Interim Report
of the Task Force Working Group 5 on Malaria

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Note to the reader
This Interim Report is a preliminary output of the Millennium Project Task Force on HIV/AIDS, Malaria, TB, Other Major Diseases, and Access to Essential Medicines. The recommendations presented herein are preliminary and circulated for public discussion. Comments are welcome and should be sent to the e-mail address indicated above. The Task Force will be revising the contents of this document in preparation of its Final Task Force report, due December 2004. The Final Task Force report will feed into the Millennium Project’s Final Synthesis Report, due to the Secretary-General on June 30, 2005.

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This publication does not necessarily reflect the views of the United Nations Development Programme (UNDP), its Executive Board or its Member States.
The Millennium Project is the independent advisory body to United Nations Secretary-General Kofi Annan that is commissioned with recommending, by June 2005, operational strategies for meeting the Millennium Development Goals (MDGs). This includes reviewing current innovative practices, prioritizing policy reforms, identifying frameworks for policy implementation, and evaluating financing options. The Project’s ultimate objective is to help ensure that all developing countries meet the MDGs.

As a United Nations-sponsored initiative, the Millennium Project proceeds under the overall guidance of the Secretary-General and United Nations Development Programme (UNDP) Administrator Mark Malloch Brown in his capacity as chair of the United Nations Development Group (UNDG). Professor Jeffrey Sachs directs the Project, which brings together the expertise of world-class scholars in both developed and developing countries, United Nations agencies, and public, non-governmental, and private-sector institutions. Ten Task Forces carry out the bulk of the Millennium Project’s analytical work with support from a small secretariat based at UNDP headquarters in New York. The Task Forces and their Coordinators are listed below.

<table>
<thead>
<tr>
<th>Task Force</th>
<th>Task Force Coordinators</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - Poverty and Economic Development</td>
<td>Mari Pangestu, Jeffrey Sachs</td>
</tr>
<tr>
<td>2 - Hunger</td>
<td>Pedro Sanchez, M.S. Swaminathan</td>
</tr>
<tr>
<td>3 - Education and Gender Equality</td>
<td>Nancy Birdsall, Amina Ibrahim, Geeta Rao Gupta</td>
</tr>
<tr>
<td>4 - Child Health and Maternal Health</td>
<td>Mushtaque Chowdhury, Allan Rosenfield</td>
</tr>
<tr>
<td>5 - HIV/AIDS, Malaria, TB, Other Major Diseases and Access to Essential Medicines</td>
<td>Agnes Binagwaho, Jaap Broekmans, Paula Munderi, Josh Ruxin, Burton Singer</td>
</tr>
<tr>
<td>6 - Environmental Sustainability</td>
<td>Yolanda Kakabadse Navarro, Don Melnick</td>
</tr>
<tr>
<td>7 - Water and Sanitation</td>
<td>Roberto Lenton, Albert Wright</td>
</tr>
<tr>
<td>8 - Improving the Lives of Slum Dwellers</td>
<td>Pietro Garau, Elliott Sclar</td>
</tr>
<tr>
<td>9 - Open, Rule-Based Trading Systems</td>
<td>Patrick Messerlin, Ernesto Zedillo</td>
</tr>
<tr>
<td>10 - Science, Technology and Innovation</td>
<td>Calestous Juma, Lee Yee Cheong</td>
</tr>
</tbody>
</table>

Additional information on the Millennium Project is available on its website at www.unmillenniumproject.org
COMING TO GRIPS WITH MALARIA IN THE NEW MILLENNIUM

DRAFT INTERIM REPORT
May 2004

Coordinators
Burton H. Singer
Awash Teklehaimanot
# Table of Contents

1. Introduction  
   1.1. The Millennium Project  
   1.2. Organization of the interim report

2. The resurgence and burden of malaria  
   2.1. Health burden  
     2.1.1. Temporal trends in the malaria burden
   2.2. Economic and social burden

3. Major initiatives and institutional policies for malaria control  
   3.1. Eradication period  
   3.2. The Global Malaria Control Strategy  
   3.3. The Harare Declaration of Malaria Prevention and Control  
   3.4. The Multilateral Initiative on Malaria  
   3.5. Roll Back Malaria Initiative  
   3.6. The Abuja Declaration on Roll Back Malaria  
   3.7. The Medicine for Malaria Venture  
   3.8. The Global Fund to fight HIV/AIDS, Malaria and Tuberculosis

4. Commonly used malaria control interventions  
   4.1. Case management  
     4.1.1. Malaria diagnosis  
     4.1.2. Malaria treatment  
     4.1.3. Malaria management at home  
     4.1.4. Malaria in pregnancy  
     4.1.5. Malaria in infancy  
   4.2. Vector Control  
     4.2.1. Insecticide-treated materials  
     4.2.2. Indoor residual spraying  
     4.2.3. Source reduction  
   4.3. Intervention strategies against epidemics  
   4.4. Information, education and communication

5. Success stories in malaria control  
   5.1. Tigray Region, Ethiopia  
   5.2. Highlands of Madagascar  
   5.3. Vietnam

6. Implementation challenges  
   6.1. Strengthening of health systems  
   6.2. Human resources capacity development  
   6.3. Social mobilization of communities  
   6.4. Scaling-up: intersectoral and public-private collaboration
7. Monitoring and evaluation

7.1. Demographic and health surveys
7.2. Health Management Information Systems
7.3. Measuring effectiveness of commodities
7.4. Development of a national GIS platform
   7.4.1. Cost-effectiveness of service promotion
   7.4.2. Impact on poverty

8. A roadmap for achieving the malaria-MDG

8.1. Goal and targets
8.2. Development of a business plan for global malaria control
   8.2.1. Coverage and impact of interventions
   8.2.2. Renewal of interventions and the products on which they are based
   8.2.3. Commodity management
   8.2.4. Linkages to the development of health systems
   8.2.5. Linkages to economic development and poverty reduction
   8.2.6. Costs and financing
   8.2.7. Monitoring and evaluation
   8.2.8. Advocacy

9. Research and development to meet current and future needs

9.1. Anti-malarial drug development
9.2. Malaria diagnostics
   9.3.1. Vector ecology
   9.3.2. Insecticide development
   9.3.3. Modification of vector populations
   9.3.4. Risk mapping
9.4. Malaria vaccines

10. Recommendations

References
1. Introduction

The Millennium Project Task Force on HIV/AIDS, Tuberculosis, Malaria and Access to Essential Medicines has been asked to propose a framework for accelerated implementation strategies for achieving the Millennium Development Goal 6 “to combat HIV/AIDS, malaria and other diseases’ in the developing world. The Working Group on Malaria within this Task Force seeks to develop an operational framework of implementation to significantly reduce malaria risk throughout the world’s tropics, particularly in Africa, so as to improve human well-being while also promoting economic growth in the following decades.

Despite a series of declarations on malaria and pledges by global partners in the second half of the twentieth century, very few health gains have been translated into sustained societal improvements in the lives of endemic populations in tropical Africa, where malaria transmission has historically been far more intense than anywhere else in the world. Success stories, notably during the Global Malaria Eradication Campaign (1955-1969), are primarily confined to areas of unstable malaria transmission with functioning health care systems, mainly in the temperate regions of the world. A curtailment of commitment and resources for malaria control and research characterizes the decades following the global eradication period, as malaria became a disease of the poor nations situated primarily in tropical areas (Shiffman et al. 2002). National malaria control programs have predominantly been fragmented, lacking organizational structure and financial and economic resources for sustainable implementation. The growing HIV/AIDS pandemic has also overstretched the already limited resources available for disease control in the past decade, particularly in Africa. The malaria problem is confounded further by the growing parasite resistance to the front-line antimalarial drugs.

Launched in 1998 by the WHO1, Roll Back Malaria – a global initiative on malaria – has successfully harnessed the necessary political commitment for the control of the disease within the international public health community. Subsequently, the level of internal commitment from African countries has risen sharply following the Abuja Summits on Roll Back Malaria (April 2000). However, national level implementation of the RBM initiative has severely been limited due to resource constraints. Experience has proven that adequate resources are necessary to keep political commitments alive. Since its inception in 2002, the Global Fund to Fight AIDS, TB and Malaria has availed additional resources for malaria control, fulfilling its role as a financial instrument. The Fund has successfully spawned several country-led multisectoral plans of action with a set of clear targets, serving as a basis for a broad-based response to the disease.

There is a broad consensus among experts of the need for a coordinated effort to strengthen health and other wider development systems to deliver malaria control interventions of proven effectiveness on a sustainable basis (Shiff 2000, Utzinger et al. 2001, Moerman et al. 2003). The success of malaria control programs also depends on adequate health information systems, relevant management skills at different levels to develop and implement appropriate policies and efficacious antimalarial drugs, diagnostic

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1 The other founding partners of RBM include the World Bank, United Nations Children’s Fund and United Nations Development Programme. Since its inception, over 90 multilateral, bilateral, non-governmental and private sector organizations have become actively engaged with RBM.
tools and insecticides. On the latter point, donor agencies hesitate to provide resources and required quantities of such commodities as anti-malarial drugs, insecticide treated bednets (ITNs) and insecticides. Consequently, resource-poor endemic countries are unable to attempt nation-wide malaria control, tending to resort to programs of limited scope. There is a sound biological and epidemiological basis for considering these services as public goods that promote health. Free distribution of available interventions tools to the poorest and most vulnerable populations would greatly reduce the malaria burden in endemic countries.

1.1. The Millennium Project

The Millennium Declaration, adopted by the 147 heads of State and Government and 189 Member States at the UN Millennium Summit in September 2000, formed the basis for eight mutually supportive goals, known as the Millennium Development Goals (MDGs) (Box 1). Originated from a series of UN resolutions and agreements over the past decade, the MDGs are intended to resolve the most important structural constraints impeding sustainable economic growth and hence social progress in developing countries. This concerted effort is committed to changing the course of policy in several key areas at all necessary levels to combat poverty, disease, illiteracy, gender inequality and environmental degradation, particularly in the poorest and most vulnerable populations. For countries trapped in entrenched poverty, the Millennium Development Compact highlighted health as a priority investment area in view of the fact that any progress in this front is mutually reinforcing and also contributes to better outcomes in the other MDGs. While national ownership by governments and communities in the developing world lies at the heart of this effort, there is a broad consensus on the need for heightened external technical assistance and financial commitment.

Headed by Professor Jeffrey Sachs, Special Advisor to the Secretary-General on the MDGs, the Millennium Project aims to identify the best strategies and the resource gaps ahead to achieve the MDGs in all developing countries by the year 2015. Ten Task Forces have been established towards that end, each comprised of scholars, policy makers and practitioners from both developed and developing countries, affiliated with United Nations agencies, public, non-governmental or private sector institutions. The Task Forces divided up the task according to their expertise to arrive at an integrated MDG strategy by the year 2005, which aims to take full account of the synergies among the MDGs. On the financial front, the Monterrey Consensus adopted by a large group of participating countries at the International Conference on Financing for Development in 2002 is

<table>
<thead>
<tr>
<th>Box 1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Millennium Development Goals</strong></td>
</tr>
<tr>
<td><strong>Goal 1</strong></td>
</tr>
<tr>
<td><strong>Goal 2</strong></td>
</tr>
<tr>
<td><strong>Goal 3</strong></td>
</tr>
<tr>
<td><strong>Goal 4</strong></td>
</tr>
<tr>
<td><strong>Goal 5</strong></td>
</tr>
<tr>
<td><strong>Goal 6</strong></td>
</tr>
<tr>
<td><strong>Goal 7</strong></td>
</tr>
<tr>
<td><strong>Goal 8</strong></td>
</tr>
</tbody>
</table>
committed to supporting this global effort through creating an enabling international and domestic economic environment, providing more extensive debt relief and improving market access to poor countries.

1.2. The organization of the interim report

This interim report draws on a large body of published literature and practical experience on malaria control efforts and identifies key implementation challenges and resources required for achieving significant reductions in the disease burden by the year 2015.

The report is intended for governments of malaria endemic countries, partners of rich developed countries, the private sector, non-governmental organizations and civil society organizations.

The Working Group on Malaria aims to put forward a number of recommendations that would promote accelerated implementation of effective integrated package of interventions to national scale. These recommendations from the interim report would feed into the overall Millennium Project report expected to be completed by December 2004.

Most commitments made by development partners to the control of malaria have regrettably been short-term and narrowly focused, paying little attention to the underlying determinants of disease propagation and strengthening of health care systems.

The Malaria Working Group would also undertake needs assessment exercise in collaboration with selected malaria endemic countries to come up with a cost estimate for scaled up program of malaria control. From these case studies, the total global need will be estimated. The cost estimate for malaria program in Ethiopia for 2005 and 2015 is in the order of million US dollars (per capita).
2. The resurgence and burden of malaria

Despite a century of systematic disease control efforts, malaria\(^2\) is still rampant in several regions of the world (Figure 1), draining the vitality of about 100 nations, particularly in Africa, south of the Sahara (WHO 2002). More than 2400 million people, nearly 40% of the world’s population, are at risk of malaria infection today (WHO 2000). During the Global Malaria Eradication Campaign between 1955 and 1964, malaria disappeared from several countries with temperate climates and was effectively suppressed in several subtropical and tropical regions in southern Europe, Latin America, in parts of Asia and the Middle East. Sub-Saharan Africa was, however, excluded from the eradication campaign and is the only region in which the malaria burden persisted throughout the twentieth century.

![Figure 1.1 Malarious regions of the world in the year 2002](image)

In the past three decades, the disease has, however, encroached upon areas where it had formerly been eradicated or had successfully been controlled (Baird 2000), offsetting the gains attained in the latter half of the past century. The intensifying parasite resistance to commonly used anti-malarial drugs is one of the most significant challenges facing malaria control efforts in all endemic countries, particularly in Africa. Chloroquine resistance is widespread where falciparum malaria is endemic, except Central America and the Caribbean (Wongsrichanalai et al. 2002). Sulfadoxine-pyrimethamine resistance

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\(^2\) Transmitted from person to person through the bite of a female Anopheles mosquito, malaria is an infection of red blood cells in human populations caused by protozoa of the genus Plasmodium. Four species of Plasmodium infect humans: Plasmodium falciparum, P. vivax, P. malariae and P. ovale. Of these four species, P. falciparum infection is the main cause mortality from malaria throughout the tropics and sub-tropics, especially in Africa, south of the Sahara (Snow & Gilles 2002).
has been reported in large parts of Southeast Asia, southern China, the Amazon basin, western Oceania, the Pacific Coast and in parts of Africa. The increasing risk of severe disease and death due to drug resistance threatens predominantly the vulnerable populations in malaria-stricken areas, such as young children\(^3\) and pregnant women.

Complicating matters further, environmental changes, socio-economic factors and political circumstances have led to a complex distribution of the disease across the globe, rendering malaria’s containment intractable with conventional currently available resources. The diversity with respect to the epidemiology and transmission intensity of malaria in endemic areas has important consequences for public health in general and for malaria control efforts in particular.

### 2.1. Health burden

Assessment of the true scale of the disease burden is fraught with formidable challenges due to insufficient surveillance and gross underreporting; however malaria is estimated to cause 300-500 million episodes of acute illness and 1.1-2.7 million deaths worldwide every year (WHO 2000). Sub-Saharan Africa where the disease transmission is most favored by a host of epidemiological, ecological and socio-economic factors bears more than 90% of the global malaria burden (WHO 2000). With an established multidrug resistance problem, the East Asia and Pacific Regions bear most of the remaining global malaria burden. Released in December 2003, the African Malaria Report states that “RBM is acting against a background of increasing malaria burden” (WHO/UNICEF 2003).

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\(^3\) For instance, Trape et al. (1998) demonstrated that the emergence and development of chloroquine resistance resulted in a 2.1 to 5.5 fold increase in mortality risk among children 0-9 years old in all study populations in the Sahel.
Lacking natural immunity to the disease, young children bear the brunt of malaria mortality, corresponding to nearly 20% of overall childhood deaths in Africa south of the Sahara (WHO/UNICEF 2003). Without effective interventions, the number of febrile episodes in children under 5 year of age is estimated to double over the next two decades (Breman 2001). Besides children, pregnant women with suppressed immune systems, particularly primigravidae in highly endemic areas, are at a greater risk of experiencing acute malaria infections with a range of clinical outcomes, from anemia to severe complications such as cerebral malaria (Menendez 1995). Malaria infection during pregnancy has been associated with low birth weight, affecting the development and survival of newborns, especially in Africa (Murphy & Breman 2001). As a risk factor, poor nutritional status has been associated with increased malaria morbidity and mortality, particularly in young children (Shankar 2000).

Several studies have shown that people living in poorly constructed houses in endemic areas have a higher risk of vector contact and malaria infection than those living in well constructed houses (Gamage-Mendis et al. 1991, Gunawardena et al. 1998, Lindsay et al. 2003, Konradsen et al. 2003). Overall, house construction type is primarily connected to the socio-economic status of households. Therefore, once infected, the inhabitants of poorly built houses are most likely to suffer from the adverse effects of malaria, owing to their limited capacity to use health care services and preventive measures to protect against the disease.

Rapid and unplanned urban growth in tropical areas creates suitable conditions for malaria transmission, mainly at the periphery of towns and cities. People who migrate from rural areas generally settle in poorly constructed houses in densely populated and underdeveloped periurban areas and bring along their traditional rural practices, such as farming in small garden plots with small-scale irrigation, that favor mosquito breeding. Today, malaria is a major public health problem in urban settings and is estimated to cause 3 to 9 million malaria cases every year (WHO 2001).

Engineering and development projects such as construction of dams, roads and industrial centers may increase the number of mosquito breeding habitats and lead to disease propagation in malaria-prone areas (Patz et al. 2000). Another concern is the incursion of non-immune people into forests and jungles for agriculture, road construction, timbering, gem mining and where malaria vectors are readily available (Nájera et al. 1992). For instance, the Amazon Basin Settlement Project attracted non-immune populations to the region for mining activities, and malaria epidemics broke out, as the principal malaria vector, Anopheles darlingi, adapted to new habitats (Marques 1987, Molyneux 1998). On the other hand, human interference may sometimes have an adverse effect on malaria transmission in endemic areas. For instance, deforestation in Thailand led to the cessation of malaria in certain regions (Oaks et al. 1991).

2.1.1. Temporal trends in the malaria burden

Historically, malaria plagued not only the tropical but also the temperate regions of the world. For instance, malaria occurred as far north as Maine and Vermont in the United States, even spilling over to Canada. Natural disappearance of the disease in the mid-nineteenth century from vast regions in North America and Central Europe was mainly
attributed to land reclamation efforts for agriculture, increased animal husbandry, improved housing and other effects of development (Bruce-Chwatt 1988).

In the beginning of the twentieth century, malaria was a major health problem in Southern Europe, Latin America, the Western Pacific, the Caribbean, in much of Asia, and the Middle East. The global malaria picture was altered considerably during the Global Eradication Campaign between 1955 and 1969. With the exception of Europe, North America and some small islands, the eradication goal of the past century was never realized (Litsios 1996). However, unprecedented reductions in the prevalence of malaria were achieved in the Middle East, the Mediterranean basin, the Far East and Latin America (Roberts et al. 2000). Despite being the cradle of the disease, African countries were only partially involved, given the vast scale of the malaria problem on the continent (Greenwood & Mutabingwa 2002).

During the 1970s and 1980s, national health systems underwent substantial reforms in many developing countries, moving from vertically organized disease-specific orientations to a strategy based on the delivery of integrated health services. “Primary health care” was adopted as a key element in the organization of the health system (Mayhew 1996, Vendiktov 1998). These developments resulted in a series of decentralized health care systems that diluted the force of disease-specific programs in most countries.

In Asia and throughout much of the Americas, today’s malaria burden is a residue of what once prevailed. It is heaviest in remote, rural areas and in situations where there is civil unrest or other conflict. In Asia, therefore, the heaviest malaria burden rests in the Mekong region, along international borders and in other conflict-stricken parts of the region. In South America, in the Amazon basin, malaria is brought to indigenous people similarly by the incursions of commercial and government-sponsored settlement activities. Although malaria is not particularly severe in Central America, India, Sri Lanka and in the islands of the Western Pacific, its burden persists at unacceptable levels (WHO 1999). Should antimalarial drugs fail completely, the global malaria situation would become catastrophic.

In tropical Africa, the extent of malaria endemicity has remained largely unchanged during the past century, and perhaps for the past several millennia (Carter and Mendis 2002). In addition to financial constraints, inadequate health systems, which would effectively deliver anti-malarial drugs or other interventions, lie at the heart of the problem. Africa is particularly vulnerable to any failure on the part of the international donor community to supply effective antimalarial drugs and other essential supplies and commodities.

2.2. Economic and social burden

The disease burden imposed by malaria carries with it a corresponding economic burden. Several studies have been undertaken to estimate the economic impact of malaria by focusing on direct prevention and treatment costs born by households and the public health sector. Some studies also considered income losses due to malaria morbidity as indirect costs of the disease. In rural communities, malaria transmission season generally coincides with that of planting or harvesting, leading to reduced agricultural productivity and output. Many subsistence farmers in Africa shoulder the heaviest burden of malaria
because their way of life is so fragile such that a brief period of illness that delays planting or that coincides with the harvest, may produce catastrophic effects. The problem becomes exacerbated, of course, where drugs must be purchased by the farmer out of his own meager cash reserves. Investments in malaria control would enhance the quality of life of the poorest of the poor: those who co-exist with this disease.

Lately, malaria control has been viewed as a developmental problem, and hence plays a key role in poverty reduction. Malaria incapacitates the workforce, leading to decreased economic productivity and output in various sectors of the economy (Sinton 1935 & 1936, MacDonald 1950, Sachs 2002). Malaria suppresses economic links between tropical countries and the more temperate regions of the world that generally are non-malarious. In today’s global economy, such isolation carries profoundly negative effects. Investors from non-malarious regions tend to shun malarious regions for fear of contracting the disease - a fear that is well-grounded by the recent experience of BHP Billiton, a London-based mining and metals company. In a US $1.4 billion joint venture investment to build an aluminum smelting facility in Mozambique, the largest foreign investment so far in that country, the company was faced with 7,000 cases of malaria in two years, and the deaths of 13 expatriate employees. Mortality among highly skilled professionals strongly discourages economic investment in malaria endemic sites. Investments in many kinds of production - in mining, agriculture and manufacture - can be crippled if the labor force faces a heavy disease burden, or if the presence of malaria raises the cost of attracting needed labor. In the colonial period between 1900 and 1950, malaria control was frequently decisive in attracting the labor force that was essential for developing rubber and tea plantations in the former Malay States (now Malaysia) and for mineral extraction in the former Northern Rhodesia (now Zambia). Since the middle of the last century, international trade and finance have become critical for economic development, and malaria-induced adverse effects on foreign trade and investment are likely to be of tremendous macroeconomic importance, slowing economic growth and further widening the gap between malaria endemic countries and the rest of the world.
3. Major initiatives and institutional policies for malaria control

The modern era of anti-malaria efforts began during the second half of the twentieth century and has continued through a series of mutations and variations. The principal initiatives, summarized below, provide an essential context for our main recommendations.

3.1. Eradication period

The availability of DDT and the experience of its profound effect on malaria transmission as well as the effectiveness of chloroquine antimalarial drugs encouraged the world to attempt to remove the burden imposed by malaria by eradicating this infection, globally. The program began during the 1950s and ended within the following decade. But even given the extraordinary efforts of the WHO in limited sites in western Kenya (the Kisumu project) and Nigeria (the Garki project), the campaign led to a reduction in the incidence of malaria but failed to eliminate transmission. Due to the perceived intractability of malaria in Africa and concerns of sustainability, the “Global Programme” largely bypassed that continent even though the malaria burden was greatest there. For the next several decades, malaria attracted little interest, and scant resources were allocated by the international community to this problem, leading to poorly coordinated and fragmented intervention efforts.

3.2. The Global Malaria Control Strategy

Malaria has been a subject of intense discussion at the annual meetings of the World Health Assembly during the last decade of the 20th Century. The 1990 meeting of this Assembly attributed the resurgent malaria situation to rapidly increased drug resistance, lack of clear strategy and shortage of financial resources. Development of an appropriate strategy and mobilization of resources to intensify effective intervention measures were recommended. The Amsterdam Ministerial Conference on Malaria of 1992 adopted a global strategy that subsequently was endorsed by the UN General Assembly in 1993. This strategy recognized that the epidemiology of malaria is exceedingly variable and that its ecological, social and operational bases should be considered locally. The four basic technical elements of the resulting strategy were as follows (WHO 1993):

1. Provision of early diagnosis and prompt treatment,
2. Selective use of preventive measures such as insecticide treated nets and other vector control activities,
3. Prevention, early detection, and containment of epidemics, and
4. Strengthening local capacities in basic and applied research.
This strategy was well received by the international community and the endemic countries and great expectations were generated for meaningful engagement in malaria control efforts. Pledges of support, however, never materialized.

3.3. The Harare Declaration of Malaria Prevention and Control

Heads of State of the Organization of African Unity took particular note of the deteriorating malaria situation in Africa at a Summit meeting in 1997 and unanimously passed a Declaration of Malaria Prevention and Control that was designed to promote African economic recovery and development. The Summit approved a comprehensive intervention plan for malaria and called upon all member states to take immediate and substantive action. UN agencies such as the World Bank, various governments and bilateral and multilateral agencies were urged to participate actively in the effort and mobilize additional resources to meet the challenge of malaria on the African Continent. This potentially powerful commitment has not yet been implemented.

3.4. The Multilateral Initiative on Malaria

In 1995, key scientific and donor agencies convened in Dakar, Senegal to discuss collaborative efforts to address health problems in Africa. In order to facilitate this process, malaria was selected as its initial focus. Out of this initial move, the Multilateral Initiative on Malaria (MIM) was created, consisting of a group of organizations and individuals that aimed to maximize the impact of scientific research on malaria in Africa. The creation of MIM was born out of several main needs. First, the investment in research was low relative to the burden of disease and there was a perceived need for effective use of existing control tools. Second, malaria was recognized as a problem that required short-, medium- and long-term research priorities in order to be contained effectively. Third, an inequality existed between knowledge of the disease – its pathology and etiology – and its reduction in endemic countries, which led to the identification of another need: to strengthen research capacity in Africa. This aim was to be accomplished through collaboration and communication between researchers in Europe and America and those in the endemic countries of Africa. The combination of these efforts has heretofore culminated in several effective partnerships between scientists from developed countries and their African counterparts.

3.5. Roll Back Malaria Initiative

Upon assuming the directorship of the World Health Organization in 1998, Dr. Gro Brundtland established an initiative designated as “Roll Back Malaria (RBM), which aims to reduce the burden of malaria throughout the world with special focus on Africa (WHO 1998). This initiative derived from an earlier African initiative for accelerated implementation of anti-malaria interventions by African Governments, and specified the goal of halving the burden of malaria by 2010. This original WHO initiative on RBM was joined by an array of international organizations, including the World Bank, UNDP and UNICEF. RBM adopted the malaria control

http://www.who.int/tdr/diseases/malaria/mim.htm accessed April 23, 2004
strategies that were accepted by the international Community in the Amsterdam Ministerial Conference of 1992 under a strong banner of dynamic societal movement, coordinated action, and partnership.

The Roll Back Malaria initiative has achieved notable momentum and consensus among the partners on malaria control. This initiative was instrumental in the development and formulation of country-led partnerships that included UN agencies, bilateral donors, various government sectors, civil societies, NGOs, the private sector, universities and research institutions. A number of malaria endemic countries have put together evidence-based strategic plans for implementation based on situation analysis of their respective ecological and epidemiological conditions to address the burden of the disease within the context of health sector development. Despite the recognition and acceptance of the RBM goals, targets and strategy, funding constraints, however, restricted the launching of countrywide implementation efforts (WHO 2002).

3.6. The Abuja Declaration on Roll Back Malaria

The African summit on Roll Back Malaria, held in Abuja, Nigeria in April 2000, reflected a real convergence of political commitment and technical consensus on methods for dealing with the prevention and control of malaria. Delegations from 44 of the 50 malaria endemic countries in Africa attended the summit. Nineteen country delegations were led by heads of state and the remaining delegations by senior government officials. The summit was also attended by senior officials from WHO, the World Bank, the African Development Bank, UNICEF, UNDP, UNESCO and various bi- and multi-lateral agencies. The heads of state and other delegates reviewed the evidence presented to them and ratified an action-oriented declaration. They endorsed the RBM movement and its objectives and set operational targets and milestones. Many of the major international donors that participated in the summit, including the World Bank and the African Development Bank, pledged increased commitment and resources. The World Bank alone pledged $750 million.

Since the Abuja Summit, many African Governments have demonstrated their commitment to anti malarial intervention efforts by allocating human and financial resources and removing taxes and tariffs on mosquito nets. No pledges, however, have yet materialized to enable RBM to support endemic countries in implementing an integrated package of interventions on the national scale.

3.7. The Medicine for Malaria Venture

The Medicine for Malaria Venture (MMV) was established as a non-profit foundation, headquartered in Geneva, in 1999. It developed in response to discussions between the WHO and the representative body for the pharmaceutical

5 http://www.mmv.org accessed April 23, 2004
industry, the International Federation of Pharmaceutical Manufacturers Association (IFPMA). MMV uses the public-private partnership model, with funding from philanthropic organizations such as the Bill and Melinda Gates Foundation to facilitate discovery, development and delivery of new, affordable anti-malarial drugs. Since its inception, the MMV has played a significant role in streamlining drug research efforts by providing managerial and logistical support through active portfolio management, which has increased the success rate of potential anti-malarial therapies, resulting in an average of one drug discovery and development every five years. As of December 2003, the MMV had a total of 21 projects: 12 in the discovery phase and 9 in the development phase.

3.8. The Global Fund against HIV/AIDS, Tuberculosis and Malaria

A Global Fund against AIDS, TB and malaria was initiated within the UN that sought to support an array of national efforts designed to reduce the burdens of malaria as well as HIV and TB. The program required formal submission of a proposal by malaria endemic countries and evaluation by a review panel that includes members who are expert in one or another of these diseases. The Global total of 5134 million dollars for the first three rounds of proposals, from 42 malaria-endemic countries were approved for support. Although the fund provides a much-needed complement to existing public health funding, the amount available to the fund is not sufficient enough for countries to launch comprehensive intervention packages on national scales. The input of the Global Fund has made significant difference and has motivated a number of malaria endemic countries to update their respective anti-malarial drug policies and to shift to effective combination therapies as well as to upscale their interventions. It will be critical for the international donor community to support and strengthen the GFATM to mobilize adequate resources.

“The input of the GFATM has motivated malaria-endemic countries to upscale their interventions.”
4. Commonly used malaria control interventions

A variety of intervention packages can, in principle, be implemented with available tools. The components of such packages consist of early diagnosis and treatment, use of insecticide treated nets, intermittent preventive treatment (IPT) of pregnant women, application of indoor residual insecticide in regions prone to epidemics and source reduction methods where feasible, coupled with a rigorous monitoring and evaluation system. The specific selection and use of these interventions as well as the nature of the monitoring system and sources of data for such assessment depend very much on the country and district or communities to be targeted for control. We briefly discuss the essential features of the intervention tools that are available today.

4.1. Case management

Coherent national plans are required for maximizing access to effective anti-malaria drugs. Particular attention should be devoted to issues relating to access and quality of treatment distributed by public as well as private providers, including the measures required for strengthening treatment practices. The initiative should also address how the health system infrastructure will support expanded service delivery, including supervision, technical support, provision of drugs, and management at all levels, and what measures are needed to strengthen the capacity of the health system to support effective treatment strategies, including community based interventions.

In many countries, particularly in sub-Saharan Africa, a solid case can be made for free distribution of artemisinin-based combination drugs for treating uncomplicated malaria, quinine for the management of severe malaria and sulfadoxine-pyramethamine (SP) for IPT of pregnant women.

4.1.1. Malaria diagnosis

A diagnosis of malaria must precede treatment with antimalarial drugs and is made first on a clinical suspicion of the disease based on fever and other constitutional signs and symptoms. A confirmatory diagnosis of malaria requires evidence of the presence of either i) blood stage malaria parasites detected by microscopic examination of stained blood films, or ii) their products - the most widely available being rapid diagnostic tests (RDTs) which are based on the detection parasite antigens or enzymes.

A confirmed diagnosis of malaria prior to treatment is highly desirable. However, it may not always be possible, nor necessary, depending on the situation. In areas of low to moderate transmission where malaria annual inoculation rates lie in the range of < 1 to about 8, people of all ages have little antimalarial immunity, the presence of malaria parasites in blood is almost always indicative of malarial disease. In such situations, which prevail in much of Asia, the Americas and other regions outside Africa, a confirmatory diagnosis of malaria must be sought wherever possible, prior to treatment with antimalarial drugs.

In areas of intense malaria transmission (annual inoculation rates of > 8) such as in tropical Africa where the burden of malaria is greatest, and where the disease and its mortality is largely confined to children under five years of age, there has been less
dependence on a parasitologically confirmed diagnosis for the treatment of malaria, particularly in children. In this situation, malaria happens to be the most frequent cause of fever in children under five years of age, and a diagnostic tool may not be readily available in situations that warrant life-saving treatment. Furthermore, because parasite prevalence rates are high in children, the presence of malaria parasites in the blood may not, in itself, be indicative of a malarial illness. Collectively these justified the widely accepted practice of treating malaria on clinical grounds of fever rather than on a parasitological diagnosis in high transmission situations, especially when antimalarial drugs were cheap, and cost considerations were not an important part of the decision to treat. Now, however, with malaria treatment artemisinin-based combination treatments for malaria costing over 10 times more than previous monotherapies, an improved diagnosis that would allow better targeting of malaria treatment is called for, to reduce the cost of malaria management to national governments and the individual. The risks associated with making a parasitological diagnosis mandatory in these situations (e.g. delays in treatment and a higher child morbidity and mortality) must be weighed carefully against the benefits (e.g. cost savings on ACTs). Other considerations include the feasibility of introducing diagnostic tools. In specific,

1. diagnosis entails a cost (RTDs cost 0.6-1 USD per test);
2. they may have to be placed in the hands of community health workers and volunteers who are increasingly playing a role in dispensing antimalarial drugs nearer the home;
3. the performance of the diagnostic tests - at present the sensitivity of several RTDs seem to be affected by stability-related problems, specially under conditions of use which prevail in the field.

In the final analysis, a parasitological diagnosis is indicated and should be made available for malaria in situations of low to moderate endemicity and unstable malaria, and possibly also in the management of adult malaria in high transmission areas in Africa. Given the nature of diagnostic tools available at present there is neither a strong case for, nor the feasibility of, making a parasitological diagnosis mandatory for the treatment of childhood malaria in stable high transmission regions of Africa.

4.1.2. Malaria treatment

Resistance against conventional anti-malarial drugs has intensified in the 1990s. Multi-drug resistant P.falciparum malaria is widespread in South-East Asia and South America. Resistance to inexpensive antimalarial drugs such as CQ and SP is universal throughout much of Africa, particularly, in the eastern, southern and central parts of the continent. In some countries for example, the level of resistance to chloroquine now exceeds 80%. However, it is important to note that CQ is still effective for the treatment of *Plasmodium vivax*. As a response to growing *P. falciparum* resistance to anti-malarial drugs, five different CT are recommended by the WHO:

1. artemether-lumefantrine (Coartem);
2. artesunate plus amodiaquine;

6 http://mosquito.who.int/cgi-bin/rbm/rbmportal/custom/home/mal/login.jsp accessed May 28, 2004
3. artesunate plus SP, in areas where SP retains its efficacy;
4. artesunate plus mefloquine, in areas with low to moderate transmission;
5. amodiaquine plus SP, in areas where efficacy of both amodiaquine and SP remains high.

Of the listed five options, Coartem is a fixed-dose combination anti-malarial drug that is co-formulated. The rest of the combinations are comprised of independently acting antimalarial drugs that are co-administered. The last combination therapy is reserved as an interim option for countries, which are unable to switch to ACTs. This new generation of antimalarial drugs is more than ten times as expensive as is the currently used package of ineffective drugs.

In the past three years, 32 endemic countries have updated their treatment policies and have adopted one of the above five combination therapies. South Africa, Zambia, Zanzibar, Burundi, Gabon, Comores, Kenya, Ghana, Equatorial Guinea, Cameroon and Sao Tome & Principe are the only countries in Africa that have moved to ACTs Mozambique, Rwanda and Senegal have switched to amodiaquine and SP. However, implementation with the public health sector is still weak. In Africa only 5 of the 14 countries and outside of Africa 10 out of 14 countries are actually deploying these drugs. In the interim, a number of countries are attempting to buy time by using a non-fixed combination of existing drugs such as CQ + SP or AQ + SP. The decision to continue with these drugs, in the face of reduced efficacy, is largely due to financial constraints.

With the introduction of CT drugs, a two prong strategy has been proposed, based on microscopic diagnosis at district hospitals and health services levels and rapid diagnostic tests at peripheral health posts and community levels in targeted countries. Because more that 80% of malaria cases are managed at home outside the health services, RDTs can effectively facilitate the performance and quality of work of community health agents in the diagnosis and treatment of cases at the community level in areas of unstable transmission. In high transmission areas, the use of RDTs can be useful, provided that it is used as complimentary to clinical diagnosis in order to target treatment to those who are clinically ill and parasitemic.

4.1.3. Malaria management at home

Health service coverage in many African countries is inadequate, and rural populations generally lack access to minimal standards of health care. In addition, delivery of drug supplies and other essential commodities, particularly for peripheral communities, generally is not reliable. Most often, service agencies run out of essential drugs such as anti-malarials. These factors, coupled with physical distance and problems of affordability, pose major obstacles and disincentives for rural populations to use health services. Instead, they resort to self-medication using anti-malarial drugs obtained from the open market or traditional herbal medicines. The diagnosis of malaria by mothers and caregivers should be based on the presence of fever or a recent history of fever. Delivery of pre-packaged anti-malarial drugs facilitates their use at household and community levels and may improve compliance.
An RBM survey, undertaken as part of a situation analysis in several African countries, indicated that between 70% and 90% of febrile children are treated at home. As a result, a number of endemic countries seek to improve their health care coverage by extending such services beyond the formal health infrastructure through the use of volunteer networks of village health workers. Communities now readily accept this approach because mothers and caretakers can obtain prompt access to effective drugs and counseling in their respective villages. This sharply reduces severe morbidity and under-five mortality (Chahnazarian et al. 1993, Ghebreyesus et al. 1996, Pagnoni et al. 1997, Kidane et al. 2000).

Countries, therefore, should address the issue of treatment for uncomplicated malaria at the community level. If the targets set at Abuja are to be achieved, large-scale introduction of such innovative ways for delivering anti-malaria treatments should receive particular attention. However, it is critical that these initiatives are backed by a well functioning health system that provides technical support and guidance to deal with referred cases.

4.1.4. Malaria in pregnancy

Malaria infection during pregnancy is a major public health problem. In most endemic African countries, pregnant women are the main adult risk group for malaria. The malaria burden during pregnancy is a result of infection with Plasmodium falciparum. At least 30 million women in stable malaria transmission areas of Africa become pregnant every year (WHO/UNICEF 2003).

In areas of unstable transmission, where risk for malaria attack is low, adult women become ill when infected with P. falciparum as they do not have significant level of acquired immunity. In these conditions, pregnant women have the risk of developing severe malaria 2-3 times higher than non pregnant women who lived in the same area (WHO/UNICEF 2003).

Where Plasmodium falciparum transmission is intense, maternal and infant mortality is associated with malaria in pregnancy. Pregnant women are most at risk from malarial infection during the first and second pregnancies. Malaria infection leads to acute disease and anemia and to sequestration of parasites in the placenta, which in turn leads to low birth weight, the greatest risk factor for neonatal death.

The administration of intermittent preventive treatment (IPT) to pregnant women as part of routine antenatal care, particularly during their first and second pregnancies, largely eliminates anemia and low birth weight. The regimen should be given during the second and third trimester. Although IPT with SP effectively reduces severe anemia and low birth weight, few pregnant women attend antenatal clinics in many African countries. An effective replacement alternative to SP is required because the efficacy of this drug has been compromised throughout much of Africa. The challenge therefore, is to build capacity of antenatal care services to provide routine and effective anti-malaria treatment to all pregnant women.

In addition to the administration of IPT, pregnant women should be encouraged to sleep under insecticide treated nets. The proposed project seeks to protect pregnant women by the free administration of IPT and distribution of ITNs through the antenatal
care services of the targeted countries. Such services will also motivate pregnant women to seek antenatal care.

4.1.5. Malaria in infancy

The need to protect infants is urgent because they are so vulnerable to malaria. Deaths and severe anemia are most frequent in this age-group. Although infants can be protected substantially by chemoprophylaxis, provided at weekly or fortnightly intervals, such measures are difficult to sustain and may accelerate the onset of drug resistance while also impairing the development of natural immunity to malaria.

Administration of intermittent preventive treatment to infants (IPTI) has reduced episodes of clinical malaria by 60% and severe anemia by 50% in a Tanzanian study. These infants, who received three SP treatments during their first year of life, experienced substantially fewer episodes of severe anemia by 60% and 50% respectively, at the time of EPI vaccination or during health center attendances. No subsequent rebound in infection was noted. Such IPT delivery may provide a major method for reducing the burden of malaria in intensely endemic sites in Africa. Additional multi-center studies on the safety and efficacy of IPT in children are being undertaken in a number of countries in order to determine whether the immune response to EPI vaccines becomes compromised. These issues should soon be clarified.

4.2. Vector control

4.2.1. Insecticide treated materials

Bed nets and other materials that are impregnated with pyrethroid insecticides provide a chemical as well as a physical barrier to contact between malaria vector mosquitoes and the human residents of a site. The measure is effective because the more important African vectors mainly bite at night. In addition to protecting the net user, such nets usually reduce local vector density provided that the level of coverage is sufficient. This population effect may be crucial, and can most rapidly and economically be achieved by providing impregnated nets, cost-free, for every bed or other sleeping place in a community and by organized annual re-treatment these nets regularly. The introduction of long lasting insecticide treated nets (LLITNs), which could last up to four years without treatment, removes the challenge of retreatment of nets with insecticides twice a year. As many as six lives have been saved each year among each 1,000 children who were served in this manner (Lengeler, 1998), and this beneficial reduction in prevalence and anemia of malaria related fever may last for several years (Maxwell et al 2002). This technology appears to be beneficial at varied latitudes, regardless of the force of transmission. This finding suggests that anti-vector measures may generally be applicable in intensely endemic as well as less endemic sites.

4.2.2. Indoor residual spraying

Applications of residual insecticide, especially DDT, to the inside surfaces of house walls and on ceilings was the main method used to eliminate malaria from southern Europe, most of the USSR, Taiwan and the highlands of Madagascar in the 1940s and 50s and its massive suppression in the 1950s and 60s in India, Sri Lanka, tropical South America,
China, South Africa, Zanzibar and in several large field trials in mainland tropical Africa. Some of these trials produced better results than did any of the more recent trials that employed treated nets (Curtis & Mnzava 2000). In Zanzibar and perhaps certain parts of West Africa, DDT resistance in *A.gambiae* now precludes effective use of DDT. In South Africa, however, reversion to DDT spraying from pyrethroid spraying during 2001 has relieved the increasing malaria problem associated with pyrethroid resistance in *A. funestus* (Hargreaves *et al.* 2000). Similar measures resolved the disastrous Madagascan epidemic of the 1980s that killed as many as 40,000 people (Curtis 2002).

The International Convention of Persistent Organic Pollutants contains an amendment specifically excluding DDT for vector control from being banned. There are effective, but more expensive alternatives, such as pyrethroids that can be sprayed where the vectors are DDT resistant. The use of indoor residual spraying (IRS) in malaria control is reserved for epidemic prone areas or in general in areas of unstable transmission. “Fire brigades” of trained and equipped spray-men may be appropriate for deployment where in the case of malaria epidemics.

4.2.3. Source reduction

Because the breeding places of *A.gambiae* are numerous and transient in many African villages, the breeding sources of these mosquitoes may be difficult to eliminate. In towns, semi-arid or in mining areas, however, where breeding sites are limited in number, and a work force of drainage engineers and/or larval surveyors can be mobilized, vector density and malaria prevalence may be vulnerable to attack. In Sri Lanka, for example, application of an insect growth regulator to gem pits effectively suppressed malaria transmission, prevalence of infection and case incidence (Yapabandara & Curtis 2002). This success probably depended on the ability of local residents to locate the many hundreds of pits present in the region. Large scale rural-urban migration in many African cities has been accompanied by substantial and ongoing ecosystem transformation. As city boundaries expand, breeding sites tend to proliferate, peripherally, in new settlement areas of the city. Simultaneously, the process of urbanization itself leads to source reduction and/or shifts in location and character of breeding sites within the changing boundaries of the inner city. Urban agriculture and its varying intensity and location necessitate agriculture-health linkages for effective control. Risk mapping of this dynamic in Dar es Salaam (Yamagata, 1996), including specification of locally tuned source reduction techniques, provides an initial basis for developing more effective urban malaria control strategies.

Many malaria endemic urban centers in Africa are surrounded by malarious rural villages – a setting that renders it difficult to differentiate between locally contracted infections and imported cases from the surrounding villages in people who come to these urban centers for treatment. Because the epidemiological factors in urban environments are not well understood, WHO has commissioned a study in multi-urban centers. Where appropriate, source reduction measures may reasonably be employed to suppress transmission.

Source reduction by intermittent irrigation strategies has been effectively used since the 1920s to control rice field malaria, primarily in Asia (Baolin 1988, Takken *et al.* 1990). In multiple instances, these irrigation schemes have not only reduced the vector
populations, but the change in nutrient cycling patterns induced by these strategies has led to increased rice production above what had been attained by conventional irrigation (continuous flooding (Keiser et al. 2002). The opportunity to expand the domain of intermittent irrigation in concert with the development of new high yield strains of rice is gradually being taken up by the International Rice Research Institute (IRRI) and linked to malaria control via the System-wide Initiative on Malaria and Agriculture (SIMA) and the International Water Management Institute (IWMI).

4.3. Intervention strategies against epidemics

In the absence of anti-malaria immunity, malaria is exceedingly debilitating and life-threatening. Where infection is infrequent, as in some parts of Africa, residents gain little or no anti-malaria immunity, and such people are peculiarly vulnerable to the outbreaks that occasionally strike the region. Introduction of malaria into non-endemic sites, migration and displacement of non-immunes into malaria endemic regions or an unusual increase in transmission in areas where endemcity is low could trigger explosive epidemics affecting people of all ages.

In addition to the direct health burden, epidemic malaria results in heavy economic losses, both at household and community levels, both in terms of health care expenses and lost productivity. In many rural communities of Africa, epidemics strike when planting or harvesting is most intense and when the demand for intensive labor is greatest. Because malaria epidemics affect people of all ages, the impact on productivity at the household, community and country level frequently is considerable. Malaria epidemics frequently occur following years of drought and famine, further impinging on populations already weakened by malnutrition and poverty.

Outbreaks of *Plasmodium falciparum* infection, which often result in high case fatality rates, have been reported throughout those parts of Africa in which hypo- and meso-endemic malaria prevails. In Africa alone, an estimated 110 million live in malaria-prone areas. These population groups are at high risk of death or severe morbidity. More than 150,000 people died out of some three million clinical cases during the malaria epidemic that hit Ethiopia in 1958 (Fontaine 1961).

Recently, devastating epidemics have struck Zimbabwe, Botswana, Mozambique, Swaziland, Ethiopia, Kenya, Senegal and South Africa. Several East African countries including Ethiopia, Kenya, Uganda and Tanzania have experienced recurrent malaria epidemics that often affect large numbers of people and are attributed to anomalies in rainfall and temperature. Other than climatic conditions, man-made changes in the environment and factors such as war and migration similarly trigger epidemics. The extent of damage caused by these epidemics is not adequately documented.

Interventions against malaria outbreaks include:

1. Detailed study of epidemic triggering mechanisms
2. Mechanism and models for forecasting, early warning and detection of epidemics
3. Organization and capacity for information analysis and utilization as well as for effective and prompt response
4. Inter-sectoral collaboration for rapid assessment and response of suspected epidemics.

Effective forecasting with efficient surveillance and adequate epidemic preparedness and timely response can markedly reduce the socio-economic impact of malaria epidemics in terms of lost lives, suffering and lost production. Development of such systems, initially on a proof-of-principle basis for a few countries, would contribute to the development of efficient forecasting and surveillance systems in the context of integrated surveillance systems (IDS).

In the event of proven malaria epidemics, indoor residual spraying, which effectively curtails transmission, is recommended. Parallel to vector control measures, febrile cases should rapidly be screened and treated with effective drugs.

4.4. Information, education and communication (IEC)

Community participation involving “information, education and communication” components (IEC) is crucial to the success of a successful malaria control program. Such efforts must create and retain open communication and fruitful collaboration with the beneficiary population, itself, and national, district or local health agency responsible for the effort. IEC components should be sensitive to local socio-cultural and environmental variables and should foster a sense of ownership by all involved. Such an approach requires that the responsibility for the program is distributed broadly across all participatory levels. All concerned must understand each other and the purposes of the program, including possible points of friction that might prevent successful implementation. Collaboration must also be sought and established with personnel and institutions already operating in the site in order to integrate the antimalaria effort. Local adaptations are crucial. Intervention strategies should be worked out and agreed upon in concert with the affected communities. Personnel with experience in IEC activities, and those with appropriate language and communication skills and a solid knowledge of the socio-cultural, political and economic contextual characteristics of the communities in question should be engaged to guide the IEC effort. Such an IEC approach requires more than simply “imparting knowledge” and “telling populations-at-risk what to do.” Aspects of IEC activities serve to monitor progress and to adapt program implementation.
5. Success stories in malaria control

Malaria-related success in Africa is particularly limited due to an acute shortage of trained personnel, lack of adequate funding, civil conflicts, drought and under-developed health systems. But, most importantly, this record of failure is due to the biological features of African vector mosquitoes, which have greater capacity as malaria vectors than have other anophelines. Endemicity in Africa, therefore, is particularly intense. Although a person is likely to be bitten annually by an infected vector mosquito in many malarious regions of the world, an infectious bite may be a nightly occurrence in Africa, and the level of transmission may be a thousand fold higher there than the level needed to perpetuate infection. The task of malaria control in Africa is therefore far more difficult and complicated than it is elsewhere, and the burden is correspondingly huge.

Despite these difficulties, the usefulness of an integrated package of interventions is evident from experiences in different parts of the world. Salient features of these programs are cited here as examples of success.

5.1. Tigray Region, Ethiopia

Ethiopia, because of its varied ecological and epidemiological features, is intensely affected by destructive malaria epidemics that occur at regular intervals. *Anopheles arabiensis* and *A. funestus* are the principal vectors there. The epidemic that struck northern Ethiopia in 1958 devastated the region, resulting in 150,000 deaths and some three million clinical cases (Fontaine 1961). The country became alarmed by the magnitude of the disaster and launched a malaria control program in 1961 which included case management, application of indoor residual spraying, limited source reduction measures and a network of extensive surveillance system. Indoor residual spraying of DDT, with an annual coverage of some eight million people, remains as one of the main modes of intervention in the country. Epidemics still occur, but at reduced levels of severity.

The Tigray Region of northern Ethiopia is populated by about four million people, of whom 75% reside in sites that are vulnerable to malaria outbreaks. Such events result in heavy morbidity and mortality. Less than half of the population lives within 10 km of a health center. The rest do not have access to the health services. In addition to the regular spraying campaign and case management services at health centers, the region introduced community-based malaria interventions for dealing promptly with such outbreaks of disease. A package of interventions was then adopted that included home management of cases through training of mothers and local village volunteers. A network of 700 volunteer health workers was assigned the tasks of social mobilization, source reduction measures, clinical diagnosis and treatment at community levels. District health management teams and malaria control program personnel provide technical support, supervision and free distribution of anti-malarial drugs. All villages are mapped by means of GIS and GPS and the use of HealthMapper software in order to facilitate surveillance and analysis of malaria trends. More than a half million people receive free treatment for malaria each year by means of a network of more than 700 volunteer health workers. A scheme was devised involving the recruitment and training of grandmothers who would, in turn, train neighborhood mothers to diagnose and treat...
their children at home. This combination of a network of village health volunteers and trained mothers coupled with free distribution of antimalaria drugs led to a 40% reduction in deaths among children under the age of five (Kidane & Morrow 2000). This community based approach practiced in Tigray is well accepted and is being implemented nation-wide.

5.2. Highlands of Madagascar

Malaria and its vector *A. funestus* were eradicated from the cool highlands of Madagascar in the late 1950s by DDT spraying of houses combined with compulsory treatment of all schoolchildren with chloroquine. Indoor spray operations were then withdrawn. In the 1970s and early 80s, the vector and the disease slowly returned from its refugium in the lowlands. A disastrous malaria epidemic that “exploded” during the late 1980s is said to have killed 40,000 people, who by then had lost any anti-malaria immunity. After about 3 years, the DDT spraying and chloroquine distribution program was re-constituted and after five years the vector was eliminated and the disease disappeared. A surveillance system was put in place that was linked to a “fire brigade” system for applying focal spraying when needed (Romi et al. 2002, Curtis 2002).

Similarly gratifying results have been derived as a result of home management efforts in parts of Burkina Faso, Kenya, Uganda and the Democratic Republic of Congo. Uganda has already initiated a national community-based malaria program with free distribution of prepackaged (CQ+SP) combination drugs. The challenge in Sub-Saharan Africa is to implement other such interventions on national scales. The community-based malaria intervention programs of Eritrea have scored significant coverage with the free distribution of insecticide treated nets. Such successful anti-malaria efforts clearly demonstrate the value of applying a locally-adapted package of interventions.

The experience of Vietnam further corroborates the advantages of an integrated application of packaged interventions.

5.3. Vietnam

Vietnam, a Southeast Asian country of 81 million people, where as many as a third of the population reside in malaria endemic regions, is a country that has been intensely affected by this disease, which was contained successfully from 1978 to 1985. In 1991, 144 outbreaks were recorded, affecting more than one million people. The commonly used anti-malaria drugs proved to be virtually ineffective due to drug resistance. Population movements enhanced the malaria epidemic. The country became alarmed by this deteriorating situation and increased its investment, adopting a package of interventions that included free distribution of ITNs, adoption of new anti-malaria drugs and application of indoor residual insecticides. The program included intensive training, establishment of voluntary health workers and supervision of the program by more than 400 mobile teams. Vector control coverage, which included the use of ITNs and indoor residual spraying, increased the number of protected people from 4 million in 1991 to 12 million in 1997/98. Specifically, the number of people using ITNs rose from 300,000 to more than 10 million (WHO 2000). This integrated package of interventions was evaluated over a five-year period from 1992 to 1997. Mortality and morbidity were reduced by 97% and 60% respectively. Local outbreaks were virtually eliminated.
6. Implementation challenges

The objective of the Malaria working group of Task Force 5 of the Millennium Project is to help create a conducive environment that would enable malaria endemic countries to launch effective and sustainable malaria control initiatives to national scale to attain the MDG targets.

At present, malaria control efforts are carried out on a small scale with limited coverage and scope and tend to be fragmented and uncoordinated. To date, none of the existing programs in Africa are undertaking country-wide multiple interventions and these fragmented approaches have not made a dent to the resurgence of malaria. It will thus be critical to identify the barriers to scaling-up malaria programs. The main barriers include:

- Lack of human resources capacity
- Lack of meaningful financial investment in malaria control efforts
- Unresponsive health systems and infrastructure
- Inappropriate global health policies dictated by donor agencies and international organizations that impede free availability and distribution of essential public goods such as antimalarial drugs, diagnostics and ITNs to the poorest of the poor.
- Low pharmaceutical interest in drug discovery and development
- Lack of stable and sensitive diagnostic tests under field conditions
- Lack of malaria vaccines
- Lack of safe and effective antimalarial drugs and insecticides due to widespread resistance
- Poor health information systems and capacity for monitoring and assessment
- Low participation of the private sector
- Extreme poverty and ignorance.

6.1. Strengthening of health systems

As part of the process of designing appropriate malaria control programs, a rigorous assessment of existing anti-malaria program policies and program organization in relation to the health care system should be carried out. The role of the health-care system and other health related institutions in each country involved in support of malaria control programs, as well as operational research activities should be specified. Thorough assessment of the infrastructure, capacity and performance of the following program components should be part of a comprehensive malaria control effort. The following components of the health care system should be assessed:

1. Availability and quality of laboratory facilities at various levels
2. Adequacy and operational relevance of health information and management systems
3. Active role of regulatory and enforcement agencies
4. Availability of quality assurance facilities for monitoring substandard drugs, diagnostics, insecticides and other reagents
5. Systems of drug procurement and distribution
6. Services offered in antenatal care services
7. Supervision and monitoring systems
8. Capacity of human resources
9. Policy on free distribution of anti-malarials
10. Policy on free distribution of ITNs through antenatal care clinics, community-based programs and NGOs.
11. Drug resistance

6.2. Human resources capacity development

Because the efficacy of any large-scale anti-malaria intervention rests on the competence of the personnel who manage the program and who deliver the interventions, a program of training is essential. The cadre of management people should include particularly skilled personnel, and their professional development requires special care. Required areas of expertise include designing and planning of programs, management, implementation, monitoring, impact assessment of interventions, and data management and analytical skills. Acquisition of special skills for undertaking antimalarial drug therapeutic efficacy studies, insecticide susceptibility of vectors, and vector ecology and behavior will also be critical for implementation successful programs. The highly qualified personnel that result would contribute strongly to regional anti-malaria efforts. Local training programs, administered by these people provide the skilled workers who conduct this work.

Community-level health workers such as health extension workers, community health agents and traditional birth attendants involved in anti-malaria efforts are trained in a system designed to stimulate their enthusiasm and prepare them for the challenges presented by their communities. They are vital to efforts to promote social mobilization and healthy behavior as well as in mobilizing political and financial support.

6.3. Social mobilization of communities

Increased awareness and knowledge concerning healthy behaviors and practices by communities are fundamental for general health promotion, prevention of malaria infection and case management. Strategies for social mobilization should be developed for implementation at district and peripheral levels. Key elements in such strategies should include promotion of community awareness, demand for services that would lead to the adoption of essential disease-prevention attitudes, such as the correct use of ITNs, application of other preventive measures, overall treatment-seeking behavior and compliance with prescribed treatments. Health workers in general, and especially those at the periphery, are inadequately prepared for mobilizing local residents and sustaining their interest in anti-malaria measures.

Control initiatives should seek to improve community awareness and health worker skills and practices concerning malaria prevention and case management. Appropriate strategies and training materials to support capacity building for social
mobilization should be developed according to the needs and requirements of particular countries and districts.

6.4. Scaling-up: intersectoral and public-private collaboration

Anti-malaria efforts in different countries may require particular inter-sectoral relationships between agencies devoted to agriculture, finance, education, urban or rural development, as well as the private sector and certain NGOs. The commitment of the finance ministry would seem essential because such agencies allocate funds to the budgets of the various sectors, including health. Inter-sectoral partnerships at national levels facilitate a coordinated approach to the implementation of selected packages of interventions. The involvement of the business and financial communities in this effort of malaria control will contribute largely to program sustainability by encouraging local procurement of program support.

A sustainable intervention must provide economic gain to the governments that are concerned because such investments can be substantial and must be transparent. One route to economic development can accrue from close links between the agriculture and malaria control sectors. The greatest contemporary burden of malaria in sub-Saharan Africa is currently associated with people engaged in subsistence agriculture. It may be that stability of rural poverty and subsistence agriculture is fostered by malaria and vice versa. Breaking out of this cycle will require conversion to cash crops and a simultaneous investment in malaria related efforts. Economically productive agriculture provides a payoff to governments via taxation. It is also linked to export businesses, and this provides a motivation for ministers of finance to invest in malaria control.

Encouraging export businesses, which operate through urban centers, many of which are linked to profitable businesses in more rural areas, introduces a demand for malaria control in both areas to minimize days of work lost due to malaria. Enhanced labor productivity and increased company profits benefits governments through substantial tax revenues. Reduced risk of malaria may corporate development, and this can induce cycles of health and wealth that provide incentives to governments at a level where investment in health initiatives becomes a clear priority. Fostering economic development through simultaneous reduction of malaria risk in rural as well as urban centers has an interesting but limited history (Watson 1921). Much opportunity remains for expanding on such development. Intersectoral collaboration will, in fact, be necessary for any sustainable reduction in the burden imposed by malaria.
7. Monitoring and evaluation

Although an initial implementation plan for a package of essential interventions should be presented in advance of the program, it is anticipated that adaptive tuning of the interventions would be an integral part of the process of moving toward stated objectives on morbidity and mortality. To facilitate adaptive tuning, it will be essential to monitor the performance of individual components of the program - e.g. effectiveness of case detection, diagnosis, and utilization of drugs, distribution and adoption of bednets, implementation of source reduction technique(s), training and performance of new workers at health clinics, reduction in larval density at designated surveillance sites, etc. This will require the specification of an ongoing program evaluation strategy, data collection protocols and the establishment of a computerized database to facilitate performance assessments and guide the adaptive tuning of interventions.

The database for reporting on implementation of individual interventions and on local morbidity and mortality rates serves to guide the adaptive tuning of the program while serving as the basis for accountability to consortia of funding partners. A number of parameters should be monitored over a 20 year period in concert with Millennium Development Goals and process milestone targets that are established in partnership between the given counties and development partners.

7.1. Demographic and health surveys

National cluster sample surveys should be undertaken through the application of modified DHS tools using the Brass Children Ever Born methods to define infant and childhood mortality patterns every three years. Sampling should be increased over traditional DHS approaches to improve the precision in the estimates of temporal changes and allow for sub-national descriptions of mortality. These data should be supplemented with more detailed DSS data derived from sentinel sites (if these exist within selected countries). Fatal events can be ascribed to broad causes using verbal autopsy tools developed by WHO and comparative tools used within the INDEPTH network. Mortality events can be linked to intervention access and compared to surviving infants to estimate protective effectiveness using nested case-control methods.

The national 3-year sample surveys can provide the platform to capture changing coverage, sources, compliance and timing of interventions provided through formal and informal channels. DHS and MICS malaria modules should be expanded to provide more detail on the precise nature of intervention use.

7.2. Health management information systems

Randomly selected in-patient and out-patient formal health service providers should be recruited to act as sentinels for changing disease presentation risks. Changing case-fatality, clinical presentation mixes and defined treatment failures will provide important impact data. Data describing overall disease presentation will permit revised estimates of commodity needs. These sentinels should form part of enhanced HMIS services and should be guaranteed adequate diagnostics and IT capacity to track changing disease burdens.
The MARA/ARMA collaboration has collected more than 10,000 historical parasite prevalence surveys in sub-Saharan Africa. These data have a good distribution over the region and can serve as baseline data in many localities and are available on a CD (MARALite CD). In places where no previous surveys have been conducted, modeled predictions of prevalence are available in some regions or simple district means may be available. However, it is necessary to make assessments on a case by case basis if such estimates are to be a sufficiently reliable substitute for an actual baseline survey.

Malaria diagnosis has historically been based on clinical symptoms, particularly in Africa. Coupled with the low cost of treatment, there has been very limited emphasis on developing functional health facility based malaria information systems. With the policy shift to the use of ACT, the increased cost per treatment dose justifies the cost of definitive diagnosis before treatment. This provides a basis for Malaria Information Systems (MIS) based on definitively diagnosed cases, and hence more accurate estimation of incidence of symptomatic cases. Computer based MIS capturing facility based malaria case data have been developed in South Africa, Swaziland and southern Mozambique; the development of such systems in Africa is seen as essential to the effective monitoring, evaluation and management of large scale malaria control.

MIS data can be used to provide:

- rapid spatial and statistical analysis to identify any localized failure of control measures enabling targeted use of malaria control resources;
- estimates of needs and monitoring of pharmaceutical and non-pharmaceutical supplies;
- input to malaria epidemic warning system;
- monitoring and evaluation of the overall impact of interventions;
- regular reports of malaria risk assessment for tourists and business that can be updated frequently;
- data for research.

The performance of services with regard to adequate commodities, provision of quality care in accordance with national guidelines, client satisfaction with services etc should all be measured in line with recent definitions of “performance” defined by the WHO World Health Report and using modified MEASURE Service Provision Assessment tools. Repeat random sampling of formal and informal service providers from the GIS platform can serve as the principal sampling frame.

### 7.3. Monitoring effectiveness of commodities

Both parasite and vector sensitivity to drugs and insecticides will be paramount to the tracking of program effectiveness. Traditional *in vivo* assays should be supplemented with molecular marker studies to form a spatially comprehensive national surveillance. Assessments of quality assurance at procurement and at the point of delivery should also form part of the surveillance system.
7.4. Development of a national GIS platform

Establishment of a national GIS platform for assessing malaria risk will require a national effort to define a high-resolution population distribution map based upon the most recent national census and linked to modeled distributions of malaria risk. In addition, GIS surfaces will be developed for transport networks and health service providers to enhance planning of service provision. All subsequent data collection will use the combined risk-population-service GIS platform as a sampling frame and analytical tool (for example coverage vs poverty mapping).

An important first step in this direction is the monitoring system associated with RBM and implemented via such a GIS system as HealthMapper. National malaria control programs are now using this system to (i) identify populations at risk, (ii) assess access of communities to health care, (iii) target and monitor implementation of control interventions including use of bednets and larvicides, (iv) monitor drug-resistance of first-line drugs, (v) integrate environmental data (such as rainfall amounts and their variability) to serve as an early warning system for epidemics and to (vi) assess impact of irrigation and other environmental factors on transmission.

An important additional step is the recently launched WHO global online atlas of infectious diseases. This provides a new tool for infectious disease surveillance and control that builds on the features of HealthMapper. More than 300 indicators for more than 20 infectious diseases are included in the database.

7.4.1. Cost-effectiveness of service provision

Itemized costing menus should be developed, where all unit costs and quantities are given explicitly. These systematic and routine cost analyses would provide a framework for ongoing analyses of possible effects of changes in unit costs (e.g. price of bednet or drugs) or quantities (e.g. number of nets delivered/sold). The data on coverage, individual effectiveness, community effectiveness and costs would form the empirical basis of a cost-effectiveness analysis of alternative intervention strategies, and would be embedded within the national GIS platform of risk, changing disease burden and service access.

7.4.2. Impact on poverty

As part of the GIS for the countries involved in malaria control initiatives, poverty mapping should accompany malaria risk mapping. This would include spatial representations of the local living standards, the sources of income generation, and the distribution of wealth. Spatial association analyses will connect malaria risk with the economic position of communities in the malaria control initiative as well as neighboring centers with which they interact. The reciprocal connections between malaria control and poverty will be an integral part of these efforts.
8. A roadmap for achieving the malaria-MDG

8.1. Goal and targets

Enunciated at the United Nations Millennium Declaration, the Millennium Project has the following time-bound goal for the disease: “Have halted by 2015 and began to reverse the incidence of malaria.” This goal is difficult to measure and the Malaria Working Group after a lengthy deliberation and consultation decided to develop a target that will be measurable. Reduce malaria morbidity and mortality by 75% by 2015 in comparison to the 2005 baseline level.

This would require significant long-term sustainable support to:

- Enhance development of human capital, technical resource, and financial capacity of district and national level health systems

- Develop inter-sectoral partnerships between the public and private sectors, with accompanying revenue management strategies.

Intervention coverage targets:

- Ensure 80% of people at malaria risk are protected by locally appropriate vector control methods by 2008 (ITNs, IRS, EM and appropriate combinations).
- Ensure 80% of malaria patients are diagnosed and effectively treated within 24 hours of onset of illness by 2008.
- These interventions should be considered public goods and made available free to the end users in malaria endemic countries.
- These interventions are expected to entrain prospects for reduction of chronic poverty.

8.2. Development of a business plan for global malaria control

It will be important to develop implementation plans at a global level that would serve as a framework for developing consensus amongst different stakeholders on the process of planning and implementing program activities and to determine required costs, mechanisms for funding dispersal, use and accountability. Such a global business plan would serve as a template for each malaria endemic country to develop national business plans according to country specific conditions.

The STP TB partnership has developed an elaborate global business plan, which is backed with successful mobilization of resources. The RBM partnership has not formulated such a business plan at the global level or mobilized resources to support implementation in endemic countries. Such a business plan would need to be comprehensive and include all of the following elements:

1. Coverage and impact of interventions
2. Renewal of interventions and the products on which they are based
3. Commodity management
4. Linkages to the development of health systems
5. Linkages to economic development and poverty reduction
6. Costs and financing
7. Monitoring and evaluation
8. Advocacy

8.2.1. Coverage and impact of interventions

The collective and integrated use of interventions based on diagnosis and treatment, intermittent preventive treatment during pregnancy, ITNs, IRS for epidemic prevention and control and source reduction methods, particularly in urban and peri-urban areas would result in significant impact. However, the level of impact that can be realized depends also on the level of coverage.

The combination of effective vector control and early treatment with ACTs, sometimes supplemented with other methods, is likely to have a considerable impact. Especially when consistently employed over several years, it can, like IRS, greatly reduce parasite rates and entomological inoculation rates. When early ACT treatment is added, it is likely that transmission will be greatly reduced. This effect will be most marked in areas, where the interventions are applied with high coverage and quality. Generally, this will be urban areas, and areas with a relatively high level of development and population density.

Malaria epidemics and complex emergencies can greatly increase costs of operations and jeopardize the possibility of attaining impact. It is questionable, whether a business plan should include full planning for such eventualities, but experience from recent years has shown that it may be important to maintain emergency funds and revolving emergency stocks of supplies. It is essential in the reporting on coverage and impact not to neglect populations affected by such emergencies, as these currently account for a large proportion of the world's malaria problems. A specific line of products for malaria control in complex emergencies is under development by industry in cooperation with WHO and NGOs.

8.2.2. Renewal of interventions and the products on which they are based

The eventual blunting of any biocide used continually on a large scale is inevitable, and the only way to avoid setbacks caused by resistance of pathogens and vectors is to have new biocides in the pipeline to replace the ones that have been blunted. Even for some types of vaccines, it is possible that plasmodia could develop resistance. Under all circumstances, there is no good method for estimating the chances that radically new methods such as vaccines or genetically modified mosquitoes become available, and for this reason they are not included in the framework. That is of course not meant to imply that investments in research on such tools are not warranted.

8.2.3. Commodity management

The core interventions are contingent on the availability of sufficient supplies of quality products, many of which are currently just becoming available such as fixed dose combinations of ACTs and LLITNs. It would be highly desirable from a viewpoint of
sustainability to have all malaria commodities managed by national procurement and distribution systems, buying products of complying with certain criteria on a competitive free market. However, given the immature markets, the rapidly increasing demands and the risk of emergence and spread of sub-standard, fake and counterfeit problems, a high degree of international intervention will be required, at least for some years. The actions required are:

- Forecasting of demand
- “Soft contracts” supported by financial guarantees with producers for products requiring considerable lead time, such as ACTs
- Bulk procurement for clusters of countries
- Pre-qualification of products based on specifications, documentation and inspection of production sites
- Quality control of products at importation and through surveys at end-use point
- Combating fake and counterfeit products through international cooperation, law enforcement and mobilization of civil society

8.2.4. Linkages to the development of health systems

The linkages of the control of malaria to health systems development is related to the following main issues (in addition to those of financing, see 8.2.6):

A. Human resource development

Malaria control including high coverage of treatment as well as prevention is only possible when a national plan of action includes a substantial human resource development plan, which would typically comprise the following:

- Central level institutional development for management of human and financial resources as well as capacity for partnership for example with private, commercial sector, economic development projects, sub-contracting and information management; cross-programme links especially with tuberculosis and HIV/AIDS
- Development of capacity at district level for micro-planning, cross-programme links with immunization and filariasis and other programmes for ITN delivery and IPT for infants, with IMCI and hospital services for delivery of treatment
- Development of community-based services, with NGOs and/or with the private (possibly informal) sector to mobilize communities for regular re-treatment services and to provide adequate treatment – and operational research will show – on the spot diagnosis by rapid tests at community level.

On the background of the general attrition of public health human resources in most African countries and many countries in Asia and the Americas, the sustainable development of human resources presents the most formidable challenge of all to malaria control. While training and supervision are necessary elements, and should be addressed at global level by the production and testing of standardized training materials and tools, it will be necessary to take unusual measures to maintain staff, probably by intervening to
ensure attractive employment conditions by such measures as salary supplements. While it is hard to raise objections to the decent payment of quality work carried out under difficult circumstances by qualified professionals who want to work for their own people, it has to be recognized that there is substantial risk of graft, wage inflation and stimulation of rent-seeking. The “ground rules” for international financial support still need to be worked out and fall outside the remit of malaria control planning, as the issues are the same for all health programmes.

B. Service delivery

The issues of service delivery are, as in any public health programme related to human resources, logistics, communication, infrastructure, programme coordination, quality control and supervision. Most of the issues are relatively mundane, though important in terms of budget. The cross-programme links have been alluded to under A. One of the important problematic coordination issues is related to the frequently conflicting demands between maintenance of stationary routine services and outreach campaigns. Such problems occur frequently in the context of polio and measles campaigns and in many countries, health services are learning to dealing with them.

8.2.5. Linkages to economic development and poverty reduction

As indicated above, the systematic implementation of case management and prevention with modern products should lead to transmission reduction to such an extent that malaria as an obstacle to investment will be substantially reduced.

Malaria control developed as a part of health systems development is normally an accompaniment to economic development, because the natural trend of health systems is to grow from centre to periphery in parallel with general social, economic, political and economic development. Such a vision of malaria control is consistent with the requirement for sustainability, but may be less satisfactory if malaria control is meant as part of a poverty reduction strategy. However, for poverty reduction, it would again be best to demand that a broad development strategy for a given population group explores the possibility for including malaria control rather than positioning one specific disease control programme as the motor of development.

8.2.6. Costs and financing

If coverage rates and benchmarks are agreed, then it is relatively simple, especially for tropical Africa, where the populations at risk are well defined to calculate the total costs. However, these will not remain constant and the following trends and issues need to be considered:

- Increasing urbanization will tend to decrease the malaria morbidity and mortality.
- Increasing AIDS burden will tend to increase severity of malaria, especially in urban populations with relatively low malaria immunity.
- Costs of commodities, especially antimalarial drugs (ACTs) are expected to decrease within a few years from approximately about US$ 2.5 per adult dose to approximately about US$ 1.2 per adult dose or less.
• Decreased malaria incidence will translate to decreased malaria hospitalizations, but may not decrease the consumption of antimalarial drugs very much, unless specific diagnosis is widely adopted and accepted by the populations as a prerequisite to antimalarial treatment by providers and population.

• Although most commodity costs for novel products tend to go down by time, the need for replacement as resistance develops will mean that prices go up again. One of the purposes of international cooperation is to absorb these fluctuations.

• In the current phase, where there is broad international consensus that effective malaria control interventions must be scaled up rapidly to achieve impact, there is hardly any alternative to external financing as the main source of funding for malaria control. This is related to not only the low purchasing power of large proportions of the affected populations, but also the need for introducing new products for which the market is still immature and for which there is a high risk of counterfeiting and faking. A more profound analysis of these aspects by the Institute of Medicine (report due in May 2004) indicates that for ACTs specifically, the best way to ensure access may be public upstream funding in the production process. However, in the longer term, it is necessary through operational and health systems research to explore how the existing motivation for paying out of pocket for individual malaria prevention and treatment (see the Africa Malaria Report 2003) can be channeled to full or partial payment for effective interventions, and whether the development of malaria control as part of public health could contribute to the development of health insurance schemes, which would be one way to protect household economy against the effects of malaria attacks.

8.2.7. Monitoring and evaluation

In a global context, monitoring and evaluation needs to be based on a very small number of generally applicable core indicators of coverage, quality and impact. In this framework, under 5 years of age malaria mortality has been selected as the impact indicator of malaria burden. It can only be measured directly, and even then with great uncertainty in the few sentinel surveillance sites (such as DSS), where verbal autopsies are continually applied. A general assessment of burden reduction will have to rely on triangulation of data collected from: DSS, Multiple indicator cluster surveys, demographic health surveys, malaria information surveys and health service data on operations, morbidity and mortality. The necessary systems for obtaining and using such data are under development by the Monitoring and Evaluation Reference Group (MERG). The measurements are possible, but at present there is a time lag of 2-3 years from data collection to presentation.

8.2.8. Advocacy

A business plan must be accompanied by an advocacy plan, of which the main purpose is to present the business plan as such, in particular its promises and its costs as well as the dimensions of the malaria problem and the collateral effects of the plan. It would be important to present the argument for sustained and substantial, but slowly decreasing donor support and obtain firm commitment.
9. Research and development to meet current and future needs

An extensive program of applied and basic research as well as program development should be implemented for improving anti-malaria interventions.

9.1. Anti-malarial drug development

The future of antimalarial chemotherapy a few years ago seemed desperate. Drug resistance was rising and few new antimalarial drugs remained in the pipeline. The current situation, however, is more promising, with several new combinations and new drugs envisaged in the next decade. The anti-malarial drugs in the pipeline are as follows:

1. Chlorproguanil-dapsone-atesunate (Lapdap artesunate);
2. Pyronaridine-artesunate;
3. Piperaquine-dihydroartemisinin;
4. Amodiaquine-artesunate.

In addition to the combinations described above, several new single agent drugs are under development that may ultimately be used in combination with other drugs. Standard industry benchmarking suggests that a number of these projects may fail to deliver a registered product. Projects include:

1. Artemisone;
2. Isoquine.

Although several new fixed dose drug combinations and new drugs are envisaged in the next decade, in order for this promise to be realized, funding levels must continue to increase for drug discovery and development activities. Drug development is a high-risk and costly activity.

To enable such sustained support, a fixed percentage of development aid funding for malaria control might be earmarked for applied research, including product R&D through public private partnerships. In addition to such a “push incentive,” industry might be encouraged to participate in drug-discovery efforts by certain “pull incentives.” A pull incentive would encourage investment by guaranteeing the price that a company might obtain by marketing a drug with certain characteristics.

9.2. Malaria diagnostics

The choice of a malaria diagnostic tool for malaria endemic situations, which rests between microscopy and rapid diagnostic tests at present, will depend on the local circumstances. Quality assured microscopy is the standard diagnostic tool for malaria in health institutions, where microscopic services provide for diagnosis of a range of other diseases beyond malaria. Rapid diagnostic tests for malaria provide a very suitable alternative to microscopy in situations where the former is not feasible, such as in remote rural settings and outside health institutions. With either method, and in whatever situation, quality assurance of the diagnostic tool is an essential requisite for malaria diagnosis to be a cost effective intervention.
Malaria RDTs seek to detect specific antigens produced by malaria parasites and can be divided accordingly into two groups: histidine-rich protein 2 (HRP-2) and parasite lactate dehydrogenase enzyme (pLDH) (Wongsrichanalai 2001). These RDTs can be incorporated onto disposable dipsticks that can readily be used under field conditions and can be performed in about 15 minute from finger-prick blood samples by technicians with minimum training (Wongsrichanalai 2001). Therefore, the use of RDTs is adaptable for use by community health workers for malaria management at home. Malaria RDTs are sensitive and can detect as many as 90% of those malaria patients whose parasite threshold exceeds 40 parasites/µl blood. However, recent field trials have revealed that specificity and sensitivity levels for \textit{P. falciparum} are well below than what is required for operational use at a large-scale (Keiser \textit{et al.} 2002). Major limitations include false positivity due to persistent HRP2 antigenemia following successful treatment and false negativity possibly due to antigen excess in association with high parasite densities and possible HRP2 gene deletion (Wongsrichanalai 2001). More sensitive assays are necessary, especially at low levels of parasitaemia, to detect therapeutic failures earlier. Most rapid tests also fail to give a measure of the level of parasitaemia and detect other plasmodia apart from \textit{P. falciparum} (Craig \textit{et al.} 2002). Finally, the published literature on recent RDT trials does not indicate the possible causes of performance differences among study sites and failures, indicating the need for continued monitoring in the clinical setting (WHO 2003).

9.3. Malaria vector

9.3.1. Vector ecology

Increased research attention should be placed on the vector ecology of malaria. More specifically,

- the environmental conditions that contribute to mosquito longevity remain virtually unknown;
- the effect of malaria infection on feeding frequency remains unexplored;
- temperature relationships are poorly understood;
- host specificity by vector mosquitoes remains a fertile field of study;
- the “zooprophylactic” potential of different kinds of domestic animals and on the relationship of human density to the force of transmission is lacking;
- Mechanisms of mosquito survival through inter-epidemic periods and signals of the onset and termination of transmission are poorly understood.

9.3.2. Insecticide development

The available repertoire of operationally useful anti-malaria insecticides is so limited that the duration of interventions should sharply be constrained. The present armamentarium is comprised solely of sodium channel blockers and acetylcholinesterase inhibitors. Needed, are chemicals that can be applied residually and that destroy insects by affecting other life processes. Another avenue of approach is to devise insecticides that are “negatively correlated.” Such chemicals would reduce the fitness of vector mosquitoes
that resist the effects of other insecticides more than they reduce the fitness of susceptible mosquitoes. No promising candidates for either of these functions have become evident.

### 9.3.3. Modification of vector populations

Notable progress has recently been registered in attempts to genetically transform anopheline mosquitoes, including incorporation into mosquitoes of genes (designated as PLA2 and as SM1) that reduce the ability of malaria ookinetes, in model systems, to develop to the sporozoite stage (Ghosh et al. 2002). Blood meal-induced expression of such genes should eventually be inducible in mosquitoes by vitellogenin or carboxypeptidase promoters. Certain anophelines are readily transformed by means of the piggyBac vector, but not the main African vector of malaria, *Anopheles gambiae* (Perera et al. 2002). The system has been routinized in the case of *A. albimanus*. Hermes or Minos vectors have also been used for transforming other mosquitoes. The three essentials of a transformation system, thereby, should soon be mobilized: various competence inhibiting genes, promoters and transformation vectors. These accomplishments will prepare the way for definitive experiments designed to determine whether the malaria-competence of confined populations of vector mosquitoes can stably and effectively be reduced.

Efforts to create genetic constructs for vector anophelines should be accompanied by a program of research designed to explore the circumstances under which these assets can be implemented. Isolated sites are required in which such releases can be evaluated and from which the released mosquitoes can be eliminated in the event that this becomes necessary. Such a release can best be evaluated in which only a single vector population perpetuates infection. The ethics of such a release should be defined. The magnitude of the release inoculum requires careful attention as well as the circumstances under which the release is to take place. Required is definitive information on the competence of natural vector populations as well as models that examine the effect of a reduction in competence on the force of transmission of malaria.

### 9.3.4. Risk mapping

A large body of coordinated experience in mapping malaria rates has already accumulated in large parts of sub-Saharan Africa. If mapping is to play a central role in the design and adaptive implementation of control programs, however, the levels of resolution of these risk maps, linked to ground-based validation, must be increased considerably beyond current capacities. High-resolution risk mapping over time will be an important ingredient in efforts designed to monitor the projected anti-malaria intervention initiatives.

### 9.4. Malaria vaccines

Despite decades of research, the development of an effective malaria vaccine has proven elusive. Natural immunity against malaria infection develops gradually after repeated infection. Yet, naturally acquired immunity is strain-specific, requires continual boosting and is disease modifying, rather than sterilizing (Webster & Hill 2003). There are 5,300 antigens encoded by the *Plasmodium falciparum* parasite, however it is not known which exact antigens produce the key protective immune response in human hosts and should be
targeted to develop a successful vaccine (Moorthy et al. 2004). Each malaria infection introduces thousands of antigens into the human immune system, which differ at each stage of the parasite’s life cycle (Moore et al. 2002). Therefore, another central issue is the choice of the stage in the life cycle of the parasite to target (Webster & Hill 2003). Despite these complexities, prospects are still high, especially with the elucidation of the genomic sequence of *P. falciparum* (Gardner et al. 2002) and the increasing research funding in recent years (Moorthy et al. 2004). There are several types of candidate vaccine targeting different stages of parasite development:

- **Pre-erythrocytic vaccines** aim to avert the clinical manifestations of malaria by preventing sporozoites (the parasite stage that is transmitted from mosquitoes to people) from entering or developing within infected liver cells (Webster & Hill 2003). Long-lived efficacy (about nine months) has been obtained solely with a pre-erythrocytic vaccine comprised of living, but radiation-attenuated sporozoites (Moorthy & Hill 2002). This vaccine strategy is burdened, however, by the exceedingly variable nature of the relevant part of the *Plasmodium falciparum* genome. Current research focuses on the use of the sporozoite surface proteins and the manipulation of the immune system (Moore et al. 2002). The lead candidate is the RTS,S vaccine, which showed significant but short-term protection against plasmodia-infected mosquito challenge and its development has been accelerated by the Malaria Vaccine Initiative (Moorthy et al. 2004).

- **Blood-stage vaccines** aim to modulate the complications of malaria by preventing invasion of red blood cells by merozoites (active parasites that infect red blood cells). Most research has focused on targeting the antigens responsible for parasite entry to cells, merozoite surface protein (MSP) 1 being the best characterized (Webster & Hill 2003). However, vaccine development has been hampered by the discovery of parallel invasion pathways (Pasvol 2003) and the fact that some antibodies to MSP1 can block the activity of malaria-protective antibodies (Moorthy et al. 2004). The PfEMP-1 (*P. falciparum* erythrocyte membrane protein – 1) antigen is another vaccine target, which may protect against the severe complications of malaria (Moorthy et al. 2004). However, this antigen is polymorphic, each new wave of parasites expressing a new variant of this antigen. Therefore, parasite development continues despite antibody production (Webster & Hill 2003).

- **Transmission-blocking (gametocyte) vaccines** would prevent vector mosquitoes from acquiring infection from an infected person, but they would not modulate the infection itself. These vaccines are useful mainly for malaria endemic populations, and there is therefore little commercial funding for their research and development (Webster & Hill 2003). The US National Institute for Allergy and Infectious Disease Malaria Vaccine Development Unit will clinically assess a *P. falciparum* gametocyte candidate vaccine, Pfs25 (Moorthy et al. 2004).

It is commonly accepted that an effective malaria vaccine should ultimately target multiple antigens and multiple stages and generate humoral (antibody) and cellular immunity as well as immunological memory. More research on antigenic polymorphism, duration of efficacy, means of antigen combination and vaccine delivery systems capable of inducing desired immune response is required. The laboratory work that is devoted to
the production of malaria vaccines should also be accompanied by epidemiological studies that will identify the people who are to be immunized. The magnitude of financial investment in vaccine development should be proportional to the benefit that might someday be accrued.
10. Recommendations

A set of eleven recommendations have been formulated by the Malaria Working Group:

**Strengthening of health care infrastructure**

The health care systems in many malaria endemic countries are weak and lack resources. Because a well-functioning health system is fundamental to the control of infectious diseases, a strengthened health care infrastructure in endemic countries is prerequisite to the provision of quality laboratory services, reliable diagnosis, effective case management. Dependable systems will be required for procuring and distributing drugs, reagents, insecticides and other essential commodities as well as an effective health information and monitoring system.

**Social mobilization and community participation**

Systems should be put in place for mobilizing communities and encouraging community participation in planning and implementing malaria control efforts. Toward this end, village health workers, traditional birth attendants and elderly village residents might be mobilized to perform specific, malaria-related tasks such as clinical diagnosis and treatment of cases, community organization for vector control activities. Experience in various malaria endemic countries confirms that such home-based and community-based approaches effectively reduce malaria-related morbidity and mortality. Community based interventions supplement the task of the formal health services and help to extend coverage of health care delivery.

**Human resources capacity development**

Cadres of skilled personnel who are able to critically assess local situations, develop appropriate intervention strategies, guide implementation activities and monitor their effects are needed. While training and supervision are necessary elements and should be addressed at the global level by the production and testing of standardized training materials and tools, it will be necessary to take unusual measures to maintain staff, probably by intervening to ensure attractive employment conditions by such measures as salary supplements.

**Strengthening malaria training centers**

Existing Regional Malaria Training Centers in Africa, for Anglophone, Francophone and Lusophone countries, should be encouraged to produce mid-level malaria professionals knowledgeable in the epidemiology of malaria, its prevention and control as well as in advocacy and community mobilization. One such center, the Nazareth Training Center was established by WHO in Ethiopia in the 1950s and trains Malaria Control Programme Managers from Anglophone African countries. Similar training programs are offered in French and Portuguese when necessary due to financial constraints. It is recommended that these centers and others be supported and strengthened to produce mid-level malaria professionals. It is also equally important for each endemic country to produce technicians for placement at the district and community levels.
**Integrated package of interventions**

Because no anti-malaria magic bullet is available, integrated sets of interventions will be required. The transmission of malaria is comprised of many facets involving the interaction of infected and recipient human hosts, vector mosquitoes with varied characteristics and requirements under a varied set of environmental conditions. Thus, it will be critical for each country to deploy a set of integrated package of interventions in accordance to their unique ecological conditions and not to rely only on a single intervention method.

**Scaling up of control initiatives to national scale**

At present, malaria control efforts are carried out as small projects with limited coverage and scope and tend to be fragmented and uncoordinated. To date, none of the existing control efforts in Africa apply multiple interventions at the national scale, and these fragmented efforts have not made a dent to the resurgence of malaria.

The barriers to scaling-up malaria programs include critical shortage of human and financial resources, lack of free access to essential drugs, diagnostics, ITNs and insecticides by the poorest of the poor, low coverage of ineffective health services, ineffective monitoring and evaluation system and poor government capacity for developing and implementing national policies. It is critical to address these barriers to scaling-up sustainable malaria control programs to national scale. The need, therefore, is for a series of packages of integrated multiple interventions that can be applied to national scale over a number of years. The human resources that are essential to such an effort require a period of development. Because programs in endemic countries differ in their levels of maturity and human resources, each country should engage in this scaling-up process at its own pace. National health services should be strengthened by incorporating functional community-based programs in order to attain the required nation-wide coverage.

**Chemoprophylactic drugs**

Lack of safe and affordable antimalarial drugs for chemoprophylactic use in general and for intermittent preventive treatment of pregnant women in particular. Development of such drugs is a priority.

**Effective drugs and insecticides**

Regular monitoring of the efficacy of antimalarial drugs is critical to human health in endemic countries. Although antimalarial drugs such chloroquine and SP have lost much of their effectiveness against *Plasmodium falciparum*, these drugs continue to be used in a number of endemic African countries where they endanger the lives of children. The association of increased malaria deaths in children correlates with an increasing trend of *P. falciparum* resistance against the commonly used anti-malarial drugs. The detection and documentation of drug resistance and the formulation of policies for a change to an effective drug should be based on acceptable sound study protocol and evidence. Because of the failure of chloroquine and SP, it is recommended that endemic countries update their policies to use artemisinin-based combination therapy for the treatment of uncomplicated falciparum malaria. The new Antimalarial drugs (ACT) which cost about
ten times more than chloroquine and other traditional drugs, will not be affordable by the poor population in malaria endemic countries and should be available at no cost to the end-user.

It is equally important to monitor the susceptibility of anopheline vectors of malaria to insecticides to ensure that these materials remain effective, whether they are applied for epidemic prevention or long-term use. It is recommended that ITNs and insecticides for IRS use such as DDT and the pyrethroids are considered as public goods and be available free of cost to endemic countries.

**Promote economic development**

In addition to the primary objective of reducing malaria related mortality and morbidity, anti-malaria intervention strategies should also be devised that most effectively promote economic development.

**Multisector collaboration**

Governments of endemic countries and multilateral/bi-lateral agencies, with a global mandate as well as agencies operating at a local level should welcome the participation of business interests in developing and implementing anti-malaria interventions. Sustainability requires the participation of the private sector. Past and current corporate malaria control programs (Spielman et al., 2002) provide an important bridge for future partnerships.

**Research and development**

Investment in applied and basic research is essential for developing improved methods for effectively and sustainably intervening against malaria. Novel antimalarial drugs, improved diagnostic methods, anti-malaria vaccines, novel anti-vector methods and more effective insecticides should be developed.
References


