Background Paper of the Task Force on Major Diseases and Access to Medicine, Subgroup on Malaria

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Note to the reader
The Background Paper provides a preliminary overview of existing knowledge and scopes out the questions addressed by this Task Force. The analysis, conclusions and recommendations contained herein should be considered as very preliminary as they are likely to evolve as the Task Force works toward its final report at the end of 2004. Comments and suggestions are welcome. Please cite this paper as “Background Paper of the Millennium Project Task Force on Major Diseases and Access to Medicine, Subgroup on Malaria”.

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I. Purpose of the Millennium Initiative on Malaria

The Malaria Task Force of the Millennium Initiative seeks to promote regional antimalaria programs designed to reduce malaria risk in a manner that improves human well-being while also promoting economic development. Sustainability requires such a linkage between health and wealth. The present confluence of interest in alleviating world poverty and in promoting globalization presents unprecedented opportunity for reducing the burden of malaria, one of history’s most resilient and deadly diseases. This working paper is intended to provide a basis for launching anti-malaria programs throughout the world’s tropics and particularly in sub-Saharan Africa.

Although the various anti-malaria programs of the past half-century saved many lives, and malaria in some countries was either eliminated or sustainably suppressed, such successes occurred mainly in sites that were reached readily and suffered only unstable levels of transmission. Transmission is far more intense in tropical Africa, where the burden of malaria is far greater than elsewhere. Such African countries tend to be so poor that little progress against this disease has been apparent, and few gains have been translated into sustained societal progress. Despite a series of repeated declarations, resolutions and pledges, during the last three decades, few antimalaria efforts have ameliorated the worsening malaria situation in much of Africa.

The malaria situation in the world’s tropics is deteriorating, with a significant and steady increase of childhood mortality. Malaria impedes the development of countries in which malaria is endemic. It is, therefore, essential for the rich countries to forge a series of sustainable partnerships with the poor countries in which malaria is endemic and to develop an array of locally-adapted interventions that provide a basis for collective international action. Such concerted action would enable malaria-endemic countries to deploy a package of effective multiple interventions at national scales.

Those countries that emerged from their previous malaria-endemic state, and the poverty that generally accompanies endemicity, have enjoyed powerful internal commitments to rid themselves of this infection. The United States, much of the former USSR, Taiwan, Italy and Palestine/Israel stand out as prime examples of this principle. Many of those countries that remain malaria-endemic have allocated few of their own human and financial resources to the problem. Internal commitment, therefore, remains a prime requirement for a self-sustaining, and hence society-transforming reductions in local malaria endemicity. Following the Abuja Declaration of 2001, the level of commitment from the endemic African countries has risen to an unprecedented level. A determination has, thereby, developed for confronting the relatively intractable challenge of endemic malaria in Africa and certain other parts of the world’s tropics. Success will require the identification and careful analysis of constraints that affect the scaling up of interventions.

In addition to a critical need for financial resources, antimalaria success requires effective health service delivery, governmental capacity for developing and implementing
policies, operational capacity, community level management, resolution of drug and insecticide resistance, community participation, a reluctance by rich countries to provide free anti-malaria intervention tools such ITNs, drugs and insecticides. Environmental management for eliminating and reducing Anopheles mosquito breeding sites, indoor residual spraying activities and utilization of nets will have little or no impact on malaria transmission and the incidence of disease if they are limited to those few people who are fortunate enough to afford those services. If coverage is sufficient, the benefit of these interventions will extend beyond the individual user or household. These tools were provided free to the general population during the malaria eradication era in recognition of their benefit as public goods. There is, thus, a sound biological and epidemiological basis for considering these services as global public goods for health (Bradely, CMH). If effective anti-malaria interventions were freely available to the poorest of the poor, and if these methods were implemented on a national scale, a major step would be taken toward alleviating the burden that malaria imposes on our own and on future generations. Numerous technical, behavioral and management issues impede implementation of sustainable antimalaria efforts. These include:

1. Rapid spread and intensification of resistance by Plasmodium falciparum to the most commonly used anti-malarial drugs. These drugs were safe, inexpensive and effective and include chloroquine and sulfadoxine-pyrimethamine (SP).

2. Lack of diagnostic facilities at district and peripheral health services, resulting in the adoption of a defective policy of treating all febrile cases with anti-malarial drugs. As much as 60% of clinically diagnosed febrile episodes that were treated for malaria cannot be attributed to malaria. This waste of drugs will become increasingly important as more expensive drugs come to replace chloroquine and SP.

3. Inadequate coverage of the health services that omits a large portion of the residents of endemic countries, forcing them to rely on self-medication and treatment with over-the-counter drugs. Poor quality and delayed health services, delivered by unfriendly medical personnel, further disenfranchise the catchment populations of many public health facilities.

4. Wide-spread use and availability of locally produced or imported sub-standard or imitation anti-malaria drugs due to an absence of laboratories that would perform quality assurance and to poor enforcement of basic standards by regulatory agencies.

5. Lack of effective health information and management systems for timely analysis of trends, thereby delaying decision-making and interventions.

6. Inadequate monitoring and evaluation systems for assessing the efficacy of interventions. As a result, many anti-malaria activities are conducted routinely and without rigorous assessment of their impact.

7. Program designs frequently rely on a single national intervention strategy rather than on local epidemiological situation-analyses. Such discrepancies include issues of rural versus urban situations, problems related to refugees, displaced populations, migrant
workers moving from non-endemic to endemic sites, nomads who lack adequate and permanent shelters and regions prone to epidemics. These unique epidemiological situations should be stratified in a manner that permits optimally designed interventions.

8. Ineffective information, education and communication (IEC) strategies, resulting in a non-participatory approach and inadequate dialogue with the concerned communities where own perceptions may be brushed aside. Peripheral front-line health workers lack the time and skill to interact with and educate the residents of their respective catchment areas concerning health promotion practices and preventive methods of such diseases as malaria. This subject is particularly lacking in attention and resources.

9. Inadequate knowledge and practice relating to timely treatment-seeking behavior for children and full compliance for the use of prescribed drugs. Houses that are sprayed with residual insecticides that are efficacious against vector mosquitoes tend in some communities to be replastered within days after spraying. Although the protective importance of insecticide treated nets is well appreciated, children and pregnant women frequently are inadequately covered because nets may not be affordable, while re-treatment is difficult to establish on substantial scales.

10. Malaria is relegated to Ministries of Health without consultation and strong collaboration with other sectors such as Agriculture, agencies concerned with water resource development, education, local governments, ministry of finance and the communities themselves. Although various categories of private medical practitioners treat many malaria-infected people, they tend not to be included in anti-malaria programs. Village pharmacies, shops and drug vendors are the primary sources of anti malarial drugs for more than 80% of febrile children who are treated at home. A sustained impact requires a rigorously planned inter-sectoral approach.

RBM has effectively established partnerships that include bilateral donors and various national agencies. The intersectoral partnerships established by the International Water Management Institute (IWMI) and the System wide Initiative on Malaria and Agriculture (SIMA) also require expansion and enhancement (http://www.cgiar.org/iwmi/). The associations that currently exist at country levels should be extended to establish more structured partnerships that include the various public and private sectors, thereby dividing work and responsibility relating to health promotion, prevention and disease. Needed, are strategies that employ existing antimalaria agencies in antimalaria efforts that are sustainable because they initiate cycles of health and wealth.

II. Objective of the Millennium project

The objective of the Millennium Malaria Project is to reduce the burden of malaria through sustainable programs in the context of health sector development
III. Strategies for achieving the MDG Malaria objective

The millennium project seeks to address the barriers to scaling-up anti-malaria interventions that

**Formulate** strategies that will strengthen the capacity of endemic countries to scale-up their malaria control programs through a package of integrated multiple interventions to national scales.

**Develop** modalities for improving access to drugs, diagnostics, insecticide treated nets and insecticides by the residents of malaria endemic countries

**Promote** mobilization of resources by developed countries and the private sector in support of antimalaria efforts for disbursement to endemic countries through the Global Fund against AIDS, TB and Malaria.

**Strengthen** the technical capacity of NGOs and other agencies involved in the support of endemic countries in the prevention and control of malaria.

**Strengthen research and development** to improve existing methods and develop technologies that seem likely to facilitate anti-malaria interventions

**Strengthen** the global partnerships linking governments, international organizations such as WHO, UNICEF and FAO, development banks, multinational corporations, NGOs and private foundations to ensure that effective multiple anti-malaria interventions are applied adapted to local conditions

These approaches guide and prioritize the work of this task force. They provide a framework through which a diversity of partners and donors can assess progress and redirect their efforts over time, as needed. They are also meant to attract and energize new participants who will facilitate effective malaria control in the tropics.

IV. The Burden of Malaria and Intervention Strategies

A. The Burden

The current outlook for malaria control is grim and getting worse. This infection is endemic in the poorest parts of the world’s tropics. Between 300 and 500 million clinical cases of malaria occur each year, causing more than 1 million malaria-related deaths. In sub-Saharan Africa, where the burden of malaria is greatest, 15% of all disability adjusted life years (DALYs) that are lost are associated with malaria. About 60% of all deaths from malaria in the world occur among the poorest 20% of the world’s population. In the absence of effective intervention strategies, the frequency of clinical cases of malaria could double over the next two decades.

People living in poor quality housing are at particular risk of infection, and once infected, such people are most likely to suffer and die, in part because their access to effective treatment is so limited. Malnutrition contributes further to malaria-induced death and disability. In intensely endemic countries, malaria during pregnancy is a
leading cause of low birth weight and one of the primary causes of neo-natal mortality. Furthermore, women living in endemic countries are four times more likely to suffer attacks of symptomatic malaria when they are pregnant.

The disease burden imposed by malaria carries with it a corresponding economic burden. Where malaria risk is high, development is impeded. This infection 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 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. [Refs.]. Investments in many kinds of production - in mining, agriculture and manufacturing - can be crippled if the labor force faces a heavy disease burden, or if the burden raises the cost of attracting needed labor to a malarious region. In the colonial period between 1900 and 1950, malaria suppression frequently was 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). International trade and finance has become critical for economic development, and malaria-induced adverse effects on foreign trade and investment are likely to be of tremendous macroeconomic importance.

Malaria directly impedes development through its effect on agricultural productivity. In such rural communities, the transmission season generally coincides with that of planting or harvesting. Many subsistence farmers in Africa shoulder the heaviest burden of malaria because their way of life is so fragile. 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.

B. Temporal Trends in the malaria burden

At the beginning of the 20th century, malaria constituted a major health burden in the Middle East, southern Asia, the western Pacific, Central America, the Caribbean and sub-Saharan Africa. To a lesser extent, malaria was then problematic in China, northeastern Asia and in parts of South America (Table 1). Sub-Saharan Africa remains the main region in which malaria-related mortality has persisted throughout the 20th Century.
With the exception of Europe and North America, the mid-20\textsuperscript{th} century goal of malaria eradication was never realized. What was achieved, however, was an unprecedented reduction in malaria-related morbidity and especially mortality, across vast regions in the tropical and subtropical world. For the most part, the methods that are used for intervening against malaria today are the same as those that were available during the ‘eradication’ era and, many were employed effectively during the early 1900s (Watson, 1921).

The malaria-suppressive methods of the past century that so effectively reduced the burden of malaria included a battery of effective approaches. Therapeutic drugs became available, which directly reduced morbidity and mortality while also helping to suppress the force of transmission of this infection by reducing the human reservoir of infection. Residual insecticides similarly became available, which directly reduced the force of transmission by reducing the longevity of the vector population. In addition, methods were developed for reducing human-mosquito contact through the use of insecticide-treated bed nets as well as source-reduction methods and environmental management techniques. Most fundamentally, housing was improved in the more industrialized nations in a manner that excluded nocturnally feeding vector mosquitoes.

During the 1970s and 1980s, the health sectors of countries where malaria eradication had been attempted, in Asia and the Americas, went through substantial reforms, moving from vertically organized disease-specific orientations to a strategy based on the delivery of integrated health services. Decentralization was promoted such that countries devolved responsibility for the operation of health systems on provinces and districts. “Primary health care” was adopted as key element in the organization of
the health system (Mayhew, 1996; Vendikov, 1998). These developments resulted in a series of decentralized health care systems that would dilute the force of any disease-specific program.

In Asia and throughout much of the Americas, the malaria burden of today 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). With the constant threat of life-threatening drug-resistant malaria, situations fluctuate between worse and better. 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). Africa now carries far more than its share of malaria’s burden. A prominent aspect of this situation is a lack of adequate health systems, which would effectively deliver anti-malarial drugs or other interventions. Africa, of course, is particularly vulnerable to any failure on the part of the international donor community to supply effective antimalarial drugs.

V. Institutional Policies for Malaria Control

The modern era of anti-malaria efforts began during the second half of the 20th Century and has continued through a series of mutations and variations. The principal initiatives, summarized below, provide an essential context for our main recommendations.

A. Eradication period

The availability of DDT and the experience of its profound effect on malaria transmission 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. Due to the perceived intractability by malaria in Africa, the “Global Programme” largely bypassed that continent even though the malaria burden is greatest there. For the next several decades, malaria attracted little interest, and scant resource were allocated by the international community to this problem, leading to poorly coordinated and fragmented intervention efforts.

B. Amsterdam Declaration on a 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 and recommended the development of an appropriate strategy and mobilization of resources to intensify effective intervention measures. The Amsterdam Ministerial Conference on Malaria of 1992 adopted a global strategy that subsequently was endorsed by the UN General Assembly. 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 (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. The 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.

C. Declaration of the Organization of African Unity

Many of the Heads of State of the Organization of African Unity took particular note of the deteriorating malaria situation in Africa at a Summit meeting in 1977 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.

D. Roll Back Malaria initiative

Upon assuming the directorship of the World Health Organization in 1998, Dr. Gro Brundtland formulated a program designated as “Roll Back Malaria (RBM), which aims to reduce the burden of malaria throughout the world. The RBM initiative derived from an earlier African initiative for accelerated implementation of anti-malaria interventions by African Governments and specified a 10-year goal of reducing the burden of malaria by half. This originally WHO initiative was joined by an array of international organizations, including the World Bank, UNDP and UNICEF. RBM adopted the malaria control 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, consensus and developed a coherent strategic implementation plan. RBM 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. Various of the endemic that participated actively in the RBM partnership, 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. Funding constraints, however, restricted the launching of countrywide implementation programs

E. The African Summit 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 other donor 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 integrated package of interventions to national scale

F. Global Fund against AIDS, TB and malaria

A Global Fund against AIDS, TB and malaria was initiated within the UN, itself, 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 Fund has approved a total of 1482 million dollars for the first and second round of proposals, out of which, proposals from 40 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. It will be critical for the international donor community to support and strengthen the GFAIDS to mobilize adequate resources.

VI. Examples of Recent Successful Malaria Control Efforts

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 are more competent than are other vectors. 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 than the level needed to perpetuate infection. The task of malaria control in Africa is therefore far more difficult and complicated in Africa than it is elsewhere, and the endemic burden is correspondingly huge. Children are frequently infected in the first few weeks of life and circulate parasites continuously until adolescence.

The usefulness of an integrated package of interventions is evident in the experience in Tigray, Northern Ethiopia and Madagascar. Salient features of these programs are cited here as examples of success.

A. 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 live 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 and Morrow 2000). This community based approach practiced in Tigray is well accepted and is being implemented nation-wide.
B. Highlands of Madagascar

Malaria and its vector An. 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).

Examples of anti-malaria success may be cited for other parts of the world. The value of an integrated application of packaged interventions is amply demonstrated by the experience of Vietnam in Southeast Asia.

C. Vietnam

Vietnam, a Southeast Asian country of 26 million people, where as many as a third of the population reside in malaria endemic regions, is a country that, until recently had been intensely affected by malaria. In 1991, for example, 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. 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. Coverage of indoor residual spraying rose from 4.3 million in 1991 to 13 million in 1997. In parallel, the number of people using ITNs simultaneously rose from 300,000 to more than 10 million. This integrated package of interventions was evaluated over a five-year period (1992 until 1997). Mortality and morbidity was reduced by 97% and 60% respectively. Local outbreaks were virtually eliminated.

These examples of successful anti-malaria efforts clearly demonstrate the value of applying locally adapted, integrated packages of interventions. Similarly gratifying results have been derived as a result of home management efforts in parts of Burkina Faso, Kenya, Uganda and Zaire. 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.

VII. Current Strategies and Objectives

Reasonable objectives for anti-malaria interventions are particularly elusive because less infection may not automatically imply less disease and because less disease
may not imply less poverty. Infection in solidly immune adults tends to be asymptomatic. Moreover, broad regions tend to be malarially heterogeneous, thereby requiring locally adapted interventions and correspondingly special indicators of improvement. A mesoendemic urban site, for example, requires different kinds of interventions, different goals and different measures of success than does the surrounding holoendemic countryside. The heterogeneous and highly focal nature of malaria transmission should be given full consideration in designing strategies for broad regions and in formulating national strategies.

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 presumptive treatment 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.

A. 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 CT drugs for treating uncomplicated malaria, quinine for the management of severe malaria and SP for intermittent presumptive treatment (IPT) of pregnant women.

1. Malaria Diagnosis

Prompt and accurate definitive diagnosis is critical for disease management. Current options for malaria diagnosis are comprised of clinical diagnosis and microscopic examination. Microscopic diagnosis, which is considered to be the ‘gold standard’ for malaria confirmation, presents such technical and personnel requirements as working microscopes, reagents, trained microscopists and supervisory personnel. The work is labor-intensive and time consuming, occupying about an hour to process and examine a blood sample.

Because many health service facilities cannot meet these requirements, laboratory facilities for microscopic examination of malaria parasites are virtually non-existent in
the many health care services. In almost all situations, malaria treatment in Africa is administered on the basis of clinical signs and symptoms and is without microscopic confirmation of parasitemia. In the absence of microscopy, the accepted case-definition for malaria focuses on a history of fever during the past two weeks without other attributable causes. The clinical features of malaria, however, are notoriously non-specific and overlap with those of other common childhood diseases. In the absence of microscopic facilities, all fever episodes are diagnosed as clinical malaria and treated accordingly. Such practice results in over-treatment by as much as 60% and increases operating costs. This approach might have been justified when presumptive treatment relied on such inexpensive and safe drugs as chloroquine, at a cost of about 0.08 dollars for an adult treatment course. The high cost of combination therapy (CT), which is about ten times as expensive as CQ and SP, therefore, will render impractical the past practice of treating all febrile episodes on the basis of clinical diagnosis alone.

The third diagnostic option that has recently been introduced is the category of rapid diagnostic tests (RDTs). Such tests seek to detect exoantigens derived from the malaria parasites. These “antigen detection tests” are incorporated onto disposable “dip-sticks” that can readily be used under field conditions. Such tests can be performed in about 15 minute from finger-prick blood samples by technicians who have had only minimum training. Because the test can be performed by laypeople, it is adaptable for use by community health workers for malaria management at home. The RDTs are sensitive and can detect as many as 90% of those malaria patients whose parasite threshold exceeds 40 parasites/ml blood.

2. Treatment of Malaria Cases

Resistance against the commonly used anti-malarial drugs has intensified and has become virtually 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%. Three combination therapeutic options (CT) have been recommended by WHO (www.WHO.int) for Africa, namely (1) Artemether-lumefantrine (Coartem); (2) Artesunate plus amodiaquine and (3) Artesunate plus SP where SP retains its efficacy. Of the three options, Coartem is a fixed-dose combination anti-malarial drug that is co-formulated. The other two combinations are comprised of independently acting antimalarial drugs that are co-administered. This new generation of antimalarial drugs is more than ten times as expensive as is the currently used package of obsolescent drugs.

A number of countries that are concerned with the level of drug resistance against such existing anti-malarials as CQ and SP are updating their treatment policies and taking the necessary preparatory steps to introduce the new generation of effective CT drugs. In the interim, a number of these 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 such drugs of reduced efficacy is due to financial constraints. Kwazulu Natal in South Africa is the only region in Africa that has introduced Coartem. Zambia and Zanzibar, which are the first round recipients of Global Fund support, are making the necessary arrangements to introduce Coartem.
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 than 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.

3. Malaria Management at Home

In many African countries, health service coverage 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 such essential drugs as the anti-malarials. These factors, coupled with physical distance and problems of affordability, pose major obstacles and disincentives for their use by rural populations. Instead, they resort to self-medication using anti-malarial drugs obtained from the open market or traditional herbal medicines. Although patients should be treated by qualified personnel, primary health care services also should contain a prominent personal component and should rely heavily on community participation. 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 (www.rbm.who.int). 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 caregivers 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, the large-scale introduction of such innovative ways for delivering anti-malaria treatments should receive particular attention.

B. 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 on sleeping people. In addition to protecting the net user, such nets usually reduce local 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. 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.

C. Intermittent preventive treatment

Mortality in pregnant women and children is somewhat ameliorated by presumptive administration of anti-malaria drugs provided in the course of routine pre- and post-natal visits.

1. Malaria in Pregnancy

Where *Plasmodium falciparum* is intense transmitted, 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.

2. 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 (1,2). Although infants can be protected substantially by chemoprophylaxis, provided at weekly or fortnightly intervals (3,4), 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 (5). 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.

D. 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 and Mnzava, 2000). In Zanzibar and perhaps certain parts of West Africa, DDT resistance in *An. gambiae* now precludes effective use of DDT. In South Africa, however, reversion to DDT spraying during 2001 has relieved the increasing malaria problem associated with pyrethroid resistance in *An. 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. No clear criterion is available for deciding between house spraying and the application of treated bednets. “Fire brigades” of trained and equipped spray-men may be appropriate for deployment where in the case of malaria epidemics.

E. Interventions 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 endemicity 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, impeding education by absenteeism from school. Malaria epidemics frequently occur following years of drought and famine, further impinging on populations already weakened by malnutrition and poverty. Indeed, the long-term consequences of severe epidemics include impairment of the health of children born to infected mothers.

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, the residents of such malaria-prone regions and who are non-immune to the malarial parasite include about 110 million people. Such people would at high risk of death or severe morbidity in the event of an outbreak. Devastating epidemics have recently struck Zimbabwe, Botswana, Mozambique, Swaziland, Ethiopia and South Africa. These epidemics have mainly been attributed to heavy rainfall following a drought. Malaria epidemics also affected various districts in Senegal in 1994 and 1998. 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. Although the extent of damage caused by these epidemics is not adequately documented, it would include poor quality of health services. Delayed service and unfriendly medical personnel further disenfranchise people from many public health facilities. These institutions include the more financially accessible, and it is here that morbidity, mortality and the overall economic impact of these epidemics are enormous. More than 150,000 people died out of some three million clinical cases during the malaria epidemic that hit Ethiopia in 1958 (Fontaine 1961).

Knowledge-based 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 (health, meteorology, agriculture, etc) of agencies

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.
F. Source Reduction

Because the breeding places of An. gambiae are numerous and transient in many African villages, the breeding sources of these mosquitoes may be difficult to eliminate. One attempt to do so, in combination with use treated nets, was unsuccessful in enhancing the effect achieved by the treated nets alone. 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 recently effectively suppressed malaria transmission, prevalence of infection and case incidence (Yapabandara et al. 20011). 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 necessitates agriculture-health linkages for effective control. Risk mapping of this dynamic in Dar es Salaam (Yamagata, 1996 JICA Final Report), 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, RBM 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 (II) strategies have been effectively used since the 1920s to control ricefield 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 II 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 Systemwide Initiative on Malaria and Agriculture (SIMA) and the International Water Management Institute (IWMI). This is also a topic that provides a very natural bridge between the Task Force on HIV/AIDS, Tuberculosis, Malaria and Essential Medicines and the Task Force on Hunger.
G. 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.

VIII. 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 generally 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 within them.

IX. Capacity building

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.
The Fogarty International Institute of the U.S. National Institutes of Health provides a model program for such training. This system encourages U.S educational and research institutions to establish links with institutions in the developing world for this purpose. The highly qualified personnel that result would contribute powerfully to regional anti-malaria efforts. Local training programs, administered by these people provide the skilled workers who conduct this work.

Community-level participants in anti-malaria efforts are trained in their own communities in a system designed to stimulate their enthusiasm and prepare them for the challenges presented by their friends and neighbors. They are key in efforts to promote social mobilization and healthy behaviors as well as in mobilizing political and financial support.

**X. Role of Health Services in anti-malaria interventions**

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 and insecticides
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

**XI. 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 data-base to facilitate performance assessments and guide the adaptive tuning of interventions.

The data base 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 15-20 year period in concert with Millennium Development Goals and process milestone targets that are established in partnership between the given counties and alliances of supporting partners.

A. Establishing National GIS Platforms of Risk, Population and Service provision

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 which builds on the features of HealthMapper. More than 300 indicators for more than 20 infectious diseases are included in the database.

B. Measuring Mortality Impacts

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.
C. Measuring changes in morbidity burdens at health facilities

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.

D. Measuring process targets - household level

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.

E. Measuring process targets - service provider level

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.

F. Monitoring effectiveness of commodities

Both parasite and vector sensitivity to drugs and insecticides will be paramount to the tracking of program effectiveness. Traditional \textit{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.

G. Economic evaluation - 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 (\textit{e.g.} price of bednet or drugs) or quantities (\textit{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.
H. Economic evaluation - impact of 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.

I. Economic evaluation - impact on national and sub-national economic growth

It will be important to document the interrelationships between the health consequences of the malaria control programs -- including business activity, particularly new investments from diverse sources -- and the effects on the local, regional, and national economies. Some quite subtle analyses, involving judicious examination of counterfactuals, will be required to convincingly establish the impact of malaria control on national economies. A role model for this kind of study is provided by Robert Fogel’s in-depth analysis of the impact of railroads on the development of the American economy in the 19th century (Fogel, 1964). Despite pervasive, but loose, claims that railroads were key to the economic development, this did not hold up under careful scrutiny. When malaria control is necessary but not sufficient for economic development, it will be important to characterize how this activity interacts with other social and economic policies over time to produce observed and desired outcomes.

Areas 1-9 provide the principal framework for measuring public health and economic impacts and the costs required to achieve them. In addition, there will be a continued need for operational research to assess potential blocks to effective program implementation and improved systems of delivery. These will be specified on an ongoing basis as part of the strategies of adaptive improvement of program implementation.

XII. Research and Development

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

A. Vaccines

The search for a malaria vaccine has been particularly elusive. Natural immunity against this infection develops only after many years of exposure, is strain-specific, is transient in the absence of boosting and is disease modifying, rather than sterilizing. In spite of these apparent obstacles, prospects remain bright. A central question in this strategy lies in the choice of a developmental stage to be targeted by such a candidate vaccine.

A sporozoite or liver-stage vaccine would protect against the stage of the parasite that induces infection but not the stage that causes disease. The use of such a vaccine
might be limited to travelers. A merozoite vaccine would modulate the disease but not prevent infection. Such a vaccine would be useful solely to the residents of endemic sites. A gamete vaccine would be altruistic because it would prevent vector mosquitoes from acquiring infection but would not modulate the infection. It would be useful solely when applied to the residents of endemic sites.

Four different immunogens (a synthetic vaccine mixture designated as SPG66, a subunit vaccine directed against sporozoites designated as CS-NANP, another such sporozoite vaccine designated as RTS,S and against merozoites designated as MSP/RESA) have already been subjected to as many as 18 field trials in Africa (Graves and Gelband 2003). The results have been mixed. Further development of such subunit DNA candidate vaccines will be greatly facilitated be the recently decoded malaria genome. This approach toward the induction of sterilizing immunity seems promising, in large part because travelers will serve as a large and remunerative market.

Long-lived efficacy (about nine months) has been obtained solely with a pre-erythrocytic vaccine comprised of living, but radiation-attenuated sporozoites, perhaps because this delivery system induces a cellular immune response that acts against the hepatic stage of the pathogen (Moorthy and Hill 2002). Such a promising cellular response can be generated by co-vaccination with a recombinant viral protein, known as the prime-boost approach. Such a vaccine strategy is burdened, however, by the exceedingly variable nature of the relevant part of the *Plasmodium falciparum* genome. Although large, the market for this kind of a disease modifying product will be limited to the poorest-of-the-poor, the people who live in heavily endemic sites.

Blood-stage or “anti-complication” vaccines mainly seek to prevent invasion of the red blood cell. A number of candidate subunit immunogens have been developed. Such a vaccine will not be boosted naturally because vertebrate hosts would not normally be exposed to gametic epitopes. Nor would the private sector be likely to assist in the development of this altruistic product. The level of coverage required for such a vaccine to reduce the force of transmission of malaria should be defined.

The laboratory work that is devoted to the production of malaria vaccines should be accompanied by epidemiological studies that will identify the people who are to be immunized. The magnitude of the financial investment should be proportional to the benefit that might someday be accrued.

**B. Anti malarial drugs**

Since chloroquine resistance was first detected in Thailand in 1960, local *Plasmodium falciparum* poulations have developed levels of multi-drug resistance that rendered them virtually invulnerable to all existing drugs, particularly in South east Asia. Resistance to chloroquine in east Africa was documented initially in 1979. Subsequently, such insusceptibility has spread throughout the continent, particularly in the eastern (Teklehaimanot, 1986), southern and central endemic countries. In some countries, the level of resistance to chloroquine now exceeds 80%. Resistance to sulfadoxine-pyrimethamine (SP), a second line drug treatment for cases of chloroquine failure is
spreading at a similarly alarming rate in southern and eastern Africa. The widespread and intense presence of chloroquine resistance has led to an overall increase in mortality in East Africa (Marsh 1998). A significant rise in mortality in children under five in Senegal, West Africa, was also reported (Trap et al. 1998). The increasing incidence of severe malaria and the severity and frequency of epidemics are also attributed to increasing antimalarial drug resistance (Bloland PB et al. 1999; Greenberg et al. 1989). Thus, the repertoire of effective antimalarial drugs suitable for treating malaria in endemic parts of the world has greatly diminished due to wide-spread resistance of *Plasmodium falciparum* parasites.

In Southeast Asia, a system of combination therapy based on artemisinin and mefloquine is being used to treat uncomplicated malaria with the objective of enhancing treatment efficacy and of delaying the potential development of parasite resistance. In Africa, three artemisinin-based combination therapeutic options (ACT) have been recommended. These combinations are: (1) artemether-lumefantrine (Coartem), (2) artesunate plus amodiaquine and (3) artesunate plus SP where SP retains its efficacy (www.WHO.int). Of these options, Coartem is a fixed-dose combination anti-malarial drug that is co-formulated. The other two combinations are comprised of independently acting antimalarial drugs that are co-administered. This new generation of antimalarial drugs is more than ten times as expensive as is the currently used package of obsolescent drugs. Kwazulu Natal, in South Africa, is the only region in Africa that has introduced Coartem. Zambia and Zanzibar, which are the first round recipients of Global Fund support, are making the necessary arrangements to introduce Coartem or similar artemisinin-based combination products.

A number of countries that are concerned with the level of drug resistance against such existing anti-malarials as CQ and SP are updating their treatment policies and taking
the necessary preparatory steps to introduce the new generation of effective CT drugs. In
the interim, many of these 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 such drugs of reduced efficacy is due to financial constraints. The international
community, therefore, should support research and development designed to replace
these obsolete antimalarial drugs. An innovative partnership with pharmaceutical
industry should be devised to encourage the private sector to embark on the neglected
area of antimalarial drug research and development. Existing public private partnerships
such as the Malaria Venture for Medicine (MMV) require support in their efforts to
discover and develop novel antimalarial drugs. Pharmaceutical plants in malaria endemic
countries should also be provided with substantive technical support such as technology
transfer to upgrade their plants to international GMP standard for producing antimalarial
drugs.

C. Overview of Malaria Chemotherapy 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. This has resulted in part because of continued
investment in basic science by a number of agencies such as NIH, European Commission
and the Wellcome Trust. USAID funding and TDR support for artemisinin combination
studies has similarly contributed. The Medicines for Malaria Venture (www.mmv.org), a
public private partnership devoted to malaria drug development, has been particularly
helpful, as has the continued activities of institutions such as the Walter Read Army
Institute of Research in the U.S. and WHO/TDR (www.who.int/tdr).

The increased engagement of industry in drug development, through the creation
of public private partnerships has been the single most important factor in the improved
situation. More than 10 companies are currently engaged in drug discovery and
development activities. Five years ago, there were no more than two or three. The
reason for this is that, through MMV and other organizations, public and philanthropic
sector funding reached a level that enabled industry and academics to engage
meaningfully in drug development partnerships. Appropriate mechanisms are now in
place that facilitate the establishment of such partnerships. In return for partnering with
companies financially and technically, the public sector receives in return an equivalent
commitment of resources and expertise from industry and a commitment to preferential
pricing in developing countries. For large pharmaceutical companies, despite the
partnership support received, their engagement is not primarily driven by commercial
concerns. The profits they may earn will be extremely limited and do not outweigh the
opportunity costs involved. The public and philanthropic sectors derive value for their
investments and are not unduly subsidizing industry.

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. The costs of the projects initiated over the last few years will
increase as they advance to clinical studies and registration. More projects are required to sustainably ensure success. Currently, the income of MMV is only half that amount. Support to other agencies working on antimalarial drug development, such as Walter Read Army Institute of Research, WHO/TDR and NIAID also needs to be maintained and, if possible, increased.

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.

D. Antimalarials in the pipeline

An array of antimalaria drugs have been developed and are being evaluated. These include:

1. The antifolate chlorproguanil-dapsone (Lapdap) has been co-developed by GSK and WHO/TDR, with support from UK DFID, and submitted to the UK Medicines Control Agency by GSK. Because this drug is not an artemisinin combination, it is unlikely to be recommended as a first or second line treatment policy in its own right. A fixed dose combination of Lapdap with artesunate, however, is also in development (see below).

2. Rectal artesunate, developed by WHO/TDR, has recently received a letter of ‘approvability’ by the US FDA for use as a single administration for malaria patients unable to take antimalarial medication by mouth, before they are referred for hospital treatment. If certain conditions are met, registration under ‘fast-track status is anticipated in 2003. A commercial manufacturer has been identified and negotiations are being finalized. This product could greatly increase survival of children residing some distance from hospital care.

3. Several fixed dose artemisinin combinations are under development and are likely to be approved 2006 or 2007. The sole fixed dose combination currently available is Coartem, which is available at $2 per adult treatment and is dosed twice daily over three days. The use of artemisinins in combination with other antimalarials is currently being promoted by WHO, due to the efficacy of the artemisinin component and the ability of partner drugs to reduce treatment times to three days (artemisinins used alone require 5 to 7 days). Combining two drugs may also reduce the propensity to generate resistance. As such, fixed dose combinations are likely to be considered as candidate drugs for inclusion in national policies. Although the large number of fixed dose combinations under development is currently justified, some may begin to appear more relevant than others. Characteristics that will affect such a decision include efficacy, safety, cost, stability, speed of development and availability. Combinations under development include:

4. Chlorproguanil – dapsone – artesunate (Lapdap - artesunate) by GSK with WHO/TDR and MMV (MMV funded): anticipated costs are competitive with Coartem and it has a
potential advantage of once a day dosing over three days. Phase 1 studies have been initiated.

5. Pyronaridine – artesunate by Shin Poong, Korea, in collaboration with WHO/TDR and MMV (MMV funded): costs will likely be similar to that of Coartem; potential advantage comes from once a day dosing. Phase 1 trials are planned for early 2003.

6. Piperaquine – dihydroartemisinin (artekin) by Holleykin, China. Co-development discussions are currently under way with WHO/TDR, WHO-MAL and MMV. Anticipated costs are likely to be competitive with Coartem; once daily dosing is anticipated. Clinical studies are in progress, but further GLP preclinical work is required.

7. Mefloquine – artesunate, a proven combination as a non-fixed treatment regimen, is being developed as a fixed dose combination for once a day dosing over 3 days. A consortium involving MSF, TROPIVAL (Bordeaux) and Far Manginos of Brazil are involved with EU funding and some WHO/TDR technical support. Costs will likely be similar to that of Coartem. Phase 1 trials are planned for 2003.

8. Amodiaquine – artesunate, another proven combination as a non-fixed treatment regimen, is in development by the same consortium as above. Once a day dosing over three days is anticipated. Costs will likely be competitive with Coartem. A commercial partner is being sought for its manufacture and production. Phase 1 trials are planned for 2003.

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, a new artemisinin derivative being developed by Bayer with MMV support. Its potential advantage over existing artemisinins is its lower neurotoxicity and enhanced efficacy. This compound may be registered by 2007.

2. Isoquine, a new quinoline antimalarial, being developed by GSK and the University of Liverpool with support from MMV and some technical assistance from WHO/TDR. This compound resembles amodiaquine but potentially has an improved safety profile and is highly active against chloroquine resistant strains. This compound may be registered by 2008.

3. A new antifolate, highly active against SP resistant strains, is under development by Jacobus pharmaceuticals with MMV support and technical assistance from WRAIR. This compound may be registered by 2008.

4. Fosmidomycin, a new class of antimalarial, is under development by Jomaa Pharmaceuticals in Germany. This drug may also be used in combination with other agents. The major issue is whether it can be utilized in a three day regimen.
5. A new class of synthetic endoperoxide, invented at the University of Nebraska, is being developed by a consortium funded and managed by MMV. A compound is likely to enter into full pre-clinical development later in 2003. The advantage of these compounds is that they have a longer half-life than the artemisinins and so could find use alone in 3 day treatment regimens and might serve as a better partner than an artemisinin as a longer half-life drugs. Such a compound might be registered by 2009. A commercial partner is being sought.

Several promising MMV-funded drug discovery activities are also under way. Such preliminary studies on these entirely new classes of antimalarial may begin to come to market soon after 2010. Several enhanced formulations of existing drugs are also under development. These include:

1. A pediatric Coartem formulation by Novartis in collaboration with MMV and TDR (MMV funded)

2. An artesunate i.v. formulation for severe malaria; a collaboration between WRAIR and MMV.

**E. Diagnostics**

Prompt and accurate definitive diagnosis is critical to disease management. Current options for malaria diagnosis are comprised of clinical diagnosis and microscopic examination. In areas of low endemicity, the sensitivity and specificity of clinical diagnosis is low and there is a risk that potentially life threatening *Plasmodium falciparum* malaria infections might be missed. In such situations, clinical diagnosis should be confirmed by microscopic examination of a blood smear.

Where malaria is hyper- or holo-endemic, clinical diagnosis can serve as the sole means of identifying malaria cases in the event that microscopic methods for confirmation are lacking. Presumptive clinical diagnosis, however, frequently results in over-diagnosed malaria with consequent waste of these increasingly expensive antimalarial drugs. Because the new generation of antimalarial drugs is about ten-fold more expensive than CQ and SP, the current practice of treating all febrile episodes will not be cost-effective.

The third diagnostic option that has recently been introduced is the category of rapid diagnostic tests (RDTs). Such tests can be performed in about 15 minutes from finger-prick blood samples by technicians who have had only minimum training. Because the test can be performed by laypeople, it is adaptable for use by community health workers for malaria management at home. The RDTs need further refinement, however, in order to increase their sensitivity and to reduce the presently unacceptable levels of false positivity that accompanies their use (Stephens et al., 1999). Because RDTs detect circulating *P. falciparum* antigens for as long as two weeks following chemotherapy and parasite clearance as confirmed by microscopic examination, the existing RDTs are not suitable for the assessment of treatment failure or drug resistance (WWW.WHO.int: Malaria diagnosis new Perspectives).
E. Risk mapping

A large body of coordinated experience in mapping malaria rates has already accumulated in large parts of sub-Saharan Africa. The MARA program represents a major initiative in this direction. 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. Furthermore, rapid assessment strategies, particularly in urban sites, should be calibrated and standardized. An important step in this direction is the WHO-sponsored ‘Rapid Urban Malaria Assessment’ study that is ongoing in five African cities. Data gaps are currently being identified in collaboration with CIESIN (based at Columbia University), and this should lead to a comprehensive set of high resolution risk maps that integrate optical satellite images, radar images, aerial photographs and data from ground-based entomological and parasitological surveys. High resolution risk mapping over time will be an important ingredient in efforts designed to monitor the projected anti-malaria intervention initiatives.

G. Anopheline ecology

The force of malaria transmission is regulated variously by the longevity of the vector population relative to the extrinsic incubation period of the pathogen, the host specificity of the vector, the duration of the transmission season, the competence of the vector mosquito and its abundance relative to that of people (Macdonald 1956). Other factors may also contribute. The venue of transmission, of course, is the human bedroom because the nocturnal mosquitoes that transmit this infection inevitably feed there. These considerations require increased research attention to the circumstances of transmission.

The environmental conditions that contribute to mosquito longevity may focus on predation or parasitism, factors that remain virtually unknown. We know little, for example, of the predation-avoidance strategies practiced by mosquitoes during their long daily periods of rest. The effect of malaria infection on feeding frequency similarly remains unexplored. Temperature relationships are poorly understood.

Host specificity by vector mosquitoes remains a fertile field of study. We lack information on the “zooprophylactic” potential of different kinds of domestic animals and on the relationship of human density to the force of transmission.

The duration of the transmission season has not been subject to rigorous study. We do not know how the major vector mosquitoes survive inter-epidemic periods and what signals the onset and termination of transmission.

Basic information on the factors that regulate the abundance of vector populations remains elusive. We do not know whether these insects are density dependent. Nor have the food sources of the larval stages of these insects been defined. Although maize pollen appears to provide a crucial nutriment for certain vector anophelines (Ye Ebiyo et al. 2000), the role of rice and other crops remains to be defined. Novel and apparently promising intervention modalities may result.
An understanding of the structure of vector populations is prerequisite to any implementation of an integrated program of interventions. In parts of Mali, for example, as many as seven distinct vector populations share in the transmission of malaria (Toure et al. 1999). Target populations must rigorously be defined.

H. 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 to develop to the sporozoite stage (Ghosh et al. 2002). Blood meal-induced expression of such genes can be induced in mosquitoes by the 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 Anopheles albimanus. Hermes or Minos vectors have also been used for transforming other mosquitoes. The three essentials of a transformation system, thereby, have been mobilized: various competence inhibiting genes, promoters and transformation vectors. These accomplishments 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.

To translate these applications of molecular biology into useful malaria-suppressive assets, construct-bearing mosquitoes must be created that can be released into endemic sites, that will thrive there and that will inject a disproportionate fraction of their genes into the local vector population. The fitness of the vector population must be preserved. Toward this end, much laboratory work remains to be done. Improved effectors, promoters and vectors are required. More critical, however, is the need for effective drive mechanisms, a subject that remains virtually unexplored. A transposable element or some other meiotic drive mechanism will be required to drive the effector-promoter construct through the ambient population of vector anophelines, and the resulting three-element construct must be stable. Transposable elements may resist such a state of fixation. The alternative may be to design a system of inundative releases in which the construct-bearing released insects greatly outnumber the ambient population.

Efforts to create genetic constructs for vector anophelines should be accompanied a program of research designed to explore the circumstances under which these assets will be released. Sites are required in which such releases can be evaluated. The ethics of such a release should be defined. The magnitude of the release inoculum should be defined 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.

XIX. Inter-Sectoral Collaborations

Anti-malaria efforts in different countries may require particular inter-sectoral relationships. 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.

**XX. Recommendations**

A set of eleven recommendations have been formulated,

**A. 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.
B. 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. Experience in various malaria endemic countries confirms that such 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.

C. Capacity Building

Cadres of skilled personnel are needed who are able to critically assess local situations, develop appropriate intervention strategies, guide implementation activities and monitor their effects.

D. Strengthening Malaria Training Centers

Existing malaria training Centers in Africa should be encouraged to produce mid-level malaria professionals who are skilled in the epidemiology of malaria and its control as well as advocacy and community participation. One such center, the Nazareth Training Center in Ethiopia, was established by WHO in the 1950s and trains Malaria Control Programme Managers from anglophone African countries. The center is not well maintained, however, and lacks the required facilities. Such programs also are provided within Francophone and Portuguese-speaking countries. Because resources are lacking, these training programs lack coordination.

E. 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.

F. 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.
G. Scaling up of Control Initiatives to a National Scale

At present, malaria control efforts are carried out as small projects with limited coverage and tend to be fragmented and uncoordinated. None of the existing control efforts in Africa apply multiple interventions to national scale and these fragmented efforts could not make a dent to the resurgence of malaria.

The barriers to scaling-up malaria programs include critical shortage of human and financial resources, lack of access to essential drugs, diagnostics, ITNs and insecticides by the poorest of the poor, reluctance by the rich countries to provide free supply of control tools, 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.

H. Chemoprophylactic Drugs

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

I. 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. Generally, the detection and documentation of drug resistance and the formulation of policies for a change to an effective drug could take as long as three years and implementing such policies might require a similar period of time.

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 suppression.

J. Promote Economic Development

Anti-malaria strategies should be devised that most effectively promote economic development. The Earth Institute of Columbia University is coordinating an inter-
institutional malaria body that will advise the Gates Foundation on this subject and has already submitted a proposal for initiating a package of integrated interventions in selected countries. The objective is to devise interventions that reduce morbidity and mortality while also facilitating economic development. The proposed package of interventions would include such components as insecticide treated nets, various antivector approaches, intermittent presumptive treatment of pregnant women, rapid diagnostic tests, treatment with effective drugs, rigorous monitoring and promotion of health information systems.

K. Public-Private 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.

References


