¬ Affordable Medicines Facility – malaria (AMFm)

Technical Design

November 2007

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Prepared with guidance from the AMFm Task Force of the
Roll Back Malaria Partnership

Acknowledgments

Table of Contents

Figures

Abbreviations

ACT	Artemisinin-based combination therapy
AIDS	Acquired immune deficiency syndrome
AMT	Artemisinin-based monotherapy
API	Active pharmaceutical ingredient
AR	Artemether
ARV	Antiretroviral
AS	Artesunate
AQ	Amodiaquine
CGD	Center for Global Development
CHAI	Clinton HIV/AIDS Initiative, William J. Clinton Foundation
CQ	Chloroquine
DALY	Disability-adjusted life year
DNDi	Drugs for Neglected Diseases Initiative
EANMAT	East African Network for Monitoring Antimalarial Treatment
FTE	Full-time equivalent
GAVI	GAVI Alliance (formerly Global Alliance for Vaccines and Immunization)
GDP	Good distribution practice
GFATM	The Global Fund to Fight AIDS, Tuberculosis and Malaria
HANMAT	Horn of Africa Network for Monitoring Antimalarial Treatment
HIV	Human immunodeficiency virus
IEC	Information, education, and communication
IFC	International Finance Corporation
IOM	Institute of Medicine
JSI	John Snow, Inc.
LU	Lumefantrine
M&E	Monitoring and evaluation
MDG	Millennium Development Goal
MoU	Memorandum of understanding
MQ	Mefloquine
MSP	Manufacturer sales price
NGO	Nongovernmental organization
OR	Operational research
OTC	Over-the-counter
PEPFAR	President's Emergency Plan for AIDS Relief
PMI	President's Malaria Initiative
PPP	Public-private partnership
PSI	Population Services International
RBM	Roll Back Malaria Partnership
RDT	Rapid diagnostic test
RRP	Recommended retail price
SP	Sulfadoxine–pyrimethamine
SRP	Suggested retail price
TB	Tuberculosis

ToR	Terms of reference
UN	United Nations
UNDP	United Nations Development Programme
UNICEF	United Nations Children's Fund
USD	United States Dollar
Booster Program	World Bank Booster Program for Malaria Control
WHO	World Health Organization

Executive Summary

1. Introduction

Quick and effective treatment are essential to prevent disability or death from malaria. The lethal form of the malaria parasite, *Plasmodium falciparum*, is increasingly resistant to the older, inexpensive drugs for treating the disease. A new class of highly effective drugs is available, but there is a dual challenge in the treatment of malaria. First, the new drugs (artemisinin-based combination treatments or ACTs) are 10-40 times as expensive as the older and failing drugs, such as chloroquine. Second, since ACTs are the only first-line antimalarial drugs still appropriate for widespread use against the most lethal forms of malaria, malaria's toll could rise if resistance to artemisinin were allowed to spread. The poor cannot afford combination treatment, and inappropriate use of single treatments, or monotherapies, greatly increase the risk of drug resistance, rendering useless the only treatment currently effective – ACTs. This technical design of the proposed Affordable Medicines Facility-malaria (AMFm) shows how *more lives can be saved* and *the clinical effectiveness of new anti-malaria drugs can be preserved for all* through an innovative public-private partnership approach.

In 2004, a Committee of the Institute of Medicine (IOM), led by Professor Kenneth Arrow, published a report recommending a global buyer co-payment for effective, coformulated antimalarials for uncomplicated malaria as the most economically and biomedically sound means to meet the dual challenge.[1] The proposed buyer co-payment would be available to both the public and private sectors. In addition to saving lives, the innovation could delay the onset of resistance to artemisinins, creating a benefit for all—a "global public good." Better access to these drugs is also an essential part of the comprehensive package of interventions required to fight malaria, which includes prevention (insecticide-treated nets, indoor residual spraying, other vector control techniques, and vaccines that are under development) and treatments for severe malaria. Subsequent analyses published in both the Development Economics Working Paper Series and a peer-reviewed journal[2] confirmed the potential impact of the IOM committee proposal. Immediate action is called for.

The Finance and Resources Working Group of the Roll Back Malaria Partnership initiated a work program in 2006 to translate the IOM proposal into reality. The work program is financed by a grant from the Bill and Melinda Gates Foundation, managed by the World Bank, and guided by the RBM Affordable Medicines Facility - malaria (AMFm) Task Force.[3] The Netherlands and Tanzania co-chair the task force. Dalberg Global Development Advisors facilitated the process of designing the co-payment system. Since January 2007, when a consultation was held among key stakeholders in Amster-

dam, this process has achieved several milestones and received strong support from endemic countries. In May 2007, the RBM Partnership Board endorsed the key design principles of the co-payment system. AMFm Task Force members have provided substantial input into this technical design and have agreed on the requirements for implementation.[4]

2. Objectives and design principles

The operational objectives of the AMFm are to increase the use of ACTs and other effective antimalarial combinations, and to eliminate the use of ineffective drugs and artemisinin monotherapies. The technical design is based on the objectives and design principles endorsed by the RBM Board in May 2007, with the recognition that that the design will evolve during implementation of the AMFm.

The AMFm will promote the use of eligible antimalarials and help to drive monotherapies and ineffective drugs from the market. Initially, the only class of eligible antimalarials will be ACTs, but this requirement is expected to change in the future as novel antimalarials emerge from ongoing research and development (R&D). It will achieve its objectives by:

- Reducing end-user prices to an affordable level through a properly supported global buyer co-payment of ex-manufacturer prices (CIF[5] basis), in line with the IOM recommendation by Professor Kenneth Arrow's committee;
- Introducing supporting interventions, including those that promote the proper use of effective antimalarials.

The objectives are reflected in the set of design principles adopted by the RBM Partnership Board. These principles state that:[6]

1. The success of the AMFm will be measured by the degree to which it lowers the consumer price of effective antimalarials to the affordable level of CQ and SP; increases access to these drugs in all market sectors (public and private)—particularly among the lower income quintiles; drives monotherapies, sub-standard drugs, and counterfeits out of the market; and maximizes the effective lifespan of effective antimalarials through responsible introduction and use.
2. The antimalarials eligible for co-payment will be available to first-line buyers in the public, private, and NGO sectors in all malaria-endemic countries at a price competitive with CQ and SP.
3. The AMFm will be managed by a small secretariat, embedded in an existing organization or organizations.

4. Product, manufacturer, and buyer eligibility will be guided by clear quality and price standards, with the concomitant aim of being as inclusive as possible.
5. In-country activities, essential to ensure the success of the AMFm, will be identified, facilitated, and encouraged.
6. The co-payment rollout under the AMFm will be informed and monitored on a learning-by-doing basis. The modalities will include concomitant operational research and monitoring and evaluation of retailer prices, access, drug quality, drug resistance, and market dynamics. These can be specific to, co-paid by, or facilitated by the AMFm.

The design of the AMFm, which follows from these objectives and design principles, emphasizes a responsible introduction of the co-payment system. Standards and requirements for manufacturers, buyers, and countries as well as supporting interventions, will result in a phase-in of demand over the first three to four years of AMFm operation.[7] During this initial period, extensive operational research and monitoring will facilitate learning and adjustments to the mechanism.

3. Mechanism

The AMFm will leverage the strengths of the public, NGO and private sectors to achieve the greatest impact possible on the effective treatment of malaria. It will combine the following elements: public sector capacity for governance, regulation, and quality safeguards; the reach and resourcefulness of NGOs and the private sector; the infrastructure for service delivery in the public, NGO and private sectors; and the collective capacity of all sectors to expand access, monitor progress, conduct operations research to fine-tune the design and implementation, and evaluate impact.

A core function of the AMFm, which serves both the public and private sectors, is the co-payment toward purchases of eligible antimalarials by first-line buyers at a level that allows these drugs to arrive in countries at a price comparable to CQ and SP. The AMFm will process co-payments upon the receipt of invoices from manufacturers in accordance with the AMFm standards and requirements. It is important to note that through the co-payment, the AMFm will reduce the prices that buyers pay for ACTs, but it will not subsidize manufacturers.

To be eligible for co-payment by the AMFm, an order must meet the following standards and requirements, which will be validated by the AMFm and its technical partners through regular audits to ensure compliance by manufacturers and buyers:

Antimalarials will be co-paid only if they belong to WHO-recommended drug classes.

WHO treatment guidelines, as the internationally recognized standard for malaria treatment, define the eligible classes of drugs. Currently, these encompass four classes of ACTs.[8] As WHO treatment guidelines evolve and new products

become available, eligible antimalarial drugs will be added to the portfolio of products offered by the facility, in line with WHO recommendations. The WHO, in collaboration with national authorities, will develop a list of approved antimalarials that is country specific, taking into consideration drug efficacy and parasite-resistance patterns. Studies should be conducted as part of country support packages to maintain up-to-date information on these patterns.

Eligible antimalarials will be co-paid only if they belong to the list of pharmaceutical preparations meeting approved quality standards.

A transparent and internationally recognized quality standard is required to ensure delivery of high-quality pharmaceutical preparations while encouraging competition among suppliers in all treatment classes. The final quality standard will be WHO pre-qualification or registration by a stringent regulatory authority.[9] Pharmaceutical preparations submitted for such approval, but not yet approved, may be eligible for a period of two years, provided that they meet interim criteria along the lines of those currently applied to the WHO/UNICEF tender list and the Global Fund (ci) compliance list. The RBM Board has asked the WHO to work with other relevant agencies to harmonize the criteria underlying these lists.[10] It is envisioned that these harmonized criteria will have been established prior to the AMFm launch and thus will apply to it.

Eligible antimalarials will be co-paid only if they are produced by manufacturers with whom the AMFm has a co-payment agreement.

Given the limited level of competition in the current market for eligible antimalarials, the setting of co-payments may initially be based on direct negotiations with manufacturers. It is expected that the manufacturer sales price (MSP) for private-sector buyers will come closer to the current price offered to public-sector buyers, with further reductions in MSPs within the ensuing three to five years. As markets become more competitive, alternative rule-based mechanisms with low transaction costs, such as competitive auctions, may be considered.

Eligible antimalarials will be co-paid only if their international freight and insurance are provided within the terms and price benchmarks defined by the AMFm.

The international distribution component (insurance and freight) might make up a significant share of AMFm co-payments. It is expected that the unit cost of international freight and insurance will be reduced over time as the volume of low-cost eligible antimalarials increases and distribution practices improve. The AMFm will benchmark insurance and freight prices and terms directly with international freight forwarding agents through a regular process of evaluation, taking into account normal market fluctuations. To ensure minimal disruption to existing distribution networks, manufacturers will use their own distribution arrangements (offering prices

on both FOB[11] and CIF bases). An order will be co-paid only if the CIF price offered for eligible antimalarials falls within the bounds benchmarked by the AMFm for a similar order.

Eligible antimalarials will be co-paid only if they have been ordered by eligible first-line buyers.

Eligibility criteria will ensure that only legal and legitimate first-line buyers of drugs have access to the AMFm and that national regulations are respected. Criteria will include:

- Registration with national authorities;
- Acceptance of terms of purchase and a record of acting in accordance with these terms;
- Confirmation that the destination country meets preparedness requirements.

Eligible antimalarials ordered by international procurement agents pooling orders on a voluntary basis will also be co-paid if those agents comply with similar eligibility criteria.

These criteria will include:

- A record of respecting national regulations;
- Acceptance of terms of purchase and a record of acting in accordance with these terms;
- Acceptance of accountability for ensuring that co-paid eligible antimalarials will be sold only to buyers who meet the eligibility criteria applied to first-line buyers.

Eligible antimalarials will be co-paid only if the ordered quantities are within upper limits.[12]

Upper limits will guard against unwarranted spikes in ordering volumes. These annual ceiling values will be set on a country-by-country basis and in consultation with national stakeholders. These thresholds may be modified by the AMFm in accordance with the availability of funding to meet co-payment commitments.

Eligible antimalarials will be co-paid only if they are destined for distribution in a country meeting a set of minimal preparedness requirements.

Country-preparedness requirements will help ensure responsible introduction of eligible antimalarials in a given country. These requirements will be both technically sound and minimally bureaucratic, to minimize delays in the rollout of the AMFm. It is expected that all malaria-endemic countries will meet these requirements within a short time.

Requirements will include:

- Acceptance of WHO treatment guidelines for antimalarials (or guidelines of equivalent standing developed by the country);

- Provision of a list of eligible first-line buyers;
- Commitment to implement supporting interventions, including a basic monitoring framework;
- Any additional preparedness requirements, to be defined, provided that the expected benefits from these requirements appear to exceed the risks of delays they may cause.

The mechanism to assess the minimal country-preparedness requirements will be based on mechanisms used by existing bodies and will not place an undue burden on countries. The mechanism could be structured as an expert panel that would carry out focused assessment missions to countries, taking into account recent assessments conducted by donor agencies and ensuring appropriate linkages to national plans.

4. In-country supporting interventions

The co-payment of eligible antimalarials meeting the above standards and requirements will ensure an affordable, high-quality drug supply at the point of arrival in endemic countries. Ensuring that the price reduction is transmitted to the patients at the point of purchase, and that patients have access to diagnosis (where appropriate) and effective malaria treatment, will require supporting interventions at the country level. A core package of in-country interventions will allow countries to manage the increased volume of eligible antimalarials, particularly in the private sector, and promote the desired outcome of improved access to affordable eligible antimalarials. The core package of supporting interventions will encompass six areas:

- National policy and regulatory preparedness;
- Wholesaler incentives and pricing/margin-control mechanisms;
- Public education and awareness campaigns;
- Provider training and supervision;
- National monitoring and quality preparedness (resistance monitoring, pharmacovigilance and quality surveillance);
- Monitoring and evaluation.

Countries will take the lead in developing rollout plans tailored to their specific situations and needs, drawing on but not limited to these interventions. Special attention will be paid to increasing broad access to ACTs, especially among those at highest risk. Although national mechanisms for planning and coordination of supporting interventions will be based on existing bodies, these can also include private-sector representation, as appropriate. International coordination mechanisms to identify funding gaps and to mobilize technical support at the global level will also be based on existing bodies. These mechanisms will reflect the results of needs assessments, including those conducted by the RBM Harmonization Working Group, and will avoid bureaucratic constraints. They will include but not necessarily be limited to those within the purview of RBM partners and structures

with emphasis on enabling rather than controlling innovations at the country level.

5. Governance and management

The governance and management of the AMFm will concentrate on how to meet the established objectives by making the best use of existing institutions. As a basic principle, no new bureaucracy will be created for the AMFm, whether it is embedded in one institution or among several institutions. The strategic intent is to ensure that it is fit for purpose, as lean as possible, and transparent.

The RBM Board will consider the parameters for the AMFm prior to its announcement, including:

- The technical design of the AMFm;
- Key performance indicators by which the success of the AMFm will be measured; and
- Terms of reference of the institution(s) that manages the AMFm.

Once these parameters have been agreed upon, two options are open to the RBM Board to support the governance and management of AMFm:

Option 1: Within agreed parameters, the RBM Partnership would grant the responsibility for governance and management to an institution to manage the AMFm. In matters of implementation, the institution would use its own judgment on approaches to implementation within the terms of agreement. The handover from RBM to the institution would be based on one of two arrangements:

A. A memorandum of understanding, in which the host would accept the design principles and conditionalities (as above) of the AMFm; it would agree not to substitute a pre-existing business model for the implementation of the AMFm; and it would commit itself to working collaboratively with RBM members and others in performing its duties to achieve success. A joint announcement of the AMFm would be made by RBM and the institution.
B. An informal commitment by the institution(s) that manages the AMFm to proceed with its implementation combined with a statement by the RBM Partnership, expressing commitment to the long-term success of AMFm co-payment and offering continuing technical support.

Option 2: The RBM Board would take a direct role in specific activities and in the ongoing governance of the AMFm. As the RBM Board is neither a legal nor operational entity, the AMFm would have to be administratively hosted in an existing institution.

In practice, it seems most appropriate to adopt Option 1, preferably with a memorandum of understanding that also commits the institution(s) managing the AMFm to provide the RBM Board with periodic updates, perhaps at each board meeting. In turn, the RBM Board will provide candid feedback and recommendations to ensure the success of the AMFm. The RBM Board will neither manage day-to-day activities nor insist on a particular approach to tasks such as procurement or payment.

The institution(s) managing the AMFm would be responsible for providing the following:

- *Governance and resource mobilization*: A legal entity within which the AMFm is governed and overseen. This entity would undertake basic strategic and general management-support functions, fiduciary responsibility, and functions to support resource mobilization.
- *AMFm mechanism*: A team that sets co-payments and terms for eligible antimalarials, processes co-payments to eligible first-line buyers on an on-demand basis, and arranges for regular audit of manufacturer and buyer compliance. This team would ensure that the AMFm responds quickly, effectively, and with low transaction costs as invoices are received, while enforcing eligibility and performance criteria.
- *Responsible introduction*: Coordination of a range of policy and supporting activities that facilitate the responsible introduction and operation of the facility. National partners will have the primary responsibility for executing in-country supporting interventions. It is expected that a portion of the cost of these interventions could be funded, or is already being funded, via existing financing mechanisms. The AMFm will be responsible for coordinating and identifying resources for these activities.

An estimated 15 to 22 staff will be required to carry out the core functions of the AMFm. It is expected that the institution(s) that manages the AMFm will draw on partners to execute functions that are outside of its own core expertise.

The implementation of the AMFm may be aided by an independent expert advisory group that meets annually (or as needed) to review the program's progress and to make recommendations as to any needed changes in the AMFm architecture or operating mechanism to better meet its objectives.[13]

6. Expected impact

If established as described here, the AMFm will contribute to the achievement of the 2015 RBM targets and to five of the eight Millennium Development Goals. AMFm has the potential, and will be measured against its ability, to reduce consumer prices of a treatment course of an effective coformulated antimalarial from the current level of USD 6–10 to a far lower level of USD 0.20–0.50 (which is competitive with current retail prices of CQ and SP) for the

majority of patients.[14] This drop in prices is expected to more than triple current ACT usage, increasing ACT demand from the current level of 110 million treatment courses per year to a projected 360 million. In doing so, the AMFm will shift most purchases away from ineffective medicines and greatly reduce the market for artemisinin monotherapies and other substandard and ineffective antimalarial drugs. The result will be an estimated 174,000 to 298,000 lives saved per year, with an estimated cost per disability-adjusted life year (DALY) of USD 33 to 56, making the AMFm a cost-effective intervention.

7. Financial requirements

The total resource requirements for the AMFm will be USD 1,400–1,944 million for the first five years.

- Co-payments to cover ACT treatment and distribution costs will require an estimated total financing of USD 1.2–1.6 billion over the first five years of AMFm operation;
- The core package of in-country supporting interventions will require financing of USD 230–330 million for the first five years of operation. This estimate principally covers financing for activities by endemic-country partners but also reflects the principle that the AMFm should not create unfunded mandates for international technical assistance;[15]
- The administrative management of the AMFm is estimated to cost USD 25–30 million over the first five years.

Based on the AMFm design principles and mechanism outlined above, RBM will now encourage donors who have shown interest in funding the facility to formalize the terms of their contribution. Institutions that are currently funding grants for the purchase of eligible antimalarials are similarly invited to work with countries and grantees to reallocate funds that may be freed up by the AMFm to the supporting interventions that are required to help countries absorb increased volumes of eligible antimalarials, particularly in the private sector.

8. Risk mitigation and implementation planning

At each stage of the supply chain and in the implementation of the co-payment, risks must be considered and mitigated. The technical design recommendations include measures to mitigate the following risks: (a) *Affordability:* Failure to sustain competition and price reductions in the global market for eligible antimalarials; cost of eligible antimalarials to patients does not decline as expected due to retailer absorption of co-payment; (b) *Availability:* Slow consumer, wholesaler or retailer uptake of eligible antimalarials; insufficient increase in scale of manufacturer production; long production cycle and restricted growing season of *Artemisia annua* making it diffi-

cult to respond rapidly to changes in product demand; (c) *Product arbitrage:* Failure to stop co-paid product from being transferred to markets/countries where the co-payment is not applied, thus allowing high profits to be collected by middlemen; (d) *Drug resistance:* Failure effectively to replace monotherapies and substandard drugs; (e) *Patient safety:* Unexpected rare adverse events; (f) *Product innovation:* Failure to maintain innovation in the market for antimalarial treatments; (g) *Funding:* Insufficient, or solely short-term funding available; (h) *Implementation:* Failure to implement supporting interventions; project-management mission creep.

A number of additional activities targeted at risk mitigation will be put in place by the time of the launch as part of the operational-planning process for the AMFm: (a) Communication and consultation with endemic-country governments and national implementation partners to facilitate preparation for responsible introduction of the AMFm; (b) Forecasting and specification of the burden on ACT manufacturers and other private-sector partners to allow preparation for scale-up in production and AMFm-specific requirements such as packaging; (c) Operational research to be launched in four to six countries; (d) Monitoring and evaluation in all countries, integrated into existing systems and surveys to the greatest extent possible. This operational-planning process will be conducted in liaison with relevant RBM working groups, including Harmonization, Procurement and Supply Chain Management, and the Monitoring and Evaluation Reference Group.

Overall, the biggest risk is that of inaction or delayed action. The status quo—that is, funding of eligible antimalarials through grant-based programs alone—virtually guarantees that only the relatively affluent and those with access to public facilities that have a sufficient supply of drugs will get timely, lifesaving treatment. The current system neglects a large part of the population who use the private sector, particularly the urban and rural poor, and those who use public-sector clinics and other facilities that have no effective antimalarials. This is the scenario to which the risks of implementing the AMFm must be compared.

Subject to RBM Partnership Board approval, the AMFm will be *announced* in November 2007, but it will take several months before it is *launched* and becomes operational. A launch is contingent upon (i) final agreement by a host institution to operate the AMFm as designed, and (ii) assurance of sufficient funds for an effective take-off of the AMFm. The launch will be without a priori exclusion of particular endemic countries or sectors. The application of standards and requirements for manufacturers, buyers, and countries as well as the implementation of supporting interventions, will result in a phase-in of demand over the first three to four years of operation. The development of these standards within the design of the AMFm is an inherent aspect of risk mitigation. Findings from the initial phase of scale-up will be collected, and appropriate adjustments to standards and requirements will be made. While the overall design is con-

sistent with the original IOM recommendations, the final recommendations have been developed on the basis of broad consultations among RBM stakeholders to facilitate the success of the AMFm.

9. A call to action

The AMFm will be a major innovation that challenges current practices and requires institutions to transcend their traditional comfort zones and business models. The consequences of inaction and further delays as measured in avoidable deaths and disabilities of malaria sufferers are clear, and so is the case for decisive and rapid action.

1. Introduction

Section summary

This section introduces the structure and contents of the AMFm technical design. It provides a description of the leadership roles played by the RBM Partnership, the AMFm Task Force of RBM, World Bank, Bill and Melinda Gates Foundation, and other key stakeholders through the design process. Finally, this section provides detailed information on endemic countries consulted in the technical design process.

1.1 Document structure and contents

In 2004, the Institute of Medicine called for a global co-payment toward purchases of artemisinin-combination therapies (ACTs) by first-line buyers directly from manufacturers. This call stemmed from the recommendations of the Institute of Medicine (IOM) committee chaired by Professor Kenneth Arrow, Nobel Laureate in economics, which were published in *Saving Lives, Buying Time: Economics of Malaria Drugs in an Age of Resistance* (2004).[16] The IOM committee advocated for "a sustained global subsidy of artemisinins coformulated with other antimalarial drugs"[17] in order to reduce malaria mortality ("saving lives") and delay resistance ("buying time").

This technical design document builds on the original IOM concept and sets out a design for the proposed Affordable Medicines Facility - malaria (AMFm) based upon a set of principles endorsed by the Roll Back Malaria Partnership (RBM) in 2007, and following extensive consultations and analysis. The technical design document outlines the impact of the proposed AMFm to address malaria treatment access, affordability, and resistance challenges, and the technical design, implementation, and funding requirements associated with its introduction.

Figure 1 provides an overview of the problem that the AMFm seeks to address, the proposed solution, and the key design and implementation questions addressed in this document.

This document places particular emphasis on the technical design and management of the AMFm. Much of the rationale and impact analysis presented is derived from the findings of the IOM report and from subsequent analysis conducted by experts in public health, economics, supply-chain management, public-private partnerships, communications, program management, and private-sector manufacturers, as well as from primary field research. Its structure is as follows:

Section 2: ACTs Are Unaffordable to the Poor and Could Become Ineffective Due to Resistance addresses the rationale for the AMFm and its dual role: to increase equitable access to effective treatments and to guard against the risk of parasite resistance to artemisinin-based therapies.

Figure 1: Overview of Document Content and Structure

Design and Implementation Questions

Problem
- High cost ACTs unaffordable for patients
- Threat of resistance due to increasing use of monotherapies

Solution
- Ex-Factory Subsidy to "Save Lives and Buy Time" (IOM Report, 2004)
- Increase access to ACTs
- Displace monotherapies that can promote resistance

- How will an ex-factory subsidy impact the ACT supply chain at each step– from production through to patient consumption?
  Section 4: Low-Cost Antimalarial Medicines and the ACT Supply Chain: Will the AMFm Work?

- What are the implications for subsidy mechanism design and the organizations/ partners that implement it?
  Section 5: AMFm Design
  Section 6: Governance and Management

- What functions, interventions and risk mitigation strategies are required for efficient and effective implementation?
  Section 7: Risk-Mitigation Strategy and Implementation Planning

- How much funding is required to support an efficient and effective mechanism?
  Section 8: Financial Requirements

Section 2: ACTs Are Unaffordable to the Poor and Could Become Ineffective Due to Resistance

Section 3: AMFm Overview, Objectives and Impact

Section 3: AMFm Overview, Objectives, and Impact describes the concept and objectives of the AMFm. It also demonstrates the facility's potential contribution to global development goals, health-financing mechanisms, and comprehensive malaria-control efforts. This section also outlines the expected impact of the proposed AMFm on the price of ACTs, including the expected increase in ACT penetration of the total antimalarial treatment market and expected impact on health outcomes in terms of lives saved.

Section 4: Low-Cost Antimalarial Medicines and the ACT Supply Chain: Will the AMFm Work? explores how a co-payment toward the purchase of ACTs as they leave the factory would impact the ACT supply chain at each step: from ACT production to product distribution and finally to patient consumption.

Section 5: AMFm Design proposes the functions, eligibility standards, and in-country supporting interventions that will be required for efficient and effective operation of the AMFm.

Section 6: Governance and Management defines the organizational and governance requirements of the AMFm.

Section 7: Risk-Mitigation Strategy and Implementation Planning addresses risks in implementation and describes the key implementation priorities and risk-mitigation strategies, such as operational research and monitoring and evaluation, that will be required to ensure an effective and responsible rollout of the AMFm.

Section 8: Financial Requirements focuses on the funding requirements for an efficient and effective AMFm. These are divided into three categories: ACT treatment and international distribution costs, targeted supporting-intervention costs, and management and organizational costs.

Section 9: Timeline and Next Steps provides a high-level timeline of activities following a November 2007 announcement of the AMFm.

Section 10: Conclusion addresses the opportunity that the AMFm presents to save lives and delay resistance.

1.2 Technical design development process and milestones

Following the publication of the Institute of Medicine report *Saving Lives, Buying Time* in 2004, the RBM Partnership decided to examine further the ACT subsidy concept. In September 2005, the World Bank, in its capacity as chair of the RBM Finance and Resource Working Group, led the preparation of a proposal for the design and operation of a mechanism to subsidize antimalarials. In 2006, the Bill and Melinda Gates Foundation provided a grant to finance the technical design process, which is managed by the World Bank.

The Expert Workshop and Consultative Forum on a High-Level Buyer Subsidy for Artemisinin-Based Combination Therapies (ACTs) took place in Amsterdam on 18–19 January 2007, and the malaria community endorsed the creation of an RBM Task Force to steer the project. The RBM Executive Committee approved the creation of the Task Force in February 2007.

Since the first meeting of the task force in March 2007, a significant work program has been under way to design the AMFm. In May 2007, the RBM Board agreed to the objectives and design principles for the AMFm and requested that the Task Force prepare a full technical design for consideration at its November meeting.

The sections of this document outline the core design features of the AMFm, summarize the discussions and decisions of the task force between March and November 2007, and summarize the supporting technical design work program. The contents, estimates, and recommendations contained in this document will be subject to refinement and revision during the implementation phase of the AMFm based on further studies and consultations. Further details on various aspects of the technical design are available in the Background Papers listed in the Appendix.

1.3 Endemic-country stakeholders engaged in the development process

The AMFm is designed to assist endemic countries in fighting malaria. From the earliest discussions within the RBM Finance and Resources Working Group, such as the meeting in Amsterdam in January 2007, ministers of health from Nigeria, Tanzania, Sudan, Cameroon, Cambodia, and other countries have led the call for sustainable, on-demand procurement of affordable and lifesaving antimalarial medicines. It remains a significant challenge for these countries to ensure access to medicines for all patients within the constraints and uncertainties of current grant- or credit-based financing of malaria control. The former health minister of Nigeria, Professor Eyitayo Lambo, said at that meeting: "The global subsidy initiative should have started yesterday. I am sure that even while we speak somebody in Nigeria is dying of the disease."[18]

Further consultations with endemic-country representatives have underlined the strong demand from endemic countries for this innovative financing initiative. At the African Union Health Ministers' Conference in Johannesburg in April 2007, Professor David Mwakyusa, Tanzanian minister of health and social welfare said: "Even though the price of new medicines has come down, it is still too expensive for Africa. We need to find sustainable solutions to raise new money to make medicines available and affordable to the poor through both the private and public sectors." Minister Mwakyusa in his capacity as co-chair of the RBM Task Force introduced

the initiative at the RBM board meeting in Geneva in May 2007, where the design principles were endorsed.

Consultations on implementation have been equally important. The AMFm technical design team held in-depth consultations with national stakeholders in Kenya, Burkina Faso, and Cameroon in April 2007. Stakeholders consulted include government officials, multinational institution staff, pharmacists, manufacturers/importers/ wholesalers, international donors, local and international NGOs with in-country presence, and academics. Consultations with endemic countries related to implementation issues were conducted at the Medicines for Malaria Venture (MMV) Access Symposium in Uganda in September/October 2007. Topics discussed included regulation, in particular over-the-counter (OTC) status of ACTs and retailers' quality; supply-chain interventions and provider incentives; social marketing and provider training; country-preparedness and buyer-eligibility criteria; and monitoring and evaluation. Country-preparedness criteria were discussed with regulatory authority representatives from Uganda, Nigeria, and Tanzania, and buyer-eligibility criteria were explored with first-line buyers from Nigeria, Uganda, and Zambia. Finally, national stakeholders from Cameroon, Ghana, and Tanzania were consulted in a meeting on country mechanisms for the AMFm that was held in Geneva at the end of October 2007. Further information on individual consultations can be found in the Appendix.

1.4 Audience for this document

This document is a submission to the RBM Partnership Board. It is of interest to malaria-endemic countries, potential donors to the AMFm, institutions contributing to the management of the AMFm, international and country partners, and other stakeholders in malaria control.

2. ACTs Are Unaffordable to the Poor and Could Become Ineffective Due to Resistance

Section summary

This section discusses the problem of poor access to effective, affordable, high-quality antimalarial medicines. It first addresses the global malaria burden and the need for action. Then, it addresses the challenge of treatment efficacy and the critical need to expand access and prevent resistance to effective medicines. Finally, it discusses the expected evolution of ACT production costs in the event that low-cost treatments were not introduced through the AMFm.

2.1 The global malaria burden calls for urgent action.

According to recent estimates, between 350 million and 500 million episodes of malaria are suffered every year,[19] resulting in between one and three million deaths[20]—deaths that could be averted through proper treatment. Malaria is a disease that disproportionately impacts poor populations, pregnant women, and young children: Children under the age of five account for 75% of malaria-related deaths.[21] The majority of this burden is shouldered by those living in Africa, where 90% of global malaria mortality occurs.[22]

Beyond the health toll that malaria inflicts on the poor, the economic impact of the disease is significant, given that disabilities suffered by survivors can last a lifetime. It is estimated that each year Africa loses USD 12 billion due to malaria in direct and indirect costs,[23] a burden that takes its greatest toll on the poorest populations. Malaria also constrains economic growth: one study found that "African nations with high levels of infestation had economic growth rates that were 1.3% lower than other countries from 1965–1990. Lifting the burden imposed by malaria would have significant effects on African economic growth."[24] While causal relationships are hard to establish at the macroeconomic level, the association is noteworthy.

A significant challenge to malaria-control efforts is resistance to antimalarial treatments. Resistance has emerged against the most commonly used first-line treatments: chloroquine (CQ), sulfadoxine–pyrimethamine (SP), amodiaquine (AQ), and mefloquine (MQ). Drug-resistant malaria today is spreading among malaria-endemic populations. In Malawi, the cumulative efficacy of SP is estimated to be a mere 21%.[25] In other words, four out of five SP treatment courses are failing the patient. Data on CQ resistance paints a similar picture: over a period of three years (from 2001 to 2003), failure rates in the CQ treatment of preschool children increased from 10% to 50% in one northwestern town in Burkina Faso.[26]

The failure of CQ, and the decreasing efficacy of SP, mean that in Africa, after a steady decrease in deaths from malaria, death rates began rising in the 1990s,[27] with evidence that the "spread of chloroquine resistance has had a dramatic impact on the level of malaria mortality in most epidemiological con-

texts in tropical Africa."[28] The Burden of Malaria in Africa research project suggests that, while overall malaria-specific mortality fell between 1960 and 1990, it then rose above pre-1960 levels from 1990 to 1995—even though total child mortality in Africa has been on a steady decline since 1960.[29] As a result, while malaria-related deaths represented 18% of total child mortality in Africa prior to 1960, and 12% from 1960 to 1990, they accounted for an unprecedented 30% of total child mortality during the 1990s.[30] Recent efforts in malaria control, including the increased supply of ACTs through the public sector, as well as the use of insecticide-treated mosquito nets, have reversed the upward trend in malaria mortality, but these gains are at risk today.[31]

Resistance-compromised antimalarials have also played a role in increasing morbidity as well as in rising treatment costs and other societal costs. A recent study conducted in East Africa suggests that increasing resistance causes secondary health problems, such as anemia, which render children's health more fragile.[32] Therapeutic failure against first-line drugs also causes an increase in overall treatment cost due to increased costs of diagnosis, additional drug purchases, and hospital admissions. For example, experiences in Central Africa show that the appearance of CQ resistance has led to an increase in hospital admissions and related costs.[33] This increase in consultations and diagnoses at the health-facility level, translates into an increased burden on health systems and into a loss of productive working days for adults and absence from school for children.[34]

Finally, the emergence of drug resistance has been shown to cause a negative change in epidemiology as it increases the proportion of the more deadly *P. falciparum* species relative to other species of malaria parasites. For example, since the advent of drug resistance in India, *P. falciparum* has accounted for more than 50% of all malaria attacks, instead of the previously reported 23%.[35]

The global health community is fighting malaria using an increasingly integrated approach that relies on preventive measures along with effective diagnostic tools and treatments. Despite these efforts, hundreds of millions of episodes of malaria occur each year, and effective and affordable treatments are often not available to patients.

2.2 Effective malaria treatments are essential to save lives, and their efficacy must be preserved.

The large-scale onset of resistance has led WHO to revise its malaria-treatment guidelines[36] so that they now recommend the use of artemisinin-based combination therapies (ACTs). WHO now urges all countries that face resistance to conventional monotherapies to rely instead on ACTs to treat *P. falciparum* malaria.

ACTs are recommended by WHO because they can save lives where conventional monotherapies are failing, and because they have the potential to forestall the development of parasite resistance to artemisinin and its partner drugs.[37] The latter is due to the independent mode of action of each constituent drug, which significantly reduces the probability of the development of a mutation that is simultaneously resistant to both drugs.[38]

Laxminarayan (2004) makes a cost-effectiveness argument in favor of a rapid introduction of ACTs to prevent the increase of monotherapy resistance based on artemisinin used alone (AMTs) or combination-therapy partner drugs used alone (e.g. SP, AQ).[39] He argues that the longer it takes to replace monotherapies with ACTs, the less effective they will be against emerging resistance, and the less cost effective it will be to introduce them.

2.3 Effective malaria treatments are too often inaccessible, and their efficacy is placed at risk by the inappropriate use of monotherapies.

ACTs have brought new hope that effective first-line malaria treatments can once again be made widely available and save lives. Since 2000, when WHO recommended the adoption of ACTs for more effective treatment of falciparum malaria, 68 malaria-endemic countries have officially adopted ACTs as their specified first- or second-line treatments.[41] As a result of

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What are ACTs? WHO Definition[40]

Over the past decade, a new group of antimalarials—artemisinin-derived compounds, especially artesunate, artemether and dihydroartemisinin—have been deployed on an increasingly large scale. These compounds produce a very rapid therapeutic response (reduction of the parasite biomass and resolution of symptoms), are active against multidrug-resistant P. falciparum, are well tolerated by the patients, and reduce gametocyte carriage (and thus the rate of malaria transmission). To date, no resistance to artemisinin or artemisinin derivatives has been reported, although some decrease in sensitivity *in vitro* has been detected in China and Vietnam. If used alone, the artemisinin compounds will cure falciparum malaria in seven days, but studies have shown that in combination with certain synthetic partner drugs they produce high cure rates in three days, and spur higher adherence to treatment by patients.

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both the WHO recommendation and a large influx of funding from the GFATM and the U.S. President's Malaria Initiative (PMI), there has been a significant scale-up in public-sector[42] purchase of ACTs, which reached roughly 90 million treatment courses[43] by 2006. Those treatments amounted approximately to a 60% share of the total public-sector antimalarial treatment market (estimated at 140 million treatments).[44]

While these figures represent substantial progress, there is evidence that scale-up remains slow.[45] Twenty-two countries that have adopted ACT policies are not yet deploying the treatment.[46] In addition, access is still insufficient in many of the other countries where public-sector delivery systems have been slow to increase ACT distribution.

In fact, poor access to ACTs remains an urgent challenge for the international community. ACTs are reaching only a fraction of the places where patients seek treatment, and lower-cost monotherapies are mostly purchased instead. The implication is clear: there is higher malaria mortality and morbidity where there is no access to effective treatment, and there is an increased threat of the emergence of resistance where AMTs are used. Figure 2 summarizes the challenge of ACT access and the impact it is having on those who suffer from malaria.

While pricing levels for ACTs differ significantly for public- and private-sector buyers, prices in both cases are considerably higher than those paid for CQ and SP. In the public sector, the manufacturer sales price (MSP), or the price paid by the first-line buyer to the manufacturer, has decreased significantly over the last four years. Today, manufacturers offer public buyers what is called "no-profit, no-loss" pricing.[47] This type of agreement was detailed in a memorandum of understanding between Novartis and WHO signed in 2001,[48] and accordingly, Novartis recently reduced the public-sector cost of an adult treatment course of the ACT Coartem® from USD 2.4 to 1.8.[49]

In the private sector, ACTs are sold as a premium product to a diverse base of wholesalers and distributors. For these premium branded ACTs, manufacturer sales prices are approximately two to three times higher than those paid by public-sector buyers, or USD 4–5.[50]

High MSPs lead to high retail prices for patients seeking access to ACTs through private-sector outlets. As shown in Figure 3, data from Uganda, Cameroon, Burkina Faso, Nigeria, and Kenya indicate that ACT prices in private retail outlets are between USD 6 and 10[51]—which is 10 to 40[52] times higher than the prices of more familiar, less effective treatments (CQ and SP) or of AMTs.

These retail pricing levels have created a major impediment to the private-sector's uptake of ACTs,[53] because 60 to 80% of patients in malaria-endemic areas rely on private providers

for treatment.[54] While public-sector penetration of ACTs has grown, in the private sector, ACTs comprise only a small fraction (2 to 5%) of antimalarial treatment sales today. Figure 4 provides an overview of antimalarial-treatment market volumes in 2006, outlining the estimated market share of ACTs and other malaria treatments in the public and private sectors.[55]

In addition to the difference in ACT penetration rates between sectors, lower priced artemisinin-based monotherapies (AMTs) have overtaken ACTs in private-sector market share, demonstrating that they pose an ongoing threat to the efficacy of artemisinin-based therapies.

Counterfeits, or drugs of inappropriate quality or dosage, although not represented in this chart, are also believed to occupy a growing share of the market.[56] Incentives to produce and sell these drugs are driven in large part by the current high market prices of ACTs. These drugs pose immediate risks to the life of the patient who takes them, as well as a long-term public health risk, as under-dosed formulations may also serve to increase the risk of resistance.

2.4 ACT prices are expected to remain unaffordable and to serve as a barrier to equitable access for the poorest patients.

Analysis of the three core components of current ACT costs (MSP, international distribution costs, and local wholesale and retail distribution costs) suggests that, in the absence of an intervention such as the AMFm, ACT retail prices in private outlets would decline only to an estimated USD 2–4 by 2013.[57]
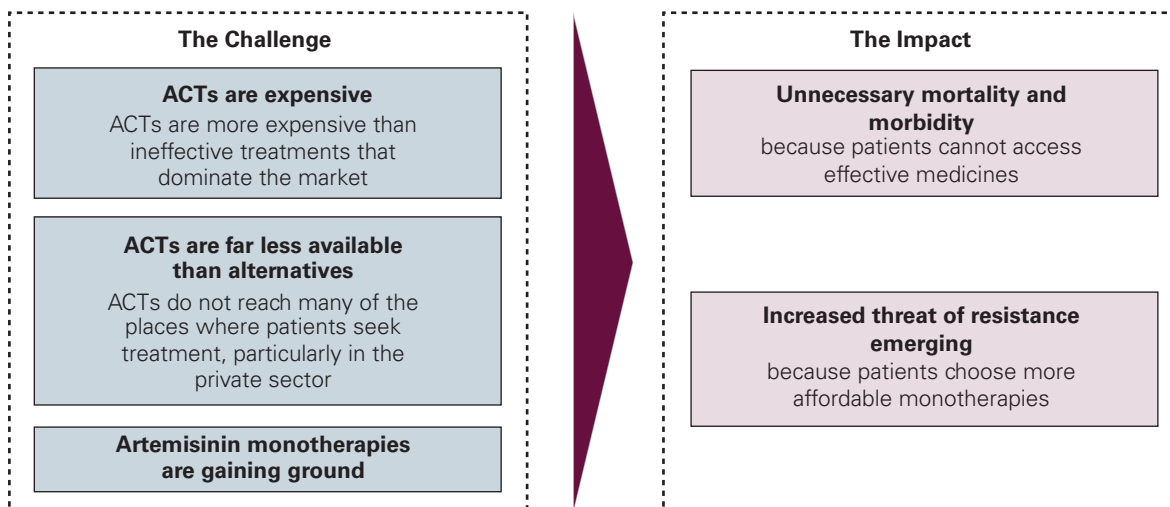
This expected decline in ACT retail prices is driven by the characteristics of the manufacturer, international distribution, and retail supply chain. MSPs of ACTs are expected to decline as cultivation of *Artemisia annua* plants and extraction capacity expands, as generic manufacturers become prequalified, and as new technologies for API production are developed. As demand for ACTs increases, international distribution costs are also expected to decline. Yet ACT retail prices are not expected to decline "naturally" below USD 2–4, therefore remaining much higher than current retail prices of CQ, which are USD 0.2–0.4. There are several reasons for this:

Note on ACT prices discussed in this document

ACT prices vary across two dimensions: treatment dosage (e.g. pediatric vs. adult) and treatment combination (e.g. AR+LU vs. AS+SP). The treatment dosages for ACTs are differentiated by the consumer's weight and are usually split into three or four classes.[58] The dosages usually differ with respect to the number of pills per treatment. For example, the adult treatment dose of Coartem® consists of 24 pills, whereas the infant dose consists of merely 6 pills. Treatment combinations differ through the use of different partner drugs paired with the artemisinin component in the combination therapy. Currently, WHO recognizes four suitable partner drugs, namely lumefantrine (LU), sulfadoxine-pyrimethamine (SP), mefloquine (MQ), and amodiaquine (AQ).[59]

Throughout this document, reference is made to prices for full ACT treatment courses at the manufacturer and retail levels. It is important to note that **two simplifications have been made unless otherwise noted:** 1) Prices refer to the adult treatment dosage, and 2) prices are a weighted average across combination treatment categories (e.g. AR+LU, AS+SP, AS+MQ, and AS+AQ). This simplification provides a single set of reference prices throughout the document, rather than a more complicated matrix of pricing. However, it should be noted that all financial modeling has incorporated the full range of treatment dosages and combinations.

Figure 2: The ACT Access Challenge and its Impact

The Challenge

ACTs are expensive
ACTs are more expensive than ineffective treatments that dominate the market

ACTs are far less available than alternatives
ACTs do not reach many of the places where patients seek treatment, particularly in the private sector

Artemisinin monotherapies are gaining ground

The Impact

Unnecessary mortality and morbidity
because patients cannot access effective medicines

Increased threat of resistance emerging
because patients choose more affordable monotherapies

- The artemisinin component is produced from a natural (herbal) ingredient, rather than a chemically synthesized one (like CQ), which increases the cost;
- The inclusion of a partner drug, especially a more expensive one like lumefantrine or mefloquine, further increases the cost of manufacturing ACTs;
- The limited scale of local production of ACTs (versus CQ) incurs relatively higher international distribution costs;
- Distribution costs for internationally shipped ACTs are high due to their short shelf-life, relatively costly packaging (blister rather than bulk), high insurance fees, and the significant percentage shipped by air rather than by sea.

ACTs are currently the only effective antimalarial drugs. The AMFm has been designed to encourage competition among ACT manufacturers, but also innovation among manufacturers and other groups to develop new antimalarials, which may or may not be based on artemisinin derivatives. The pipeline of new antimalarial medicines from the Medicines for Malaria Venture,[60] the Drugs for Neglected Diseases Initiative (DNDi),[61] and the Institute for OneWorld Health are encouraging, and it is expected that the AMFm will, over time, also subsidize other effective antimalarials.

Figure 4: Estimated Antimalarial Treatment Volumes, 2006 (millions)

2006 Antimalarial treatment volumes (Million)
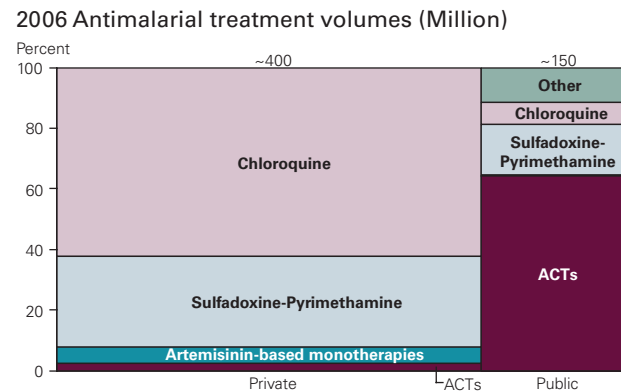
Note: Other category includes MQ, AQ, and others. ACT data based on WHO estimates and manufacturer interviews.

Source: Biosynthetic Artemisinin Roll-Out Strategy, BCG/Institute for OneWorld Health, WHO, Dalberg.

Without the AMFm, ACTs and other new antimalarials will remain out of reach of the poor in malaria-endemic countries.

Figure 3: Indicative Prices of Malaria Treatments to Patients (Private-Sector Retailers)

Average Prices (USD)

Note: Ranges indicate variance across countries and products excluding outliers, N (observations): (ACT, 222); (AMT, 227); (CQ, 37); (SP, 118).

Source: Dalberg field research (Burkina Faso, Cameroon, Kenya, Uganda). Observations by World Bank and Research International (Nigeria). SP and CQ data complemented with HAI and IOM observations.

3. Affordable Medicines Facility – malaria: Overview, Objectives, and Impact

Section summary

Based on the affordability, access, and resistance challenges highlighted in the previous section, Section 3 describes the history and RBM-endorsed design principles that guided the technical design of the AMFm. It then lays out the AMFm concept and the goals and objectives that the AMFm seeks to achieve—namely to save lives and delay resistance to the 'A' in ACT.

This section presents an analysis of the expected impact of the AMFm, based on two goals and three objectives. It discusses the numbers of lives saved and the potential effects of the AMFm on delaying resistance, on affordability and availability of ACTs, and finally on crowding-out monotherapies from the marketplace.

Finally, the section outlines the contribution of the AMFm to strengthening health systems and to supporting other malaria control efforts.

3.1 RBM–endorsed design principles for the AMFm

In May 2007, the RBM Partnership endorsed a set of objectives and design principles for a facility to improve access to ACTs and delay resistance. The technical design of the proposed AMFm presented here is consistent with the principles summarized in Figure 5.

3.2 AMFm Concept

Based on the concept developed by the IOM committee and on the principles adopted by the RBM Partnership, the primary function of the proposed AMFm is to lower the manufacturer sales price (MSP) paid by first-line buyers for ACT treatments as they leave the factory (ex-factory). Specifically, the AMFm mechanism will lower the ACT price paid by first-line buyers (such as private national wholesalers or ministries of health) so that it is comparable to the price paid for less effective alternatives, such as chloroquine (CQ), sulfadoxine–pyrimethamine (SP), or artemisinin-based monotherapies (AMTs). In turn, the lower purchase prices will allow first-line buyers to sell lower priced ACTs to private distributors, retailers, and public-sector hospitals and clinics. This technical design document also recommends a set of eligibility criteria and in-country interventions aimed at ensuring that the co-payment of first-line buyer ACT purchases ultimately results in both public- and private-sector distribution of quality ACTs to patients at significantly reduced prices.

The process of co-paying treatment purchases will be simple. First-line buyers will place orders for ACTs with manufacturers; eligibility for purchase will then be established; orders will be fulfilled by manufacturers; and (upon receipt of product by the buyer) co-payment will be sent to the manufacturers by both buyers and the AMFm.

Figure 6 provides an overview of this process, including the flow of medicines, money, and information among the various stakeholders involved.

The co-payment process is further described in Section 5.1 and detailed in Figure 19.

Figure 5: RBM Partnership Board Objectives and Principles for AMFm Design (Summary Form)

Objective: Increase Overall Use of ACTs[62]

The AMFm will promote the use of ACTs and drive monotherapies and ineffective drugs from the market by:
- Reducing end-user prices to an affordable level through a properly supported global co-payment toward manufacturer sales prices (MSPs), on a CIF basis, in line with IOM recommendations;
- Introducing in-country supporting interventions, including support for proper use of ACTs.

Principle 1:	The success of the AMFm should be measured to the extent that it lowers the consumer price of ACTs, increases access to ACTs in all market sectors (public and private), drives monotherapies out of the market, and ensures that the effective lifespan of ACTs is maximized through responsible introduction and use;
Principle 2:	The low-cost ACTs should be available to first-line buyers in the public, private, and NGO sectors in all malaria-endemic countries at a price competitive with CQ and SP;
Principle 3:	The AMFm should be managed by a small secretariat, based in an existing organization or organizations;
Principle 4:	Product, supplier, and buyer eligibility should be guided by clear quality and price standards;
Principle 5:	In-country activities will be important to ensure the success of the AMFm;
Principle 6:	The AMFm rollout should be informed and monitored on a learning-by-doing basis by concomitant AMFm-specific and AMFm co-paid operational research and monitoring and evaluation of retailer prices, access, drug quality, drug resistance, and market dynamics.

Figure 6: Diagram of AMFm Mechanism and Medicine Flows

Multiple eligible ACT Manufacturers

Co-payment

AMFm

Eligible first line buyers

Private Buyers (e.g. National Wholesalers)

NGO Buyers

Public Buyers (e.g. Ministry of Health)

Distributors

Distributors

Central medical stores, for example

Retailers, private clinics and public providers

Medicines
Money
Information

Patients
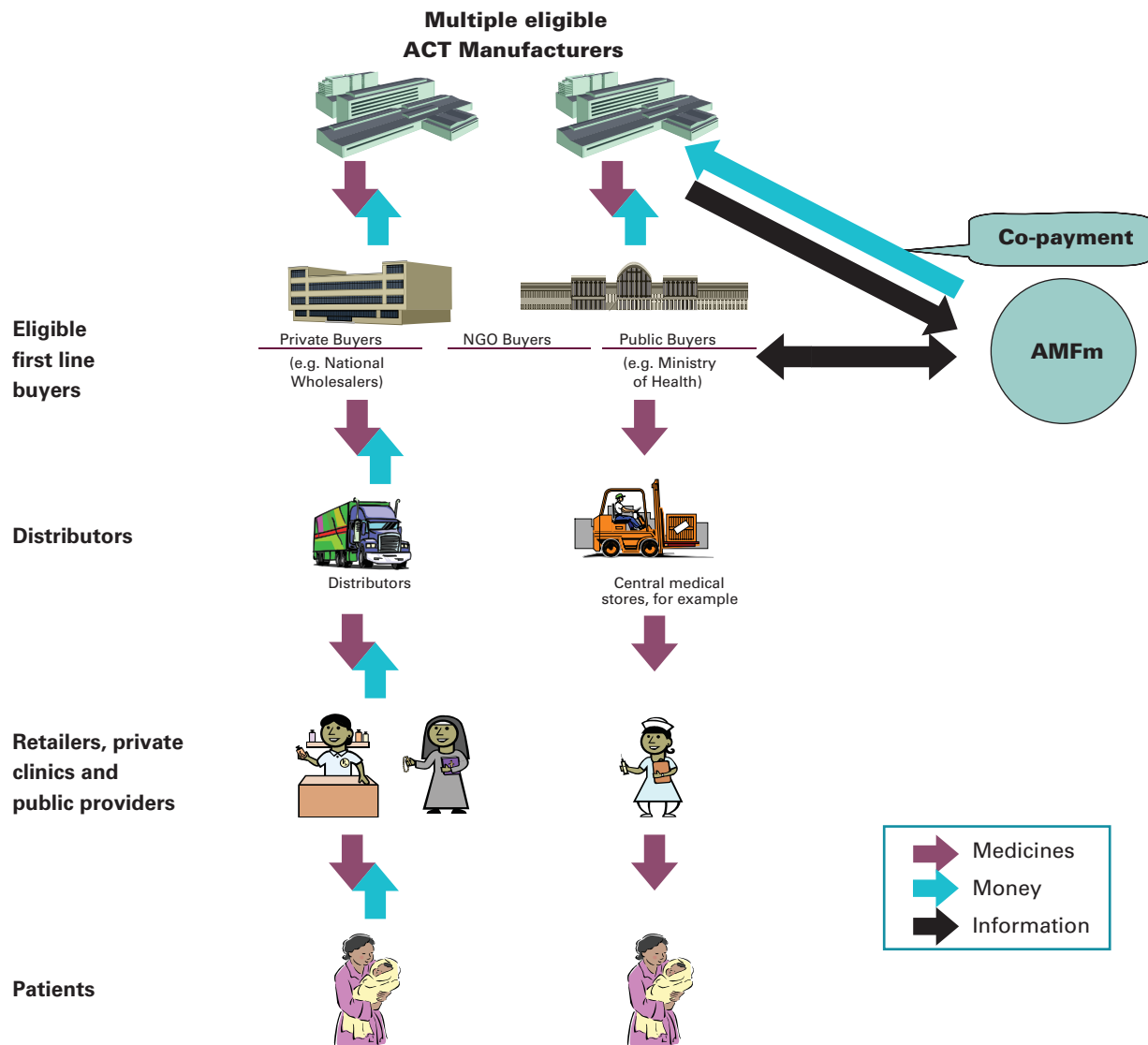
3.3 Goals, Objectives and Impact

3.3.1 Objectives and Goals

The ultimate goal of the AMFm is to work within the existing health system—including the public, NGO, and private channels—to reduce malaria-related mortality and to delay resistance to effective treatment. Within these parameters, the AMFm has three measurable objectives to achieve 1) increasing affordability, 2) increasing availability, and 3) crowding monotherapies out of the marketplace. These goals and objectives are described as follows:

Goal 1 – Reduce Mortality: The AMFm, by achieving its objectives, will contribute to a reduction in malaria mortality.

Goal 2 - Delay Resistance: The AMFm, by achieving its objectives, will decrease the likelihood that resistance to effective treatment will emerge.

Objective 1 – Increase Affordability: The AMFm offers low-cost ACTs to first-line buyers, which must translate into reductions of final purchase prices paid by patients.

Objective 2 - Increase Availability: The AMFm must contribute to making ACTs widely available through public, private, and NGO channels.

Objective 3 – Crowd out Monotherapies: ACTs must contribute to displacing monotherapies that increase the likelihood of resistance developing.

The success of the AMFm will be measured according to these three objectives. It is important to note, however, that progress toward these outcomes may be attributed to a variety of factors, only one of which is the introduction of low-cost ACTs via the AMFm. Further detail on measuring the performance of the AMFm is available in Background Paper 3.

3.3.2 Expected Impact

Figure 7 summarizes the expected impact of the AMFm based on its objectives and goals:

Goal 1 - Reduce Mortality: Fully funding the AMFm will save 174,000 to 298,000 lives per year and is a cost-effective intervention.

It is expected that a fully funded AMFm—requiring between USD 1,400 and 1,944 million over the course of five years— would dramatically expand the market penetration of ACTs, from 20% to 65% of total antimalarial treatment courses. This growth of ACT usage would save an estimated 174,000 to 298,000 lives per year.[63] From a cost-effectiveness perspective, this translates into a cost per life saved of USD 980 to 1,700 and a cost per disability-adjusted life year (DALY) of USD 33 to 56.[64] This analysis is based on modeling that is further detailed in Background Paper 8.[65]

The World Bank considers any health intervention with a cost-per-DALY-averted of less than USD 150 to be "cost-effective,"[66] and the AMFm would thus rank as a cost-effective health intervention, as illustrated by Figure 8.[67]

Further, it should be noted that these cost-effectiveness estimates for the AMFm are conservative in two respects: 1) they do not include the benefits of reduced morbidity (only mortality), and 2) they reflect global impact; estimates for sub-Saharan Africa alone would be even more cost-effective, likely meeting the USD 25/DALY benchmark for "highly cost-effective" interventions according to the World Bank and WHO.[68] In terms of the ability to increase in scale quickly, the AMFm is also expected to rank as "highly cost-effective." In achieving these results, the AMFm would contribute to the achievement of five of the eight Millennium Development Goals[69] and the 2015 RBM targets.[70]

Goal 2 - Delay Resistance: Fully funding the AMFm will decrease the likelihood that

resistance to effective treatment will emerge.

Analysis presented in Laxminarayan et al. (2006) shows how a global AMFm could delay the emergence of resistance.[71] Using a mathematical model of malaria transmission, resistance, immunity, and economics, they demonstrate that a global subsidy for ACTs would delay the development of resistance to artemisinin and its partner drugs and that "even a partial subsidy could delay the emergence of resistance."[72] The authors urge that the time to act is now, as a "delay (even by two years) in implementing a subsidy for ACTs could facilitate the emergence of resistance and lower the economic value of ACTs."[73]

Objective 1 - Increase Affordability: The AMFm will lower retail prices of ACTs to USD 0.2–0.5 for the majority of patients.
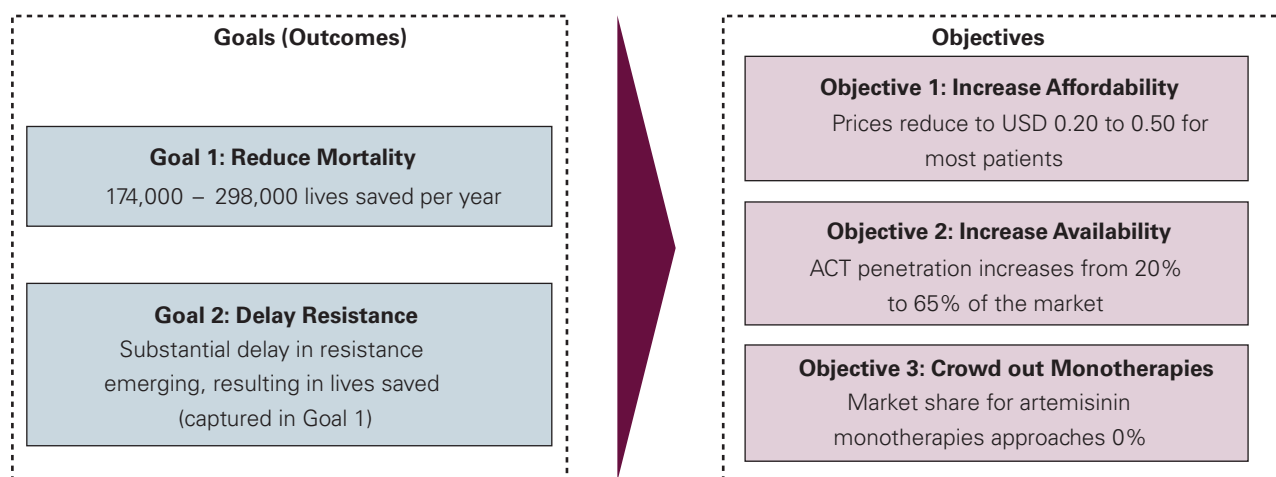
The AMFm would make ACTs more affordable by offering low-cost ACTs to first-line buyers in private and public channels alike. An analysis of conditions in several markets indicates that the AMFm has the potential, and will be measured against its ability, to reduce consumer prices of a treatment course of an effective coformulated antimalarial from the current level of USD 6–10 to a far lower level of USD 0.2–0.5 (which is competitive with current retail prices of CQ and SP) for the majority of patients, depending on market conditions, as illustrated in Figure 9.[74] The ability of the AMFm to achieve and sustain low prices for patients will be a critical measure of its success and a focus of additional pre- and post-launch research and analysis.

Background Paper 7 summarizes the country field visits that were conducted to collect pricing data, and Background Paper 8 outlines the methodology used to estimate post-AMFm retailer margins.[75]

Objective 2 - Increase availability: The AMFm will increase ACT penetration to more than 65% of the antimalarial market.

The AMFm would make ACTs widely available and significantly increase their penetration into both the public and

Figure 7: Summary of Expected Impact of the AMFm

Goals (Outcomes)

Goal 1: Reduce Mortality
174,000 – 298,000 lives saved per year

Goal 2: Delay Resistance
Substantial delay in resistance emerging, resulting in lives saved (captured in Goal 1)

Objectives

Objective 1: Increase Affordability
Prices reduce to USD 0.20 to 0.50 for most patients

Objective 2: Increase Availability
ACT penetration increases from 20% to 65% of the market

Objective 3: Crowd out Monotherapies
Market share for artemisinin monotherapies approaches 0%

Figure 8: Cost-Effectiveness Ratio of Various Health Interventions (USD per DALY averted)

Comparative cost-effectiveness: Interventions for high-burden diseases in SubSaharan Africa
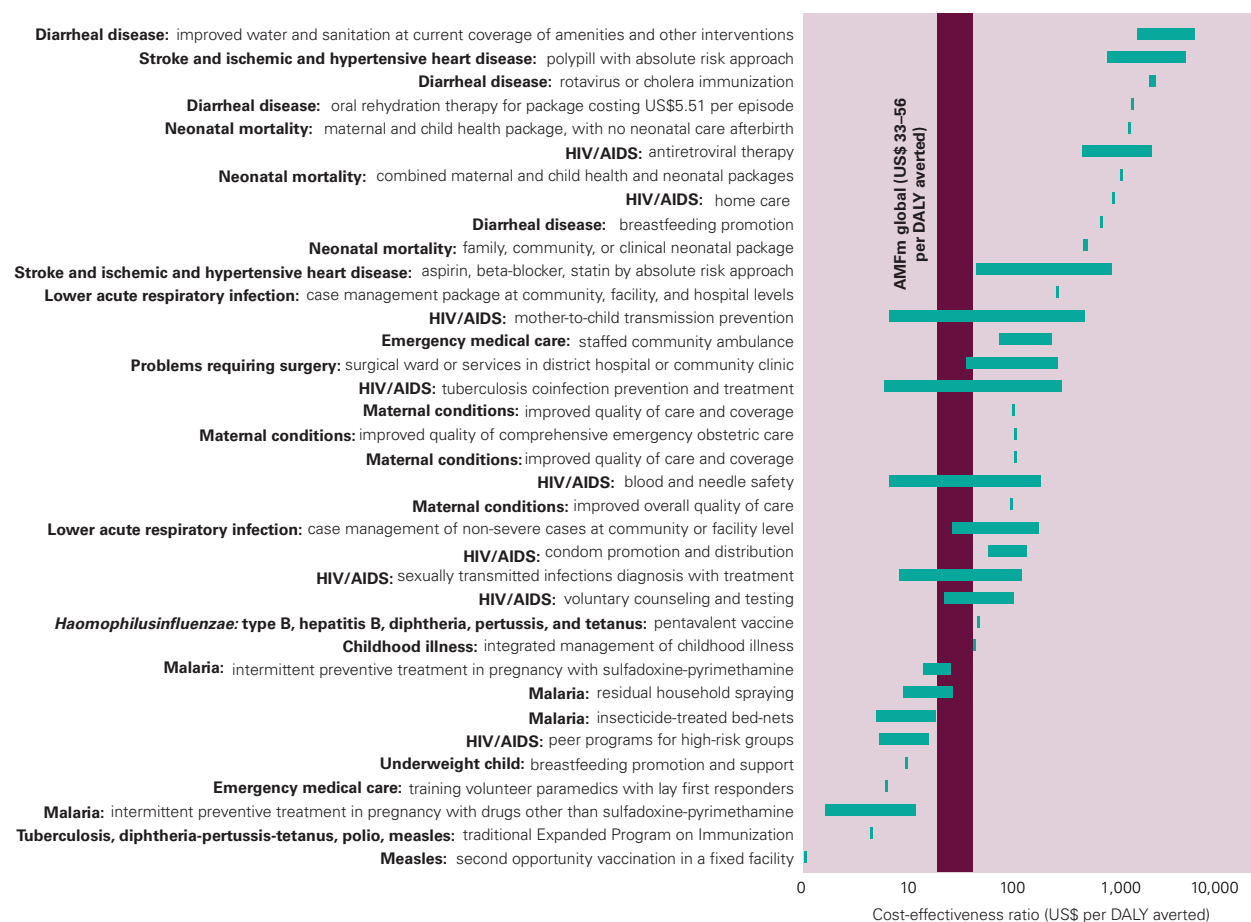
Source: Disease Control Priorities Project, 2006, Chapter 2, Ramanan Laxminarayan, Jeffrey Chow, and Sonbol A. Shahid-Salles.

private sectors. Specifically, the AMFm is expected to expand the penetration of ACTs in the public sector from 60% today to 90%. It is also expected to expand coverage of ACTs in the private sector from 5% today to 60%, as predicted by uptake modeling based on price elasticity and demand curve estimates. This increase, illustrated in Figure 11, will correspond to a penetration of more than 65% among providers of antimalarial medicines. The penetration of ACTs in the private and public sectors is outlined in Figure 10.

For further analysis of the projected impact of the AMFm on the global supply of ACTs, local markets, and ACT demand volumes, refer to Background Paper 8.

Objective 3 - Crowd out monotherapies: The AMFm will displace monotherapies.

The availability of low-cost ACTs combined with supporting interventions across the public and private sectors is expected to rapidly shift consumer purchasing patterns toward ACTs, while displacing monotherapies that are ineffective and increase the likelihood of resistance. Artemisinin-based monotherapies (AMTs), with retail prices averaging

USD 6 in the private sector, are likely to be more quickly displaced by low-cost ACTs, thereby delaying the onset of resistance to the active ingredient artemisinin. This shift will occur even if prices to patients are significantly higher than projected in this document. As the price of ACTs will soon become comparable to that of less-effective treatments such as CQ, SP, or AQ monotherapies, they too will soon be supplanted by ACTs.

In addition to displacing AMTs and other monotherapies, the availability of lower-priced ACTs resulting from the AMFm will make the ACT counterfeit market less attractive. As noted in a 2006 report documenting the deaths resulting from fake artemisinin derivatives in Southeast Asia, it is believed that there is high risk for counterfeit ACTs to proliferate in Africa.[76] The same report suggests that a subsidy for ACTs in the private sector would best tackle counterfeit manufacturing of AMTs because it would leave thinner profit margins to counterfeiters. An estimate of the future ratio of ACTs to other antimalarials under the AMFm is outlined in Figure 11. Background Paper 8 contains the methodology and calculation behind these estimates.

3.4 AMFm Contribution to Strengthening Health Systems

Malaria places a very significant burden on health systems in high-endemic countries. In countries such as Nigeria, Benin, and Zambia, malaria-related illness accounts for as much as 40% of public health spending and up to 50% of outpatient visits.[77] This burden affects health staff workload and leads to significant expenditures for essential commodities such as medicines. By lowering the financial burden of malaria medicines, the AMFm would allow endemic-country governments to increase the availability of effective medicines throughout the health system. Improved productivity of malaria treatment in areas where effective medicines are currently not available will free up health-system resources for both malaria and other illnesses. These positive effects are expected to impact public and nonprofit, as well as private health-service providers.

3.5 Role of the AMFm in global health financing and comprehensive malaria-control efforts

3.5.1 The AMFm will complement existing donor-funded malaria programs.

Grants from the GFATM and bilateral donor programs including PMI, as well as funding from endemic-country governments, multilateral institutions, and foundations, have been crucial in enabling the switch to ACTs in the public sector. The proposed introduction of subsidized antimalarials does not seek to displace the achievements made in scaling up public-sector delivery of ACTs, but rather to complement and expand those accomplishments to the private sector. One important design feature of the AMFm is that it will also provide a more streamlined approach for the public purchasing of effective antimalarials than do current grant-based mechanisms.

The AMFm will work with existing malaria-control programs and funding mechanisms to avoid duplication of partner efforts. The proposed AMFm is a natural complement to the efforts of organizations such as GFATM, the Booster Program, and PMI.

It is increasingly recognized that improving access to affordable, effective ACT treatments is part of an integrated malaria-control program. Recent experiences in Vietnam have revealed the effectiveness of integrated malaria control, reducing malaria deaths from about 4,500 per year to fewer than about 100 over the period of a decade.[78] The South African province of Kwazulu Natal witnessed similar success resulting from an integrated approach to malaria control.[79] Given the wide range of interventions required for effective malaria control, the AMFm is expected to increase national and partner capacity to execute the required suite of critical malaria-control interventions. The AMFm will assist by lowering the manufacturer sales price of ACTs for all first-line buyers and thereby free existing donor funds to support programs and interventions on a large scale.

As laid out in the RBM Global Strategic Plan 2005–2015, an integrated malaria-control program needs to combine prevention, accurate diagnosis, and treatment while maintaining a long-term strategy for pharmaceutical innovation.[80] Home-based management of malaria (HMM) is one strategy being employed to increase coverage and enable the scale-up and
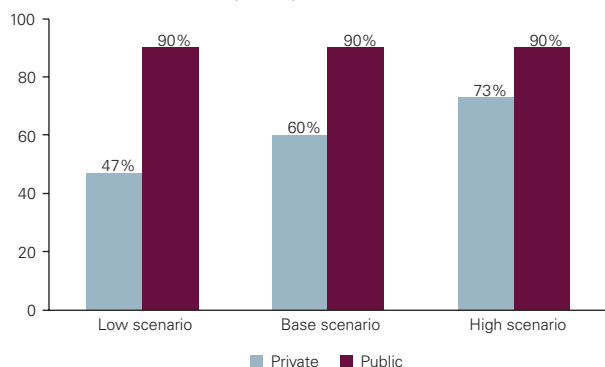
Figure 9: Expected impact of AMFm on ACT Treatment Prices along the Supply Chain
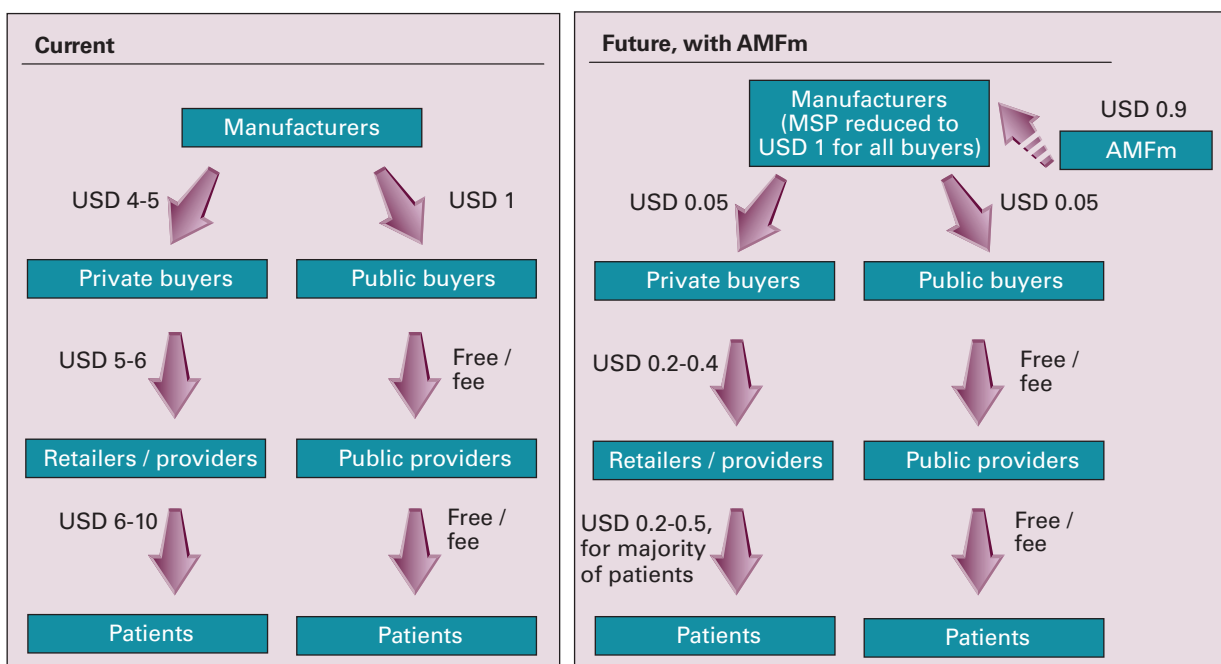
Figure 10: Estimates of Post-AMFm ACT Penetration in Public and Private Sectors (Years 1–5)

Estimated uptake by sector and by scenario

ACT treatment share of overall antimalarial treatment volumes (Percent)

Source: Modeling by Ramanan Laxminarayan, Dalberg analysis.

sustainability of malaria-control interventions. The Abuja declaration made by African heads of state in April 2000 called for HMM as well as integrated partnership approaches to malaria control that more broadly bridge the gap between public and private health sectors to ensure that diagnosis and treatment of malaria are made available as widely as possible.[81] More recently, the WHO declared that HMM "has become a cornerstone of malaria case management and, more generally, of malaria control in sub-Saharan Africa. Many countries have incorporated HMM in their strategic plans to roll back malaria, or in their successful applications to GFATM, and are now moving to large-scale implementation of HMM."[82]

Figure 11: Estimates of Increases in ACT Treatment Coverage Post AMFm Introduction

Treatment coverage (doses)

Percent
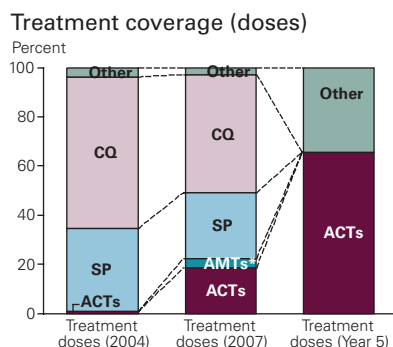
* Artemisinin monotherapies.

Note: Split between CQ/SP in 2004 assumed to be equal to today. Increase in ACT usage to 360 million doses (from 100 million today) assumed, with 235million in the private sector (55% penetration) and 125 million in the public sector (90%).

Source: Dalberg analysis, BCG/Institute for One World Health Institute.

3.5.2 The AMFm will contribute to Millennium Development Goals and RBM targets for 2015.

In achieving its two outcome goals, the AMFm will contribute to five of the eight Millennium Development Goals (MDGs):[83]

Direct Impact

- **MDG 4: Reduce child mortality.** MDG 4 refers specifically to reducing by two-thirds the mortality rate among children under 5. These children are most at risk from malaria, accounting for 75% of malaria mortality.[84]

- **MDG 6: Combat HIV/AIDS, malaria, and other diseases.** MDG 6 explicitly aims to "halt and begin to reverse the incidence of malaria."[85] As highlighted in a recent RBM press release, malaria control will reduce malaria mortality and morbidity not only due to malaria but also due to opportunistic infections.[86]

- **MDG 8: Develop a global partnership for development.** Underlying the AMFm design is a public-private partnership mechanism that can be extended to other disease areas.

Indirect Impact

- **MDG 1: Eradicate extreme poverty and hunger.** Malaria imposes a significant financial burden on the poorest households as well as on public-health systems. In some countries with a heavy malaria burden, RBM estimates that the disease can consume up to 25% of household incomes and 40% of public-health expenditure.[87]

- **MDG 2: Achieve universal primary education.** Malaria is a leading cause of illness in children and teachers, and can cause lasting neurological and cognitive damage in children. As such, malaria affects attendance and learning and impedes efforts to achieve universal primary education.

The AMFm will also directly contribute to the RBM targets for 2015, which it lays out in its Global Strategic Plan 2005–2015, namely:

- Reduce malaria morbidity and mortality by 75% compared to 2005, not only by national aggregate but particularly among the poorest groups across all affected countries;

- Achieve malaria-related MDGs, not only by national aggregate but also among the poorest groups, across all affected countries;

- Ensure universal and equitable coverage with effective interventions.[88]

4. Low-Cost Antimalarial Medicines and the ACT Supply Chain: Will the AMFm Work?

Section summary

This section summarizes the findings of an in-depth analysis of ACT market dynamics and cost drivers along each stage of the ACT supply chain. Based on an analysis of the AMFm's potential impact on the ACT supply chain and cost structure, this section illustrates that, through the combination of sound design and in-country interventions, the AMFm can achieve its goal of increasing the availability and affordability of effective antimalarial treatments to patients at the point of purchase. Furthermore, the AMFm can also improve the ability of public-sector buyers to access ACTs sustainably.

Finally, this section includes findings from field research in Senegal on the GFATM-supported government sell-through scheme, which demonstrates that low-cost ACTs can successfully be made available through the private and public sectors.

While the first-line buyer co-payment mechanism described in the previous section is the core feature of the AMFm, it will not alone guarantee the successful achievement of the AMFm's objectives. Success will require reduced treatment costs not only to first-line buyers, but along each step of the ACT supply chain. This price reduction will then render ACTs affordable to patients and encourage their purchase instead of readily available alternatives, whether CQ, SP, or AMTs.

This section presents four key opportunities along the ACT supply chain to ensure ACTs are delivered at an affordable price:

1. **Negotiate lower manufacturer sales price (MSP):** Today, there is a significant opportunity to negotiate lower prices for ACTs. As discussed previously, the private sector pays USD 4–5 per treatment, while the public sector pays USD 1–2. The AMFm could immediately reduce, and potentially eliminate, this differential by negotiating with manufacturers based on the substantial sales volumes that it will engender. Current prevailing interim quality standards [per the WHO/UNICEF tender list and the GFATM (ci) compliance list] are expected to yield a sufficient supply of antimalarials to respond to the increased demand created by the AMFm.
2. **Include international distribution in the co-payment:** International distribution costs contribute significantly to the prohibitively high retail price of ACTs. International distribution costs also must be incorporated into the buyer co-payment supported by the AMFm.
3. **Provide incentives for wholesalers:** The AMFm will be able to provide volume incentives to wholesalers to carry ACTs with measures that minimize the risk of price gouging.
4. **Suggest recommended retail prices and educate providers and consumers:** Either recommended or maximum retail pricing can serve as an incentive for retailers to stock ACTs while preventing price gouging. Patient and provider training, as well as social marketing, can create demand for ACTs at the retail level.

The AMFm design has taken into account the opportunities laid out above, and, with the inclusion of appropriate eligibility criteria and interventions in the supply chain, it is expected that the retail prices of ACTs can be reduced from USD 6–10 today to USD 0.2–0.5 for the majority of patients.

4.1 AMFm impact on costs and prices along the ACT supply chain

Each ACT treatment delivered to patients in malaria-endemic countries must journey through six supply-chain stages, accumulating costs that build to the ultimate patient purchase price. These stages are identified in Figure 12.
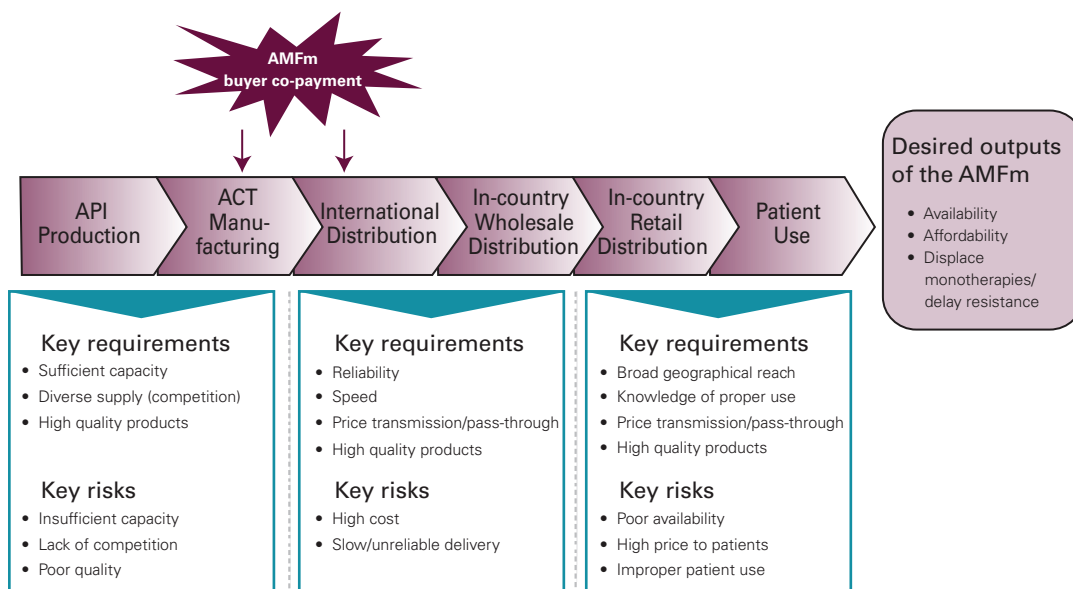
4.1.1 ACT manufacturer sales prices have reduced slightly, but require negotiations by the AMFm to reduce them to an affordable level.

The current average manufacturing cost of an adult course of ACT treatment ranges from USD 0.95 (for AS+AQ) to USD 1.83 (for AR+LU).[89] These price differences are largely driven by the relative cost of partner drugs and the use of various artemisinin derivatives. For all treatment combinations, manufacturing costs have declined over the past year as a result of price reductions in the cost of artemisinin-derived raw materials and active pharmaceutical ingredient (API) production. This development is illustrated by Novartis's lowering of the public-sector MSP of Coartem® from USD 2.4 to USD 1.8 per adult treatment course in October 2006.[90]

As discussed in Section 3, prices charged by manufacturers to public- and private-sector buyers differ significantly. Private-sector ex-factory prices of ACTs are estimated at roughly USD 4–5, or double the public-sector "no-profit, no-loss" prices. These MSPs have translated into an average ACT retail price of around USD 8.4 in the private sector[91] (the prices range from USD 6 to USD 10), as illustrated in Figure 13.

Average ACT manufacturing costs are only expected to decline 30 to 40% in the coming years, as noted in Section 2.4. As a result, ACT retail prices will remain unaffordable to

Figure 12: Supply Chain for Antimalarials

| | | Key requirements | Key requirements | Key requirements |

Desired outputs of the AMFm
- Availability
- Affordability
- Displace monotherapies/delay resistance

the majority of patients in the malaria-endemic developing world. Through negotiations with manufacturers, the AMFm can immediately reduce, and potentially eliminate, the public-private MSP differentials from USD 4–5 to below the current public sector MSP of USD 1–2.

A further reduction in the average MSP will be feasible after the introduction of the AMFm due to an expected change in the current product mix of ACTs as a result of greater competition and the entry of new treatment categories.
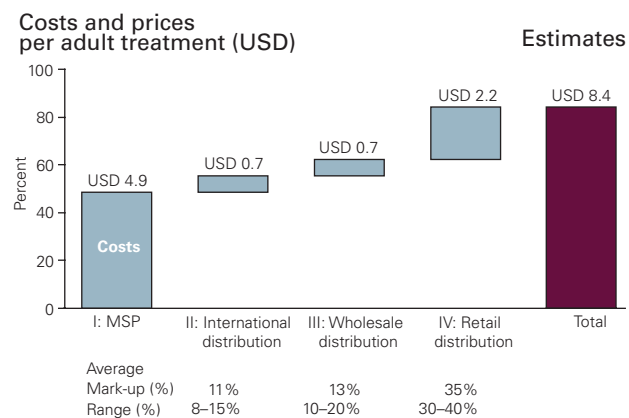
Finally, a larger projected global demand following the introduction of the AMFm should lead to a further reduction in manufacturing costs and MSPs due to economies of scale achieved in procurement, production, and overhead, and in time to improvements in artemisinin plant yield and potential innovations in synthetic artemisinin.[92, 93]

4.1.2 International distribution costs for ACTs are substantial and will also need to be covered by the AMFm buyer co-payment.

Today, costs associated with international distribution of ACTs from the manufacturer to endemic countries ("factory gate" to port) total an average of USD 0.7 CIF (cost, insurance, freight) per treatment course. Fees paid to international distributors constitute the largest component of this cost, which is driven by the mode of transport chosen, the level of competition among distributors, the average ACT order size, the level of quality assurance required by buyers, and customs costs, which are determined by the total value of the ACT shipment. Without reducing the cost of international distribution, the retail prices that patients pay for ACTs will remain significantly higher than for SP and CQ, which rely to a greater extent on local production and can be packaged and shipped more efficiently.[94]

Although support of international distribution costs will continue to be essential to sufficiently lower prices to con-

Figure 13: Current ACT Markup Structure

	II: International distribution	III: Wholesale distribution	IV: Retail distribution
Average Mark-up (%)	11%	13%	35%
Range (%)	8–15%	10–20%	30–40%

Note: Average mark-ups are calculated over the sample Burkina Faso, Cameroon, Kenya, Uganda. This data is in line with more recent observations made in a pricing study conducted in Uganda by the Ministry of Health/MMV.

Source: Dalberg field analysis (Burkina Faso, Cameroon, Kenya, Uganda).

sumers, the level of subsidization will decline substantially over time. Increases in ACT demand may allow for the establishment of more regularly scheduled international distributions of drugs using sea freight.[95] This likely change is expected to reduce international distribution costs per ACT treatment to between USD 0.1 and 0.2[96] by the fifth year of AMFm operation. However, overall international distribution costs are nevertheless expected to remain above those of CQ.[97]

4.1.3 Wholesale margins for ACTs (on an absolute basis) have the potential to decline significantly after AMFm introduction.

Wholesaler structures and markets vary widely by country. There is significant diversity among business models and within the competitive environments of malaria-endemic countries, with national regulations playing a significant role

in shaping market dynamics. These dynamics are particularly pronounced in sub-Saharan Africa where there is a distinction between those less-regulated countries, in which wholesaler margins are largely market-driven, and those where the ministry of health regulates fixed percentage margins for wholesalers and retailers (which is typically the observed norm in Francophone Africa). Figure 14 illustrates the in-country ACT supply chain in Tanzania—a typical wholesale distribution model.

Today, wholesale distribution is estimated to account for about 8 to 15% of the average retail sale price of ACTs to patients, or about USD 0.4–0.7.[100] Where wholesalers carry a range of medical supplies, and margins are not officially stipulated, a fixed percentage margin is typically applied, based on the purchase price paid for a particular medicine.

According to current estimates, the wholesaler margin averages 13% of the landed cost.[101] Wholesalers typically set higher percentage margins for lower-cost commodities, in part to reflect the costs of handling greater volumes. For example, wholesaler margins for SP are estimated at 20% of landed cost.[102] If wholesaler markups after the introduction of the

AMFm are similar to those for CQ or SP (approximately 20% over the landed cost), wholesaler markups will fall from the current level of ~USD 0.69 to ~USD 0.01 per adult ACT treatment course.[103]

Wholesalers would stand to maintain, or increase, their overall profitability only if there were a significant increase in the volume of ACTs they sold—which would be achievable only by substituting sales of CQ and SP with sales of ACTs. This increase could be driven either by both higher patient demand for ACTs and by other direct incentives to wholesalers, such as volume rebates that yield somewhat higher margins for ACTs than for CQ and SP.

4.1.4 The AMFm should aim to achieve retailer margins that more closely resemble those for CQ or SP, resulting in retail prices between USD 0.2 and USD 0.5 for the majority of patients.

There is a wide range of retail outlets distributing antimalarial treatments to patients in malaria-endemic markets. In the public sector (discussed in Section 4.4), drugs are distributed in hospitals and various health clinics, while in the private sector, they are distributed via pharmacies, dispensaries, corner shops, private hospitals, and faith-based organizations or NGOs.

Average retail margins are estimated at USD 2.0–2.2 per treatment (41–45% above MSP).[104] Margins are driven by fixed-price regulation, elasticity of demand, and competition (where fixed-margin regulation does not exist); by the strength of the public sector; and by patients' perceptions toward pricing. Of the USD 2.0–2.2 average margin, profits are estimated to account for approximately 60%, and costs account for the remaining 40% (USD 0.9), driven by overhead, staff, and transport expenses.

Retailer margins for lower-priced antimalarial treatments such as CQ or SP are, in relative terms, significantly higher than current ACT margins. As noted previously, there is an inverse relationship between the level of input (wholesale) price and the relative retailer margin. For example, the current average markup on ACTs in Uganda (currently priced at ~USD 8) is 40%, whereas the average markup on the far lower cost generic SP is 190%.[105] However, in absolute terms, this still implies a markup of ~USD 3 for ACTs vs. ~USD 0.3 for generic SP.

Following the introduction of the AMFm, the overall retail price of antimalarials will have the potential to decline significantly, from its average of USD 8.0, provided the buyer co-payment is passed along the supply chain. The target post-AMFm retail margins have been estimated based on current margins for other antimalarial treatments, such as generic SP and CQ treatments.[106] The post-AMFm average relative retail markup has been estimated at approximately 150%, which implies an expected post-AMFm ACT price of approximately USD 0.3. The table below illustrates how this

margin compares to various in-country observations of markups on generic SP and CQ:

Current retail margin (%)			
Country	CQ Generic	SP Generic	Comment
Uganda	160%	190%	Average across multiple brands
Kenya	—	140%[107]	Industry norm: 33%; outliers up to 400%[108]
Cameroon	—	70%	Fixed retail margin for low-priced goods
Burkina Faso	100%	100%	Fixed retail margin for low-priced goods

Source: Dalberg field analysis (Burkina Faso, Cameroon, Kenya, Uganda).

Post-AMFm retail prices can be expected to vary across endemic countries, as they do today. Drivers of post-AMFm differences in retail prices will include: government regulation, ACT status as an over-the-counter (OTC) drug, level of competition in the wholesale and retail market, and consumer awareness and education. Many of these characteristics are specific to individual countries and are thus outside the control of the AMFm. Variation in prices within a country, particularly in prices expected in non-competitive markets, has been a source of concern for stakeholders.

To assess this risk, previous studies and field observations were analyzed, and, based on these analyses, a simple randomized model was created to estimate likely pricing distribution across retail outlets within a country, yielding estimates of post-AMFm consumer prices of USD 0.2–0.5 per treatment course for an effective coformulated antimalarial for the majority of patients.[109, 110]

In-country supporting interventions will be instrumental to achieving these margins and are discussed in Section 4.2. Detailed assumptions are discussed in Background Papers 5 and 8.

4.1.6 Summary: The AMFm introduction can result in low-cost ACTs by lowering costs and margins at every step of the supply chain.

Following the introduction of the AMFm and the buyer co-payment at the manufacturer level, costs are expected to decrease along each stage of the global ACT supply chain. A buyer co-payment of approximately USD 0.9 is highly leveraged to deliver an approximate decrease of USD 5.5– 9.8 in retail price to patients, from USD 6–10 to USD 0.2–0.5 for the majority of patients, as shown in Figure 15.

4.2 Supporting interventions to enable transmission of low-cost products through the in-country supply chain

Analysis indicates that supporting interventions can be deployed to facilitate the pass-through of lower prices at the

Figure 15: ACT Markup Structure Following AMFm Introduction
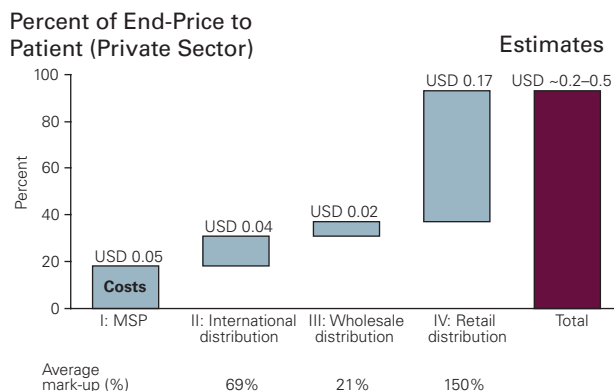
Note: Average mark-ups are calculated over the sample Burkina Faso, Cameroon, Kenya, Uganda. Retail margin is conservatively taken as the highest margin (Uganda, 150%). International distribution includes customs and clearance charges. This data is in line with more recent observations made in a pricing study conducted in Uganda by the Ministry of Health/MMV.

Source: Dalberg field analysis (Burkina Faso, Cameroon, Kenya, Uganda).

wholesaler/importer level, to align retailer incentives, to set prices directly, and to stimulate demand for products. Possible supporting interventions include:

- Recommended or suggested retail pricing—to aid margin control and prevent price gouging in markets without strong price regulation;
- Wholesaler and retailer incentives, such as retroactive volume rebate contracts, to align incentives of wholesalers and retailers to market and sell low-cost ACTs; and
- Patient education and awareness, which will be instrumental in informing patients about the greater efficacy of ACTs vis-à-vis other antimalarials.

Supporting interventions will play an important role in enabling the transmission of low-priced ACTs to patients. They are discussed in more detail in Section 5.3 and Background Paper 6. For in-depth analysis of the ACT supply chain and such interventions, refer to Background Paper 9, containing an analysis provided by supply-chain expert and MIT-Zaragoza International Logistics Program Professor Prashant Yadav.

4.3 Learning from the impact of existing efforts to subsidize ACTs

A range of subsidies supporting distribution of low-cost health products, including through the private sector, have proven effective in other contexts. A key example is a 2006 Brazilian Ministry of Health initiative that enables patients to purchase a range of subsidized health products through private pharmacies. As a result, an average of 400,000 Brazilians access low-cost hypertension and diabetes medicines each month - and the program has recently been expanded to also include contraceptive pills.[111] The Brazil example offers an encouraging model for successful private sector distribution of nationally subsidized products. Its reliance on

national financing rather than donor funding further makes Brazil a relevant model for the possible eventual shift in AMFm ownership to country governments.

Furthermore, research is currently being conducted to identify the likely impact of the AMFm in more detail. Although no existing international financing mechanism mirrors the characteristics of the AMFm exactly, field research can help estimate its potential impact, as well as suggest key success factors and challenges that the AMFm may face during implementation.

Four research studies have been or are being conducted in this regard:

- Senegal: The Institut de Recherche pour le Développement (IRD) conducted a pricing study to establish whether price transmission in the national, GFATM-funded ACT subsidization scheme is efficient or whether price gouging is occurring.
- Cameroon: The Malaria Consortium is using the same methodology as IRD to study the national subsidization scheme.
- Uganda: as part of the implementation planning for the ACT access pilot scheme, the Ministry of Health of Uganda and MMV conducted market research into the prices and availability of antimalarials in the country.
- Tanzania: The Clinton Foundation is conducting a

demonstration project, in which subsidized Coartem® is being distributed in a number of pilot districts, with availability and prices being monitored, evaluated, and compared with baseline data.

At the time of writing, results were available from the research in Uganda, and the IRD study in Senegal, which is summarized in Figure 16. Research results from Uganda on prices and availability of antimalarials were broadly in line with earlier observations by the Dalberg team and reconfirmed the price ranges described earlier in this Section. Further indications on the likely impact of the AMFm will become available as results from the Cameroon and Tanzania research are published.

4.4 Impact of the AMFm on public-sector health channels

The public sector will have access to the AMFm at the prices available for all eligible first-line buyers. Procurement volumes are expected to rise to approximately 130 million doses over the next three to five years, driven mainly by GFATM, PMI and Booster Program grants, as illustrated in Figure 17. Expected volumes and prices are discussed in more detail in Background Paper 5.

The effect that significant reductions in ACT prices (from ~USD 1-2 to ~USD 0.05) will have on the funding alloca-

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Figure 16: Country Case Study: Co-Paid ACTs in Senegal

Subsidized ACT Distribution in the Public and Private Sectors: Senegal Case Study[113]

In September 2006, the Senegalese government began the distribution of subsidized ACTs through both public- and private-sector outlets. With funding from GFATM, the National Medical Store (Pharmacie Nationale d'Approvisionnement) procured adult, adolescent, and infant doses of the Cipla AS-AQ product Falcimon®.

Under the subsidization scheme, adult doses were to be sold at CFA 600 (USD 1.29) and adolescent and infant doses at CFA 300 (USD 0.65) per dose in public clinics, NGO clinics, and private pharmacies. Public-sector and NGO clinics purchased the medicines at CFA 575 (USD 1.24) per adult dose and resold it virtually at cost, while private-sector pharmacies purchased it at CFA 460 (USD 0.99), yielding a gross margin of 29% on the product, in line with margin regulation for the pharmaceutical sector in Senegal.

In August and September 2007, the Institut de Recherche pour le Développement (IRD) conducted a pricing study in 67 facilities to test whether outlets were conforming to government price regulations and were passing the subsidy on to patients, or whether price gouging was occurring. In line with international practice, Health Action International (HAI) methodology was used, as well as a 'mystery shopper' technique, in which an investigator purchased the product either for himself or his child without revealing the aim of the purchase.

Price adherence was consistently high in all sectors, in both urban and rural settings: observed prices for adult doses varied between CFA 600 and CFA 650, with an average of CFA 604 in the urban public sector, CFA 621 in the urban private sector, CFA 600 in the rural public sector, and CFA 615 in the rural private sector. Some of the price differences were attributable to uncertainty around the applicability of a CFA 30 'risk premium' for 'class C' medicines, which some pharmacies added to the price of CFA 600.

Mystery shopping yielded price results very similar to those collected using the HAI methodology, with a maximum of CFA 650 paid for an adult dose in urban areas and CFA 630 in rural areas. On one occasion, significant overcharging occurred, when CFA 400 was demanded for an infant dose.

Medicine availability was generally high in the public and NGO sectors, with at least one of the three dosage forms available in all rural outlets and in at least 80% of urban outlets. In the private sector, stocking was much poorer, with merely 57% of urban outlets and 31% of rural outlets carrying subsidized Falcimon®. Interviews revealed that this was due to the first batch of publicly procured Falcimon® nearing its expiration date and, concomitantly, to a pending decision by the National Medical Store to refund expired stock. This issue has led to significantly decreased stocks and a reduced availability of Falcimon® in private-sector outlets in recent months.

Figure 17: Public-Sector Expected Volumes over Time

Expected public-sector demand
(post-AMFm, million treatments)

	2007	Year 1	Year 2	Year 3	Year 4	Year 5
ACT penetration (% of public sector)	64%	77%	77%	90%	90%	90%
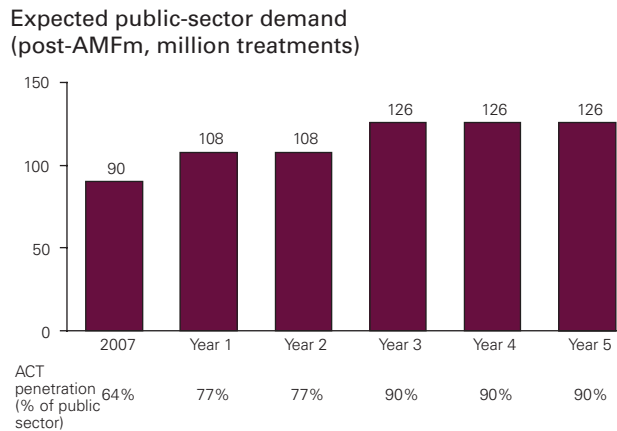
Source: Dalberg analysis based on information from PMI, WB Booster Program and GFATM.

tions of large donors, and on their reprogramming of planned expenditures, is difficult to estimate before donors have set their policies in response to the AMFm. There have been some indications, for example in Kenya,[112] that the overall share of public-sector drug provision could be expanded.[114] However, this effect will likely take some time. Therefore, the case for working additionally through the private sector remains.

The AMFm co-payment mechanism also holds some advantages over the current grant-based public-sector mechanisms:

- *Reduction of transaction costs:* Current grant-making mechanisms are characterized by high transaction costs (application processes, review panels), delays, and a general lack of flexibility. Similarly, financing through credits comes with high transaction costs and multiple reviews. A co-payment mechanism will, in contrast to this "stop-and-go" approach, "flow" in a more natural manner, and will provide responsive and fast delivery of commodities against much lower transaction costs.
- *Reduction of uncertainty:* Current grant-making mechanisms create uncertainty for recipients, as grants always have the potential to end without renewal. This uncertainty could prevent an entity from switching to a first-line ACT treatment protocol and could undermine the establishment of a stable and predictable country-owned rollout strategy.
- *Alignment of incentives:* Grant-making mechanisms can create inappropriate incentives for recipients, for example to stockpile or over-order. The credible, long-term operation of the AMFm would reduce these incentives.

In the split between public and private sectors, NGOs have been included in the private sector for analysis purposes. Current NGO procurement is fairly limited, and is estimated to account for less than 10% of the overall current ACT purchases in the private sector (10 million). The AMFm will increase NGO procurement in absolute terms, but overall this channel is likely to remain a small part of overall private-sector procurement. The NGO sector will benefit in the same way as other sectors do—through sustainable access to low-cost ACTs via a simple and transparent mechanism.

5. AMFm Design

Section summary

Based on the goals of the AMFm, and taking into account the characteristics of the ACT supply chain identified in Section 4, this section outlines the core functions of the AMFm. In addition to managing the buyer co-payment process, the AMFm will set eligibility requirements and help coordinate critical in-country supporting interventions essential to the responsible introduction of the AMFm. These supporting interventions will be executed largely by countries with technical assistance from international RBM partners.

To meet the price and access objectives of the AMFm, and to address the ACT supply-chain issues discussed in Section 4, the AMFm will need to manage a core set of co-payment functions and have a direct role in managing the conditions for co-payment or eligibility requirements. In-country supporting interventions will be monitored or coordinated by the AMFm but carried out by individual countries and supported by partners in the global health community.

5.1 Core functions of the AMFm facility

5.1.1 Negotiation of terms for low-cost antimalarials

A core activity of the AMFm will be to negotiate with manu-facturers the terms under which the AMFm will offer co-payments for effective antimalarial treatments. The objective of these terms will be to enable first-line buyers to access effective antimalarials at a price comparable to CQ and SP.

The negotiation approach to setting co-payment levels and price ceilings

Copayment agreements between the AMFm and manufacturers will aim for a balance between achieving the best prices and maintaining a sustainable global market for ACT manufacturers. Given the limited competition in the current market for eligible antimalarials, the setting of co-payments may initially be based on direct negotiations with manufacturers.

Figure 18: Core AMFm Functions and In-country Supporting Interventions

CORE AMFM FUNCTIONS
(Executed by Facility)

5.1.1. **Negotiating terms for low-cost antimalarials**
5.1.2. **Negotiation of terms for international distribution**
5.1.3. **Processing first-line buyer co-payments**
5.1.4. **Transparent sharing of information and forecasts**

ELIGIBILITY CRITERIA / REQUIREMENTS
(Set by Facility)

5.2.1. **Antimalarial treatment requirements**
5.2.2. **Buyer-eligibility requirements**
5.2.3. **Country-preparedness requirements**

5.3 RESPONSIBLE INTRODUCTION: IN-COUNTRY SUPPORTING INTERVENTIONS
(Monitored or coordinated by Facility)

- **National policy and regulatory preparedness**
- **Wholesaler incentives and pricing/margin-control mechanisms**
- **Public education and awareness (IEC)**

- **Provider training**
- **National monitoring and quality preparedness (resistance monitoring, pharmacovigilance, and quality surveillance)**

The AMFm will negotiate co-payment levels rather than prices. The co-payment level will be based on the lowest-cost producer of a given ACT combination and dose, and ACTs will retain price differences based on their original MSPs. Under this approach, a target or average first-line buyer price of USD 0.05 is expected, although individual MSPs to first-line buyers will vary. The AMFm may also set price ceilings as part of the agreement with manufacturers, to ensure that the benefits of the co-payment are passed on to first-line buyers and ultimately to patients. Orders for antimalarials with prices above these ceilings would not be eligible for co-payment.

Under this negotiation approach, incentives for innovation and competition will be retained by allowing for MSP differentials, and potentially setting the co-payment level by treatment classes and formulations. Innovation and competition is also encouraged by the antimalarial treatment requirements outlined in Section 5.2.

Negotiations with eligible manufacturers are expected to take place on a regular basis to reflect changes in the market for effective antimalarials. To achieve the desired negotiation outcomes, a highly skilled team with international procurement and negotiations experience, as well as the ability to undertake market and product cost analysis will be required.

Impact on product flows and purchasing relationships

The AMFm has been designed to ensure that first-line buyers maintain their existing purchasing relationships with manufacturers while encouraging new buyers of ACTs, and to minimize disruption to the efficient operation of the global antimalarial market. Buyers will continue to place orders directly with manufacturers and may continue to conduct their own competitive tenders with multiple manufacturers. Manufacturers may also continue to market existing premium-branded antimalarial formulations.

Use of international procurement agents

First-line buyers will have the option to use international procurement agents voluntarily to pool their purchases. Current major agents that already purchase ACTs include UNICEF, MissionPharma, IDA Solutions, and Crown Agents, among others.

Future considerations for negotiating co-payment levels and price ceilings

As markets become more competitive, alternative rule-based mechanisms with low transaction costs may be considered. Regular negotiations or tendering with an increasing number of manufacturers may over time become unwieldy, inefficient, or expensive, and may not yield the most competitive co-payment levels or sufficient incentives for ACT product innovation. Over time, the AMFm may consider moving to a more automated, rule-based mechanism, such as a competitive pricing auction, to set co-payment amounts in response to changes in market conditions. In addition to greater com-

petition and lower transaction costs, an auction may also increase the bargaining power of the AMFm and assist in managing a healthy and competitive market.

5.1.2 Negotiation of terms for international distribution

As discussed in Section 4, a co-payment from the AMFm toward international distribution costs (insurance and freight) will be required to ensure that ACTs decline to a sufficiently low price to consumers. The international distribution component will make up a significant share of AMFm co-payments. It is expected that the unit cost of international freight and insurance will decline over time as the volume of low-cost eligible antimalarials increases and distribution practices improve. The AMFm will benchmark insurance and freight prices and terms directly with international freight forwarding agents through a regular process of evaluation. To ensure minimal disruption to existing distribution networks, manufacturers will use their own distribution arrangements (offering prices on both an FOB[115] and CIF basis). The international distribution portion of an order with a manufacturer will be co-paid only if the price falls within the bounds benchmarked by the AMFm for a similar order.

The final AMFm agreement with manufacturers on co-payments may also include more specific terms relating to the distribution of effective antimalarials, such as conditions for shipping, packaging, and marketing.

5.1.3 Processing first-line buyer co-payments

Another core function of the AMFm is the processing of co-payments. This function will be similar to a standard payment process and should be as simple and streamlined as possible. It is recommended that the process be fully automated, using an existing electronic platform. It could be outsourced to a commercial provider for low cost and fast processing times. The steps required to process the co-payment amount are outlined in Figure 19.

Several of the steps specified here as performed by the AMFm, including confirmation of eligibility and of receipt of goods, could be performed by manufacturers, subject to regular audits to ensure compliance by both the manufacturers and first-line buyers. The final placement of activities will be determined as part of the agreement on co-payments with manufacturers.

Many of these processes can be performed electronically. It is estimated that the workload could be handled by as few as one to two administrative employees, that the order processing time would be under 24 hours, and that the number of orders is likely to be fewer than 2,000 per year. The electronic order processing platform and/or an outsourcing partner will be chosen during the implementation phase. The electronic platform should capture the transaction, customer, country, order, and volume information required for

transparent tracking, auditing, and global-demand-forecasting activities, as described in Background Paper 6. The subprocesses required by the AMFm to process co-payments are detailed in the same paper.

5.1.4 Transparent sharing of information and forecasts

As emphasized in a recent publication by the Center for Global Development (CGD),[116] accurate and credible demand forecasts are critical to the successful delivery of health products and to enabling players in the global health supply chain to make appropriate decisions and investments. Recognizing the importance of demand forecasting, the report recommends three reinforcing solutions to address current obstacles to credible demand forecasting in the global health context:

- Improving the capacity to develop credible forecasts by taking forecasting seriously and understanding the far-reaching negative implications of poor demand forecasts.
- Mobilizing and sharing information in a coordinated way through the establishment of an "infomediary."[117]
- Better sharing of risks and aligning supply-chain incentives by employing a broader range of contractual arrangements among key players.

The AMFm has a clear role to play in capturing consumption information and forecasting future demand for malaria medicines. Yet many global health institutions do not currently share this data, and those that do may not share them fully, or in a transparent manner. Given the solutions recommended by the CGD Global Health Forecasting Working Group, the AMFm will publicly share on its Web site demand forecasts and aggregated purchase data, including pricing and volumes, with manufacturers, buyers, funders, governments, and NGOs. The AMFm will also provide data to specialized forecasting bodies, such as an infomediary, as suggested by CGD.[118]

For manufacturers, access to quality market information and credible demand forecasts are minimum requirements for their investment decisions, particularly with regard to the capacity-expansion decisions required to meet the global demand that will be spurred by the AMFm. Without quality information about the market, existing manufacturers and potential market entrants are less likely to make the capital and marketing investments required to increase the global supply of ACTs.

5.2 Product/supplier, buyer eligibility, and country preparedness

To be eligible for the co-payment by the AMFm, orders must meet the following standards and requirements, which will be validated by the AMFm and its technical partners. The

Figure 19: First-Line Buyer Order Process for Low-Cost ACTs Purchased through the AMFm

Step	Who	Description
1. Place order	First-line buyer	• Eligible first-line buyer places an order for eligible ACT treatments directly with an eligible manufacturer.
2. Establish eligibility	**AMFm**	• The AMFm confirms the order against eligibility and pricing criteria, checking for the correct ACT treatment, supplier and buyer eligibility, MSP pricing, international-distribution price, and the order volume being within an upper limit. • Once a new buyer, product, or supplier is added to the eligibility lists, this function will be automatic for orders within safe ordering parameters and will require no AMFm staff input.
3. Process invoice	Manufacturer	• ACT manufacturer submits invoices to the first-line buyer (for the low AMFm price) and to the AMFm (for co-payment).
4. Receive delivery	Manufacturer/shipping agent	• The order is shipped to the first-line buyer at the specified destination. • Upon receipt, a delivery notification is sent to (a) the AMFm and (b) the manufacturer, stating that drugs have been received. • Buyer pays the AMFm price to the manufacturer (according to manufacturer terms). • The AMFm will not interrupt normal manufacturer-buyer payment terms based on standard credit practices.
5. Process co-payment	**AMFm**	• The AMFm receives the delivery notification and reconciles it against (a) the manufacturer invoice and (b) the international distributor invoice (this step is performed electronically). • If approved, a payment authorization is sent to the AMFm's bank, and the co-payment amount is transferred electronically to the manufacturer (which includes the international distribution cost component). • The co-payment processing is complete. • Transaction data are stored for records, financial auditing, and global demand forecasting.
6. Local distribution	Distributors, pharmacies, public health-care providers, other private retailers	• First-line buyer distributes ACTs to in-country distributors who then distribute ACTs through in-country supply chains to private retailers and/or public-health-care providers of ACTs, and on to patients.

standards and requirements include ACT treatment requirements, buyer eligibility, and country preparedness.

5.2.1 Antimalarial treatment requirements (quality, combinations, geography)

Eligibility requirements for medicines will be crucial to ensure that the AMFm delivers appropriate, high-quality ACTs to patients. This need will affect manufacturer participation in the AMFm at three levels:

- Antimalarial combinations: WHO treatment guidelines, as the internationally recognized standard for malaria treatment, define the eligible classes of drugs to be co-paid by the AMFm. Currently, these encompass four classes of ACTs. As WHO treatment guidelines evolve and new products become available, eligible antimalarial drugs will be added to the portfolio of products offered by the facility, in line with WHO recommendations.
- Geographic exclusions: The WHO, in collaboration with national authorities, will develop a list of approved antimalarials that is country-specific, with consideration given to drug efficacy and parasite-resistance patterns. Studies should be conducted as part of country-specific support packages to maintain up-to-date information on these patterns. The AMFm will co-pay only for combinations in specific regions and countries in a manner consistent with treatment guidelines and on the basis of their efficacy and their potential to delay resistance.
- Medicine quality: A transparent and internationally recognized quality standard is required to ensure delivery of high-quality pharmaceutical preparations while encouraging competition among suppliers in all treatment classes. The final quality standard will be WHO pre-qualification or registration by a stringent regulatory authority.[119] Pharmaceutical preparations submitted for such approval, but not yet approved, may be eligible for a period of up to two years, provided that they meet interim criteria along the lines of those currently applied to the WHO/UNICEF tender list and the Global Fund (ci) compliance list. The RBM Board has asked the WHO to work with other relevant agencies to harmonize the criteria underlying these lists.[120] It is envisioned that these harmonized criteria will have been established prior to the AMFm launch and thus will apply to it.

Figure 20 details those ACT treatments that currently meet these quality standards:[121]

Additional manufacturers of ACTs, for example those producing in developing countries, will be encouraged to meet the required quality standards so they can provide their products through the AMFm. To this end, interventions to support manufacturers in reaching quality standards will be required. These are discussed below.

5.2.2 Buyer-eligibility requirements

Buyer-eligibility requirements are needed to ensure that only legitimate buyers access the AMFm, in compliance with national regulations. In accordance with the on-demand nature of the AMFm, individual purchases by first-line buyers will not be subject to technical review. Instead, the list of eligible buyers will be updated on an annual basis. Initially, first-line buyer vetting will be conducted by manufacturers rather than by the AMFm on a global scale. Over time, public-sector buyers may require fewer criteria than for-profit buyers, given their missions and history of purchasing ACTs.

The following minimum requirements for access by first-line buyers are recommended:

- Registration with national authorities;
- Acceptance of terms of purchase and a record of acting in accordance with these terms;
- Confirmation that the destination country meets preparedness requirements.

First-line buyers supplying more than one country with medicines will be required to respect the requirements in each country in which they operate.

ACTs ordered by international procurement agents pooling orders on a voluntary basis will also be co-paid if those agents comply with similar eligibility criteria. These criteria will include:

- Record of respecting national regulations;
- Acceptance of terms of purchase and a record of acting in accordance with these terms;

Figure 20: Current ACT Treatments Meeting International Quality Standards

	AR-LU	AS-AQ	AS-MQ	AS-SP
WHO or SNRA[122] pre-qualified	Novartis	Guilin		
WHO/UNICEF tender list	Novartis	Guilin Ipca Strides-Arco	Mepha	Guilin Ipca
GFATM compliance list (ci level and above)[123]	Cipla Dafra	Cipla Dafra Guilin Ipca Lachifarma Sanofi-Aventis		Dafra Guilin

- Acceptance of accountability for ensuring that co-paid eligible antimalarials will be sold only to buyers who meet the eligibility criteria applied to first-line buyers.

In addition, upper limits on orders by first-line buyers will guard against spikes in ordering volumes. These ceiling values will be set and reviewed on a country-by-country basis in consultation with national stakeholders, and will not interfere with normal buying behavior.

5.2.3 Country-preparedness requirements

Effective implementation of the AMFm will require both an effective co-payment mechanism and responsible introduction at the country level. Country-preparedness requirements will help ensure the success of the AMFm by providing essential assurances that the country conditions under which AMFm–supported antimalarials are introduced will be conducive to responsible introduction of ACTs. Assessment of country preparedness will also be key to identifying appropriate supporting interventions and implementing them.

In consultation with endemic-country representatives and international stakeholders, the following have been identified as potential country-preparedness requirements:

- Acceptance of WHO treatment guidelines (or guidelines of equivalent quality developed by the country) to promote the objectives of rational use of ACTs and the crowding out of monotherapies;
- Provision of a list of eligible first-line buyers to ensure that only legitimate wholesalers are able to access the AMFm;
- Commitment to implement supporting interventions, including a basic monitoring framework, to ensure that essential supporting interventions will be implemented in a timely manner;
- Minimum levels of regulatory preparedness and wholesaler regulation/incentive setting to ensure the promotion of WHO treatment guidelines and the transmission of low ACT prices to patients.

It is recommended that requirements remain both technically sound and minimally bureaucratic, to minimize delays in the rollout of the AMFm. When possible, existing grant mechanisms, such as the GFATM, Booster Program, or PMI, should be used to assess country preparedness. Where preparedness assessment using existing mechanisms is not possible, light and flexible approaches should be used to minimize both bureaucracy and the workloads of individual countries. For example, a dedicated expert panel, similar to the one used for the Stop TB Initiative's Green Light Committee, could be used to assess country preparedness in a joint problem-solving approach. Under such a scenario, experts would visit decision makers in endemic countries, and plans and documentation would be developed jointly.

Furthermore, the RBM Harmonization Working Group is supporting the preparation of gap assessments for a number of highly endemic countries. These gap assessments and other working group tools may also be very relevant to the assessment of country preparedness.

5.3 Responsible introduction: In-country supporting interventions

Whereas the AMFm will focus on ensuring access to affordable ACTs, there are also important non-price factors that contribute to effective malaria case management and rational treatment use in endemic countries. These factors include patient treatment-seeking behavior, product availability, the national regulatory environment, provider knowledge, local distribution capacity and supply-chain efficiency, patient demand and education, and product efficacy. The interrelationships among these factors are outlined in Figure 21.

A core package of supporting interventions has been developed based on a comprehensive review of supply-chain challenges and required responses. These core interventions will help countries manage the increased volume of ACTs, particularly in the private sector, and will help reach desired outcomes.

Only those supporting interventions that are directly linked to the management of low-cost ACTs, particularly in the private sector, have been included in the core package detailed in Figure 22. Cost estimates for the delivery of the interventions described in this section are included in Section 8, which estimates the financial requirements of the AMFm. It is recognized that there are significant links among the core supporting interventions and wider regulatory and programmatic efforts required to roll back malaria and promote safe and effective product use.

The core package of supporting interventions comprises five categories, and is summarized in Figure 22.

Further information on the implementation of specific supporting interventions can be found in Background Paper 6.

5.3.1 Planning in-country supporting interventions

Endemic countries are at differing stages of preparation for the rollout of ACTs in the private sector, and each will thus need to implement a unique package of supporting interventions targeted to its particular conditions. Significant differences in pharmaceutical policy and culture exist among endemic countries, for example between Anglophone and Francophone Africa, and between Africa and Asia.

The need for supporting interventions will be determined through the implementation plan for supporting interventions described above. These plans will be based on existing country plans and may need to be adjusted to reflect the availability of low-cost ACTs through the AMFm. National partners will hold the primary responsibility for the planning of core supporting interventions, which should be linked to existing

Figure 21: Effective Malaria Case Management and Rational Use

Effective "Malaria Case Management" and "Rational Use"

1. Patient seeks treatment through appropriate channel
2. Provider takes medical history, completes physical exam, and correctly diagnoses patient
3. Provider knowledge enables prescription of correct treatment and dosage
4. Prices are not prohibitive and patient can afford to purchase entire treatment course
5. Correct treatment course is available and in-stock via selected channel
6. Patient understands/complies with dosing regimen and completes treatment course
7. Treatment is effective

The price of ACT is only one component of access to effective treatment. Others include:

- Treatment-seeking behavior
- Availability in appropriate channels
- Regulatory environment
- Provider knowledge
- ACT price/affordability
- Local distribution capacity/supply-chain efficiency
- Patient education
- Product safety, efficacy, and quality

national malaria-control programs and health-sector plans. In cases where countries do not already receive grants from lead implementers (e.g. GFATM, PMI, or the Booster Program), there is a strong rationale for providing targeted support to ensure that supporting interventions will be planned and designed. Special attention will be paid to increasing broad access to ACTs, especially among those at highest risk. This is part of the AMFm's role in promoting equity of access.

It is recommended that coordination at the national level be implemented as far as possible through government mechanisms or appropriate existing grant-coordination mechanisms, such as the GFATM country coordinating mechanism. At the global level, existing RBM mechanisms should be used. The different working groups will assume responsibility for different parts of coordination, in line with their mandates.

5.3.2 The role of operational research

Operational research will play an important role in ensuring that the AMFm is implemented responsibly in endemic countries. Intensive operational research will be conducted in four to six endemic countries and will consist of intensive monitoring and evaluation to ensure that the AMFm is reaching its goals and that supporting interventions are effective. The countries in which operational research will be conducted should be representative of the majority of endemic countries. Lessons learned in these countries will then be shared with other endemic countries and with the international community to inform the choice and implementation of supporting interventions elsewhere. As countries decide on

supporting interventions and their design, they will benefit from the experiences and lessons learned in other countries.

5.3.3 The role of international technical assistance

Technical assistance will be required to assist individual countries, particularly those that have not met the country-preparedness requirements. Countries that already have aligned national malaria-control programs with ACT delivery will require less assistance, but may nevertheless benefit significantly from coordinated planning of core supporting interventions. Figure 23 summarizes partners currently providing technical assistance to endemic countries.

International technical assistance will also play a critical role in ensuring rapid and effective planning and implementation of core supporting interventions, particularly in endemic countries demonstrating low levels of preparedness. A number of the public institutions mentioned above have as part of their core mandates the development of policy guidelines and technical guidance for endemic countries. However, these mandates often do not include capacity-building activities to provide extensive operational assistance to large numbers of countries.

To ensure that critical technical assistance does not go unfunded in the design of the AMFm, the funding requirements as detailed in Section 8 include an allocation for international technical assistance related to the core package of supporting interventions.

Figure 22: Overview of Five Core Supporting Intervention Areas

Supporting Intervention Categories	Description
National policy and regulatory preparedness	Update national policies to align with WHO treatment guidelines and build capacity of drug regulatory policies to meet requirements of the AMFm.
Wholesaler incentives and pricing/ margin-control mechanisms	Regulate economic operators of the drug-distribution chain involved in distributing low-cost ACTs, including treatment prices and alignment of incentives to enable an appropriate price/margin structure, through mechanisms such as: • Wholesaler volume rebates • Suggested/recommended retail pricing • Maximum suggested retail price
Public education and awareness (IEC)	Build awareness of availability, efficacy, pricing, and rational use of ACTs through media campaigns directed at patients and by packaging and labeling products appropriately.
Provider training	Train health professionals and private wholesalers/retailers to promote safe and effective use of ACTs, including diagnosis, prescription, and treatment.
National monitoring and quality preparedness	Assess and enforce the quality and efficacy of ACTs distributed through both public and private channels through pharmacovigilance, resistance monitoring, and quality surveillance.

Figure 23: Examples of International Technical-Assistance Providers

Area of Supporting Interventions	Sample of Current Implementers
National policy and regulatory preparedness	• WHO Global Malaria Program • WHO Regional Offices (e.g. AFRO) • WHO Department of Medicines Policy and Standards • Management Sciences for Health (MSH) / Rational Pharmaceutical Management Plus (RPM Plus) • World Bank • Malaria Action Coalition (MAC): USAID, Management Sciences for Health (MSH), WHO/AFRO, U.S. CDC, and the Maternal and Neonatal Health Project (ACCESS) • Malaria Consortium
Wholesaler incentives and pricing/margin-control mechanisms	• Population Services International (PSI) • Clinton Foundation HIV/AIDS Initiative • WHO Department of Medicines Policy and Standards
Information, education, communication (IEC)	• Population Services International • UNICEF • Plan International • Sanofi (Impact Malaria), other manufacturers
Provider training	• Population Services International • CARE • Sanofi (Impact Malaria), other manufacturers • Health Action International (HAI)
National monitoring and quality preparedness (e.g. resistance monitoring, pharmacovigilance, and quality surveillance)	• WHO Collaborating Centre for International Drug Monitoring (Uppsala Monitoring Centre) • WHO Global Malaria Program • Regional networks (HANMAT, EANMAT) • Procurement agents, e.g. UNICEF • Management Sciences for Health (MSH) / Rational Pharmaceutical Management Plus (RPM Plus) • Malaria Control and Evaluation Partnership in Africa at PATH • John Snow, Inc.

6. Governance and Management

Section summary

This section addresses the governance and management implications for the organization and partners that implement the AMFm. The secretariat managing the AMFm will be responsible for ensuring that all key activities related to the facility's core functions, including the setting of co-payment conditions, are performed.

To ensure a lean architecture for the AMFm, with minimal overlap with existing institutions in the global health community, the secretariat should be embedded as a new business line within an existing organization, which is expected to meet a set of objective performance criteria. The secretariat will require a maximum of 15 to 22 full-time-equivalent (FTE) staff members to ensure that all functions of the AMFm are effectively performed.

Actual staffing will depend on the degree to which the AMFm functions are outsourced or provided by the organization managing it. Depending on the strengths and competencies of the selected organization, several of the technical and management functions of the AMFm will likely be outsourced.

6.1 AMFm operations

The core functions of the AMFm have been described in Section 5. An analysis of the facility's organizational requirements against benchmark organizations yields three operational areas required to govern and execute those functions. These operational areas are summarized in Figure 24.

The experience of other institutions and a growing emphasis in the global health field on targeted, efficient institutions have led the RBM Partnership to endorse the principle of a lean and focused secretariat for the AMFm. No new organization or governance structure should be created. To achieve this objective, a secretariat with a focused mandate will make use of the expertise of partners as well as private-sector service providers to perform the full range of functions required of the AMFm. It will avoid taking responsibility for functions currently per-

formed by other international partners or by endemic countries themselves and may outsource functions, such as order processing and cash payments, which can be provided efficiently and effectively by commercial service providers.

Based on an analysis of a variety of organizational options, the recommended approach is a "hybrid" arrangement that combines the expertise and brand identity of a multilateral institution in the global health community, with appropriate supply-chain expertise and private-sector outsourcing arrangements. An existing example of such an arrangement is the International Financing Facility for Immunizations, set up in partnership with the GAVI Alliance and Goldman Sachs.

The size of the core secretariat will depend significantly on the operational model established by the institution manag-

Figure 24: Overview of AMFm Operational Areas

Operational Area	Key Activities
Governance and resource mobilization The governance and oversight of all AMFm functions. This area also comprises basic strategic and general management-support functions.	• Governance and oversight • General management and performance measurement • Resource mobilization
AMFm mechanism The negotiation of terms with manufacturers and provision of co-payments to eligible first-line buyers on demand. The AMFm will need to respond quickly, effectively, and with low transaction costs, while enforcing eligibility and performance criteria. These needs will require the establishment of a dedicated fund with management procedures tailored to the buyer co-payment mechanism.	• Assurance that eligibility criteria are met and maintained for products, suppliers, and buyers • Negotiation and price-setting • Order management • Co-payment processing • Demand forecasting • Transparent information sharing/ management of online resources • Financial audit/quality assurance
Responsible introduction The financing and coordination of supporting activities that facilitate the responsible introduction of the first-line buyer copayment	• The provision of in-country supporting interventions • Review of country preparedness • Provision of technical assistance • Provision of financing for core supporting interventions • M&E and operational research

ing the AMFm. Under current assumptions, an estimated 15 to 22 staff will be required to carry out the core functions of the AMFm. A potential structure of the secretariat is illustrated in Figure 25.

Background Paper 6 describes in more detail the core function processes, key performance indicators for success, and types of supporting interventions.

based on a set of transparent criteria and key indicators for the performance of core functions. The key performance indicators are outlined in Figure 26.

Key performance indicators to measure the success of the AMFm are discussed in more detail in Background Paper 2.

6.2 Selection of institutions for governance and management of the AMFm

The selection of the institution that will govern and manage the AMFm and coordinate its operating partners will be

Figure 25: Resource Requirements for Delivery of Key AMFm Functions

Operational Area	Total Resource Requirements	Estimated Resource Requirements
Governance and resource mobilization	• 5–8 FTEs, not including board members and technical advisors	• Executive director, 2 FTEs • General management at 20% of core staff, 1–2 FTEs • Partnership/contract management, 1–2 FTEs • Resource mobilization, depending on funding situation, 1–2 FTEs
AMFm mechanism	• 5–7 FTEs	• Eligibility monitoring, transparent information reporting and forecasting, 2–3 FTEs • Negotiating terms with suppliers, 2–3 FTEs • Co-payment authorization/processing, 1 FTE
Responsible introduction	• 5–7 FTEs, not including in-country activities and international technical assistance	• Coordination of M&E and operational research, 3–4 FTEs • Funding and coordination of supporting interventions, 2–3 FTEs

Figure 26: Governance and Management: Key Performance Indicators

Operational area	Key performance indicators
Governance and resource mobilization	• Fit of mission and policies with existing governing body • Legitimacy, transparency, efficiency of decision-making • Credibility of fiduciary mechanisms • Value of privileges and immunities • Cost-effectiveness • Flexibility and effectiveness of general management procedures • Acceptability to donors • Resource mobilization track record
AMFm mechanism	• Ability to implement the AMFm according to the technical design agreed by RBM partners • Skills and ability to outsource core functions
Responsible introduction	• Feasibility of allowing access to AMFm on inclusive basis • Ability to collaborate with RBM partners in line with current global health architecture • Ability to access required technical skills

7. Risk-Mitigation Strategy and Implementation Planning

Section summary

This section addresses the likely range of risks in implementing and operating the AMFm. It describes the risk-mitigation strategies incorporated into the design of the AMFm and outlines additional strategies. Monitoring and evaluation (M&E) and operational research are explored, as are the strategies that may be needed to identify and mitigate implementation risks and to determine the effectiveness of supporting interventions for a responsible global AMFm introduction.

7.1 Risks and risk-mitigation strategies

The launch of any new venture requires careful consideration of the risks that may impede its success. The identification of implementation and operational risks has enabled the incorporation of mitigating features into the technical design of the AMFm, and has supported the development of strategies to address these risks as they arise during operations. While it is impossible to predict all scenarios and contingencies before making a decision to launch the AMFm, the careful attention that has been paid to risk identification will increase the chances of implementation and operational success.

Figure 27 summarizes the key risk areas that could impede the achievement of AMFm goals and their attending mitigation strategies. Many of the mitigation strategies have been incorporated into the design of the AMFm and are articulated throughout the document. Specific mitigation strategies are discussed in Sections 7.2 to 7.6.

7.2 Market positioning: Low-cost AMFm ACT treatments and premium-branded ACTs

ACTs are currently sold as a premium branded product in the private sector on a prescription-only basis. ACTs distributed through the public sector typically have distinct ("generic") packaging, although the formulation and name of the product are the same. Similar dual-market positioning will continue after the introduction of the AMFm, as described in Figure 28.

From the start, low-cost ACT products available through the AMFm will be branded distinctly to facilitate safe and effective patient use, and to minimize the impact on the premium-branded ACT market. Manufacturers, experts in international branding and social marketing, and endemic-country partners will be consulted in the development of AMFm packaging to ensure it is attractive to consumers, takes into account country differences, and remains sufficiently distinct from the premium product. Branding will be integrated into product packaging and into supporting interventions in endemic countries, including patient information and education campaigns, provider training, and recommended retail pricing.

7.3 Options for a partial or limited-scope rollout of the AMFm

There are several options for partial- or limited-scope rollout of the AMFm. These include a partial buyer co-payment and several alternatives for restrictions on buyers, regions or countries, or consumer groups. The final option is to manage the AMFm on a first-come, first-served basis, in which co-payments are made until funds are exhausted in a given time period. An analysis of each option for the AMFm rollout against its likely impact toward AMFm goals clearly indicates that a full global launch will yield the greatest benefits, particularly with regard to measures of equity, given that a full AMFm rollout will most effectively broaden access to affordable ACTs and save more lives relative to partial rollout alternatives.

In the event that the AMFm were not fully funded, even if only for a short period of time, reducing the buyer co-payment level per treatment, either to a fixed level or to a level based on country gross national income per capita, would be the most attractive option. This option would result in a significant number of lives being saved, would be cost effective, and could realize a significant reduction in required funds. Additionally, this option would present relatively few operational or organizational hurdles. In the event that this scenario were realized, at a minimum, the goal should be to co-pay ACTs to the extent that they can effectively compete with, and drive out, artemisinin monotherapies to accomplish the goal of delaying resistance. Laxminarayan et al. (2006) concluded that even a partial co-payment could delay the emergence of resistance.[124]

It is important to note that the recommended full AMFm rollout is expected to result in a natural and gradual 'phase-in' of ACTs from the baseline level of 100 million treatment courses to more than 350 million treatment courses over five years. This increase will occur due to the de facto phasing that will occur, as countries and buyers become eligible to purchase low-cost ACTs via the AMFm, and as patients and markets respond to the significant reductions in price and to social marketing and education campaigns. Assumptions and scenarios for the phase-in are discussed in more detail in Background Paper 8.

Responding to unexpected variations in demand and funding requirements

Because the AMFm is a market-based intervention, ultimate

Figure 27: Key Risk Areas and Mitigation Strategies

Risk Area	Description	Mitigation Strategy
Affordability	• Failure to sustain price reductions in the global market for ACTs	• Open, competitive, repeated process of setting price ceilings and buyer co-payment levels • Support of pre-qualification for additional suppliers of high-quality ACT treatments to expand supply • Transparent sharing of information about forecasted and actual antimalarial demand to enable suppliers appropriately to expand production
	• Cost of ACTs does not decline as expected due to retailer absorption of buyer co-payment	• Terms and conditions/MoU with wholesalers, addressing margins and expectations • Local supply-chain incentives, including incentives to wholesalers such as retroactive volume rebates • Supporting interventions in local supply chains including M&E, preparedness, recommended retail pricing, communication, and education campaigns • Maintain premium branded product as a distinct product offering
Availability	• Slow consumer uptake of ACTs	• Social marketing, media campaigns, and other supporting interventions targeting patients and providers • Rollout with gradual scale-up of ACTs over a five-year period (see Section 7.3) • Work with endemic-country partners to assess viability of OTC availability for ACTs (see Section 7.4)
	• Insufficient increase in pace of production, due to long ACT production cycle, restricted growing season of Artemisia annua, or inaccurate demand forecasts/country targets	• Long-term funding commitments • Promotion of local quality manufacturing • Careful verification of targets by in-country (RBM) partners (which could require oversight from RBM centrally, similarly to systems in place for access to vaccine stockpiles) • Clear communication and transparent demand data provided to market
	• ACTs not available where most needed due to fraud or over-ordering of low-cost medicines (e.g. hoarding or profiteering)	• Ministry of Health certification of accredited ACT buyers • Electronic order processing to maintain transparency and to track order patterns • Authority to suspend or delay orders for individual first-line buyers
Product Arbitrage	• Failure to stop co-paid product from being transferred to markets/countries where the co-payment is not applied, allowing high profits to middlemen	• Use of maximum retail price mechanisms to reduce undue profiteering; requires significant consumer education • Global rollout expected to reach large share of endemic countries in 3 to 5 years, reducing opportunities and incentives for arbitrage
Drug Resistance	• Failure to effectively replace monotherapies and substandard drugs	• Communication and consultation with endemic countries to facilitate responsible introduction of AMFm • Support for appropriate policy change (e.g. illegalizing marketing and/or sale of monotherapies) • Support for national quality-preparedness measures (e.g. through resistance monitoring and quality surveillance) • Education, branding, and social marketing of co-paid ACTs to demonstrate their superiority to consumers and providers
Patient Safety	• Unexpected rare adverse events	• Support for national quality-preparedness measures (e.g. through pharmacovigilance)
Product Innovation	• Failure to maintain innovation in the market for antimalarial treatment	• Eligibility criteria enabling AMFm to support all effective WHO-recommended antimalarial treatment combinations—not just ACTs (thus enabling new, innovative combinations to benefit from the buyer co-payment)
Funding	• Insufficient funding available, or funding is solely for the short term	• Multi-stakeholder engagement in AMFm design and advocacy (as has occurred throughout the AMFm design process) • Options for partial or limited-scope rollout of the AMFm (see Section 7.3)
Implementation	• Failure to implement supporting interventions	• Formalize partner commitments to supporting interventions critical to AMFm success, with particular attention to programs that support the most vulnerable (in rural areas), through home- and community-based care and public-education campaigns • Funding of supporting interventions included in AMFm funding requirements, preventing unfunded mandates • M&E systems developed in advance of launch (see Section 7.5) • Country-preparedness requirements • Operational research (see Section 7.6)
	• Project management mission creep	• Highly targeted mandate and secretariat functions • Outsourcing/partnering for non-core activities
	• Perceived conflict of interest for managing organization (if the same institution were to take on the role of both manager and ACT buyer)	• Full separation of operations/transactions will be required if the same institution were to act as both manager and buyer
	• Accreditation of pooled procurement buyers (e.g. UNICEF) may be difficult if done on a country-by-country basis • Local manufacturers do not reach required quality levels	• Mechanism will be needed to guarantee access by pooled procurement buyers (such as UNICEF) to the AMFm • Early involvement of local ACT manufacturers in implementation phase to share information and create certainty for manufacturers • Targeted technical assistance to help manufacturers prepare quality approval dossiers
Buyer purchase behavior	• Lack of transparency in establishing buyer eligibility	• Transparency, including the required public availability of the list of accredited buyers (via the AMFm Web site) • Close monitoring by partners for any signs of corruption • Ministry of health certification of accredited ACT buyers
	• Buyer hoarding and profiteering	• Use of maximum retail price mechanisms to reduce undue profiteering
	• Buyer collusion: some local buyers purchase full country target and keep out other buyers	• Monitoring of ordering patterns to detect signs of collusion (manufacturer responsibility in the long-term agreement) • Upper limits on ordering

Figure 28: Market Positioning of ACTs—Current and Post-AMFm Introduction

Current Positioning of ACTs	Anticipated Positioning of ACTs with a Buyer Co-payment
• Highly regulated donor-funded market with largest volumes distributed through public-sector channels • Two-tiered pricing structure with low- or zero-margin price for public and nonprofit buyers • ACTs are branded as "premium products" in private-sector channels and targeted to relatively high-income populations, typically in registered pharmacies in cities.	• Low margin price for public and nonprofit buyers extended to low-cost purchases via the AMFm for the private sector • Branded "premium product" will continue to be distributed in registered pharmacies in parallel to low-cost alternatives (with distinct packaging) • Market dynamics will over time determine demand levels for premium ACTs and low-cost alternatives.

funding requirements will be driven by consumer demand and thus susceptible to unexpected variations in any given year. While the projected annual funding requirements for the AMFm are based on well-informed demand forecasts, the market will always contain a degree of uncertainty. If the consumer response is less than the funding committed, the AMFm will have an excess of funds. If this occurs, it will be recommended that the funds be held for subsequent years when consumer demand has grown.

If consumer response is greater than the donor funds available, there will be insufficient funds to support all purchases at least for a short period of time. During implementation, a plan to create a credit line or financial guarantee mechanism backed by future funding commitments, or to implement a system to prioritize fund use, will be recommended. It is also important to recognize that insufficient funds will also be a sign of success: It will mean that drugs are reaching patients at a sufficiently low price to stimulate demand. In this case, donors may be interested in increasing financial support.

7.4 Over-the-counter (OTC) status of antimalarials

A primary goal of the AMFm is to replace monotherapies, including alternatives such as CQ and SP, with safe and effective combination therapies. CQ is widely distributed to consumers beyond the reach of clinics and registered pharmacies. While SP still has prescription-only status in many countries, it is also widely distributed, and its wide distribution is tolerated. ACTs, however, are distributed in a much more limited way due to their high price and prescription-only status in almost all endemic countries.

ACTs are not currently recommended for use by pregnant women due to safety concerns. To date, pharmacovigilance studies and safety databases relating to ACTs do not have the reach and controlled management to provide for a rigorous testing of these concerns. As a result, only a few countries have granted OTC status to ACTs.

In the course of implementation planning, it will be necessary to consider the impact of possible OTC status on patient demand and to identify approaches to the distribution of ACTs that facilitate broader use while taking fully into account safety concerns. Country differences in OTC status, such as that between Nigeria and its neighbors, could also promote cross-border arbitrage of low-cost ACTs, suggesting that harmo-nized policies on OTC status may be beneficial to responsible rollout of low-cost ACTs.

7.5 Monitoring and evaluation

A large component of the AMFm's risk-mitigation strategy will be achieved through rigorous monitoring and evaluation (M&E) for the life of the mechanism, underpinned by operational research during the implementation phase.

M&E will be essential to (1) demonstrate progress toward the AMFm goals of reducing mortality and morbidity and of delaying resistance, (2) adjust the AMFm design as needed to fit various endemic countries, (3) guide the use of supporting interventions, and (4) plan an exit strategy.

Management of the AMFm will be guided by the following M&E principles:

- Routine monitoring of whether the facility is achieving its goal in endemic countries.
- Integration, where possible, into existing tools and activities to obtain the necessary information, minimizing the burden on endemic countries and existing investments in M&E.
- Collation, analysis, and feedback of data to all operational levels, including stakeholders in endemic countries and the international malaria community.

The M&E activities will measure the success of the AMFm at country and international levels. At the country level, M&E instruments will be focused on measuring availability and affordability of ACTs, and measuring the crowding-out of monotherapies from the market.

At the international level, M&E instruments will monitor flows, volumes, and prices of ACTs along the supply chain. The outputs and regular reporting of M&E activities will feed into AMFm management decision-making and inform any policy or operational adjustments to the co-payment mechanism as in-country or international market conditions change.

The M&E framework contains 10 core indicators and 10 supplementary indicators. Of the 10 core indicators, 4 measure the cost to patients and markups in the supply chain; 4 measure the accessibility of ACTs to patients; and 2 measure the use and cost of monotherapies. Supplementary indicators provide additional information in the area of supply-

chain markups, adherence to treatment courses, quality of dispensing, and quality of medicines available. Detail on the indicator set, its integration into existing M&E mechanisms, and specifications can be found in Background Paper 3.

The M&E framework has been developed through a two-stage process: in July 2007, an M&E concept note was shared widely among M&E experts for feedback and comments. DfID, WHO, and the RBM Monitoring and Evaluation Reference Group (MERG), among others, commented on the concept note, as have a number of experts from other organizations, including Médecins Sans Frontières (MSF), the London School of Hygiene and Tropical Medicine (LSHTM), and the Malaria Control and Evaluation Partnership in Africa (MACEPA). In the second stage, the full M&E framework was developed in collaboration with LSHTM and other M&E stakeholders. A wide range of malaria M&E experts have been invited to comment on its design.

7.6 Operational research

While M&E activities will measure the success of the AMFm and provide data for AMFm management decisions, operational research (OR) activities will focus on mitigating the identified risks of the AMFm introduction and on evaluating the effectiveness of in-country supporting interventions. OR activities will be concentrated in four to six sentinel countries and will be limited in duration. These sentinel countries will be chosen to provide a representative set of information from the OR phase. For example, criteria for selecting sentinel countries may include the level of country preparedness, geographic location, antimalarial market characteristics, and malaria burden. During this phase, two types of activities will be conducted:

First, in-country M&E indicators will be collected with higher frequency to mitigate potential risks of introduction and to assess the success of the AMFm introduction. To col-

lect these indicators, dedicated surveys that go beyond the standard set of M&E indicators will be implemented in sentinel countries, if necessary. This M&E method will be similar to that of the Clinton Foundation project in Tanzania, where uptake and price data have been collected monthly during the first quarter of implementation and quarterly thereafter.

Second, OR activities will determine the impact of supporting interventions in the countries under study. As laid out in Section 5.3 on supporting interventions, these will vary from country to country based on the characteristics of each country and their corresponding needs. The corresponding OR activities will be structured around the nature of the interventions under review.

A key aspect of OR will be to provide information on lessons learned to other endemic countries and to the international community. This information will help in-country decision makers choose the most appropriate strategies for rolling out and scaling up the availability of low-cost ACTs. To facilitate this communication, OR reports will be disseminated among in-country partners, with workshops as needed.

Accelerated M&E activities may be implemented by local consultants or country representatives of AMFm partner organizations, or through specialized projects such as the Gates Foundation's Antimalarial Market Research Study project,[125] depending on the specific situation in each country. To evaluate the effectiveness of supporting interventions, endemic-country governments will be enlisted to guide and approve OR activities, while in-country donors and technical subcontractors will be needed to support implementation. The proposed approach to OR is discussed in more detail in Background Paper 3.

CHAI is currently supporting low-cost ACT distribution in Tanzania. These results will inform the implementation planning and launch of the AMFm. The case study presented in Figure 29 outlines the approach being taken by CHAI in Tanzania.[126]

Figure 29: Indicators Case Study: Clinton Foundation Operational Research in Tanzania

The Clinton Foundation has recognized that key technical partners and funding agencies often raise two critical questions about the impact of a global buyer co-payment for ACT purchases: 1) whether a first-line buyer co-payment will be passed through the supply chain to benefit patients at the point of purchase, and 2) what kinds of interventions must accompany the introduction of a facility for affordable malaria medicines to ensure the quality and affordability of treatment?

To answer these questions and inform the design and implementation of a global buyer co-payment mechanism, the Clinton Foundation has launched a pilot subsidy project that is expected to significantly increase ACT access in targeted areas in Tanzania. Minister of Health David Mwakyusa expressed interest in such a pilot project, and the project plan was created in collaboration with key partners in Tanzania, including the Tanzanian Food and Drug Authority and the National Malaria Control Program.

Recommended first-line ACTs (AR+LU) are being procured by the Clinton Foundation and distributed to a single designated wholesaler in Dar-es-Salaam, the capital, at low cost. The objective of such a pilot is to replicate an unregulated supply chain as much as possible, and the Clinton Foundation has avoided unnecessary intervention in the distribution of drugs, instead observing wholesalers, regional distributors, and semiformal drug shops (*duka la dawa baridis*) conducting business as usual. Because the wholesaler used by CHAI uses multiple models for distributing to district retailers, the pilot results will enable an initial analysis of differences in price and other key outcomes, according to the distribution model chosen.

In addition, the project is being implemented in two Tanzanian districts (Kongwa and Maswa) to enable several key interventions to be assessed. In both districts, publicly focused information and awareness campaigns will accompany the distribution of low-cost medicines. In one district, however, drugs will be repackaged with suggested retail prices accompanied by social-marketing interventions to inform patients of suggested retail pricing, while in the other district, drugs will be sold in their original packaging. The district of Shinayanga Rural will serve as a control. Accordingly, it will not receive low-cost medicines, but retail prices of ACTs and other antimalarials will be monitored frequently.

The Clinton Foundation recognizes the importance of extensive monitoring and evaluation of pilot results "to best inform the global and national decision makers." The key metrics that are being measured include: 1) the actual price paid by patients for low-cost ACTs distributed, 2) the extent to which ACT sales increase in the area, and 3) associated factors such as patients' socioeconomic status and perceptions of ACTs. A variety of data-collection methods, including patient exit-interviews, "mystery shoppers,"[127] and retail audits, have already been used to gather baseline data along these metrics. Such activities will be conducted four times during the year-long pilot project.

8. Financial Requirements

Section summary

This section describes the funding required to implement the AMFm, estimated at between USD 1,400 million and USD 1,944 million over the first five years of operation. It then describes the components of AMFm costs: ACT treatment and international distribution represent the bulk of the funds, with additional funding required for targeted in-country supporting interventions and for management and organizational expenses. Finally, opportunities to leverage and reprogram existing funds for supporting interventions—representing up to half of the total funding required for such interventions—are discussed.

The estimated funding requirements for the AMFm can be grouped into three cost components, namely:

1. **ACT treatment and international distribution costs**
2. **Management and organizational costs** related to AMFm operation
3. **Targeted supporting interventions** to address local ACT supply-chain risks and requirements.

It is essential to note that figures provided in this document for each cost component are estimates. Since the AMFm is a market-based intervention, ultimate funding requirements will be driven largely by consumer demand. Thus, while the projected funding required for the AMFm is based on well-informed demand forecasts, the ultimate response of the market must be characterized by an element of uncertainty. Ongoing funding requirements will be further refined based on the outcomes of additional field research to be conducted before the AMFm is launched and as part of the operational research to be conducted during its implementation.

Current projections place the total cost of the co-payment for ACT purchases and international distribution at between USD 1,145 million and USD 1,582 million over the first five years. For the same time period, USD 25–30 million will be required to cover organizational and management costs of the facility, and an additional USD 230–332 million will be required to cover the core package of supporting interventions.

The annual costs are projected to increase from a low of USD 263–346 million in Year One to a peak of USD 289–405 million in Year Four before beginning to decline (Figure 30). The projected decline in annual costs from Year Four onward is attributed to a combination of factors, including a projected decrease in the cost of treatments, a shift in product mix, and a reduced need for many supporting interventions, particularly those directly linked to the launch and start-up period. Figure 30 details each of these costs over the five year period.

The estimates for each cost component depend on a number of inputs and assumptions that are summarized in subsequent sections and in Background Paper 5.

One critical assumption underlying the funding estimates is the rate of ACT uptake and resulting market penetration that can be expected following the introduction of the AMFm. Modeling of the demand curve for ACT treatments[128] suggests that market penetration of ACTs is likely to range between 47% and 73% of the total market for antimalarials once the AMFm is fully operational. Base case scenarios have been based on a mid-point between these values, which is 65%. However, recognizing that there is uncertainty around this assumption, the potential impact of high or low market-penetration scenarios is addressed in Background Paper 8.

8.1.1 ACT treatment and international distribution costs are estimated at USD 1,145–1,582 million during the first five years

The ACT first-line buyer co-payment and international distribution costs constitute the largest cost category for the AMFm. The combined cost of these two categories has been estimated at USD 1,145–1,582 million during the first five years of operations.

Beyond Year Five, cost projections anticipate a steady decline in the annual cost of the direct buyer co-payments as ACT volumes approach a steady state. This decline in costs would be driven primarily by:

1. Reduction in manufacturer sales prices (MSPs) for ACT treatments as a result of production efficiencies, product innovation, and increased competition, and
2. Reduction in ACT international distribution costs as a result of the switch from air freight to sea freight for a growing proportion of the treatments, and of scale economies from larger shipments.

Additional information on the assumptions associated with the first-line buyer co-payment and international distribution funding requirements can be found in Background Paper 8.

8.1.2 Management and organizational costs are estimated at USD 25–30 million over the first five years.

Successful implementation of the AMFm and its key supporting interventions will greatly depend on its having a flexible and responsive management and administrative

Figure 30: Estimated AMFm Funding Requirements (Years One to Five)

Facility Funding Requirements (USD million)

Base Case

| USD264M | USD287M | USD282M | USD289M | USD274M |

High Case

| USD347M | USD397M | USD398M | USD406M | USD387M |

■ Medicines and International Distribution   ■ Supporting Interventions   ■ Organizational Costs
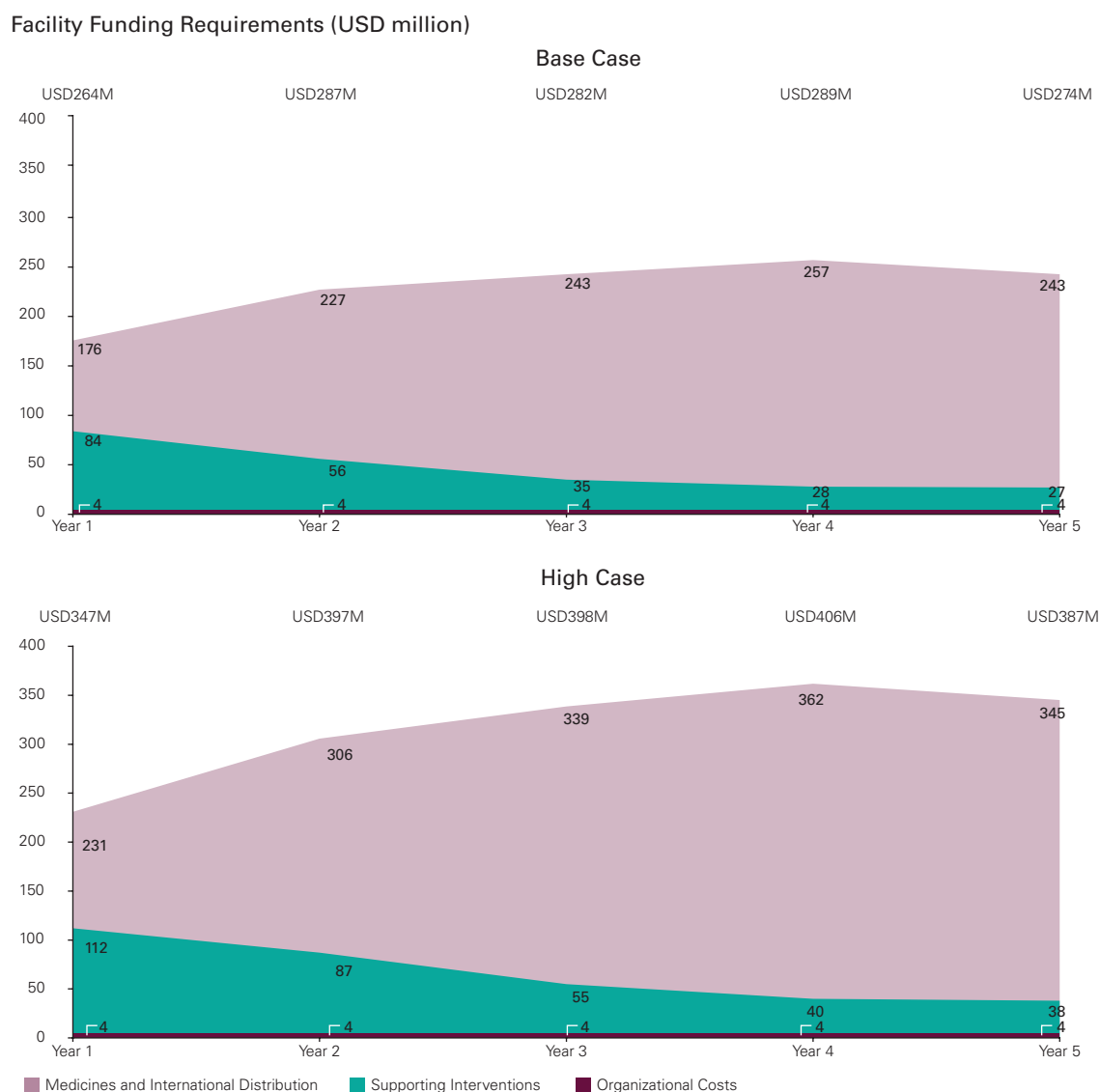
structure. As outlined in Section 6.1, a lean secretariat is recommended—one that is managed by an existing institution and that outsources core processes where appropriate. Depending on the management arrangement, it is estimated that operating cost (based on 15 to 22 full-time staff members) will require an annual budget of USD 5–6 million or a total of USD 25–30 million over the first five years of operations. This funding level is anticipated to remain steady over the first five years of the AMFm but may need to be revisited as it enters a steady state. These estimates will be refined during the implementation phase.

8.1.3 Supporting-intervention costs are estimated at USD 230–332 million over the first five years.

As discussed previously, based on stakeholder input and an assessment of ACT supply-chain requirements, a core package of in-country interventions has been established. The package is composed only of those interventions most crucially linked to achievement of AMFm objectives. The cost of this package is estimated at between USD 230 million and USD 332 million over five years. Costs are expected to be higher at the beginning of operations—between USD 84 million and USD 112 million in Year One, declining to a steady-state cost of between USD 19 million and USD 26 million by Year Five.

This recommended package has been met with broad agreement from stakeholders and in many cases reflects activities that are already taking place. The costing estimates in this technical design document aim to take into account pre-existing spending on similar activities that can be reoriented in line with the AMFm. However, it is likely that still more of these estimated costs will be offset by reprogramming a portion of donor funds previously spent on ACT purchases that could potentially become available as a result of the facility's effect on drug prices.

Additional information on the assumptions associated with supporting-intervention funding requirements can be found in Background Paper 8.

8.1.4 Existing grant funding and incremental AMFm funding requirements

Both the demand and supply of ACTs have risen sharply since 2001, when the WHO recommended the use of artemisinin-based products as first-line treatments for malaria.[129] Public-sector ACT sales increased from ~200,000 in 2001 to ~90 million treatments in 2006, and account for the vast majority of the global ACT market (90–95%).

In 2007, it is expected that the major public-sector buyers of ACT treatments will spend a total of USD 90 million for roughly 90 million treatments (at an average price of USD 1). PMI is estimated to spend USD 19 million, GFATM to spend USD 50 million, the World Bank to spend USD 10 million, and other public-sector buyers (such as governments) to spend approximately USD 11 million.

In 2008 alone, the reduction of ACT prices to 0.05 for first-line buyers has the potential to lower total public spending on ACTs from USD 108 million to USD ~11 million, if grantees purchased all ACTs with the AMFm co-payment. This change would free USD ~97 million for reprogramming for other malaria-related uses.

It is expected that, in Year One of AMFm operations, PMI will choose not to purchase medicines through the AMFm, maintaining its USD 40 million procurement at current prices. The remaining USD 68 million of global donor funding budgeted for ACTs in 2008 would be reduced to USD 7 million, freeing USD 61 million for reprogramming for the associated supporting interventions. In this case, the AMFm would require a total of USD 156 million in Year One, compared with the USD 264 million outlined in Section 8.1. This scenario, illustrated in Figure 32, would require agreement with the largest funders as well as with grantees, in terms of rules, amounts, programming, and management of funds.

Figure 31: Estimated Costs for Supporting Interventions

In-Country Supporting Intervention	Total Cost over First Five Years (Base Case, USD millions)
National policy and regulatory preparedness	16
Wholesaler incentives and price/margin-control mechanisms	15[130]
Public education and awareness (IEC)	68
Provider training	45
National monitoring and quality-system preparedness (resistance monitoring, pharmacovigilance, and quality surveillance)	50
Monitoring and evaluation	36
TOTAL	230

The reprogramming of public-sector funds is one option for funding supporting interventions. Other options include direct contributions from AMFm donors to the core interventions or contributions from other partners to country-specific interventions or to a central fund. Each of these options will be explored in more detail in discussions with potential donors and with the major grant-making institutions during the process of establishing the funding arrangements for the AMFm.

8.2 Exit strategy and sustainable financing

Although the funding analysis in this document focuses on the first five years of operations, it is expected that the AMFm will require sustainable long-term financing.
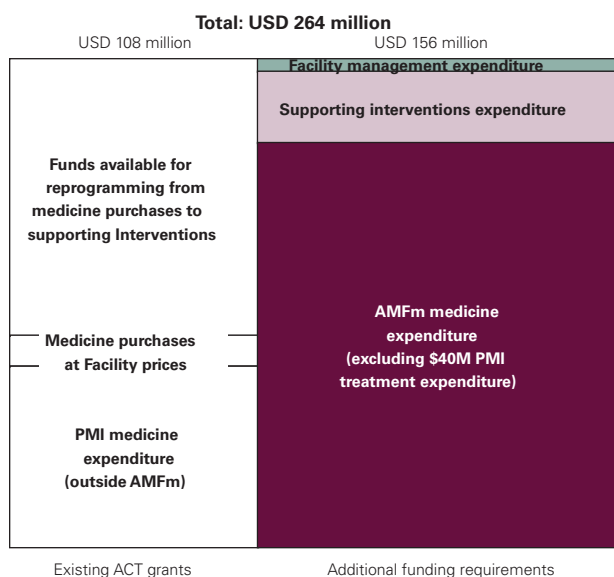
8.2.1 Cost reductions due to market innovation

Breakthroughs in the manufacture of ACTs could precipitate significant reductions in the financing requirements for the AMFm. One such breakthrough could arise from drastically lower costs of active pharmaceutical ingredients (APIs). A widely anticipated breakthrough would be the development of synthetic or semi-synthetic artemisinin compounds. The production of these APIs would be significantly less labor-intensive, and the market for them subject to less cyclicality than the current market for agriculturally derived artemisinin APIs. The first ACT containing a semi-synthetic artemisinin compound is expected to be launched in 2010.[131] However, there are several questions that must be resolved, including the selection of a commercial manufacturing partner, commencement of technology transfer and scale-up, and completion of the Drug Master File (DMF) or equivalent. The first fully synthetic artemisinin molecule is not expected until 2013. Because a fully synthetic molecule will be considered a new chemical entity (NCE), it will require all of the safety, toxicology and clinical trials that go along with full regulatory approval.

The effectiveness of the AMFm will depend on whether it can make ACT prices competitive with those of the full range of monotherapies such as CQ and SP. Because the high cost of ACTs is driven by a number of factors beyond manufacturing cost, such as the need for international shipping, more expensive packaging, and more restricted distribution, market innovation is not likely fully to remove the need for this facility in the short to medium term. However, continued innovation could significantly reduce the financing requirements for the AMFm over time.

8.2.2 External factors that could affect exit strategy

Other events that could impact the financing requirements for the AMFm, without eliminating it entirely, include the successful scale-up of current technologies for the prevention of malaria (such as long-lasting insecticide-treated bed

Figure 32: AMFm First Year Funding Requirements in Addition to Existing Grant Funding

Total: USD 264 million

USD 108 million USD 156 million

Facility management expenditure

Supporting interventions expenditure

Funds available for reprogramming from medicine purchases to supporting Interventions

AMFm medicine expenditure (excluding $40M PMI treatment expenditure)

Medicine purchases at Facility prices

PMI medicine expenditure (outside AMFm)

Existing ACT grants Additional funding requirements

nets and indoor residual spraying, where appropriate) and the successful development and introduction of a malaria vaccine.

Emergence of resistance to specific ACT combinations or artemisinin more generally would present the need to refocus the AMFm on distributing the remaining effective drug classes. Preliminary results of two recent *in vivo* studies have shown increased treatment failures with ACTs along the Thai-Cambodian border.[132] These treatment failures cannot be unambiguously attributed to artemisinin resistance and could stem from a number of causes including the failure of the partner drug, inadequate dosing, or inaccurate measurement of clinical failure. If the treatment failure in Cambodia were indeed the consequence of a failed partner drug, the AMFm would provide an effective solution in that it will introduce multiple ACTs with various partner drugs. Indeed, Cambodia is currently planning to change its first-line treatment guidelines in favor of an ACT with a different partner drug. If the treatment failure were the result of growing resistance to artemisinin due to the continued use of AMTs, a fast-tracked

AMFm could indeed be one solution, helping to contain the spread of resistance to artemisinin as well as to partner drugs.

8.2.3 End clauses and sustainable long-term financing

Explicit end clauses defined before the launch of a major mechanism in the global health field are the exception rather than the rule. Most funding facilities have no explicit sunset clause, as illustrated in Figure 33.[133]

Although most funding facilities have no explicit time limitations, there are examples of facilities that have taken steps to improve the sustainability of long-term financing. GAVI is one such case (see Figure 34), which provides insight into ways in which the funding mechanism may be strategically adjusted over time to gradually transfer responsibility toward endemic-country governments as treatment prices become more affordable.

Over time, the AMFm could evaluate similar arrangements for adjusting funding levels based on per capita income and consider taking other steps to improve sustainability of long-term financing. Termination of the AMFm could be triggered by distinct events, for example the manufacturer sales prices of effective antimalarials falling and remaining below the average daily per capita income in most (e.g. >80%) countries, artemisinin monotherapy being banned in most countries, or resistance having developed against the remaining effective antimalarials. The use of clear criteria will create certainty for manufacturers entering the market that the AMFm will be sustainable and that termination would be contingent on a fact-based assessment of market conditions.

Figure 33: Limitation Clauses in Existing Global Health Initiatives

Funding Agency	Sunset Clauses or Time Limitations
GFATM	"The foundation shall remain in operation indefinitely"
GDF	Facility is expected to operate at least for 10 to 15 years with no clear time-limitation
UNITAID	No clear time limitation
GAVI	Second phase of the facility ends in 2015, although continuation is possible

Figure 34: Case Study: GAVI's Strategy for Sustainability

Exit Strategy Case Study: GAVI[134]

At GAVI, support provided to countries is determined by the level of country need: Countries with lower immunization rates and higher numbers of non-immunized children receive higher levels of support. During the first phase of GAVI financing, all vaccines were provided on a grant basis as part of an attempt to stimulate manufacturer investments that would reduce the cost of production, accelerate competition, and drive prices down. A co-financing strategy was introduced in 2006 as an adjustment mechanism to require countries to pay part of the cost of vaccines purchased.

The contribution of countries is determined by allocation to groups based on national income:

1. Highest income group of GAVI countries, [those with a 2005 gross national income (GNI)/capita over USD 1,000] will be required to co-finance a gradually increasing portion toward a target between USD 0.7 and USD 0.95 by 2010 (to be determined following consultations).
2. Poorest group of GAVI countries (those classified by the United Nations as "least developed countries,"[135] or LDCs) will be asked to contribute a fixed amount of between USD 0.1 and USD 0.25 per dose (to be determined following consultations). This amount would increase after 2010.
3. GAVI countries falling below the USD 1,000 GNI/capita cutoff, but not classified as LDCs, will be asked to contribute a fixed amount between USD 0.2 and USD 0.5 (to be determined following consultations). This amount would be increased after 2010.
4. Countries facing difficult circumstances ("fragile"/post-conflict states) will be exempted from co-payment. A clear set of criteria is proposed to identify such countries.

9. Timeline and Next Steps

Section summary

This section outlines the high-level timeline for implementation of the AMFm and the key issues driving the implementation work plan. The RBM Board will be asked to endorse the announcement of the AMFm at its meeting in November 2007. Following this announcement, five key challenges must be addressed before the launch of the AMFm, targeted between July and September 2008.

9.1 Endorsement and Announcement of the AMFm

The Roll Back Malaria Partnership Board endorsed the objectives of the AMFm in May 2007 and agreed to a set of design principles for its implementation. Over the following months, the AMFm Task Force served as the RBM mechanism guiding the finalization of this technical design, engaging other RBM working groups as necessary, including: the Monitoring and Evaluation Reference Group, the Harmonization Working Group, the Procurement and Supply Chain Management Working Group, and the Malaria Advocacy Working Group.

Following the anticipated announcement of the AMFm at the RBM Partnership Board meeting at the end of November, the focus of work will be on implementation planning to take the AMFm from announcement to launch.

9.2 Activity plan from announcement to launch of the AMFm

A significant work program must be carried out between the announcement of the AMFm and the operational launch. The announcement is targeted for the period of July to September 2008.

The work program will focus on five key challenges that must be addressed to ensure a successful launch of the AMFm:

Figure 35: Key Challenges in Implementation of the Work Program

Implementation Challenge	Key Activities
1. Ensure quality assurance, pharmacovigilance, and strengthening of national regulatory authorities	• Provide guidance on treatment guidelines and regulatory alignment in preparation for the launch • Harmonize quality-assurance policies • Put in place prerequisite pharmacovigilance activities
2. Ensure management/ coordination of in-country supporting interventions, particularly around patient information, education, retail price setting, communication, and country-level monitoring	• Support countries in conducting needs assessments and prepare plans for AMFm-related supporting interventions • Coordinate short- and medium-term financing frameworks for supporting interventions at the country level, including reprogramming of existing plans and new grants • Provide training and technical assistance to prepare implementation of the AMFm • Execute communication strategy in preparation of AMFm launch
3. Identify an appropriate organization to manage the AMFm	• Reach agreement on organization with comparative advantages to take on management of core functions of AMFm • Obtain approvals required for this organization to accept the task of managing the AMFm • Complete prerequisite operational steps to launch the AMFm
4. Negotiate co-payment levels with manufacturers and monitoring of in-country supply chains	• Prepare framework for negotiation with manufacturers • Consult with manufacturers on operational aspects of AMFm-related agreements, including packaging, terms of purchase, communications, provider training • Monitor supply-chain dynamics for global and local antimalarial markets, including up-to-date demand forecasting • Negotiate agreements with manufacturers
5. Secure additional resources	• Sustain dialogue with interested donors • Establish financing framework for AMFm funding requirements • Reach medium- to long-term donor commitments

10. Conclusion

The call for a global buyer co-payment for artemisinin-combination therapies first issued by the Institute of Medicine three years ago remains urgent. Commonly used antimalarials are failing, and the rising use of artemisinin-based monotherapies threatens the efficacy of these more expensive combination therapies. Unacceptably, while life-saving antimalarials exist, they remain too costly for most patients in the malaria-endemic developing world to afford.

The global health community has explicitly recognized the need for an intervention to increase equitable access to low-cost ACTs. Grants from The Global Fund to Fight AIDS, Tuberculosis and Malaria, donor government programs, and endemic-country government funds currently support public-health systems in this ongoing switch to ACTs. Significant progress has been made in the delivery of these essential medicines via the public sector, yet these efforts reach only a minority of patients. The proposed AMFm seeks not to displace current efforts to scale up public-sector delivery of ACTs, but rather to support continued progress in public-sector ACT delivery and build on this success by achieving similar access in the private sector, where the majority of patients seek treatment.

To save lives and delay resistance to ACTs, not only must ACTs continue to be accessible in public channels, but access to low-cost ACTs must be extended to the private sector. The analyses summarized in this document reaffirm the AMFm's rationale and its feasibility.

10.1 Detailed design and responsible introduction

The recommended AMFm technical design is the result of extensive consultations with partners from all RBM constituencies. The AMFm is designed to be an innovative, demand-driven intervention to expand access to essential medicines and to complement existing health systems and global malaria-control strategies. A core feature of the design is reliance of the AMFm on existing delivery channels and the availability of low-cost to national malaria-control programs, public clinics, mission hospitals, community health workers, home-based management of malaria programs, NGOs, and pharmacists alike.

Implementing the AMFm will demand knowledge of global and national pharmaceutical markets. The technical design takes into account the complex dynamics of the ACT supply chain, as demonstrated by its insistence on standards, transparency

mechanisms, incentives, and the in-country supporting-intervention package. It emphasizes the importance of supporting interventions in ensuring proper ACT use, and recognizes that country infrastructure and resources already exist. Finally, monitoring and evaluation and operational research functions are built into the design and implementation strategies. This will allow the AMFm to make design adjustments during implementation and ensure a transparent process.

10.2 High impact and cost-effectiveness

The AMFm is part of a broader portfolio of interventions for effective malaria prevention, diagnosis, and treatment. As one tool in the fight against malaria, it will address one barrier to ACT access—price—so as to make ACTs more affordable and available. In lowering ACT prices to a level below artemisinin-based and partner drug monotherapies, the AMFm will strengthen national malaria-control programs not only by increasing access to affordable, effective medicines but by allowing ACTs to supplant resistance-promoting monotherapies. Paired with supporting interventions, ACT penetration is projected to increase from 20% to more than 65% of the total treatment market. The impact of such an increase is significant: up to 300,000 lives can saved per year at a cost-effectiveness rate of USD 980 to 1700 per life.

10.3 Estimated resource requirements and potential exit strategies

Funding requirements for the AMFm, including the core package of supporting interventions, are estimated at USD 1,400 to USD 1,944 billion over five years. ACT treatment and international distribution costs represent the bulk of these costs. Although the funding estimate is limited to a five-year period, the AMFm is expected to continue beyond 5 years, barring a breakthrough that renders ACTs cost-competitive with the lowest cost monotherapies.

There is no time to waste. Lives are being lost as patients attempt to access effective and affordable lifesaving malaria medicines but cannot find them where and when they need them—or cannot afford them even if these treatments are available. The growing use of monotherapies poses a real and immediate risk to the most effective antimalarial treatments (i.e., ACTs) on the market. It is now essential to mobilize the political support and financial commitments necessary to move from concerns about malaria to actions on malaria that make a difference to the lives of so many.

11. Appendix

11.1 List of stakeholders consulted

Global Stakeholders:		Endemic-Country Stakeholders/Groups:	
Yann Derriennic	Abt Associates	**Burkina Faso**	
Janhavi Bonneville	Accenture	Mahamadou Compaore	DGPML (Direction for Pharmaceuticals, Medicines, and Laboratory Supplies), Directeur General
Khalil Elouardighi	Act Up-Paris		
Jean-Marie Kindermans	AEDES		
Richard Tren	Africa Fighting Malaria	Pierre Crozier	AfD DGPML, Technical Advisor
Susan Dykes	All Party Parliamentary Malaria Group, UK	Zacharie Balima	PADS (Programme d'Appui au Développement Sanitaire), Coordinateur
Sylvie Chantereau	Amis du Fonds Mondial Europe		
Karen Bissell	Asthma Drug Facility		
Paulo Teixeira	Brazil, Ministry of Health	Lazare Bansse	CAMEG, Directeur General
Charles Griffin	Brookings Institute	Ida Sawadogo	CAMEG, Directeur d'Achats /Logistique
Ruth Levine	CGD	A. Salam Kappar	Ordre des Pharmaciens
Raphael Okalla	Cameroon, National Malaria Control Program	Alfred Sandouidi	Ordre des Pharmaciens, Secretary General
Anil Soni	CHAI	Victoire Benao	L'Ordre National des Pharmaciens du Burkina Faso; Pharmacie de l'Avenir, President Pharmacist
Inder Singh	CHAI		
Kanika Bahl	CHAI		
Oliver Sabot	CHAI	Amidou Kabore	Distribution pharmaceutique du Burkina Faso SA, Directeur General
Lorrayne Ward	CHAI		
Pascal Bijleveld	CHAI	Malick A. Ba	Laborex, Directeur Commercial
Ernest Loevinsohn	CIDA	Stephane Francisco	Cophadis S.A, Directeur General
Louise Holt	CIDA	Aoua Idani	Pharmacie des Ecoles, Pharmacist
Chris Collinson	DfID	Francoise Yerbanga	Pharma Plus, Directeur General
Delna Ghandi	DfID	Ryssalatouphie Diawara	Pharmacy Diawara, Pharmacist
John Worley	DfID	Jan van der Horst	Netherlands Ministry of Foreign Affairs, Health Advisor
Michael Borowitz	DfID		
Veronica Walford	DfID Consultant	Robert Clark	PSI, Technical Advisor
Bernard Pecoul	DNDi	Thomas Zoungrana	UNFPA, NPO
Graciela Diap	DNDi		
Jean-François Alessandrini	DNDi	**Cameroon (Yaoundé)**	
Doug Koplow	Earth Track	Raphaël Okalla Abodo	PNLP (National Malaria Control Programme), Directeur
Giorgio Roscigno	FIND		
Vinand Nantulya	FIND	Alexis Tougordi	OMS, Responsable Programme Malaria
Louis-Charles Viossat	France, Ministry of Foreign Affairs		
Alexandra Melby	Bill & Melinda Gates Foundation	Felix Fotso Simo	Ministère de la Santé, Chef du service de la médecine traditionelle
Gabrielle Fitzgerald	Bill & Melinda Gates Foundation		
Girindre Beeharry	Bill & Melinda Gates Foundation	Jean-Marie Ngono	RACTAP (Réseau de surveillance des résistances du parasite au anti paludique), Administrateur
Regina Rabinovich	Bill & Melinda Gates Foundation		
Tom Kanyok	Bill & Melinda Gates Foundation		
Alice Albright	GAVI Fund	Marie Louise Ngoko	CENAME (Centrale d'Approvisionnement en Médicaments Essentiel), Responsable d'Assurance Qualité et Gestion des ARV
Andrew Jones	GAVI Fund		
Marc Hofstetter	GAVI Fund		
Robert Matiru	GDF		
George Amofa	Ghana Health Service	Ada Jeanne	Syndicat des pharmaciens, Pharmacie Theriaque
Barry Greene	GFATM		
Bartolomeo Migone	GFATM	Eric Sungu	Syndicat des pharmaciens
Christina Schrade	GFATM	Gaetan Bahiol	l'Ordre des Pharmaciens du Cameroun, Secrétaire National
Elisabetta Molari	GFATM		
Friederike Teutsch	GFATM	Sibiri Konkobo	UC Pharm, Directeur General
Helen Evans	GFATM	Yolande Tangang	Laborex
Ines Garcia-Thoumi	GFATM	Yves Dsamou	Pharmacam
Mark Grabowsky	GFATM	Stella Feka	Catholic Health Organization of Cameroon
Michel Kazatchkine	GFATM		
Nosa Orobaton	GFATM	Theresa Gruber-Tapsoba	Permanent Secretary, Association Camerounaise pour le Marketing Social
Rajat Gupta	GFATM		
Stefano Lazzari	GFATM		
Louis da Gama	Global Health Advocates	Felix Tietche	Faculté de médecine, Directeur centre Mère - enfant fond. C. Biya
Patrick Bertrand	Global Health Advocates		
Ian Boulton	GSK	Leopold Lehman	Université de Douala
Margaret Ewen	HAI		

Global Stakeholders:		Endemic-Country Stakeholders/Groups:	

Global Stakeholders:

Clarisse Morris	IDA Solutions
Henk den Besten	IDA Solutions
Erwin van Boven	Imres
Christa Hook	Independent
Evan Lee	Independent
Peter Evans	Independent
Philippe Baetz	Independent
Robert Chisholm	Independent
Ximena O'Reilly	LPK
Richard Skolnik	Population Reference Bureau
Hellen Gelband	IOM
Keith Gristock	Irish Aid
Carolyn Hart	JSI
David Sarley	JSI DELIVER
Lois Todhunter	JSI DELIVER
Miguel Jaureguizar	JSI DELIVER
Catherine Goodman	KEMRI / Wellcome Trust / Oxford University Collaboration
Anne Mills	LSHTM
Chris Whitty	LSHTM
Kara Hanson	LSHTM
Shunmay Yeung	LSHTM
Dieter Meppiel	Mepha
Laurent Lombart	Mission Pharma
May Ongola	MIT-Zaragoza
Prashant Yadav	MIT-Zaragoza
Anna Wang	MMV
Chris Hentschel	MMV
Ian Bathurst	MMV
Jaya Banerji	MMV
Penny Grewal	MMV
Renia Coghlan	MMV
Prudence Hamade	MSF
Tido von Schoen-Angerer	MSF
Tom Ellman	MSF
Unni Karunakara	MSF
Julie McFadyen	MSH
Malick Diara	MSH
Rima Shretta	MSH
Harry van Schooten	Netherlands, Ministry of Foreign Affairs
Marijke Wijnroks	Netherlands, Ministry of Foreign Affairs
Paul Richard Fife	Norway, Ministry of Foreign Affairs
Sigrun Møgedal	Norway, Ministry of Foreign Affairs
Hans Rietveld	Novartis
Heiner Grueninger	Novartis
Silvio Gabriel	Novartis
Ronald Steenblik	OECD / Global Subsidies Initiative
Bernard Baudrand	OTECI / Artepal
Jacques Pilloy	OTECI / Artepal
Mohga Kamal-Yanni	Oxfam
A. Alfidja-Cisse	Pharmacist Niger
Bernard Nahlen	PMI
Sonali Korde	PMI
Timothy Ziemer	PMI
Desmond Chavasse	PSI
Manya Andrews	PSI
Ricki Orford	PSI
Arun Purohit	Ranbaxy
Sandeep Juneja	Ranbaxy
Awa Coll-Seck	RBM Secretariat
Betty Udom	RBM Secretariat
Jan van Erps	RBM Secretariat
Prudence Smith	RBM Secretariat
Ramanan Laxminarayan	Resources for the Future
François Bompart	Sanofi-Aventis
René Cazetien	Sanofi-Aventis

Endemic-Country Stakeholders/Groups:

Kenya (Nairobi)

Stephen Kimatu	Head - Medicines Information Department, Pharmacy and Poisons Board, Ministry of Health, Kenya
Jayesh Pandit	Head - Department of Pharmacovigilance, Pharmacy and Poisons Board, Ministry of Health, Kenya
Julius Kimitei	Programme Officer, Division of Malaria Control, Ministry of Health
Joanne Greenfield	WHO Malaria Country Support, WHO
Larry Kimani	Company Pharmacist, UNGA Farm Care Limited
Wellington Muiruri	Region Head, Novartis
Vijai Maini	Managing Director, Surgipharm Ltd
Rakesh Vinayak	Sales and Marketing Director, Surgipharm Ltd
Prakash Patel	Chairman / Managing Director, Cosmos Ltd
Vimal Patel	Director, Cosmos Ltd
Rohin Vora	Regal Pharmaceuticals Ltd
Marilyn McDonough	Chief, Health Section, UNICEF Kenya
Moses Mwaniki	PSI Kenya
Manya Andrews	MCH Coordinator, PSI Kenya
Sylvia Khamati	Regional Senior Health Officer, East Africa, the Horn, Great Lakes and Indian Ocean Islands, IFRC
Raghu Krishnaswamy	Regional Pharmacist, East Africa, MSF
Patrick Mubangizi	HAI Africa
Gladys Tetteh	Senior Program Associate, Rational Pharmaceutical Management Plus, MSH
Alex Mwaura	Program Development Officer, Kenya, Samaritans
Rose Kipchumba	Samaritan's Purse
Oresmus Muinde	Assistant Country Manager, Action Against Hunger
Jeff Orero	Kergatuma
Abdinasir Amin	Malaria Public Health & Epidemiology Group, KEMRI / Wellcome Trust / Oxford University Collaboration
Tim Abuya	KEMRI / Wellcome Trust / Oxford University Collaboration

Uganda (Kampala)

Public sector group:

Henry Akpan	NMCP / FMOH Abuja
Ngemera Mwemezi	NDA Tanzania
Amos Atumanya	NDA Uganda

Private sector group:

John Kerry	Sky Pharmaceuticals, Zambia
Kinny Nayer	Surgipharm, Uganda
Obiyo Nwaiwu	Novartis Pharma, Nigeria

Groups (in addition to the RBM Task Force)

African Union Health Ministers' Conference (Johannesburg 10-13 April 2007)

All Party Parliamentary Malaria Group (London 18 July 2007)

MMV Access and Delivery Advisory Committee (Amsterdam 6 March 2007)

Kenya, Cameroon and Burkina Faso consultations (April 2007)

MMV Stakeholder Meeting (Kampala 9 May 2007)

RBM Board Meeting (Geneva 10-11 May 2007)

Global Stakeholders:		Endemic-Country Stakeholders/Groups:
Robert Sebbag	Sanofi-Aventis	RBM Finance and Resources Working Group (Amsterdam 18-19 January)
Brian Fahey	Save the Children UK	
Jeff Mecaskey	Save the Children UK	RESULTS Annual Conference (Washington 10 June 2007)
Maggie Huff-Rousselle	Social Sectors Development Strategies, Inc	
Aloka Sengupta	Strides-Arco	RBM Harmonization Working Group (Geneva 10 September 2007)
David Mwakyusa	Tanzania, Minister of Health	
Renata Mandike	Tanzania, National Malaria Control Program Manager	Global Fund Policy and Strategy Committee (Geneva 19-21 September 2007)
Franco Pagnoni	TDR	
Jane Kayondo	TDR	Uganda MoH-MMV Workshop on Improving access to ACTs (Kampala 26 September – 2 October 2007)
Piero Olliaro	TDR	
Melanie Renshaw	UNICEF	
Stephen Jarrett	UNICEF	All Party Parliamentary Malaria Group (London 9 October 2007)
Alan Court	UNICEF	
Angus Spiers	UNICEF	RBM Procurement and Supply Chain Management Working Group (Washington 11 October 2007)
Kevin Starace	UN Foundation	
Mark Amexo	UNITAID	
Jorge Bermudez	UNITAID	
Philippe Duneton	UNITAID	
Benny Moldovanu	University of Bonn	
Michael Thiede	University of Cape Town	
Achim Wambach	University of Cologne	
Nicholas White	University of Oxford	
Richard Peto	University of Oxford	
Kim Sweeny	University of Melbourne	
Carolin Samouel	World Economic Forum	
Anarfi Asamoa-Baah	WHO	
Andrea Bosman	WHO	
Arata Kochi	WHO	
Hiroki Nakatani	WHO	
Howard Zucker	WHO	
Kamini Mendis	WHO	
Marthe Everard	WHO	
Maryse Dugue	WHO	
Matthias Staul	WHO	
Paul Lalvani	WHO Consultant	
Richard Laing	WHO	
Sergio Spinaci	WHO	
Aizhan Imasheva	World Bank	
Andreas Seiter	World Bank	
Joy Phumaphi	World Bank	
Olusoji Adeyi	World Bank	
A.-M. Pierre-Louis	World Bank	
John Paul Clark	World Bank	
Suprotik Basu	World Bank	
Malama Muleba	Zambia Malaria Foundation	

11.2 Background Papers

Background Papers are available, upon request, from Charlotte Heime (charlotte.heime@dalberg.com):

Background Paper 1: Stakeholders Consulted
Background Paper 2: Management Terms of Reference
Background Paper 3: Monitoring & Evaluation and Operational Research
Background Paper 4: Subsidy Case Studies
Background Paper 5: Supply Chain Analysis
Background Paper 6: Operational Framework
Background Paper 7: Summary of Field Research

Background Paper 8: Methodology: Market Dynamics and Funding Scenarios
Background Paper 9: Yadav and Ongola – 'Analysis of Complementary Supply Chain Interventions' and 'Estimating Private-Sector Demand for Anti-Malarials in Ghana, Uganda and Zambia Using Household Consumption Expenditures and Willingness-to-Pay Estimates'

Endnotes

1. Arrow, Kenneth J, Claire B. Panosian, and Hellen Gelband, eds. Saving Lives, Buying Time: Economics of Malaria Drugs in an Age of Resistance. Washington DC: National Academies Press, 2004.
2. Laxminarayan, Ramanan, Mead Over and David L. Smith. "Will a Global Subsidy of Artemisinin-based Combination Treatment (ACT) for Malaria Delay the Emergence of Resistance and Save Lives?" Health Affairs 25.2 (2006): 323-336.
3. Originally called the RBM Global ACT Subsidy Task Force.
4. The Task Force met in Geneva, Switzerland on 11 September 2007.
5. Cost, insurance and freight (CIF) included, i.e. the landed cost.
6. Principles presented in summary form. For details refer to Section 3.
7. The scope and speed of AMFm phase-in will take account of any potential effects that could negatively affect AMFm objectives such as product arbitrage.
8. The four WHO-recommended ACT combinations are artemether-lumefantrine, artesunate-amodiaquine, artesunate-mefloquine and artesunate-sulfadoxine-pyrimethamine.
9. Stringent regulatory authority is defined as a national drug regulatory authority (NDRA) participating in The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) or the Pharmaceutical Inspection Co-operation Scheme (PIC/S).
10. At the Task Force meeting in Geneva, Switzerland on 11 September 2007, Task Force members agreed to speed up this task.
11. FOB stands for "Free On Board." "FOB" indicates that the seller pays for transportation of the goods to the port of shipment, plus loading costs. The buyer pays freight, insurance, unloading costs and transportation to/at the port of destination.
12. The operationalization of these limits is still under discussion by the AMFm Task Force. It is emphasized that limits must not interfere with normal buying behavior.
13. It is expected that this Independent Expert Advisory Group will be drawn mainly from the Committee on the Economics of Antimalarial Drugs and Board on Global Health that drafted the IOM Report.
14. It is estimated that first quartile retail price for ACTs under the AMFm will be USD 0.25, second quartile USD 0.30, third quartile USD 0.60.
15. Consideration will be given to a block grant to ensure that essential mandates are funded, including international technical assistance.
16. Arrow, Kenneth J, Claire B. Panosian, and Hellen Gelband, eds. Saving Lives, Buying Time: Economics of Malaria Drugs in an Age of Resistance. Washington DC: National Academies Press, 2004.
17. Ibid.
18. Professor Eyitayo Lambo, Former Health Minister of Nigeria. Comments made at the RBM Finance and Resources Working Group Meeting in Amsterdam, January 2007
19. World Health Organization. World Malaria Report 2005. Geneva: World Health Organization, 2005.
20. Breman, J. "The Ears of the Hippopotamus: Manifestations, Determinants, and Estimates of the Malaria Burden." American Journal of Tropical Medicine and Hygiene 64.1 Suppl (2001): 1-11
21. Snow RW, et al. "Estimating Mortality, Morbidity and Disability Due to Malaria Among Africa's non-Pregnant Population." Bulletin of the World Health Organization 77.8 (1999): 624-640
22. Roll Back Malaria Partnership, "Malaria in Africa," Website, July 2007 <http://www.rbm.who.int/cmc_upload/ 0/000/ 015/370/RBMInfosheet_3.htm>.
23. Ibid., Also see: Dalrymple, Dana G. "Artemisia, Agriculture, and Malaria in Africa: The Interplay of Tradition, Science, and Public Policy." USAID and Roll Back Malaria Working Paper (July 1, 2006): 4.
24. Ibid.
25. Laufer, Miriam K., et al. "Return of Chloroquine Antimalarial Efficacy in Malawi." The New England Journal of Medicine 355.19 (November 2006)
26. Bocar, Kouyaté, et al. "The Great Failure of Malaria Control in Africa: A District Perspective from Burkina Faso." Policy Forum 4.6 (June 2007).
27. World Health Organization. Susceptibility of Plasmodium Falciparum to Antimalarial Drugs Report on Global Monitoring 1996-2004. Geneva: World Health Organization, 2005.
28. Pison, Gilles, et al. "Impact of Chlorquine Resistance on Malaria Mortality." InDepth Network. Scientific and General Meeting. Johannesburg, South Africa. June 2000: Session 2. <http://www.indepth-network.org/events/1agm/AGM2000 Report%20final.htm>.
29. The Burden of Malaria in Africa (BOMA) project, which the IOM report identifies as "the most plausible current estimate" of malaria-specific mortality and "the best opportunity to chart malaria's past in Africa", worked to assemble a single database of all evidence on morbidity, disability and mortality related to falciparum malaria in Africa. (p. 171-2) in Arrow, Kenneth J, Claire B. Panosian, and Hellen Gelband, eds. Saving Lives, Buying Time: Economics of Malaria Drugs in an Age of Resistance. Washington DC: National Academies Press, 2004.
30. Ibid.
31. Ibid.
32. World Health Organization. Susceptibility of Plasmodium Falciparum to Antimalarial Drugs Report on Global Monitoring 1996-2004. Geneva: World Health Organization, 2005.
33. Ibid.
34. Ibid.
35. Ibid.
36. World Health Organization. WHO guidelines for the Treatment of Malaria. Geneva: World Health Organization, 2006
37. The unique mode of action associated with ACTs includes: (1) rapid and substantial reduction of the parasite biomass, (2) rapid parasite clearance, (3) rapid resolution of clinical symptoms, (4) effective action against multidrug-resistant P.

falciparum, and (5) reduction of gametocyte carriage, which potentially reduces transmission of resistant alleles.

38. World Health Organization. *Antimalarial Drug Combination Therapy, Report of a WHO Technical Consultation.* Geneva: World Health Organization, 2001.

39. Laxminarayan, Ramanan. "Act Now or Later: The Economics of Malaria Resistance," *American Journal of Tropical Medicines and Hygiene.* 71.2 suppl (2004): 187-195.

40. Roll Back Malaria Partnership, "Facts on ACTs: January 2006 Update," Website. January 2006. http://www.rbm.who.int/cmc_upload/0/000/015/364/RBMInfosheet_9.htm

41. World Health Organization. "Meeting Global Demand." MMV WHO Conference on Artemisinin Production and Market Needs. Bangkok, Thailand. 25 June 2007

42. The public sector includes federal governments, municipalities, or other health facilities run by local authorities.

43. Sales by Novartis to the public sector were roughly 62 million treatments in 2006, out of an estimated total public-sector delivery of approximately 90 million treatments. Private sector market size was estimated based on data from Boston Consulting Group & Institute of OneWorld Health and then adjusted accordingly per manufacturer conversations. Please see: The Boston Consulting Group & Institute for OneWorld Health. *Biosynthetic Artemisinin Roll-out Strategy- Study Overview and Key Results,* July 2006.

44. The Boston Consulting Group & Institute for OneWorld Health. *Biosynthetic Artemisinin Roll-out Strategy- Study Overview and Key Results,* July 2006.

45. Kouyaté Bocar, et al., "The Great Failure of Malaria Control in Africa: A District Perspective from Burkina Faso," *Policy Forum* 4.6 June 2007.

46. World Health Organization. "Meeting Global Demand." MMV WHO Conference on Artemisinin Production and Market Needs. Bangkok, Thailand. 25 June 2007.

47. Sanofi-Aventis terminology. See: Sanofi-Aventis. "Driving Back Disease Around the World." February 2006.

48. Memorandum of Understanding (i.e. the agreement betwern Novartis Pharma AG and representatives of WHO) on public-sector MSP for Coartem® was signed on 23 May 2001

49. "Novartis announces initiative to improve access to state-of-the-art antimalarial treatment Coartem®," www.novartis.com. Press Release. 29 September 2006 <http://www.novartis.com/newsroom/news/2006-10-04_malaria.shtml>.

50. Estimates based on field research in Kenya and Uganda, as well as the pricing policy of Sanofi-Aventis. See: Sanofi-Aventis. "Driving Back Disease Around the World." February 2006.

51. Pricing observations in Burkina Faso, Cameroon, Kenya, Nigeria, and Uganda.

52. Ibid.

53. Retail prices are lower in Asia; data obtained from Professor Nicholas White.

54. Goodman, Catherine Anne. "An Economic Analysis of the Retail Market for Fever and Malaria Treatment in Rural Tanzania." Doctor of Philosophy Thesis. Health Policy Unit, London School of Hygiene and Tropical Medicine, University of London, 2004.

55. The Boston Consulting Group & Institute for OneWorld Health. *Biosynthetic Artemisinin Roll-out Strategy- Study Overview and Key Results,* July 2006

56. Roll Back Malaria Partnership, "Facts on ACTs: January 2006 Update," Website. January 2006. http://www.rbm.who.int/cmc_upload/0/000/015/364/RBMInfosheet_9.htm

57. Based on modelling by Dalberg Global Development Advisors. For details, please see Background Paper 8.

58. For example, for Coartem® there are four weight classes: 5-14 kg (infant), 15-24 kg (toddler), 25-34 kg (child) and finally 35 and above (adult).

59. Roll Back Malaria Partnership, "Facts on ACTs: January 2006 Update," Website. January 2006. http://www.rbm.who.int/cmc_upload/0/000/015/364/RBMInfosheet_9.htm

60. The MMV portfolio <http://www.mmv.org/IMG/pdf/MMV_Portfolio_2Q_2007V2.pdf> cites Chlorproguanil – Dapsone – Artesunate, Dihydroartemisinin – Piperaquine and Pyronaridine – Artesunate in 3rd stage trials and dispersible Coartem® in regulatory approval

61. The DNDi portfolio (http://dndi.org/cms/public_html/insidearticleListing.asp?CategoryId=92&ArticleId=348&TemplateId=1) shows an AS-MQ combination in late stage development, next to its known AS-AQ combination

62. Summarized RBM Partnership principles. Full principles can be found in: Roll Back Malaria Partnership. "RBM Change Process." Internal Board Communiqué #1, 2006 <http://rbm.who.int/partnership/board/meetings/docs/9th_RBM_Board_Meeting_Communique.pdf>

63. Based on modeling conducted by Ramanan Laxminarayan. Current annual number of deaths used for calculation is 1.5 million, so reduction in annual mortality is 12-20%. See: Laxminarayan, Ramanan, Mead Over and David L. Smith. "Will a Global Subsidy of Artemisinin-based Combination Treatment (ACT) for Malaria Delay the Emergence of Resistance and Save Lives?" *Health Affairs* 25.2 (2006): 323-336.

64. Base-case scenario, assuming a DALY/life saved ratio of 33.

65. Theoretical model assumes two ACTs are subsidized, given that the AMFm will begin by subsidizing four WHO-approved ACTs. Consequently, there is strong potential to surpass estimates provided by model. See: Laxminarayan, Ramanan, Mead Over and David L. Smith. "Will a Global Subsidy of Artemisinin-based Combination Treatment (ACT) for Malaria Delay the Emergence of Resistance and Save Lives?" *Health Affairs* 25.2 (2006): 323-336.

66. Jamison, Dean T., W. Henry Mosley, Anthony R. Measham, and Jose Luis Bobadilla, eds. *Disease Control Priorities in Developing Countries.* New York: Oxford University Press for the World Bank, 1993.

67. See section titled "Intervention Cost–Effectiveness: Overview of Main Messages" in Ibid.

68. The World Bank considers a health intervention of less than USD 25 / DALY to be "highly cost-effective." See: Jamison, Dean T., W. Henry Mosley, Anthony R. Measham, and Jose Luis Bobadilla, eds. *Disease Control Priorities in Developing Countries.* New York: Oxford University Press for the World Bank, 1993.

69. UN Millennium Development Goals,", Website, United Nations Organization, July 2007 <http://www.un.org/millenniumgoals>.

70. Roll Back Malaria Partnership. *Global Strategic Plan 2005 – 2015.* Geneva: Roll Back Malaria, 2005.

71. Laxminarayan, Ramanan, Mead Over and David L. Smith. "Will a Global Subsidy of Artemisinin-based Combination Treatment (ACT) for Malaria Delay the Emergence of Resistance and Save Lives?" *Health Affairs* 25.2 (2006): 323-336.

72. Ibid.

73. Ibid.

74. It is estimated that under the AMFm first quartile retail price

for ACTs will be USD 0.25, second quartile USD 0.30, third quartile USD 0.60.

75. Price distributions have been estimated using a numerical model, incorporating data on the density and spread of retail outlets and data on price variances collected during field studies and pricing observations, as well as findings from an extensive literature review. See Background Paper 8 for additional detail on price distribution analysis. Key sources include:
    – Goodman, Catherine Anne. "An Economic Analysis of the Retail Market for Fever and Malaria Treatment in Rural Tanzania." Doctor of Philosophy Thesis. Health Policy Unit, London School of Hygiene and Tropical Medicine, University of London, 2004.
    – Health Action International and World Health Organization. "Medicine Prices." Online Database. Health Action International Europe. Website. July 2007. <http://www. haiweb.org/medicineprices/>.
    – Health Research for Action. *Review of the Accredited Drug Dispensing Outlets (ADDO) Roll out Program in Tanzania.* Belgium: Health Research for Action, 16 March 2006.
    – HAI Africa and Republic of Kenya, Ministry of Health. *Medicine Price Monitor.* Nairobi: Kenyan Ministry of Health, October 2006.
    – HAI Africa and Uganda, Ministry of Health. *Medicine Price Monitor.* Kampala: Ugandan Ministry of Health, October – December 2006.
    – Additional data received from HAI
    – Field research conducted in Uganda, Kenya, Burkina Faso, and Cameroon.
    – Personal correspondence, with special gratitude toward Libby Levison and Marg Ewan.

76. Newton, P.N, et al. "Manslaughter by Fake Artesunate in Asia—Will Africa Be Next?" *PLoS Medicine* 3.6 (June 2006).

77. Roll Back Malaria Partnership. "Looking Forward: Roll Back Malaria." Pamphlet on website. (2004). http://www.rbm .who.int/docs/rbm_brochure.pdf

78. Roll Back Malaria Partnership. *Global Strategic Plan 2005 – 2015.* Geneva: Roll Back Malaria, 2005.

79. Novartis. "Coartem in Africa: Gaining Momentum on the Ground." Website. (17 April 2007). <http://www.novartis .com/newsroom/news/2007-04-17_coartem-africa.shtml#>

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81. "The Abuja Declaration," *Roll Back Malaria Partnership,* Website, 25 April 2000, July 2007 <http://www.rbm.who.int /docs/abuja_declaration_final.htm>.

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83. "UN Millennium Development Goals", Website, United Nations Organization, July 2007 < www.un.org/millennium goals>.

84. Snow RW, et al. "Estimating Mortality, Morbidity and Disability Due to Malaria Among Africa's non-Pregnant Population." *Bulletin of the World Health Organization* 77.8 (1999): 624-640

85. "UN Millennium Development Goals", Website, United Nations Organization, July 2007 < www.un.org/millennium goals>.

86. "Millennium Development Goals for Malaria: Reaching the Halfway Point," *Roll Back Malaria Partnership,* Press Release,

4 July 2007, July 2007 <http:// rbm.who.int/docs/press/ prRBM2007-07-04.pdf>.

87. Roll Back Malaria Partnership. "Economic Costs of Malaria." Website. <http://www.rbm.who.int/cmc_upload/0/000/015/ 370/RBMInfosheet_10.htm>

88. Roll Back Malaria Partnership. *Global Strategic Plan 2005 – 2015.* Geneva: Roll Back Malaria, 2005.

89. Cost-price data for AR+LU based on Coartem®.

90. "Novartis announces initiative to improve access to state-of-the-art antimalarial treatment Coartem®," www.novartis .com. Press Release. 29 September 2006. <http://www .novartis.com/newsroom/news/2006-10-04_malaria.shtml>

91. Pricing observations are in line with results from MMV field research in Uganda, presented at the joint MoH-MMV planning conference in Kampala, October 2007 <http://mmv .org/rubrique.php3?id_rubrique=149>

92. Cost-price reductions over time include assumptions on the improvement of A. Annua plant yield. See: The Boston Consulting Group & Institute for OneWorld Health. *Biosynthetic Artemisinin Roll-out Strategy- Study Overview and Key Results,* July 2006.

93. As noted in Section 2 of this document, only a fraction of this reduction in MSP could be expected in the absence of the AMFm.

94. CQ and SP can be packaged in bulk (e.g. jars), which would minimizes required volumes, while necessary blister packaging of ACTs does not allow for bulk packaging.

95. In the long run, it is assumed that sea freight will account for an estimated 80% of international ACT distribution, and air freight for the remaining 20%.

96. This range is driven by differences in distribution distances, ease of country accessibility and variations in clearance and customs charges.

97. Lower international distribution cost of CQ relative to ACTs is driven by the greater proportion of local CQ production and by efficient lower-cost bulk-packaging that is not possible for ACTs (see reference note 91).

98. The Clinton Foundation HIV/AIDS Initiative (CHAI). "Increasing Access to Effective Malaria Treatment in Tanzania Through a Private Sector ACT Subsidy: Pilot Project Implementation Plan", The Clinton Foundation, June 5, 2007.

99. Cited in Ibid, 18. Original Source: Goodman, Catherine Anne. "An Economic Analysis of the Retail Market for Fever and Malaria Treatment in Rural Tanzania." Doctor of Philosophy Thesis. Health Policy Unit, London School of Hygiene and Tropical Medicine, University of London, 2004

100. Assumes an USD 0.69 average wholesale markup on ACTs as a percentage of an average USD 8 retail price.

101. Based on Dalberg field research conducted in Uganda, Kenya, Burkina Faso, and Cameroon.

102. Ibid.

103. The wholesaler margin falls within a range of 10% to 30%. For example, 10% margins for generic SP and CQ were observed during field research in Uganda, whereas 30% margins were observed in Cameroon and Burkina Faso. Average markups of 14% on an input price of USD 0.11, or USD 0.02 (generic CQ), and 19% on an input price of 0.10, or USD 0.02 (generic SP), were observed during the course of 365 price observations in Uganda.

104. Based on Dalberg field research conducted in Uganda, Kenya, Burkina Faso, and Cameroon.

105. Field research in Uganda (2007) performed for the ACT subsidy.

106. Field observations in Uganda, Kenya, Cameroon, and Burkina Faso revealed a range of USD 0.2–0.4 for CQ and USD 0.4–0.7 for SP.

107. Straight average across all antimalarial products (including AQ) with a price lower than 50KSH or USD ~0.7.

108. Outliers composed largely of particular SP generics including Falcigo and Falcidin, which appear to have extraordinarily high retail margins (roughly 400%).

109. Price distributions have been estimated using a numerical model, incorporating data on the density and spread of retail outlets and data on price variances collected during field studies and pricing observations, as well as findings from an extensive literature review. See Background Paper 8 for additional detail on price distribution analysis. See Reference Note 73 for a list of key sources

110. It is estimated that under the AMFm first quartile retail price for ACTs will be USD 0.25, second quartile USD 0.30, third quartile USD 0.60.

111. Brazil. Ministério de Saude, Definidos preços de contraceptivos no "Aqui tem Farmácia Popular". 15 June 2007. <http://portal.saude.gov.br/portal/aplicacoes/noticias/noticias_detalhe.cfm?co_seq_noticia=31777>

112. Amin, Abdinasir A., et al. "The Challenges of Changing National Malaria Drug Policy to Artemisinin-Based Combinations in Kenya." *Malaria Journal* 6.72 (May 2007).

113. Assuming an equal number of overall required treatments, this would have little impact on the AMFm or funding requirements.

114. Kone, Karna Georges, et al. "Subsidized ACTs Available for Sale in Private Drugstores: Experience in Senegal." *Institut de Recherche pour le Developpement* (2007).

115. FOB stands for "Free On Board." "FOB" indicates that the seller pays for transportation of the goods to the port of shipment, plus loading costs. The buyer pays freight, insurance, unloading costs and transportation to the port of destination.

116. Center for Global Development Global Health Forecasting Working Group. *A Risky Business Saving Money and Improving Global Health Through better Demand Forecasts.* Washington, DC: Center for Global Development, 2007.

117. Terminology used in Ibid.

118. Ballou-Aares, Daniella and Priya Mehta. *Information Sharing & Gathering as a Public Good.* Background Paper accompanying Report of the Center for Global Development Global Health Forecasting Working Group, Washington, DC: Dalberg Global Development Advisors and Center for Global Development, October 2006.

119. Stringent regulatory authority is defined as a national drug regulatory authority (NDRA) participating in The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) or the Pharmaceutical Inspection Co-operation Scheme (PIC/S).

120. At the Task Force meeting in Geneva, Switzerland on 11 September 2007, Task Force members agreed to speed up this task.

121. Artepal Project. Website. Status Q2 2007. <www.artepal.org>

122. SNRA refers to a strict national regulatory authority (see End Note 8).

123. Excludes the Global Fund compliance list cii category.

124. Laxminarayan, Ramanan, Mead Over and David L. Smith. "Will a Global Subsidy of Artemisinin-based Combination Treatment (ACT) for Malaria Delay the Emergence of Resistance and Save Lives?" *Health Affairs* 25.2 (2006): 323-336.

125. The ACT Watch project has been set up to provide transparency on ACT markets in developing countries. Data will be collected in 8 countries and will be made available in a close to real-time manner. At the time of writing the project has not been finalized, thus a complete reference cannot be given.

126. The Clinton Foundation HIV/AIDS Initiative (CHAI). "Increasing Access to Effective Malaria Treatment in Tanzania Through a Private Sector ACT Subsidy: Pilot Project Implementation Plan", The Clinton Foundation, June 5, 2007.

127. Ibid.

128. Based on modeling conducted by Ramanan Laxminarayan for the AMFm technical design (2007). See also: Laxminarayan, Ramanan, Mead Over and David L. Smith. "Will a Global Subsidy of Artemisinin-based Combination Treatment (ACT) for Malaria Delay the Emergence of Resistance and Save Lives?" *Health Affairs* 25.2 (2006): 323-336.

129. World Health Organization. *Antimalarial Drug Combination Therapy,* Report of a WHO Technical Consultation. Geneva: World Health Organization, 2001.

130. The Boston Consulting Group & Institute for OneWorld Health. *Biosynthetic Artemisinin Roll-out Strategy- Study Overview and Key Results,* July 2006.

131. Cost estimate includes costs of RRP/SRP interventions only; cost estimates for the proposed package of wholesaler volume rebate and any further incentives or price/margin control interventions pending further study.

132. Denis, May Bouth, R Tsuyuoka, et al. "Efficacy of Artemether-lumefantrine for the Treatment of Uncomplicated Falciparum Malaria in Northwest Cambodia". *Tropical Medicine and International Health* 11.12 (2006). See also: Vijaykadag, S., C. Rojanawatsirivej, et al., "In vivo Sensitivity Monitoring of Mefloquine Monotherapy and Artesunate-mefloquine Combinations For the Treatment of Uncomplicated Falciparum Malaria in Thailand in 2003." *Tropical Medicine and International Health* 11.12 (2006).

133. Key sources behind table include:
    – "The Global Fund To Fight AIDS, Tuberculosis & Malaria By-Laws". The Global Fund. Website. July 2007 <http://www.theglobalfund.org/en/files/about/governance/Bylaws_governance.pdf>.
    – "Prospectus - Global TB Drug Facility." Website. Global Drug Facility. July 2007. <http://www.stoptb.org/gdf/whatis/prospectus.asp>.
    – "Unitaid Constution." Website. Unitaid. July 2007 <http://www.unitaid.eu/uploaded/unitaid-acte-constitutif-eng.pdf>.
    – GAVI Principles Memorandum. GAVI Alliance. Website. July 2007. <http://www.gavialliance.org/resources/Guiding_ Principles_adopted.doc>.

134. GAVI Alliance Proposed Co-financing Levels. GAVI Alliance. Website. February 2007 <http://www.gavialliance.org/resources/Proposed_Co_Financing_Levels_Feb07.doc>

135. UN Office of the High Representative for the Least Developed Countries, Landlocked Developing Countries and Small Island Developing States, "List of Least Developed Countries". Website. <http://www.un.org/special-rep/ohrlls/ldc/list.htm>