The Right Drug at the Right Time

The Power of the Affordable Medicines Facility - Malaria to Save Lives

Report for the All-Party Parliamentary Malaria Group (APPMG)
based on evidence presented to the APPMG from July to October 2007

House of Commons
All-Party Parliamentary Malaria Group

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Contents

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HOUSE OF COMMONS

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The All-Party Parliamentary Malaria Group

Foreword
From The Chairman

The All Party Parliamentary Malaria Group (APPMG) remains busier than ever. The Parliamentarians from all parties and from both Houses are pleased to note that the level of activity both in the UK and around the world to combat malaria, saving and improving the lives of millions of people, grows apace. Following our first two groundbreaking reports this third APPMG report is short and focussed, reflecting the strength of evidence in supporting and advocating the Affordable Medicines Facility – malaria (AMFm). The AMFm is on the agenda for the Roll Back Malaria Board meeting on 29th November in Addis Ababa. This report will be submitted to those involved in the decision-making processes with our strong recommendation to support, develop and utilise AMFm as one of the range of tools to save and improve lives.

In meeting the costs of producing and distributing this report, I wish to acknowledge the APPMG's enormous debt of gratitude to Malaria Medicines Venture (MMV), the Malaria Consortium and the European Alliance Against Malaria. Both for this and their unwavering support for the work of the APPMG, we are eternally grateful.

I thank our authors Sylvia Meek and Sarah Pickwick of the Malaria Consortium and Professor Chris Whitty of the London School of Tropical Medicine for their time and expertise in marshalling the evidence from the excellent series of presentations to the Group in July and October this year.

I commend this report to all who care about doing everything possible to relieve people from the avoidable blight of malaria.

Stephen O'Brien MP
Chairman, All Party Parliamentary Malaria Group

The All-Party Parliamentary Malaria Group

Executive Summary

Malaria kills more than a million people a year, mostly those living in the poorest countries of the world. It can be treated very successfully, but increasing resistance to older cheap drugs means that the right drugs cost the patients several dollars (varying from $0.5 to $10) per treatment. This may not seem much, but is out of reach of those who need them most.

This report for the All Party Parliamentary Malaria Group focuses on a fundamental gap in delivering effective malaria control to those most in need: effective and high quality treatment that is affordable and available where it is needed. Specifically, it looks at an idea to bring down the price of artemisinin-based combination therapies (ACTs) through an Affordable Medicines Facility to ensure widespread use and to discourage use of single drugs which may accelerate development of resistance to artemisinin derivatives. This idea has been developed into a proposal to set up the Affordable Medicines Facility - Malaria (AMFm), which will provide a co-payment at the factory gate to allow first-line buyers to purchase effective antimalarials at prices comparable to those of ineffective older drugs, such as chloroquine. The report describes the rationale and design of the AMFm, and explores some of the risks associated with either promoting or not supporting it.

The conclusions of the report are that:

1. The APPMG has decided on the basis of the evidence presented that the concept of the AMFm is sound, and it is right to proceed.
2. The APPMG considers that the mechanism still needs more work to make it able to deliver its objectives to greatest effect and to ensure a market mechanism to provide competition and incentive to drive down prices, but that there cannot be a delay in initiating the Facility given the extremely poor current access to effective antimalarials and the real risks of allowing continued use of inappropriate drugs. Improvements to the mechanism can best be made on the basis of early implementation experience.
3. The APPMG recognises that subsidies and the Facility alone are not sufficient to ensure availability and use of effective antimalarials by those who need them most. There is a huge need to strengthen health systems in countries most affected by malaria in order to make them better able to provide prompt and effective treatment of this common and treatable disease.
4. The APPMG expects that the financial requirements for the AMFm will taper down in a few years, as the market for effective antimalarial drugs matures and stabilises.

Three recommendations arising from these conclusions are:

1. Coordinated international support of the AMFm
For the AMFm to be successful it will need buy-in from multiple funding partners to cover the cost for long enough to achieve its purpose. It will also need full support from user countries. The Roll Back Malaria Partnership needs to create unity of purpose in fostering the AMFm, both encouraging support and tackling remaining challenges in perfecting the design.

2. Addressing developing country pharmaceutical manufacturing capacity.
Further in-depth consultation is needed urgently with governments and pharmaceutical manufacturers in developing countries, both to explore ways to encourage a competitive market that will lead to unsupported price reduction and to avoid anticipated bottlenecks if recipient countries perceive that their own industries are at a disadvantage.

3. Monitoring and evaluation
Monitoring and evaluation need to be intensive, particularly in the first few years. This is a new approach carrying some risks. We believe these risks can be managed to do little harm, but they should not be swept under the carpet. Public scrutiny and transparency of management are key to making the AMFm work.

1 Introduction

This is the third in a series of reports developed by the All Party Parliamentary Malaria Group addressing critical issues relating to malaria. The first report made the case for taking action to tackle one of the most important yet tractable problems that keeps much of the world in poverty[1], and the second report reviewed financing mechanisms and recommended ensuring that increased funding should be predictable and sustainable[2]. After determining the need for and feasibility of tackling the malaria problem, then examining the mechanisms for financing necessary action, the group is turning its attention to issues of effectively delivering successful control measures.

This report focuses on a particularly fundamental gap in delivering effective malaria control to those most in need: effective and high quality treatment that is affordable and available where it is needed. Specifically, it looks at an idea arising from a committee convened in 2002 by the Board on Global Health of the US Institute of Medicine (IOM) to examine the economics of alternative strategies to treat malaria given the increasing resistance to commonly used treatments. The idea was to bring down the price of newer effective but costly antimalarial drugs to the level of the older ineffective drugs to ensure that they would be universally used through a global subsidy, which has been developed into the proposal for the Affordable Medicines Facility.

[1] APPMG 2005. Tackle Malaria Today. Give Tomorrow a Chance

[2] APPMG March 2007. Financing Mechanisms for Malaria

2 Current situation

The major burden of malaria rests on the poorest people in the world. It is a deadly disease, which can kill within 24 hours of first symptoms. Fortunately, there are very effective medicines to treat it, but still there are 300 to 600 million cases a year of which more than a million die. The vast majority of deaths are in young children in Africa (20% of all childhood deaths in Africa), but there are also still problems in the most marginalised populations of Asia and Latin America. Children and pregnant women are especially vulnerable. Drug resistance has increased so much in recent years that the drugs, which have been commonly used for decades, and cost only a few cents – chloroquine and sulfadoxine-pyrimethamine – are no longer useful. The best drugs now for treatment are the artemisinin-based combination therapies (ACTs).

These drugs combine the very fast and effective action of an artemisinin derivative (based on an extract of the plant *Artemisia annua*) with protection from development of resistance by using a second drug at the same time with a different mechanism of action. This means that malaria parasites not killed by one of the drugs in the combination should be killed by the other, so resistant mutations should not spread. The disadvantage of the ACTs is that they currently cost US$6 to 10 for a single treatment in the private sector (the public sector can buy for lower prices $0.5-$3), which is far beyond the reach of the most vulnerable populations.

The people with the highest chance of being infected with malaria are those with the lowest disposable income for treatment (Photograph: S.Meek, Malaria Consortium).

Since the time of the IOM committee's deliberations and report[3] a great deal has happened to improve the chances of effective malaria treatment reaching those most at risk. Most countries have changed their malaria treatment policies to recommend artemisinin-based combination therapy (ACT) as first-line treatment. Funding for malaria from international donors has increased 10-fold in the last 10 years, and some of the initial bottlenecks to supply of ACTs have been overcome.

However, the reality is that a large proportion of malaria patients are not able to obtain ACT in time or at all. Although ACTs are beginning to reach public sector health facilities, problems with stock management and staffing often mean patients are not offered ACTs. In several countries, many people live far from the nearest health facility. As a result a large proportion of patients or the carers of patients resort to buying drugs from the nearest store they can reach. Many of these people will buy incomplete doses of inappropriate drugs, as that is all they can afford. One of the greatest threats to future sufferers from malaria is that resistance could develop to the excellent artemisinin derivatives, if they are used on their own (as a "monotherapy" as opposed to a combination therapy). Indeed the evidence that resistance is already developing in parts of Southeast Asia is becoming clear.

[3] Arrow, K. Panosian C. and Gelband H. (eds.). 2004. *Saving Lives, Buying Time: Economics of Malaria Drugs in an Age of Resistance.* Washington, DC: The National Academies Press.

3 Options appraisal

So what are the options?

One approach is to flood the public sector with free ACTs, and hope that this will attract all patients and carers to use the public facilities. This can reach more people than before, but unless there is substantial improvement in management of drug stocks and of health workers (by paying reasonable salaries and providing appropriate incentives to work full-time) there will remain great reluctance to give up other sources of treatment. Additionally in many settings, the financial barrier of indirect and transport costs of accessing public healthcare mean the poorest cannot afford to access the public sector and use the private sector, especially shops, which are much closer and therefore have much smaller indirect costs. Improvements in public healthcare should be strongly supported, but realistically it will take many years of steady increased investment to bring about fully functional health systems. In the meantime, substantial numbers of people will have to use the treatment sources they can access, and the risks of ineffective treatment will remain high if we ignore the private providers, who will sell what people can and will buy.

A second approach would be massively to scale up community health worker programmes to provide free ACTs at village level. This approach is being tested in countries, such as Uganda and Cambodia, with initially promising results, but to date the community medicine distributors have not displaced the private drug sellers, and sustainability is likely to be difficult in some settings. This approach can indeed improve access, and deserves support, but is unlikely for some time to suppress the sale of inappropriate drugs in the private sector. It is therefore not sufficient on its own.

A third approach may be to provide grants to governments to import sufficient ACTs, so that they can be sold from the public sector on to the private sector at lower prices. This would be a subsidy, but would be complex to administer.

A fourth approach is to apply the funds at the level of the manufacturer through a global buyer co-payment mechanism, which would be available to both public and private sectors. This is the approach proposed by the IOM report, and supported by a modelling exercise, which showed that even a partial subsidy could delay the emergence of artemisinin resistance, although there were conditions where it could speed up emergence, whilst a delay in implementing an ACT subsidy could facilitate the emergence of resistance and lower the economic value of ACTs[4].

While the report focuses on this fourth option and recommends support, it is important to emphasise that these options are not exclusive. Support for the first two together with AMFm can ensure that all routes leading to a successful treatment are opened, while support for only one would provide a partial solution, and would not offer the promise of long-term effectiveness of ACT.

[4] Laxminarayan, R., Over M, Smith D. 2006. Will a global subsidy of new antimalarials delay the emergence of resistance and save lives? Health Affairs. 25, 325-336.

4 Rationale and Description of AMFm

4.1 Rationale for AMFm

The rationale for AMFm is that it has the potential to prevent many deaths by ensuring that correct treatment is accessible to far more people. It also responds to the need to minimise use of artemisinin monotherapy, which could lead to more rapid development of resistance to extremely valuable and at present irreplaceable drugs (until some major new drug classes are discovered). The sooner it is introduced successfully, the fewer lives will be lost. The rationale for a global mechanism is that resistance developing in one country will spread to others, regardless of how well the other countries manage their malaria treatment. Other benefits of global introduction are to save more lives and to reduce the likelihood of leakage and misuse.

4.2 What is AMFm?

The Affordable Medicines Facility - Malaria (AMFm) is a mechanism designed firstly to increase the overall use, affordability and availability of eligible, good quality Artemisinin-based Combination Therapies (ACTs) and other effective antimalarial co-formulations (a co-formulation is more than one drug in the same tablet; this is better than administering two separate tablets, as it ensures that both drugs are taken). Secondly, the AMFm is designed to work across multiple channels, benefiting both the public and private sector. Yet since current global public health efforts have effectively increased the supply of antimalarials in the public sector, the focus of this new initiative is to help increase access through the private sector as well as public. A further objective of AMFm is to help drive out monotherapies and ineffective drugs from the market, in line with the recommendations of the original Institute of Medicine (IOM) proposal.

Box: Goals of the AMFm

Goals

1. **Reduce mortality.** The AMFm will contribute to a reduction in malaria mortality
2. **Delay resistance.** The AMFm will decrease the likelihood that resistance emerges to effective treatment

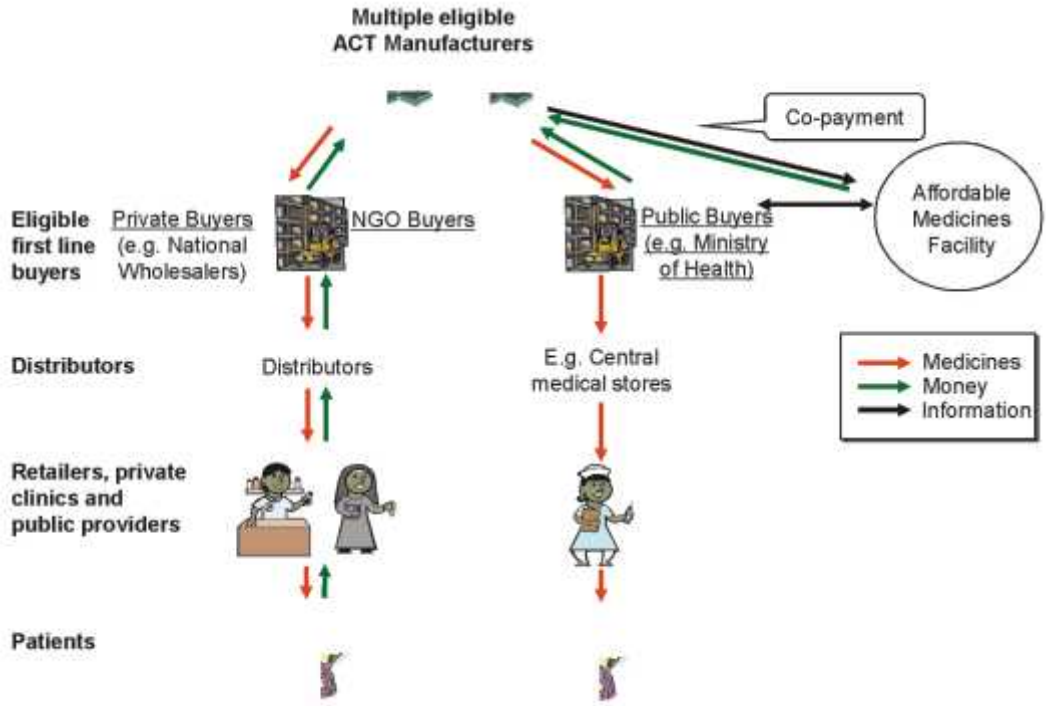
Objectives

1. **Increase affordability of artemisinin combination therapies (ACTs) by lowering price.** The AMFm offers low-cost ACTs to first-line buyers, which must translate into reductions of final purchase prices paid by patients
2. **Increase availability of ACTs.** The AMFm must contribute to making ACTs widely available through public, private and non-governmental organisation (NGO) sector providers.
3. **Crowd out artemisinin monotherapies (AMTs).** ACTs must contribute to displacing AMTs that increase the likelihood of resistance

Derived from: Saving Lives, Buying Time[3]

4.3 How will AMFm achieve its goals?

AMFm will achieve these objectives, firstly by quickly reducing end-user prices of ACTs to an affordable level, through a properly supported global buyer co-payment of ex-manufacturer prices. The price level will then be comparable to what is currently being paid for less effective alternatives such as SP - sulfadoxine-pyrimethamine - or CQ - chloroquine. Secondly, it will also introduce in-country supporting interventions, including those for the proper use of effective antimalarials/ACTs.



These measures should encourage uptake of ACTs due to a more regular and cheap supply of effective antimalarials. It is predicted though not certain that there would be an improved forecast of ACT needs, and there would be stabilisation of the ACT market and reduced ACT prices overall. At the same time it should delay drug resistance and undermine the counterfeit market, although it will be important to anticipate and monitor the effects on behaviour of those suppliers not granted access to co-paid drugs. The approach would improve predictability and sustainability for public sector and for manufacturers, as drugs would be ensured to all sectors and would further facilitate the involvement of the private sector in ACT distribution.

Through supporting interventions in-country AMFm will promote the strengthening of national capacities in procurement and drug management, drug quality assurance, pharmacovigilance and drug resistance monitoring.

The total resource requirements for AMFm will be USD 1.4-1.9 billion for the first five years. This is made up of (for 5 years):
Funding for commodities and transport - $1.2-1.6 billion
Funding for supporting activities and technical assistance - $230-330 million
Secretariat and administrative expenses - $25-30 million.

4.4 How does AMFm work?

AMFm would operate out of an international secretariat (hosted by an existing institution, to avoid building a new global heath institution) which would perform certain core functions, making sure it is not replicating existing services.

1. It would set the eligibility criteria for the products and manufacturers to ensure high quality standards and simplicity of access to the Facility. This would be based on existing WHO treatment recommendations and prequalification standards, while providing some flexibility for an initial two-year period for new manufacturers. Those antimalarials which meet international quality standards would be eligible for the co-payment. Initially, the only class of eligible antimalarials will be ACTs but this should change in the future as novel antimalarials emerge from ongoing research and development.

2. The secretariat would agree with manufacturers on the co-payment levels and the maximum sale price of the co-paid medicines. The prices would be set through negotiations and a competitive tendering process to encourage competition and innovation and the AMFm would be responsible for processing any payments to manufacturers and orders from wholesalers.

3. It would co-pay for orders from buyers for ACTs (it would not purchase the drugs itself). When a first-line buyer orders an eligible ACT, the buyer would only pay the reduced price while the Facility secretariat would make the co-payment. The co-payment would also cover international transport costs and buyers would be free to choose between manufacturers.

4. It would determine criteria for buyers and distributors eligibility

AMFm will provide a high-level co-payment i.e. at the factory gate. Importers / distributors in both the public and private sectors would be able to procure effective antimalarials such as ACTs at the cost of US$ 0.05 CIF[5] per treatment course (current public sector cost is US$ 0.95 to 1.95, private sector even higher). AMFm would monitor end-user prices to ensure the price reduction reaches patients. Procurement and sales would use existing channels, avoiding disruption to markets and ensuring optimal access for patients. By choosing a high-level entry point, AMFm avoids complex channel entry and keeps access open to all channels and patients.

4.5 What else would AMFm do?

AMFm would also assist in global antimalarial demand forecasting (although primary responsibility for this would rest with the Health Forecasting Working Group), health system technical assistance and providing or contracting promotion, distribution and marketing programmes in each malaria endemic country.

While the Facility co-pays for eligible antimalarials, ensuring an affordable and quality drug supply at the point of arrival in endemic countries, it will also introduce (in-country) supporting interventions, including those for the proper use of effective antimalarials. This is in order to ensure that the price reduction is transmitted to the patients at the point of purchase and that patients have access to effective malaria treatment. 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. These supporting interventions include things like public education and awareness campaigns, provider training, national monitoring, wholesaler incentives and pricing/margin control mechanisms. In-country activities will be important to ensure the success of the AMFm.

AMFm would also fund, contract and coordinate limited monitoring and evaluation which would include concomitant AMFm-specific and AMFm co-paid operational research as well as monitoring on a learning-by-doing basis.

4.6 How does the co-payment mechanism differ from existing malaria grants?

ACTs are already provided through several grant programmes (e.g. Global Fund for AIDS, Tuberculosis and Malaria, donor government programmes including the President's Malaria Initiative and funding from endemic country governments). These grants have been key in enabling the policy switch to ACTs in most countries, but these mostly flow currently to public sector health services and are short term commitments. The AMFm will ensure the drugs continue to be affordable in the longer term, and reach the private sector where 60-80% of people buy their medicines. The initiative will rely on the existing aid architecture

[5] Cost, insurance and freight included, i.e. the landed cost.

and drug supply channels. It will complement support to national malaria programmes and health systems, and providing there are no onerous pre-conditions for access to the scheme, offers a way to scale up use rapidly even where Governments have limited capacity.

In conclusion, AMFm is based on six broad guidelines:

1. Measurement of success based on the three objectives of the facility, to lower prices of effective antimalarials, improve availability of ACTs and drive out ineffective monotherapies
2. Competitive and affordable pricing to private, public and NGO sectors in malaria endemic countries
3. Management by a small AMFm secretariat of 10-20 staff
4. Eligibility of products, suppliers and buyers that meet standards and requirements of entities such as WHO and AMFm secretariat
5. Importance of in-country supporting activities to ensure success of AMFm
6. Monitoring and evaluation of retailer prices, access, drug quality, drug resistance and market dynamics.

5 What are the risks of investing in AMFm?

Several legitimate concerns have been raised about a financing mechanism of sufficient scope to allow co-paid drugs to penetrate the private and non-formal market where most people currently obtain their treatment. Some of these are practical, some theoretical.

1) Will pushing a co-payment through the private sector lead to less investment in public sector delivery, including health system strengthening?
There is a concern regarding the risk that investment that would otherwise be put into the public health sector is siphoned off to support the co-payment. This is plausible, and the main way to mitigate this risk is clearly to identify separate and new funding streams; recycling old money to fund any subsidy does risk this becoming a reality. Public sector provision of health care faces many problems, and, although it may be difficult to improve access in many settings, the long-term goal should be to ensure that its reach increases greatly. Efforts to mitigate its failure to reach those most in need by improving the quality of care in the private sector must not be allowed to undermine this overall goal. Close tracking of global investment in health and malaria should continue, and rigorous monitoring of subsidy management and evaluation of impact are essential.
This is strongly argued by some groups with a legitimate wish to strengthen the public sector. There is limited evidence that allowing effective rather than ineffective drugs to be used in the private sector weakens the public sector. The AMFm will simply ensure that effective and affordable drugs are available in line with patients' treatment seeking preferences - whether public or private. The private sector includes formal and informal outlets such as pharmacies, drug shops and general stores.

Public sector health-systems strengthening is clearly essential both for malaria and for many other diseases. However, malaria, unlike HIV/ AIDS and TB, is often treated with drugs purchased through the private sector due to the need for immediate treatment, particularly for the most vulnerable. Informal and formal private outlets are accessed for their convenience and proximity rather than their excellence. The poorest cannot afford to access public healthcare on a regular emergency basis, even if excellent and free, if it takes them hours to get to it. The majority of the costs of malaria episodes are indirect costs such as opportunity costs, and non-health costs such as transport[6]. Patients will therefore continue to use informal private outlets which are much more widely dispersed and thus accessible — the question is whether they get effective drugs or ineffective drugs through this route.

The AMFm is based on the world as it is, rather than as everybody would want it to be. The only serious risk is that funds that would otherwise be invested in the public health sector are siphoned off to support the AMFm. This is a plausible concern, and the main way to mitigate this risk is clearly to identify separate and new funding streams for the AMFm; recycling old money could lead to this risk becoming a reality. In addition, close tracking of global investment in health and malaria should continue, and rigorous monitoring of AMFm management and evaluation of impact are essential.

2) *Will wider use of the drugs as a result of their lower prices lead to more rapid development of resistance?*
There is a tension between widening access and increasing the pressure for development of drug resistance. This is a real risk that applies to all methods of increasing access to antimalarials, including increased use through the public sector and community distribution systems. In areas where malaria is common and drug resistance to cheap drugs is widespread, however, restricting the drugs to the formal healthcare system will usually mean that most of those with malaria will not get effective antimalarials. There is no evidence that *unnecessary* prescription is lower in the public sector- indeed what evidence there is points

[6] Wiseman, V., Onwujekwe, O., Matovu, F., Mutabingwa, T. and Whitty, C. 2005 *Differences in willingness to pay for artemisinin-based combinations or monotherapy: experiences from the United Republic of Tanzania,* Bull. WHO 83, 845-852.

to massive over-prescription in the public sector, and (largely random) under-prescription in the private sector[7].

The argument that access to newer antimalarials should be restricted holds much greater force in countries where older drugs, or combinations of drugs, are still effective; this applies whatever method of delivery is used. These risks can be reduced, but not eliminated, by methods to improve targeting of drugs, but this is not easy to achieve in practice. There is, however, a good case for examining options to link co-paid ACTs with improved access to better diagnosis (i.e. improved microscopy and rapid diagnostic tests for parasitological diagnosis). While the costs of un-co-paid diagnosis would be relatively high when the drugs are co-paid, the value of moving towards more rational use of drugs argues for also co-paying for diagnosis, providing behaviour change to promote appropriate use of diagnostic results could be shown to be effective.

There are counter-risks of increasing drug resistance by not creating an AMFm, and these are a key part of the rationale for the AMFm. High costs of legitimate combination drugs in the private market increase the risk that more affordable monotherapies will continue to be used, and that counterfeit drugs, many of which have trace amounts of active drug, penetrate the market. Both of these risks are best mitigated by having genuine effective antimalarial combinations available at affordable costs.

Private drug outlets are often poorly managed. In this shop in Tanzania the medicines are being sold by a child. At least if the right drugs were available at competitive prices, and consumer demand was enhanced by consumer education, more people would receive better treatment than now.

(Photograph from Battersby A, Goodman C, Abondo C and Mandike R 2003. Improving the Supply, Distribution and Use of Antimalarial Drugs by the Private Sector in Tanzania, Malaria Consortium report for DFID.)

3) Will the AMFm lead to suppression of diversification of manufacturers, especially in developing countries leading to reduced competition and less incentive to lower prices and to innovate?

This is a strong argument, and any subsidy mechanism needs to minimise the impact of this in the way it is designed. Competition in the market is the best way to ensure a steady supply of new drugs as drug resistance emerges (as it almost certainly will in time) and has clearly been demonstrated to minimise the factory gate cost of antimalarial drugs more effectively than central negotiation. In the long run diversity of supply, and local production, are likely to be essential components in bringing down the underlying cost of drugs and their

[7] Amexo, M *et al*. 2004. Malaria misdiagnosis: effects on the poor and vulnerable, Lancet, 364; 1896-1898; Reyburn, H *et al.* 2007. Rapid diagnostic tests compared with malaria microscopy for guiding outpatient treatment of febrile illness in Tanzania: randomised trial. BMJ 334.

ingredients. More consultation with developing country manufacturers, business leaders and politicians is urgent in finalising the design of the AMFm, and may require parallel investments in strengthening local pharmaceutical manufacturing capacity to enable competition. The mechanisms to do this need urgent consideration.

4) Will the co-payment applied at factory gate benefit middle-men more than end-users?
There is a risk that despite low original purchase cost the mark-ups along the distribution chain will increase to the extent that little of the benefit goes to the end-user or even that the prices remain so high as to deter use altogether. Simultaneous initiatives, such as MeTA (the Medicines Transparency Alliance), and regular drug price and availability monitoring as undertaken by Health Action International and WHO, should mitigate this risk, provided there is support for them to continue. As markup is likely to depend on competition and availability, the co-payment may reduce the opportunities for markup.

5) If user countries are left to make technical decisions on which drugs to use, but the cost of the drugs chosen is fixed, does this mean there is no competition on grounds of cost?
This reduces the incentive for manufacturers to compete on the basis of cost, and if real costs of manufacture decrease over time, it reduces their incentive to pass these cost savings on. To avoid this any mechanism must ensure cost is part of the decision user governments make.

6) If a system based on AMFm were stopped abruptly would it lead to chaos?
This risk is not a question, but a fact. It is anticipated that the AMFm would be likely to taper down with time, partly because underlying costs of raw materials are likely to reduce, partly because the market will stabilise, and partly due to potential reduced demand as a result of the success of malaria control interventions. The time-frame is not easy to predict at this point, and substantial financial commitment may be needed for several years. A sudden stop would, however, mean those with malaria would suddenly not have access to the drugs, so at a patient level it could be catastrophic. It would also lead to a major shock to the market, and achieve exactly the opposite of stabilising the market. It is only sensible to launch the AMFm if it will be sustained; it would be better not to start at all than to start then suddenly pull out. The key to mitigating this potential risk is political commitment to being in this for the long run, and it is essential to have a starting commitment of five years.

7) *Will those most in need of the subsidy be able to access it?*
If the subsidy is to have a major impact on those least able to access public services, it must ensure that the informal private sector is able to provide greatly subsidised ACTs. While the difficulties of involving some of these providers are great, particularly if quality diagnosis and treatment is to be ensured, the impact of the subsidy without these providers will be small. Greater efforts are needed to define how they will be safely included as well as efforts to monitor the benefits and harms following from their involvement.

Of these risks the most significant is that any AMFm will in effect reduce the competition in the market- so that a mechanism brought in to lower costs in the market has the perverse effect of slowing the natural drift down in prices over time. It is essential that the mechanism chosen retains as much incentive to compete on price as is possible, and choices between different mechanisms need to concentrate on this. This is, however, achievable by a variety of mechanisms. Additionally, clear new funding streams must be identified rather than switching funding from the public sector to the AMFm.

6 What are the risks of not creating the AMFm?

The risks of not creating an AMFm are at both individual and system-wide levels.

1) The greatest risk is to children and pregnant women who are vulnerable to malaria, and who can neither afford to access public healthcare, nor to buy effective drugs in the private sector. The majority will continue to use the private sector, and therefore continue to be prescribed antimalarials which are affordable, but ineffective or in some cases useless. In all studies undertaken the great majority of febrile illnesses are treated in the private sector. Reports in the literature on the use of medicine sellers in sub Saharan Africa during recent child illnesses ranged from 15–82% with a median around 50%[8]. Currently ACTs are simply unaffordable in the private sector to any but the richest. Even where people probably can pay they are not willing to pay anywhere near the amounts ACTs cost in the market[9]. People who could have been treated with an effective drug will be prescribed an ineffective one, many will deteriorate to severe malaria, and a significant number will die.

2) The risk of counterfeit drugs penetrating the market will increase significantly. This is already a serious problem in Southeast Asia, and is spreading to Africa[10]. Counterfeiting is most likely when there is a significant gap between what people are prepared to pay, and the cost of the true product. Greater efforts to detect counterfeiters and to prosecute have a part to play, but even in highly regulated markets counterfeit drugs are a significant problem. The only way effectively to deal with counterfeit drugs and drive them off the market is to undercut them; where true products cost no more to end users than the fake products the fakes soon cease to be profitable. Fake drugs are very dangerous themselves; parents will treat children in good faith, and the condition of the children will deteriorate because they have no active drug. This is even more dangerous than no drug, as parents will think they have acted, and are likely to delay further. If fake drugs become widespread to the point when patients and their families cease to trust the drugs, the whole ACT deployment could collapse.

3) The current market for ACTs is highly unpredictable, and this is exacerbated by the fact that they have shorter shelf-lives than older antimalarials (two years), so where there is a surplus of stock over orders the drug has to be destroyed. The price, therefore, allows for both waste and risk. Expanding the market will reduce this risk, and if the market depends on many more individual purchases, there will be a more predictable expansion and contraction. This should feed through into prices of drugs directly, and encourage other producers into the market. Without this artificial boost the market may take a very long time to mature and become stable.

The key problem with doing nothing, however, remains the first; most of those who need effective antimalarials will not get them. Without an AMFm which brings down the cost in the private sector the chances of this changing are remote. Therefore despite the risks of proceeding, which should not be ignored, the risks of not proceeding are considerably greater.

[8] Brieger W, Unwin A, Greer G, and Meek S. 2005. *Interventions to Improve the Role of Medicine Sellers in Malaria Case Management for Children in Africa.* London, UK and Arlington, Va., USA: the Malaria Consortium and BASICS for the United States Agency for International Development; prepared for Roll Back Malaria's Sub-group for Communication and Training and Malaria Case Management Working Group.

[9] Wiseman (as in footnote 5)

[10] Newton, P *et al.* 2006.*Manslaughter by Fake Artesunate in Asia—Will Africa Be Next?* PLoS Medicine 0752. Newton P, Green M and Fernandez F 2007.*Counterfeit Artemisinin Derivatives and Africa*: Update from Authors, PLoS Medicine 0598.

7 What next?

Dealing with unresolved issues, making it happen, research, monitoring and evaluation

A clear plan is needed to deal with remaining design issues following the presentation of the AMFm proposal to the RBM Board meeting at the end of November 2007 and prior to launch if the current design is endorsed. A number of key outstanding challenges have been identified, and responsibilities for addressing them are being assigned. For instance, there is a need to clarify the scope of supporting interventions to improve proper use of antimalarials; if this were a pre-condition, it may exclude for some time the informal private sector, and so greatly delay access for rural poor.

In addition to agreeing on the organisation to host the AMFm, negotiating co-payment levels with manufacturers, establishing supporting measures in-country and ensuring strengthening of regulatory authorities, the major outstanding challenge is to secure sufficient funding.

A monitoring and evaluation framework is being developed[11], which will draw on a number of existing monitoring and evaluation tools and events to collect necessary data, and a final plan to ensure this happens will be needed.

In order to address a number of questions which remain, there is scope and need for diverse operational research efforts linked to the initiation of the AMFm, and possible areas for research are being considered. Some urgent operational research efforts are underway:

1. Medicines for Malaria Venture in collaboration with the Ugandan Ministry of Health will soon be launching a pilot intervention in 6 districts in Uganda that will provide a subsidised ACT via the private sector and measure the health impact achieved.
2. The Clinton Foundation in collaboration with the Tanzanian Ministry of Health has launched a pilot ACT subsidy to improve malaria treatment in Tanzania.
3. The Malaria Consortium with national research collaborators in Cameroon and the Institut de Recherche et Développement in Senegal are assessing the effects and progress of ongoing subsidy of ACTs.

The results of these and other pilots will inform the design and evolution of the AMFm.

[11] Affordable Medicines Facility for Malaria (AMFm) Monitoring and Evaluation Framework, working draft 17 October 2007.

8 Conclusions and Recommendations of APPMG

8.1 Conclusions

1. The APPMG has decided on the basis of the evidence presented and the discussions of the presentations in parliament that the concept of the AMFm is sound, and it is right to proceed.

2. The APPMG considers that the mechanism still needs more work to make it able to deliver its objectives to greatest effect, and to ensure a market mechanism to provide competition and incentive to drive down prices, but that there cannot be a delay in initiating the facility given the extremely poor current access to ACTs and the real risks of allowing continued use of inappropriate drugs. Improvements to the mechanism can best be made on the basis of early implementation experience.

3. The APPMG recognises that the AMFm alone is not sufficient to ensure availability and use of effective antimalarials by those who need them most. There is a huge need to strengthen health systems in countries most affected by malaria in order to make them better able to provide prompt and effective treatment of this common and treatable disease. Development of AMFm should be used as an opportunity to advocate for stronger systems, and should not be allowed to displace investment in system strengthening. In the longer term it is anticipated that better control of malaria would be a significant contributor to lightening the burden on the health system, as up to 40% of all health facility visits and as many as 20-30% of inpatient admissions are due to malaria in some malaria affected countries.

4. The APPMG expects that the financial requirements for the AMFm will taper down in a few years, as the market for effective antimalarials matures and stabilises. The rate is currently unknown.

8.2 Recommendations

1. Coordinated international support of the AMFm
For the AMFm to be successful it will need buy-in from multiple funding partners to cover the cost for as long as it takes to achieve its goals. It will also need full support from user countries. The Roll Back Malaria Partnership needs to create unity of purpose in fostering the AMFm, both encouraging support and tackling remaining challenges in perfecting the design.

2. Addressing the important issue of developing country pharmaceutical manufacturing capacity.
Further in-depth consultation is needed urgently with governments and pharmaceutical manufacturers in developing countries, both to explore ways to encourage a competitive market that will lead to unsupported price reduction and to avoid anticipated bottlenecks if recipient countries perceive that their own industries are at a disadvantage.

3. Monitoring and evaluation
Monitoring and evaluation needs to be intensive, particularly in the first few years. This is a new approach carrying some risks. We believe these risks can be managed to do little harm, but they should not be swept under the carpet. Public scrutiny and transparency of management are key to making the AMFm work.

9 Presentations on AMFm to All-Party Parliamentary Malaria Group (APPMG)

Session 1. 18 July 2007

Dr. Vinand Nantulya *ACT Global Subsidy: Perspective from Diagnostics,* Foundation for Innovative New Diagnostics (FIND). Emphasized importance of linking diagnosis to subsidised ACTs to avoid misuse and wastage of ACTs.

Prof. Richard Peto *Global high-level subsidy for ACT procurement to facilitate low-cost commercial, & other, distribution (allowing effective, affordable home treatment or healthcare facility treatment of suspected malaria)***,** Clinical Trial Service Unit & Epidemiological Studies Unit (CTSU),University of Oxford, UK. Stressed the importance of home based management of malaria with ACTs and outlined rationale for the AMFm.

Prof. Awa Marie Coll-Seck *Global ACT Subsidy: Role of RBM Partnership,* Executive Director, RBM Partnership. Described the objectives and design of the AMFm and noted the role of the Roll Back Malaria partnership in consensus building, design, fundraising and launch preparation. Anticipated that more affordable prices would triple uptake of ACTs.

Dr. Ian Boulton *Presentation on behalf of manufacturers.* GSK. Large manufacturers welcome the subsidy. Discussed potential road-blocks, emphasised the need for high quality products and reliable supplies, so ACTs are always in stock and highlighted the importance of diagnosis.

Session 2. 9 October 2007

Baroness Shriti Vadera *Representing DFID in House of Lords,* noted importance of AMFm to make drugs affordable, urged that it should work through existing systems, and emphasised DFID's support for malaria control and commitment to long-term predictable funding.

Dr. Stefano Lazzari *The Global Fund and the Affordable Medicine Facility-malaria (AMFm),* Senior Health Advisor, The Global Fund to Fight AIDS, Tuberculosis and Malaria. Described GFATM support, described the AMFm design, noted a number of issues to be addressed including a need to define, manage and support interventions for a "responsible introduction" of AMFm and the need to define a clear operational model for price negotiation with manufacturers. Noted that RBM Partnership has approached GFATM to consider hosting the AMFm, that initial analysis shows potential synergies and that the GFATM Board would consider the idea at its November meeting.

Dr. Joy Phumaphi *Affordable Medicines Facility for Malaria (AMFm)*, Vice President, Human Development Network, The World Bank. Described World Bank's growing commitment to malaria and its role in developing the AMFm, and gave a full description of how the AMFm would work.

Prof. Christopher Whitty *ACT subsidy- operational pitfalls and opportunities*, London School of Hygiene & Tropical Medicine. Noted the large proportion of children with malaria who never reach a formal health facility in many countries. He noted that there would be overdiagnosis and wastage of drugs, but that this is already the case. The subsidy is needed now but would taper down in time due to greater competition, reduction in risk pricing and potentially reduced overprescription and reduced incidence lowering demand.

10 Bibliography

Other documents consulted while preparing the report.

MEETING REPORT: Expert Workshop and Consultative Forum on a High-Level Buyer Subsidy for Artemisinin-Based Combination Therapies (ACTs), January 18 – 19, 2007 at the Royal Tropical Institute (KIT) Amsterdam. Organised by: The Ministry of Foreign Affairs of the Netherlands, Roll Back Malaria (RBM) Partnership Secretariat, and the World Bank.

Global ACT Subsidy: Information Pack, February 2007.

Global ACT Buyer Subsidy: Organization, Governance and Hosting Annex, 2 March 2007.
Global ACT Buyer Subsidy, Market Analysis and Methodology Annex:, 2 March, 2007.
Global ACT Buyer Subsidy, Buyer Subsidy Mechanism Annex, 2 March 2007.
DRAFT Proposal: Global ACT Buyer Subsidy, Summary, Submission to RBM Task Force on the Global ACT Buyer Subsidy, 2 March 2007.

Improving Access to Malaria Medicines with a Global ACT Buyer Subsidy: Executive Summary, 7 March 2007.

Outcomes of the first meeting of RBM Global ACT Subsidy Task Force, 13 March 2007, Washington DC.

ACT Subsidy – Future research: proposed way forward, final version 4 April 2007.
Monitoring & Evaluation and Operational Research, Stakeholder meeting, Geneva, 25 April 2007.

Global ACT Subsidy Project: RBM ACT Subsidy Task Force (Pre-read for 6 June meeting).

Additional Research Options – June to November: Consultation Draft, 4 June 2007.

RBM - Terms of Reference for RBM Global ACT Subsidy Task force.

Global ACT Subsidy, Public Information: Frequently Asked Questions, June 2007, Commissioned by the World Bank and funded by the Bill & Melinda Gates Foundation.

Increasing Access to Malaria Medicines: Draft Technical Proposal for a Global ACT Subsidy, Submission to Roll Back Malaria Global ACT Subsidy Task Force 10 August 2007. Dalberg

Jack, A. *Attack on malaria drugs subsidy*, Financial Times, London, April 11 2007.