm and consider public-private models for implementation and monitoring. AMFm may be a source of funding for the ACTs used in the MFT and this has to be part of the selection criteria if there are certain ACTs not covered by AMFm.

Element	Key Actions	Issues to Consider	Potential Challenges and Cost Implications	Potential Effect of the Subsidy	Strategy for Way Forward
	Analysis of the regulatory environment	***Option A (public/private)*** Analyze regulatory body capacity to regulate public and private sector. ***Option B (children/adults)*** Analyze regulatory body capacity to regulate private sector implementation and adherence to recommended treatment children under and over age five.	Regulatory capacity may have to be extended to private sector. Likely to be more challenging and cost more.	Subsidy to recommend range of eligible products. May be harder to regulate both AMFm and MFT requirements unless they are coordinated and complementary.	Strengthen regulatory body to monitor public and private sectors without introducing too many limitations on use of other ACTs.
	Building of consensus and advocacy for change among appropriate stakeholders	Involve key decision makers at global and country levels, researchers manufacturers and private sector stakeholders	May face challenges with local manufacturers if their product is not among those recommended and if there is no plan to provide support to country-based manufacturers to increase their GMP.	If MFT not coordinated with AMFm, MFT not likely to be accepted by implementers as ACTs procured through AMFm will be highly subsidized and preferred.	Ensure consensus amongst those involved in AMFm. Plans for MFT roll-out should be incorporated into consensus and advocacy meeting presentations.

POLICY INTRODUCTION AND IMPLEMENTATION: TECHNICAL CONSIDERATIONS					
Revision of Drug Regulation	• Registration of new drug components of MFT policy • Establishment of fast-track registration system as needed	Registration documents to include indication and target group for implementation.	Need to evaluate registration of locally manufactured products to ensure this is in concordance with the MFT strategy	AMFm will have a list of eligible products which will be registered in country	Consider restricted registration for target group AMFm drug recommendations for registration must include MFT
	Evaluation of whether regulatory requirements may have a negative impact on implementation and establish mechanisms to alleviate this	Decide if MFT implementation will change requirements for registration (i.e., will only the two selected ACTs be allowed for registration)? Change the schedule to "over-the-counter" perhaps only for the private sector	Changing regulatory status may require considerable consensus building as well as the establishment of a system to track ADRs which is costly.	Regulatory status of MFT and ACTs procured through AMFm should be the same.	May need to change the regulatory status of the medicine or review regulatory law
	Evaluation and strengthening of regulatory enforcement capacity if needed	Determine role of the regulatory body in controlling or monitoring in the private sector.	***Both options*** Extending regulatory jurisdiction to MFT in the private sector more complex and costly. ***Option B (children/adults)*** May be more complicated to regulate dispensing by age group in the private sector	If the subsidy has support interventions for strengthening regulatory capacity, MFT policy change should be able to ride on them	Coordinate closely with AMFm on planning for supporting interventions targeting regulatory body

	• Promulgate regulations for appropriate importation, distribution, prescribing and dispensing of ACTs and ensuring that they are consistent with the MFT policy. • Evaluation of "prescription only" status for increased access through the private sector	Should all other ACTs be removed?: If yes, prevent importation, distribution, prescribing and dispensing of all other ACTs and how to control ***Option A (public/private)*** Allow procurement/ importation and/or distribution of public sector product only for public sector and private only for private sector ***Option B (children/adults)*** Difficult to regulate same product used in different age groups	***Option A (public/private)*** Even with regulations there is likely to be movement between the two sectors ***Option B (children/adults)*** More costly than option A to regulate	Cannot introduce regulations preventing import of all other ACTs if AMFm takes free market approach	Coordinate closely with AMFm's strategy with regards to the market approach. May need to regulate other ACTs that are not recommended in the policy.

Review, Harmonization, Dissemination of Guidelines, Medicines Lists, etc.	• Determine which guidelines need to be revised and where harmonization should occur (with STGs, EML, IMCI, insurance lists) • Determine process for revision and the groups involved • Determine whether new guidelines need to be published or an addendum made to the existing guidelines • Publish revised guidelines/EML and/or addendum and disseminate • Develop dissemination strategy	***Option A (public/private)*** May or may not revise guidelines if the same ACT is recommended in public sector as previously. Will need to develop guidelines for the private sector (different from public sector). ***Option B (children/adults)*** Revise guidelines for public sector for each age group. Develop guidelines and disseminate to private sector (may be the same or different). IMCI guidelines will need to be revised For both—coordinate with training, insert into IMCI training, coordinate with BCC actions.	Revision of guidelines is a costly exercise and must be accompanied by adequate training in both sectors. ***Option A (public/private)*** Developing and disseminating guidelines for the private sector may be expensive. ***Option B (children/adults)*** If different guidelines are developed for the public and private sectors, costs will be higher.	Timeline for implementation of subsidy and for support activities should determine timeline for updating guidelines in support of MFT.	MFT implementation should be coordinated within timeline of subsidy implementation

Review and Dissemination of BCC Materials and Targeted IEC	• Develop/review behavior change communication strategies, and coordinate with IEC strategy • Development/review BCC and IEC materials (job aids, posters, content of TV, radio spots, documentaries, Interpersonal communication) • Development/review plan for implementing the BCC strategies	Coordinate with STGs and EML work. Involve private sector. ***Option A (public/private)*** Different IEC and BCC will need to be developed for public and private sectors. IEC messages need to inform public of what to expect in public sector versus private sector ***Option B (children/adults)*** Considerable IEC and BCC will be required to change prescribing behaviors. Need to consider how to simplify case management messages given different dosage regimens. Facilitate potential packaging requirements	***Option A (public/private)*** IEC and BCC will need to be coordinated in public and private sectors. ***Option B (children/adults)*** IEC and BCC will need to be coordinated in public and private sectors. Messages need to be consistent. Wider dissemination needed with more media outlets	Potential to confuse providers and disrupt MFT introduction process if not appropriately coordinated.	Coordination and planning essential to success. Use similar mechanism as AMFm
Update of Training Curriculum, Training, Supervision of Health Workers	Revision of pre-service and in-service training curricula to incorporate MFT	Both options require revision of training curricula to include current recommendation. Decision needs to be taken on whether one set or different sets of training curricula and materials will be needed.	Expensive to develop different sets of curricula for each option.	AMFm will also require revision of training curricula. Potential for confusion if not coordinated.	Coordinate with schools of medicine and pharmacy. Involve professional organizations. Consider input from public and private sectors.

	Development/review plan for training of health workers (public and private sectors) and development of training materials	***Option A (public/private)*** Plan for training in public and private sectors separately but within an overall plan. Different materials may be needed. ***Option B (children/adults)*** Consider joint trainings in public and private sectors.	***Option A (public/private)*** Expensive to train different trainers for different sectors/options. This will lead to fragmentation. Cost of developing different materials. ***Option B (children/adults)*** May be challenging due to the varied level of training of those in private sector.	Training of treatments for AMFm may be different from MFT and will likely lead to confusion.	Coordinate training. Plan to train a core group of trainers (pulled from both sectors and with expertise in malaria management across age groups) to train different sectors using one curriculum with different modules relevant to different sector trainings.
	Convene training workshops soon after procurement of new MFT for the public sector and carry out a cascade training	***Option A (public/private)*** Train in public and private sectors separately. ***Option B (children/adults)*** Need to involve private sector. Consider joint training. Need to ensure quality of training	***Option A (public/private)*** Will need to carry out separate trainings for public and private sectors. Private sector providers often untrained personnel—potentially more costly. ***Option B (children/adults)*** More expensive. Will need to train public and private sector providers—often untrained personnel—potentially more costly.	Training timelines and strategies might be different for AMFm and will likely lead to confusion	Cost savings and consistency gained from training the trainers in both sectors together initially. Coordinate training plans with AMFm.

POLICY INTRODUCTION AND IMPLEMENTATION: OPERATIONAL CONSIDERATIONS					
Phasing out old and phasing in new	Determination of phase-in plan for MFT policy	***Option A (public/private)*** Can be done by sector. ***Option B (children/adults)*** Can be done by sector or geographical area.	***Option A (public/private)*** If done by sector, will need strategy on what to do in the interim in the other sector. ***Option B (children/adults)*** If done by sector will need strategy on what to do in the interim in the other sector. If done by geographical area will need to coordinate with IEC, training, etc.	AMFm might be phasing-in in a different manner and could cause confusion.	Consider a phased implementation. Need to coordinate phase-in plan with AMFm for both options
	Determination of pipeline for the "old" drugs (if existent)	It is unlikely that large pipelines of ACTs exist in the private sector.	It may be challenging to determine pipeline in public sector if there is no centrally assembled data. This is practically impossible in private sector	If AMFm is introduced before MFT, there is likely to be a large pipeline of old medicines	Introduce both strategies together
	Adjustment of future procurements of MFT based on available viable old treatments and ensuring that large pipelines of outgoing drugs do not accumulate when the new drugs are procured.	If new therapies are being recommended for MFT, consider that stocks may accumulate if new policy is introduced before stocks are used. If one of the medicines are the same, consider existing stocks and adjust future procurements	Potential for wasted resources from expired medicines.	Potential for wastage of medicines.	

	Development/review of a plan for the phase-out of old unneeded drugs (especially monotherapies) from the health system (public and private sectors) as the new MFT becomes available	For MFT to achieve objectives, need to remove all circulating monotherapies. No existing mechanisms for recall in most endemic countries.	If new products are different from old, recall in the public sector will be challenging. Recall in private sector is practically impossible. Both will be costly.	If AMFm is launched before MFT, any change or removal of existing medicines will be challenging with a potential for wastage of medicines.	Consider adjusting regulatory status of "old" medicine(s) not on new policy
Forecasting of demand and quantification	• Inclusion of MFT in overall quantification. • Selection of appropriate quantification method for each first-line treatment based on data available (include RDTs if appropriate). • Use of treatment guidelines, development of appropriate assumptions for frequency and duration of treatment use • Adjustments for inventory position, lead time, safety stock, growth and losses	***Option A (public/private)*** Need to quantify for treatment for the public and private sector according to data available. If new ACT, use morbidity data. ***Option B (children/adults)*** Need to quantify separately for children under age five and over age five expected to be treated in the public and private sector according to data available. If new ACT, use morbidity data.	***Option A (public/private)*** Quantifying for the private sector is challenging. ***Option B (children/adults)*** Quantifying for children under age five and adults for one ACT is already challenging in the public sector. It is likely to be more complicated in the private sector.	Need to determine market share of the subsidized treatment versus other treatments-unless MFT components will be subsidized through AMFm	Need to monitor episodes and consumption in both public and private sectors or develop forecast models. Coordinate with AMFm
	Ensure that forecasts for any parallel procurement efforts of the MoH and grants (including GFATM and AMFm) are harmonized.	Consider private sector and public sector procurements. Private sector procurements currently usually done by myriad of importers and wholesalers.		Forecast efforts of AMFm may assist with understanding the burden and market for antimalarials.	Need to harmonize AMFm forecasts with MFT.

	Support for quantification in public and private sectors	Support public and private sectors to quantify. Capacity building needs for forecasting.	***Option A (public/private)*** Little data on consumption and or morbidity particularly in private sector. ***Option B (children/adults)*** More difficult as no data on consumption and or morbidity by age group.	***Option A (public/private)*** Need to determine markets served by AMFm versus other ***Option B (children/adults)*** Need to determine markets served by AMFm versus other.	Need clear definitions of the target populations for intervention target and implementation
	Establish consumption tracking through LMIS to guide future quantification	Consumption tracking needed to validate quantification. Need to establish system for public and private sectors.	Challenging in the public sector; likely to be more challenging and costly in the private sector.		Need to establish system for public sector monitoring. Consider using a market research company for in-country data generation in the private sector, although this is expensive.
Procurement	Depending on source of funding for treatment, adherence to procurement requirements	***Option A (public/private)*** Depending on whom does procurement in public and private sectors, may have different requirements. ***Option B (children/adults)*** Consider using same procurement agency doing procurement for public and private sectors.	Determining who procures for the private sector may be challenging due to independence of private sector. Leaving the market to procure may lead to quality concerns as well as.	Potential for conflicting procurement requirements.	Clear definition on sources of procurement and roles and responsibilities for each sector or each component of MFT strategy. Need to harmonize procurement mechanisms with the AMFm. Coordinate requirements.

	Ensuring incorporation of MFT in national procurement plan for antimalarials and diagnostic commodities	***Option A (public/private)*** May not need to be done if private sector procuring own medicines. ***Option B (children/adults)*** Procurement more likely to need harmonizing between both sectors.	***Option A (public/private)*** Not likely to have one procurement plan for the private sector due to variety of suppliers ***Option B (children/adults)*** Likely to be more challenging.	Potential for confusion is products and procurement mechanisms are different.	Harmonize procurement plans for all antimalarials (particularly ACTs) procured in country. Harmonization with AMFm needed.
	Facilitation of private sector procurement approach	This may facilitate monitoring of quality.	Private sector may be opposed to external procurement.	AMFm will be facilitating private procurement through eligible buyers.	Include multiple private sector buyers to facilitate acceptance and avoid monopolies. Consider adoption of similar principles as AMFm.
	Processing of procurement through selected procurement agent	This may facilitate monitoring of quality.	Private sector may be opposed to external procurement and use of a procurement agent		Use of procurement agents or eligible buyer approach may facilitate uniform and coordinated approaches in private sector. Harmonize with AMFm
	• If need to repackage product, identification of supplier/ manufacturer that can repackage • Development of packaging and labels for prepackaged product if needed and pretesting of package	***Option A (public/private)*** Consider different packages for public and private sectors. ***Option B (children/adults)*** Consider different packages and or color coding for children and adults.	***Option A (public/private)*** — ***Option B (children/adults)*** Manufacturer may not be willing to repackage.	If AMFm uses its own packaging, there may be confusion and branding.	Consider packaging differently for public and private or children and adults to facilitate monitoring.

	• Development of tender documents, initiate and management of procurement • Supplier performance monitoring	***Both:*** Private sector procurement likely to be different and not involve tenders. Will need feedback from public and private sectors for supplier monitoring.	Challenging and costly to sample facilities for feedback not routinely included in system.		Consider using eligible suppliers identified by AMFm.
Distribution	• Development/review distribution plan for MFT approach • Review/development of distribution systems for MFT approach	Determine how distribution will occur in private (and public) sector, who will handle it, where the goods will be stored at district level. Determine quantities to be supplied to each level.	Coordination of supply from different funding sources may be challenging.		Ensure development of distribution plans for all ACTs regardless of funding source. Delineation of processes and roles and responsibilities.
	Development/review of strategies to avoid leakage between MFT groups	***Both:*** need careful monitoring of prescriptions and dispensing in both sectors ***Option A (public/private)*** These two sectors are more heterogeneous, therefore monitoring movement may be easier particularly when different treatments are being used in each. ***Option B (children/adults)*** Monitoring movement will mean monitoring prescribing and dispensing in the public and private sectors	***Option A (public/private)*** May have some leakage between public and private sectors. ***Option B (children/adults)*** More challenging and costly.	Need to monitor movement of ACTs procured through AMFm. Complex to monitor if strategies are not complementary	Develop mechanisms and indicators to monitor leakage.

	Development/review storage capacity and conditions	Evaluate storage quality and capacity in public and private sectors ***Option B (children/adults)*** Need larger storage area because of two different products with potential total of eight packages	***Option B (children/adults)*** More challenging and costly.	If product procured through AMFm is different, storage will be a bigger issue	Ensure accurate estimation of storage capacity needed. Develop mechanisms to improve capacity if needed. Consider outsourcing storage facilities if needed
	Development/review of human capacity for efficient implementation of distribution plan and supervision	Need to mobilize capacity in public and private sectors.	***Option A (public/private)*** Supervision of implementation in private sector challenging. ***Option B (children/adults)*** More challenging to supervise and monitor.	Need capacity to supervise and monitor implementation of subsidized ACT. May over-extend staff.	Use simple supervisory tools for supervision
	Development/review of transportation systems for delivery to MFT groups	***Both:*** Determine who will do this in the public and private sectors? Monitor quality ***Option B (children/adults)*** Determine if same system to be used in public and private sector	Coordination of transport to remote private sector outlets may be challenging and costly.		Consider outsourcing transport systems
	Development/review of redistribution systems and systems to remove expired or excess stocks from one group to another.	How will this occur in public and private sectors?	Potential for procuring different medicine than the one recommended when initial stocks depleted.		Develop system to monitor near expiry products

	Development/review systems to monitor efficiency of distribution system and redistribution mechanisms	Develop indicators of success. Who monitors these indicators?	Monitoring in private sector a challenge.		Develop system to monitor in private sector.
	Develop incentives for adherence to strategy	Develop incentives for adherence for right product for child and adult.	***Both:*** Challenge in monitoring adherence. Incentives in private sector difficult to implement ***Option B (children/adults)*** Monitoring of two products in private sector particularly challenging.		Consider market centered incentives in private sector
Inventory management	Review/development of inventory management systems to improve the management of the medicines in all facilities serving MFT target groups.	Both options will require review/development of inventory management systems in private sector.	Private sector inventory management monitoring more complex and expensive—may be setting up new systems.		Implement training programs and tools for appropriate inventory management. Leverage AMFm funding to implement supporting interventions. Consider sector-wide improvements in inventory management rather than vertical system.

	Development/review of security measures and tracking systems to prevent theft of stored products.	***Option A (public/private)*** These two sectors are more heterogeneous, therefore monitoring movement may be easier particularly when different treatments are being used in each. ***Option B (children/adults)*** Monitoring movement will mean monitoring prescribing and dispensing in the public and private sectors.	***Option B (children/adults)*** More challenging and costly.	Need to monitor movement of AMFm procured ACT.	
	Development/review of systems to ensure management of the shelf life of products (including capacity building and supervision).	Difficult to develop new systems in private sector	Development of new supervision mechanisms in private sector likely to be costly.	Systems overburdened by tracking and monitoring multiple products.	
	Development/review of systems for dealing with expired products.	To do this, the previous system has to be established.	Recall in both sectors is challenging but especially difficult in private sector.		
Revision of quality assurance mechanisms (pharmacovili-gance and product quality surveillance)	Development/review of system and tools for monitoring of adverse events.	Use existing systems if they exist in public sector. System will need to be adapted or developed for private sector.	Harder to implement in private sector.	Leverage resources from AMFm for the intervention.	Consider developing integrated system for monitoring adverse events rather than parallel system.

	• Development/review of systems for quality assurance during drug registration and procurement • Development/review of system for dealing with violations of drug quality standards • Establishment of mechanism to coordinate the various surveillance systems—ADR, product quality, effectiveness, etc. • Development/review of plan for post- marketing product quality surveillance	Outline quality criteria for MFT (e.g. WHO prequalified) Consider simple systems for monitoring product quality Ensure local manufacturers supplying components of MFT adhere to same quality principles	Regular monitoring of product quality in private sector challenging and costly to implement.	ACTs procured through AMFm likely to have particular quality requirements. Important to ensure harmonization to avoid confusion during procurement.	Ensure product requirements including prequalification are harmonized. Need coordinated approaches for requirements of product quality between donors.
M&E	Definition of policy change milestones	Develop indicators and monitor them. Determine who monitors them in both sectors. In the case of private sector, determine where the data goes.	Monitoring more challenging in private sector.	AMFm will be collecting information on coverage, access and price providing opportunities for leveraging. Collecting information for different indicators may be confusing and difficult.	Harmonize indicators with AMFm.

	• Inclusion of outcome and impact targets within overall country targets (indicators) • Identification of data needs and sources (priority areas – routine data recording & collection; planning, budgeting, monitoring for donor funded activities; survey based data; LMIS; sentinel sites; training data)	Develop indicators and monitor them. Determine who monitors them in both sectors. In the case of private sector, where does this data go?	Monitoring more challenging in private sector.	As above	Harmonize indicators with AMFm
	Ensuring the collection of data through existing information systems and collate appropriately.	May need to establish new system in private sector. Include professional bodies for facilitation in private sector.	Existing systems may not be collecting information needed. May need to expand system.	As above	Consider using market research companies to monitor
	• Strengthening of M&E capacity at NMCP • Facilitation of linkages and partnerships for M&E	May need to build capacity at NMCP.	***Option B (children/adults)*** More challenging to monitor.	AMFm can be leveraged to strengthen capacity in M&E	Develop integrated M&E systems rather than donor driven systems

DISCUSSION AND WAY FORWARD

The change of global and country level policies to MFT will require significant challenges and associated costs with adoption, introduction, and implementation.

The change in first treatment policy to ACTs occurred due to widespread resistance to currently used therapies such as chloroquine and SP with subsequent global technical and donor recommendation for the need for change. Although evidence from Southeast Asia has indicated low levels of treatment failures with ACTs there is little documented parasite resistance to ACTs in Africa. Clearly, any change in policy where there is no perceived urgent need will be challenging. WHO defines the purpose of an antimalarial drug policy "to ensure availability 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 minimize the development of antimalarial drug resistance." While MFT offer potential to achieve the latter, under the current epidemiological context, the impetus to change to a new strategy is likely to be limited.

To garner acceptance of an MFT approach, a policy change to MFT will first need a presentation of the evidence for (1) the need for change including an understanding of the societal benefits of change, and (2) efficacy of the option for change—in this case MFT. The challenge will lie in the fact that there is little hard direct evidence or parameter estimates of the effectiveness of MFT versus maintaining the status quo—the evidence for change to MFT is based on theoretical models. As a result, significant efforts will need to be invested in obtaining additional evidence. This means that consensus building at this level should therefore start early along with an evaluation and presentation of the consequences of doing nothing and a presentation of potential savings accrued from having to change first-line treatments every five years.

At the national level, a change to a new strategy without drug resistance will mean significant changes in perception of the purpose of an antimalarial treatment policy and a potential strategy such as MFT may offer including a risk-benefit analysis. Assuming global technical and political support for MFT, engaging national stakeholders early in the discussion may facilitate policy uptake.

The criteria for selection of the treatments used for MFT must be widely circulated to garner acceptance and avoid irrational use. The perception of the various components of MFT may be a potential significant barrier to the uptake of MFT. A negative perception to one or more of the components may result in ethical and equity issues concerning the allocation of particular ACTs to particular portions of the population.

MFT should be considered not as a new strategy or policy but a different approach of combination therapy to facilitate a more rapid uptake; in addition, they should be offered with a potential source of funding, be it AMFm, GFATM, or other donors. For the most part, ACTs are currently available free in the public sector. A few countries have cost-sharing approaches. Most private sector sales of ACTs occur with out-of-pocket expenditures, therefore, the ACT being promoted in the private sector as part of the MFT strategy must be affordable. This is unlikely to

occur in the immediate future unless subsidized products are procured either through the AMFm or through other sources such as GFATM grants and made available through the private sector.

Furthermore, implementation of MFT are likely to face significant challenges and costs associated with forecasting or quantification; storage and distribution; training and behavior change communication messages to ensure adherence to the strategy; changing and disseminating treatment guidelines; and quality assurance, quality control, and monitoring of adverse drug reactions. Clearly, many of the steps described are pertinent to changing a policy to another single first-line policy. With new ACTs becoming available and with AMFm possibly starting up, change is inevitable. However, introducing MFT presents specific challenges in a number of areas. Firstly, traditional models of implementation have been focused on the public sector. If MFT are to be widely available, inclusion of the private sector in the strategy is desirable, particularly the private-for-profit sector. Scaling up in this sector is likely to require significant resources for training, communication and monitoring. Indeed, on the flip side MFT also offer the potential for improving practice in the private-for-profit sector where all kinds of antimalarials are being sold by people who lack training or information. Therefore, regardless of MFT, there is a need to invest resources in capacity building of the private-for-profit sector through some level of training. Nevertheless, responsible introduction of a new strategy that advocates implementation in this private sector will need to incorporate such investments.

Similarly, the reasons to restrict the use of monotherapies, poor quality medicines, or counterfeits are not specific to MFT policies, the higher demand of multiple ACT products is likely to increase challenges associated with quality. Higher investments in sampling products for monitoring of product quality will need to be made. Wider use of multiple ACTs will also require active monitoring of adverse drug reactions. Again, while these are not issues that are specific to MFT, widespread use of a larger number of products is likely to multiply the resources required for monitoring.

MFT are likely to pose specific challenges in the area of forecasting and quantification. MFT require *segregation* of the target population with estimates of proportions of the population which will receive each of the recommended therapies. Forecasting for ACTs in the public sector is currently a challenge due to a lack of data on actual demand. Forecasting and quantification for the multiple components of MFT are likely to present even greater challenges. The unavailability of morbidity data, particularly segmented by age groups is largely unavailable or inaccurate. The private sector ACT market is even more daunting. In both sectors, there is no systematic collecting and assembling of accurate data on morbidity or consumption of currently used ACTs; also, treatment seeking in the private sector is influenced by a variety of factors including medicine availability there the actual market for ACTs is unknown. Estimating the market share of each component of MFT will be challenging. AMFm is planning on working on this issue and these findings can be leveraged for MFT.

Planning and coordination will be essential and will need to include the private sector, which is often not involved in public sector programs and interventions. Roles and responsibilities for each component of the implementation process lines of accountability need to be clearly defined. Any overlap or coordinated functions must be elaborated at the planning stage particularly

between the public and private sectors. Operational research will be needed and pilot implementation of MFT may provide valuable lessons for scaled up implementation.

Most treatment seeking for malaria in sub-Saharan African occurs in the commercial private sector, so it is therefore natural to include them in the potential MFT strategy. However, the commercial private sector has thus far been relatively unregulated and implementing such interventions will require considerable capacity building of the regulatory body and behavior change of private providers. Furthermore, MFT policies may be considered to the free market models by which the private sector traditionally tends to function. In most malaria endemic countries in Africa, antimalarial availability in the respective public and private not-for profit and the for-profit sectors follow "parallel" or separate supply chains. These traditional frameworks will need to be changed, particularly if procurement and distribution of ACTs will be integrated. Mechanisms for accountability in private sector will also need to be developed. A decision will need to be made on how much control and regulation of the private sector is desirable without influencing its being able to provide wider access and without disrupting the market. Although strict control of the private sector may not be desirable or indeed feasible, some level of monitoring will need to occur to ensure some adherence according to the desired objectives.

The majority of countries in Africa are already deploying some sort of MFT, albeit by default in an uncoordinated way without a formal adoption and not always with two co-formulated treatments. While theoretical models (Boni 2008) indicate that MFT are beneficial regardless of implementation, it is unclear whether such an uncoordinated approach plays a role in delaying the emergence of resistance in practice. In countries where there is limited funding for procurement of first-line treatment for the entire public sector such as Nigeria, the first-line treatment for children is AL in selected states with the use of AS/AQ as the alternate first-line treatment for adults. In other countries such as Uganda, Malawi, Nigeria, and Ghana, the policy lists two first-line treatments. Given the erratic nature of the supply chain for ACTs as well as poor forecasting, a decision was made to ensure that ACTs are always available in the public sector. In many countries, even when only a single first-line treatment is listed because there is no public sector provision schemes for private sector treatment, the private sector is prescribing and dispensing many ACTs other than those recommended in the policy. Furthermore, as ACTs are not recommended in the first trimester of pregnancy, an alternative (usually quinine) is used in this population. AL is not recommended in children who weigh less than five kilograms, and therefore quinine is often recommended for this population as well. Also, although the policy states an ACT as the recommended first-line treatment, SP continues to be available for intermittent preventive treatment for pregnant women to prevent malaria during pregnancy and in some countries providers continue to prescribe SP.

Many countries are using microscopy and RDTs for diagnosis prior to treatment. In practice, data from Kenya, Madagascar, and Zambia indicate that in the event that the test(s) is negative but the provider (1) suspects malaria based on the clinical symptoms, or (2) is pressured by the patient or caretaker to give out some treatment for malaria, providers have been prescribing antimalarial monotherapies (AQ in Kenya, SP in Zambia, and chloroquine, quinine, or AS/AQ in Madagascar).

Although this current situation can be considered multiple first-line therapy, in the context of this paper where MFT is understood to be explicitly recommended policy, the "natural" and haphazard individual prescriber's decision/selection may not necessarily be desired, unless it is explicitly defined to be one of the "components" of the policy. For example, a specific ACT is recommended for the public and the not-for-profit private sector, while the choice of a different ACT is left open for the private sector to be potentially influenced through the AMFm mechanism on private sector suppliers.

Annex 1 summarizes information on current policies and practice in select countries in Africa.

Both options A and B will require interventions in the private sector which are harder to implement and monitor than single drug policies being implemented only in the public sector. However, option B which will require implementation and monitoring separate treatments for children under the age of five and the population over five years of age is possibly more challenging in the private sector. Given that most treatment seeking for malaria occurs in the commercial private sector in absence of effective interventions including affordable options, it is likely that the volume of ACTs distributed through the private sector will continue to remain small. A possible option for consideration is the use of one treatment in the public sector, on in the not-for-profit private sector with a third in the commercial private sector.

CONCLUSION

MFT have the potential to offer a mechanism for delaying the emergence of drug resistance, however, development of malaria policies also require consideration of their ease of implementation and sustainability. Given that some type of MFT already exists in most countries, it seems prudent to recommend MFT to ensure coordinated approaches to MFT while increasing the useful therapeutic life of the existing combinations.

The private for-profit sector has traditionally always operated as a separate entity with little interaction with the public sector and with public sector interventions. Controlling and monitoring the informal private sector however limited is likely to remain challenging with little chance of immediate resolution. It will be important to initially focus interventions such as MFT on the formal private sector, possibly including registered drug shops or outlets that are easier to monitor.

While some monitoring and interaction with the private sector will be essential for either MFT option discussed in this paper or involving implementation in the private sector, it would seem prudent to recommend an MFT alternative such as option A in which the private sector continues to remain somewhat independent with less operational challenges and cost.

Furthermore, given that implementation of MFT is likely to be accompanied by the need for increased resources for supportive functions, the strategy should be presented with potential funding sources. Also, because a lack of evidence for MFT is likely to be a potential barrier for adoption, considerable effort will be needed immediately for compiling and presenting the evidence, conducting operational research, and garnering technical, political, and donor support for MFT as a potential strategy to prolong the useful therapeutic life of ACTs.

This paper outlines critical issues for MFT and those pertinent to AMFm. However, the success of MFT will require that several issues within the AMFm be resolved and given that both strategies will be rolled out in tandem it will be essential to address both.

REFERENCES

Abdulla, S., C. Goodman, P. Coleman, et al. 2000. *The Costs, Effects and Cost-Effectiveness of Changing the First-line Drug for the Treatment of Malaria in Tanzania.* Technical report prepared for the National Malaria Control Programme, Tanzania.

Affordable Medicines Facility for malaria (AMFm). http://www.rbm.who.int/partnership/tf/globalsubsidy/080227AMFmBriefingDocument.pdf.

AMFm. 2007. Technical Design. Prepared with guidance from the AMFm Task Force of the RBM Partnership Secretariat. Geneva.

Amin, A.A., D. Zurovac, B. B. Kangwana, et al. 2007. The challenges of changing national malaria drug policy to artemisinin-based combinations in Kenya. *Malaria Journal* 6:72.

Brabin, B. J., F. H. Verhoeff, P. Kazembe, et al. 1997. Antimalarial Drug Policy in Malawi. *Annals of Tropical Medicine and Parasitology* 91(Suppl. 1):S113–S115.

Boni, M.F., D. Smith, and R. Laxminarayan. 2008. Benefits of using multiple first-line therapies for malaria. (unpublished).

Davey, P., E. Brown, L. Fenelon, et al. 2005. *Interventions to improve antibiotic prescribing practices for hospital inpatients.* The Cochrane Database System Review (4):CD003543.

Fevre, E. M., and G. Barnish. 1999. Malaria Treatment Policies: When and How Should They Be Changed? *Annals of Tropical Medicine and Parasitology* 93(6):549–60.

Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM). 2004. *Guide to the Global Fund's Policies on Procurement and Supply Management.* Geneva: GFATM. http://www.theglobalfund.org/en/about/policies_guidelines/

Goodman C. A., P. G. Coleman, and A. J. Mills. 2001. The Cost-Effectiveness of Antenatal Malaria Prevention in sub-Saharan Africa. *American Journal of Tropical Medicine & Hygiene* 64(1–2 Suppl):45–56.

Gugliemo, B.J. 1995. Practical strategies for the appropriate use of antimicrobials. *Pharmacy world & science* 17(4):96-102.

Institute of Medicine. 2004. *Saving Lives, Buying Time*. Ed. Kenneth J. Arrow, Claire B. Panosian, and Hellen Gelband. Washington, DC: National Academies Press.

Kitua A. Y. 1999. Antimalarial Drug Policy: Making Systematic Change. *Lancet* Suppl:SIV32:354.

Management Sciences for Health (MSH) and World Health Organization (WHO).1997. *Managing Drug Supply: The Selection, Procurement, Distribution, and Use of Pharmaceuticals.* 2nd ed. W. Hartford, CT: Kumarian Press.

Rational Pharmaceutical Management Plus. 2005. *Changing Malaria Treatment Policy to Artemisinin-Based Combinations: An Implementation Guide.* VA: Management Sciences for Health.

Roll Back Malaria Partnership Board. 2004. *Assuring Access to Effective Malaria Case Management.* Geneva: Roll Back Malaria Partnership.

Shretta R., J. Omumbo, B. Rapuoda, et al. 2000. Using Evidence to Change Anti-malarial Drug Policy in Kenya. *Tropical Medicine and International Health* 5(11):755–64.

Shretta, R. 2007. *Global Fund Grants for Malaria: Summary of Lessons Learned in the Implementation of ACTs in Ghana, Nigeria, and Guinea-Bissau.* Submitted to the U.S. Agency for International Development by the Rational Pharmaceutical Management Plus Program. Arlington, VA: Management Sciences for Health.

Smith, D.L., M.F. Boni, and R. Laxminarayan. 2008. *Multiple first-line artemisinin combination therapies to delay the emergence of resistance.* (unpublished)

USAID/DELIVER. 2008. Engaging the Non-Public Sectors in the SPARHCS Process. Draft.

White, N.J. 2008. Qinghaosu (Artemisinin): The Price of Success. *Science* 320:330-334.

White, N.J. 1998. Preventing antimalarial drug resistance through combinations. *Drug Resistance Updates: Reviews and Commentaries in Antimicrobial and Anticancer Chemotherapy* 1(1): p. 3-9.

White, N.J. 2004. Antimalarial drug resistance. *Journal of Clinical Investigation* 113(8):1084-92.

White, N.J., and W. Pongtavornpinyo. 2003. The de novo selection of drug-resistant malaria parasites. *Proceedings. Biological sciences/The Royal Society*. 270(1514):545-54.

World Health Organization (WHO). 2007. Containment of malaria multi-drug resistance on Cambodia-Thailand border. Report of an informal consultation, Phnom Penh, 29-30 January, 2007. http://www.wpro.who.int/NR/rdonlyres/602064E7-45FE-4BB1-A99A-834F20A98C0E/0/MAL246.pdf (accessed Aug. 2008)

WHO. 2007. New technologies for tuberculosis control: A framework for their adoption, introduction and implementation. Geneva: WHO. http://whqlibdoc.who.int/publications/2007/9789241595520_eng.pdf. (accessed Aug. 2008)

WHO. 2004. *Position of WHO's Roll Back Malaria Department on malaria treatment policy*. Statement. Geneva: WHO. http://www.who.int/malaria/docs/who_apt_position.htm (accessed Aug. 2008)

WHO/AFRO. 2003. Framework for Developing, Implementing and Updating National Antimalarial Treatment Policy: A Guide for Country Malaria Control Programmes. *Malaria: Liaison Bulletin of the Malaria Program* 2(2):1–4. http://www.afro.who.int/malaria/bulletins/1999-12_vol2-2.pdf (accessed Aug. 2008).

WHO. 2001. *Antimalarial Drug Combination Therapy*. Report of a WHO Technical Consultation. Geneva: WHO. http://whqlibdoc.who.int/hq/2001/WHO_CDS_RBM_2001.35.pdf (accessed Aug. 2008).

Williams, H. A., D. Durrheim, and R. Shretta. 2004. The Process of Changing National Treatment Policy: Lessons from Country-Level Studies. *Health Policy and Planning* 19(6): 356–70.

Wirima, J. J. W. 1999. Development of an Antimalarial Drug Policy. *Malaria and Infectious Diseases in Africa* No. 9. http://chez.com/malaria/som10an.htm

Zikusooka, C.M. 2008. *Multiple first-line treatment policies: global perspective on delaying resistance to antimalarials*. Draft consultancy report submitted to Resources for the Future.

Zinc Task Force. 2006. *Implementing the new recommendations on the clinical management of diarrhea: guidelines for policy makers and programme managers.* Geneva: WHO.

ANNEX 1. CURRENT FIRST-LINE RECOMMENDATIONS AND OBSERVED PRACTICES FOR THE TREATMENT OF UNCOMPLICATED MALARIA IN SELECT AFRICAN COUNTRIES

	First-line	Alternative First-Line (if this exists)	Second Line	First Trimester of Pregnancy	Children < 5 kilograms	Home-Based Management	Private Sector
Angola	AL	-	Quinine	Quinine	Quinine	-	AL
Practice	*AL*	-	Quinine	Quinine	Quinine	-	*AS/AQ, AL, and other registered ACTs and monotherapies*
DRC	AS/AQ		Quinine	Quinine	Quinine		AS/AQ
Practice	*AS/AQ,SP*		Quinine	Quinine	Quinine		*SP, AS, AL*
Kenya	AL	-	*Quinine*	Quinine	*Nothing on record*	*Some pilots of AL in drug shops underway*	*AL is first-line as per policy*
Practice	*AL*	*Amodiaquine still in stock. Used when AL is stocked out in public sector and also when lab is negative and there is strong suspicion of malaria*	*Quinine*	*Quinine*	*AL* *AQ*	*AL and other registered ACTs and monotherapies*	*AL and other registered ACTs and monotherapies*
Ghana	AS/AQ	AL and dihydroartemisinin-piperaquine	*Quinine*	Quinine	Quinine	*Nothing on record*	AS/AQ
Practice	*AS/AQ; AS and AQ monotherapy in combination*	*AL and other ACTs and monotherapies bought from the private market when there AS/AQ stock-outs*	*Quinine*	*Quinine and AS/AQ*	*AS/AQ*	*HBM being implemented through communication to mothers to report early to facilities*	*AS/AQ, AL, and other registered ACTs and monotherapies*

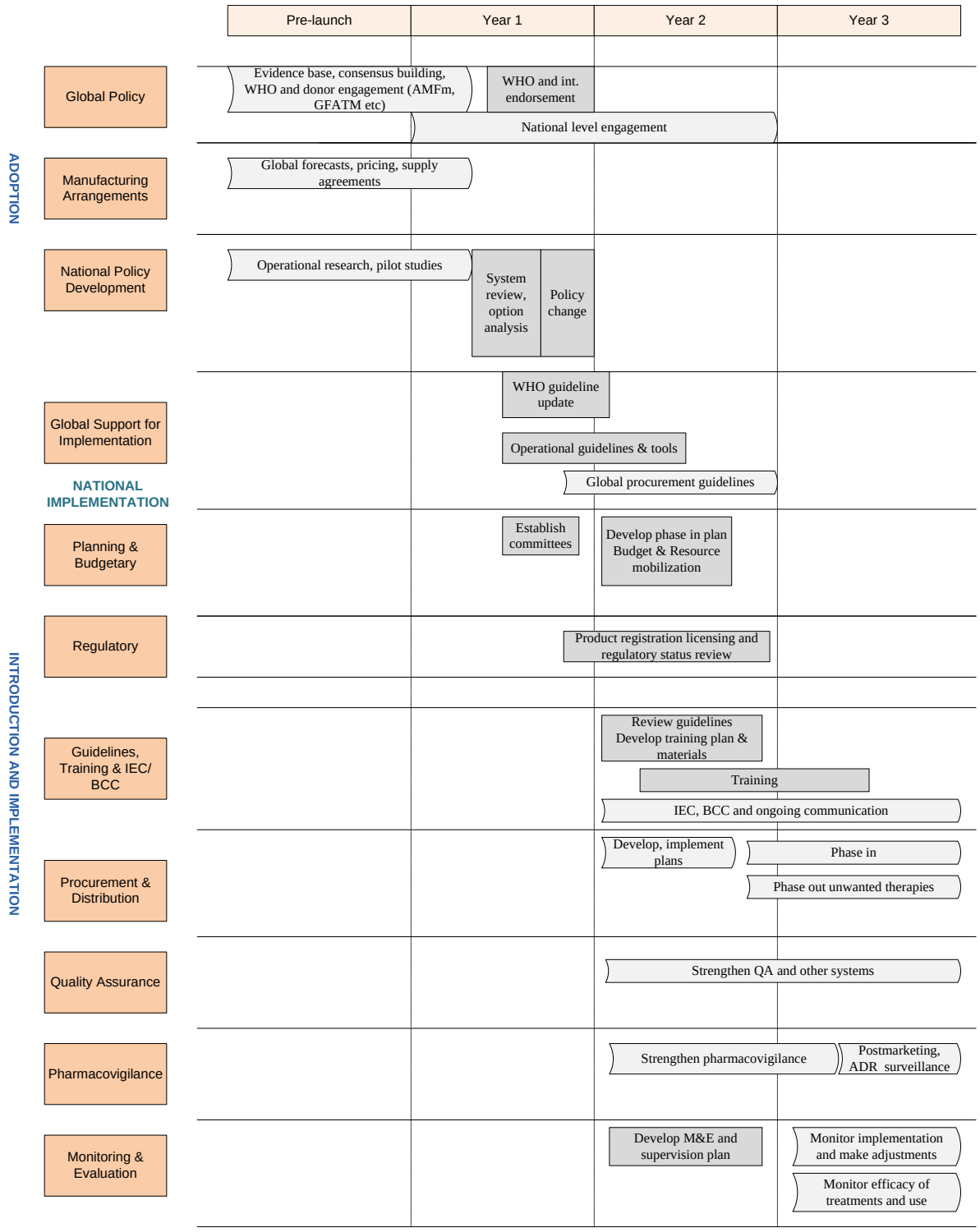
	First-line	Alternative First-Line (if this exists)	Second Line	First Trimester of Pregnancy	Children < 5 kilograms	Home-Based Management	Private Sector
Liberia	AS/AQ	None currently (AL under review)	Quinine	Quinine	Quinine	AL under review	
Practice	*AS/AQ, SP*	-	*Quinine*	*Quinine*	*AS/AQ*	-	Monotherapies including CQ and artemisinins
Madagascar	AS/AQ	-	AL or quinine + tetracycline/ doxyclycline	*Quinine*	AS/AQ	-	
Practice	*AS/AQ; RDT –severe cases–CQ, quinine, AS/AQ*	-	*No AL has been procured yet*	*Quinine*	*AS/AQ*	-	*AS/AQ, AL and other registered (and unregistered) ACTs and monotherapies*
Malawi	AL	AS/AQ	Quinine	Quinine	Quinine	-	AL
Practice	*AL*	*Quinine*	*Quinine*	*Quinine*	*Quinine*	-	*AL and other registered (and not registered) ACTs and monotherapies*
Mali	AS/AQ	-	Quinine	Quinine	Quinine	-	AS/AQ
Practice	*AS/AQ*		*Quinine*	*Quinine*	*Quinine*	-	*AS/AQ and other registered (and not registered) ACTs and monotherapies*
Nigeria	AL	AS/AQ		Quinine	Quinine	AS/AQ	AL
Practice	*AL, SP*	*(starting procurement)*	-	*Quinine*	*Quinine*	*Not implemented yet*	*AL and other registered (and not registered) ACTs and monotherapies*
Rwanda	*AL*	*Artemether*	*Quinine*	*Quinine*	*Quinine*	*AL*	*AL*
Senegal	AS/AQ	-	Quinine	Quinine	Quinine	-	AS/AQ
Practice	*AS/AQ*		*Quinine*	*Quinine*	*Quinine*	-	*AS/AQ and other*

	First-line	**Alternative First-Line (if this exists)**	**Second Line**	**First Trimester of Pregnancy**	**Children < 5 kilograms**	**Home-Based Management**	**Private Sector**
							registered (and not registered) ACTs and monotherapies
Tanzania	AL	-	Quinine	Quinine	Quinine		AL
Practice	*AL*	-	Quinine	*Quinine*	*Quinine*		*AL, SP, AQ, AS*
Uganda	AL	AS/AQ	Quinine	Quinine	Quinine	AL	*AL is first-line as per policy*
Practice	*AL* *CQ, SP*	-	*Quinine*	*Quinine*	*Quinine*	*CQ/SP*	*AL and other registered ACTs and monotherapies*
S. Sudan	AS/AQ	None	AL	Quinine	Quinine	AS/AQ	AS/AQ
Practice	AS/AQ, AS/SP,	AS/AQ, various monotherapies - CQ, SP, Quinine	AL, AS/SP Quinine	CQ, SP/ sometimes ACTs	CQ, SP sometimes ACTs	-	various ACTs and monotherapies like CQ, SP
Zambia	AL	-	Quinine	Quinine	Quinine	-	AL
Practice	*AL or SP*[4]	-	*Quinine*	*Quinine*		-	*AS/AQ, AL and other registered (and sometimes non-registered) ACTs and monotherapies*

AL=Artemether/lumefantrine
AS/AQ=Artesunate/amodiaquine
CQ=chloroquine
SP=sulfadoxine/pyrimethamine

[4] When there is no AL or when the RDT test is negative

ANNEX 2. ILLUSTRATIVE TIMELINE FOR IMPLEMENTATION OF MFTS[5]



[5] Adapted from: WHO. 2007. *New technologies for tuberculosis control: A framework for their adoption, introduction and implementation*. Geneva: WHO.