

# Working Paper

## Malaria Research

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## Malaria Research

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### **Introduction.**

Despite the fact that malaria is a major cause of global morbidity and mortality, particularly among young infants and children in Africa, research funding has never been a high priority for civilian research agencies in the developed countries. National funding agencies, even those with significant global health research agendas, but pressed with the need to address domestic agendas, have invested disproportionately small portions of their research budget in relation to the global burden of illness and death due to malaria. At the same time, research funding in most endemic countries has been seriously limited by their resource constraints and limited infrastructure. In contrast, the military of developed nations has had a consistent interest in malaria, as it represents a threat to troops sent to endemic regions. However this research has focused principally on drug discovery and development, without particular concern for the ultimate cost of the drug, and therefore not necessarily relevant to civilian needs of developing countries. .

### **The Historical Perspective**

Looking back over the history of malaria research since the identification of the parasite and its complex transmission cycle, there have been a number of attempts to examine trends in malaria research support so as to learn lessons from the past to apply to the future. All of these reviews point to the difficulty in obtaining accurate and comprehensive data for analysis. Two recent studies, however, are of particular interest and provide the qualitative and quantitative background to explore the role and relevance of research partnerships. In 2004, Alilio, Bygbjerg and Breman<sup>1</sup> reviewed 100 years of malaria research in Africa by means of a computerized literature search of

databases at the National Library of Medicine. The search returned 61 publications with “relevant information”. On the basis of these papers they divided the past 125 years of malaria research into three eras. 1. 1880-1949: Era of Ingenuity and Discovery; 2. 1950-1979: Era of Optimism and Hope; 3. 1980-2003: Proliferation of Multilateral Activities. It is valuable to examine their interpretation.

The first era was initiated with the discovery of the malaria parasite by Laveran and the identification of the transmission cycle in mosquitoes by a number of investigators, including Ronald Ross, who closed the loop by identifying parasites in wild mosquitoes in Sierra Leone.<sup>2, 3</sup> DDT was discovered in 1874 but it wasn't until 1939 that its residual insecticidal properties were identified.<sup>4</sup> With this finding, DDT became a mainstay of malaria control efforts during World War II. In some instances the colonial governments in Africa invested in malaria control following the end of the war, however this was primarily for economic reasons. Using a combination of chemoprophylaxis, DDT, and landscape engineering to reduce mosquito breeding sites, there was enough success in a number of sites to suggest it was possible to achieve major reductions in the disease burden of malaria. In fact, these measures were applied sparingly and primarily in areas of economic rather than public health interest.

The second era characterized by Alilio et al included four malaria “landmarks”: 1) WHO's Kampala Conference in 1950 on the technical needs for an action plan for malaria control<sup>5</sup>; 2) the start of the WHO Global Eradication Program in 1955, based on the Kampala Conference report; 3) independence for most former African colonies beginning in 1960 and the subsequent political instability in the continent; 4) the establishment of the Special Programme for Research and

Training in Tropical Diseases (TDR) at WHO in 1979. The Kampala Conference recommended that modern methods of control be applied in Africa immediately, because, in the view of the conferees, there was no need for further studies to prove the principle that it could be achieved. The WHO Eighth World Health Assembly in 1955 adopted resolutions stating<sup>6</sup>: 1. “Request governments to intensify plans of nation-wide malaria control so that malaria eradication may be achieved; 2. Decide that the World Health Organization should take the initiative, provide technical advice, and encourage research and co-ordination of resources in the implementation of a programme having as its ultimate objective the world-wide eradication of malaria; 3. Authorize the Director-General to obtain financial contributions for malaria eradication from governmental and private sources.” However, by the time the WHO program was implemented, Africa had been excluded from the eradication effort because indoor residual spraying with DDT, the mainstay of the program, was not considered to be feasible. Selected countries elsewhere in the world were excluded as well because of administrative, technical, financial, social or ecologic constraints. Musing about the goals and challenges of malaria control in 1957, Paul Russell of the Rockefeller Foundation wrote:<sup>7</sup> “the progress has been so great that world-wide malaria eradication seems a practical goal. But we are in the midst of a stern battle and not at its end... There is a need for greater international monetary and technical assistance, far more trained malariologists, and particularly for more malaria research”. We could say the same today, some 50 years later.

In reality, then, the global eradication program was hardly global, bypassing many of the most intense malaria endemic countries. In addition, the difficulty in achieving coordinated control measures across national boundaries due to weak governments, little funding, and political turmoil in Africa precluded the implementation of a program scaled to cover large areas of malaria

infected countries, the only way it seemed possible to achieve long lasting results. With limited resources and ongoing debates about whether or not malaria was of high enough priority to command a major portion of available funds, limited human capacity, and limited surveillance systems to track progress and problems, malaria eradication was, in fact, impossible with or without new research. The creation of TDR in 1975 was intended to overcome some of the capacity limitations through training, and in conjunction, the generation of new knowledge and information relevant to control. However, its funding from a variety of sources was divided among a number of infectious diseases problems, not just malaria, thus diluting the potential impact of the program on malaria in particular. None the less, TDR was a critical program, sustaining ongoing investment in research capacity and research in Africa and other developing regions of the world into the 1980's and 1990's

Alilio et al dubbed the third era from 1980-2003 as one of proliferation of multilateral activities. The period began with a new program created and supported by the Director of Health Sciences at the Rockefeller Foundation, Kenneth Warren, which he called the "Great Neglected Diseases of Mankind", generally known as the GND, perhaps the first use of the term neglected diseases. In Warren's view, the new biology focusing on human disease was flourishing in schools of medicine and departments of medicine, not in schools of public health. The new focus on molecular and cellular biology and genetics was also not being directed towards tropical infectious disease. Warren set out to change the status quo by engaging researchers in medical schools and research departments of medicine. It did not take a great deal of funding to support the 14 groups he hand selected at a level of \$150,000 per year, groups that were by and large not working on the diseases he was most interested in, for example malaria, leishmaniasis and schistosomiasis. He

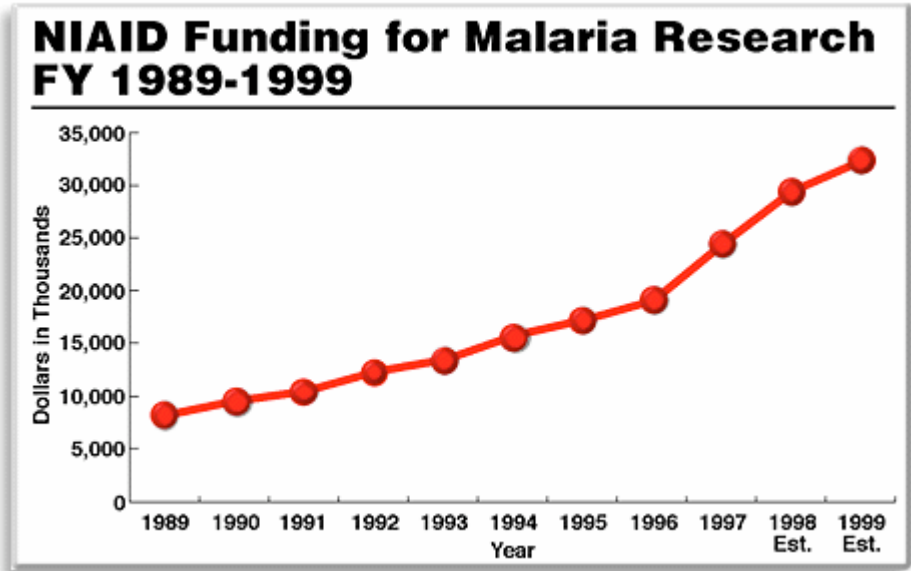
promoted a “bench to bush and back” approach, and collaboration among the 14 units was encouraged. The biological challenge these diseases represented and the availability of a sum of money to be spent however the unit director chose, together with Warren’s enthusiasm for the potential of science, if applied correctly by committed experts to solve problems, was sufficient enticement for many scientists to join the network and change the focus of their work. Malaria research now attracted both established and new scientific talent, and as only great talent can readily accomplish, new funding from many of the already existing sources was competitively and quickly secured, dwarfing the contribution in dollars from the Foundation but not diminishing its ongoing importance. And with that new funding, a stream of new doctoral and post-doctoral candidates were attracted to work on tough problems such as malaria with great scientists such those in the GND units. Catalyzed by the GND funds, the publication record for the decade or so of the Rockefeller program is truly outstanding. Not often credited to Warren was his further accomplishment in convincing the MacArthur Foundation to invest in a program of basic research support in molecular parasitology, a field that had not existed before, which kept the momentum going when the GND itself came to a halt. However, as Tim Evans, former director of Health Equity at the Rockefeller Foundation, later noted, “The primary output of these activities was improved basic knowledge about poorly understood tropical diseases, mainly in the form of research papers. There was no explicit strategy to translate new knowledge into drug or vaccine development.”<sup>8</sup>

### **Malaria Research in the Era of HIV/AIDS**

This third era also began with the advent of a deadly new disease, AIDS, which was rapidly spreading throughout much of Sub-Saharan Africa, and elsewhere in the world. AIDS soon

consumed the attention of public health and research workers everywhere, in part because of the activism of one of its target groups, homosexual men in the United States and in other rich countries. But in developing countries, HIV was heterosexually transmitted, and because it primarily attacked young adults, the economically productive age group, the impact of illness and death was felt much beyond the suffering of the individual, as family structure and economic sustainability deteriorated. The very nature of the disease, transmitted silently and developing clinically slowly at first, and the failure to find ways to effectively and cost-effectively address its consequences for a decade and a half overshadowed the resurgence of malaria where once it had been controlled, and the continuing toll of morbidity and mortality, primarily on young children, who had little to no political clout. Thus, while huge resources were invested in all aspects of research on HIV, from epidemiology to drug discovery and vaccine development, funds for malaria research grew slowly, failing to keep up with inflation in many funding agencies, and actually diminishing in some.

Figure 1 shows the malaria research budget at the National Institutes of Health, the world's largest funder of basic and clinical research, from 1989 to 1999, a period of huge expansion in HIV research. In contrast, there was a slow steady increase in funding for malaria through 1996, however from 1997 on there was a sharp increase, representing substantial new dollars in this research area. Importantly, this happened several years in advance of the increase in NIH funding to achieve a doubling of the budget over a period of 5 years, from 1999 to 2003. What is the explanation for this sudden change?



### **Creation of the Multilateral Initiative on Malaria (MIM)**

In 1996, NIH Director Harold Varmus decided it was time to turn his attention to the limited support at NIH for global health research. He spoke about the reasons for his decision in an address to the graduating 1997 class at the medical school at Columbia University. “Ours is a world in which knowledge and science have become more important than arms and political realignments. A world in which foreign policy and defense should be closely tied to education and health. A world in which recent accomplishments in biology and medicine should be powerful instruments to secure peaceful societies”.

NIH has, in fact, for many decades used approximately 1% of its budget for what was classified as international research. In reality, however, half of that support was used to support foreign research fellows doing research within the intramural program at the NIH itself and a good portion of the rest was provided to researchers in Canada, the UK, and elsewhere in the developed world to study the same diseases of domestic priority in the U.S. Varmus requested the Fogarty

International Center (FIC) at the NIH to conduct an analysis of spending vs. global health research needs, now focused on “neglected diseases”. The analysis concluded that malaria was an excellent target because of the burden of disease and death, that new research insights could yield new strategies for treatment and prevention, and new opportunities to build a global coalition among researchers and funding agencies. Accordingly, in January 1997 FIC organized a meeting of 120 malaria experts from 35 countries, including 50 from Sub-Saharan African countries, in Dakar, Senegal. In addition, representatives of the world’s major national funding agencies participated. Eight working groups were formed on a range of topics to identify both the research challenges and opportunities for collaboration. Each group reported back with a current situation analysis and recommendations for investment in research and capacity building. The final comments of the meeting report added two specific objectives: first, “to develop the mechanisms needed to ensure that systems are available for the timely communication of information to scientists working in Africa”, and second, “to establish mechanisms which will enhance the capacity to conduct collaborative/multicenter research in Africa”. The group also called for the establishment of parasite repositories, resources for host genetic studies of malaria, and malaria vector collections, available to all involved in relevant research. It was a remarkable conference of consensus in many ways, and at the end it was decided to go forward to create a globally cooperative Multilateral Initiative on Malaria, the MIM.

In the subsequent months, however, at several follow-up meetings, the funding agencies involved experienced difficulties in interacting with counterparts from other countries, often over the personality conflicts for which one was in the lead, and the lack of mechanisms in place to support a multilateral effort. But, after a truly rocky road fraught with the danger of collapse, the MIM

was born in 1998, with its first Secretariat established at the Wellcome Trust in the U.K., one of the seven funding agencies represented at the Dakar meeting. Almost immediately, the National Institute of Allergy and Infectious Diseases at the NIH began to provide new resources to the Special Programme Research and Training in Tropical Disease , TDR, at the World Health Organization, WHO, for a MIM-TDR research and capacity building program. The dynamics of malaria funding had suddenly changed through the commitment of a few leaders of major funding agencies and the stroke of a few pens, not to mention the stroking of a few egos. That commitment at the highest levels of the funding agencies is what is graphically represented in the funding trends of the NIH after 1996.

It was fortunate that the Wellcome Trust had decided to conduct an “Audit of International Activity” in malaria research, which became available a few months in advance of the Dakar meeting. It presented a state of the then current reality as the basis for the Dakar conferees to consider, as they attempted to look forward. This report, authored by Anderson, MacLean and Davies, noted the low global investment in malaria research, in contrast to other diseases, and the dominance in research publications by scientists from the north. Increases in the number of publications from French, Australian and Thai researchers could be tracked, in large part, to the support from the GND. They noted that more than one third of the research output from the UK was co-authored by scientists from the endemic countries, in large part because of the support by UK funders, Wellcome Trust and the Medical Research Council, for collaborative research centers in malaria-endemic countries. Research classified as “clinical” accounted for more than 40% of the total, mostly on pathophysiology and treatment, while the basic science focused on the parasite,

with much less on the human host or vector. There was also little in the way of intervention or health services research in the publication record.

A survey of leaders in the field of malaria called attention to the lack of research on parasite genetics and biology and the potential of high return from future investment, as well as the lack of support for intervention and health services research. The connection between funding and publication type is no great surprise, but the fact that these experts also highlighted the inadequate translation of research into practice is rather unusual. Specifically, they commented on the insufficient orientation of research programs to public needs, failure to standardize field methods, inadequate assessment of results and opportunities for application, the resource limitations in the endemic countries, and interestingly, the need for better and active communication amongst researchers and more training opportunities for endemic country scientists. The Wellcome Trust study called for “a coordinated response from the international malaria community”. As clear and appropriate this message was, perhaps the concordance between the U.K. and the U.S. was the source of the friction following the Dakar meeting, pointing to the need to overcome personal and personality differences at the same time that the importance of key leaders is emphasized. Creating genuine collaboration, where every stake holder feels that they gain something through their participation, and each has something of value to bring to the community, is more difficult than it appears to be at the outset. It is obvious that sustainable programs require sustained effort, but that it is an achievable goal

MIM focused on scientific communication, including establishing connections between malaria researchers and control program personnel in the subsequent MIM Pan African Malaria

conferences organized by the rotating Secretariats in Durban, South Africa in 1999, in Arusha, Tanzania in 2003, and in Yaounde, Cameroon in 2005. The number of participants, especially those from Africa, has dramatically increased by over 10 fold over the decade from the first meeting in Senegal to the most recent in Cameroon. MIM-COM, a MIM driven effort led by a team at the National Library of Medicine at the U.S. NIH, was devoted to increasing communication among scientists at the research centers in Africa and counterparts in northern partner institutions, working to provide data sharing and library access through the building up of internet based capacity, center by center. MR-4, the Malaria Research Reference Reagent Resource Center, supported by the National Institute of Allergy and Infectious Diseases at the NIH, together with partners, and housed by the American Type Culture Collection, was established to meet the need to bank and make available libraries of patient, parasite, and vector derived chemical entities and genome for research purposes. When evaluated in 2002 by a team of 7 experts<sup>9</sup>, chaired by Dr. Enriqueta Bond, President of the Burroughs-Wellcome Fund, MIM was judged to be “a healthy, growing group of four component organizations—an administrative arm (the Secretariat), a funding arm (MIM/TDR), an electronic-communications arm (MIMCom), and a research-materials arm (MR4)”. The review team made four recommendations: 1. Refine and clarify MIM’s vision, goals and objectives for the next five years, and develop a strategic plan to fulfill them; 2. Enhance communication and coordination between MIM’s four component organizations; 3. Strengthen MIM’s organizational structure by creating an Advisory Board, increasing the tenure of MIM’s Secretariat, and planning for transferring the Secretariat responsibilities to African institutions; and 4. Plan strategically to augment and secure MIM’s long-term resources and funding. Through the continued partnership of national and multinational research funding agencies, MIM has moved ahead in each of these areas, with the Secretariat

moving to its first African home in Tanzania in 2006, although securing long-term financial support continues to be a vexing problem.

There is no doubt, however, that creation of the MIM has pushed forward the visibility of malaria as a problem and the need for a global research network to effectively link research to practice and to move both areas forward. Increases in malaria research funding support, documented by Catherine Michaud in another paper, has been built upon the north-south and south-south collaborations established through the MIM, carried out by the MIM partners, and driven by the energy of the research community and their strong commitment to connect research to practice, and thereby reduce the morbidity and mortality due to malaria in the endemic countries. MIM has been a beneficiary of prior efforts on the part of the Rockefeller and MacArthur Foundations, and the historical investment by developed country research funding agencies in field research stations and sites in the endemic regions of the world, particularly Africa. Without this background, the new product development public-private partnerships, could not have developed or taken off and moved ahead so quickly.

### **Malaria Research and Leadership in Africa**

Malaria research in Africa is also a century old; its introduction in the continent coincided with early colonization by European nations among whose aims was to protect colonial administrators and traders residing in urban areas, agriculture estates and mines in rural areas which fed the booming industrial revolution in Europe. Trials and implementation of treatments and mass malaria control measures were initially intended to benefit mainly these early colonial enterprises. During the period preceding World War I (WWI) cultivation of cinchona for quinine was

undertaken in some African countries; while botanical pesticides (e.g. pyrethrum) and inorganic chemicals were explored, along with environmental manipulation, as vector control measures. Interest in developing new antimalarials and tools for vector control waned during the period between WWI and WWII. Then WWII, which was fought also in the tropics, exposed European military forces to vector-borne diseases, and, denied access to quinine, ushered in frantic efforts to discover and experiment with new chemicals. The most notable of these were chloroquine, discovered in Germany in 1934, and DDT, first synthesized (again in Germany) in 1874, which were crucial in the war effort. They entered civilian use after the war, starting in urban areas, mines and agricultural estates. Their early success in combating malaria among large civilian populations led to the global malaria eradication efforts, although as noted, in Africa these were primarily in the form of pilot malaria eradication projects. When the global malaria eradication policy was re-evaluated by WHO at the 22<sup>nd</sup> World Health Assembly in 1969, it was decided that alternative approaches for malaria control needed to be developed in areas where malaria eradication was considered unfeasible. Africa unwittingly abandoned malaria vector control even where it was proving successful. In the aftermath of the decision, malaria prevention and control were, unfortunately, medicalized, and in most situations malaria prevention and control unwisely relied on only a single drug (chloroquine). In retrospect, it should have been appreciated at the outset that this would precipitate the fast development of high levels of chloroquine resistance. Beyond this, it soon became clear that the principle fall-back strategy, sulphadoxine plus pyremethamine, was endangered too because of emerging parasite resistance. Rampant drug resistance coupled with abandoning or neglect of malaria vector control, and weak, poorly functioning health systems, were followed by serious malaria resurgences across sub-Saharan Africa.

The decision to abandon malaria eradication coincided with Africa's ascendance to independence. This was a time when Africans were yet to take on leadership and decision making positions in public health. For most African countries, there were hardly any malaria researchers at the time of political independence in the early 1960s. With time, and as Western nations established malaria research capacity in the sub-continent, a few Africans were recruited to start on the long road of research capacity building. This small group represented the indigenous capacity for malaria research in Africa when the first MIM conference was organized in Senegal in 1997. The detailed directory of African research capacity, compiled by the National Institute for Medical Research of Tanzania in 1997, described 29 research institutions in 20 countries across sub-Saharan Africa<sup>10</sup>. Unfortunately the majority of the institutions were weak and the stronger institutions in Africa, had historical ties to northern institutions.

None the less, the African malaria research capacity built over the last three decades has contributed immensely towards the development of new tools for the management, control and prevention of malaria. This is best presented by reviewing the development of Insecticide Treated Nets (ITN), which now constitute a leading tool in malaria prevention and control in Africa. The introduction of synthetic pyrethroids for use in agriculture during the 1970s soon led to studies of their potential use for public health. They were found to be highly insecticidal on surfaces, including fabrics, and of low toxicity to mammals including humans. Early studies of mosquito nets treated with pyrethroids, leading to the term insecticide treated nets (ITNs), demonstrated the safety of pyrethroids and their effects on various entomological parameters, such as the feeding success, survival, vectorial capacity, and human-biting rates of mosquito vectors of malaria, which

they both repelled and killed. Follow up studies, mainly undertaken in rural Africa, showed that use of ITNs reduced malaria parasite densities, and the frequency and severity of malaria, with a median reduction of 45% in malaria disease rates in areas with varying malaria endemicity. Subsequent randomized multi-country controlled field trials of ITNs showed a reduction of 17-63 per cent in childhood mortality. But mosquito nets treated by dipping retained their insecticidal power for a short time, 3-6 months, after which they required re-treatment to restore the killing effect. Early studies identified low re-treatment rates as a major drawback to the effectiveness of ITNs. At every stage, the increasing number of trained African malaria researchers participated and contributed to the studies, usually together with colleagues from the North. Subsequently re-treatment kits were developed, followed by the successful effort of small to medium entrepreneurs to coat nets with an insecticide and a binder, thus producing long-lasting insecticidal nets (LLINs). A further innovation by Sumitomo Chemical Co of Japan incorporated insecticide in the yarn. The result was a slow release of insecticide over the life of the net, guaranteed for at least 5 years, and therefore needing no retreatment. These achievements involved combined investments by major bilateral and multilateral donors, R&D institutions, philanthropy, malaria endemic countries and affected communities themselves, and lately LLIN manufacturers. It is worthy of note that the development of Artemisinin Combined Therapy, ACT, which now constitute the standard of care in malaria treatment in most malarious countries, followed a more or less similar path,

Previous efforts, particularly the highly commendable work of WHO/TDR, to train African researchers and build research capacity within Africa, have contributed immensely to malaria research in Africa. Trainees in molecular biology, immunology, biochemistry, parasitology, entomology, epidemiology, biostatistics, data management, sociology, behavioral sciences, public

health and the like, are now playing key roles beyond their participation in research, as they are also deeply involved in institutional leadership and management. African scientists now are able to prepare research proposals and protocols, mobilize research and training funds, undertake consultancies, network with the scientific, health and donor communities, and liaise with policy and decision makers.

The nature of the training however did not prepare these individuals to take key roles in the development of new tools, especially malaria vaccines, drugs or diagnostics. To fill this gap the African Malaria Vaccine Testing Network (AMVTN) was founded in 1995, succeeded by the African Malaria Network Trust (AMANET) in 2002, with the Malaria Clinical Trials Alliance (MCTA) added in 2006. Both AMANET and MCTA are African-led institutions aiming at strengthening malaria related R&D capacities in Africa, especially those pertaining to the development of malaria vaccines, drugs and devices. These two institutions are working closely with malaria product development initiatives in Europe and the U.S., and are bringing together African researchers and their institutions to undertake coherent product development, starting from phase 1b onwards to phase III. Both AMANET and MCTA put great emphasis on capacity strengthening of prospective trial centres and sites.

In building a comprehensive capacity for product development, AMANET has trained over 1000 African malaria researchers at one-week workshops relevant to clinical trials of candidate malaria vaccines that will meet scientific, ethical and international Good Clinical Practice standards. These training workshops have already included 2 on design and methodology in malaria vaccine trials, 6 on data management in intervention trials, 6 on good clinical practice, 6 on molecular biology

and immunology in malaria vaccine development, 12 on health research ethics, 2 on the harmonization of ethics committees, 2 on leadership of malaria research institutions, 1 on financial accounting and procurement procedures, and 1 on data safety monitoring. AMANET is particularly well known for its training in health research ethics, including web-based programs, as well as supporting 21 selected ethical review committees across tropical Africa. In addition a score of African malaria researchers are sponsored by AMANET to undertake relevant postgraduate training.

AMANET has also established a system for developing research centers geared towards new malaria interventions. African centers selected for development under AMANET sponsorship initially undergo a needs assessment, followed by filling gaps in short- and long-term personnel training, provision of essential equipment, and infrastructure improvement. Four centers from different malaria eco-epidemiological settings in eastern, central and western Africa are at present being strengthened, and two of these have already been approved for carrying out malaria vaccine trials. AMANET also sponsors mentorship of researchers at northern institutions undertaking Phase 1a and/or 2a trials. AMANET has sponsored four successful Phase 1b trials (MSP3, GMZ2 and AMA1), and a phase 2b trial of a candidate malaria vaccine (MSP3) is underway (Kilima, Chilengi and Wanga 2007). AMANET receives major funding from the Netherlands Ministry of International Cooperation, the Danish Development Agency, the European Developing Countries Clinical Trials Partnership, the European Commission Directorate—General Research, the European Cooperation AID Office (AIDCO), and the Bill and Melinda Gates Foundation [www.amanet-trust.org](http://www.amanet-trust.org). AMANET support from AIDCO is through the good will of the African Caribbean Pacific, ACP, Secretariat,

The MCTA is an African-led institution which aims to strengthen clinical trial capacity, share results of real, on-the-ground trial activities and codify best practices. Since its founding in 2006 MCTA has worked in collaboration with the Malaria Vaccine Initiative (MVI) and the Medicines for Malaria Venture (MMV) to support African malaria research institutions in the development of the malaria vaccine (RTS.S) and some malaria drugs. In its first Annual Report (2007) MCTA reported that during the year they undertook site preparation for clinical trials, guided infrastructure development, visited prospective trial sites, and carried out GCP training in collaboration with AMANET. MCTA is funded by the Gates Foundation and is based within the Indepth demographic surveillance systems network ([www.indepth-network.org](http://www.indepth-network.org)).

In addition to AMANET and MCTA there are a number of new African networks addressing specific malaria research issues, including: Malaria Immunology and Pathogenesis Consortium (MIMPAC); Worldwide Antimalarial Drug Resistance Network (WARN); Central Africa Network on Tuberculosis, HIV/AIDS and Malaria (CANTAM); East African Network for Monitoring Anti-Malarial Treatment (EANMAT); Malaria in Pregnancy Consortium and others. These have arisen because of need and the presence of an enlarging cohort of trained African malaria researchers who have gained the skills to conduct scientific studies and generate the funds needed to carry them out.

Over and above the traditional funders previously mentioned, malaria research in Africa has greatly benefited from increased interest in the disease in the Nordic countries and Europe, which has led to the establishment of new major funding sources including:

- [Bill & Melinda Gates Foundation Global Health Program](#)
- European Commission (EC), European Cooperation AidOffice (AIDCO)
- European Commission (EC) Directorate General Research (DG-Research)
- European Developing Countries Clinical Trials Partnership
- European Malaria Vaccine Initiative
- [Malaria Vaccine Initiative](#)
- [Medicines for Malaria Venture](#)
- PATH

Furthermore, a number of bilateral donor agencies across Europe are now including malaria research support in their development aid packages. It is also gratifying that some African governments are including malaria research support in their budgets. However, above and beyond the international funding agencies, and the researchers themselves, there are a number of players whose engagement seems to be essential. Table 1 lists the different constituencies playing key roles and elaborates their major functions. To a considerable extent, the ultimate success of malaria research to control of the disease burden it imposes is dependent on the increasing role of these diverse groups.

Table 1. Identification and role of different constituencies in promoting malaria research

Constituency	Role
Developing country governments	Commitment; insuring connections between relevant government departments and industry; mobilization of essential financial resources both internally and externally; creation and maintenance of research infrastructure; setting health care priorities and strategies; participating in setting research priorities and research agenda; creating public awareness

	through IEC, creating demand for research, providing needed personnel; establishing and enforcing regulatory environment; supporting public-private partnerships at national and local levels; ensuring standard of care is provided; rapidly make successful research products readily and widely available
Developing country R&D institutions	Mobilizing needed financial resources both nationally and externally; participating in setting and implementing agreed upon research priorities and agenda; identifying and recruiting needed personnel and ensuring their development and retention; networking with north and south institutions; implementing regulations, including ethics review and oversight; disseminating research results to appropriate end users, and promoting their early utilization
Developing country training institutions	Addressing tasks similar to those of the south R&D institutions and, in addition, training undergraduate and graduate students; conducting research; appropriately disseminating research findings to peers and students.
Malaria endemic communities	Participating in identifying research problems and in research, including but not restricted to participation as research subjects; attending information, education and communication (IEC) activities; membership on ethics review committees; actively support the implementation of research findings.
NGO's	Advocacy to government and the private sector; involvement in the local community

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### **Conclusions.**

Malaria research continues to be included in the research portfolios of developed country funders, spurred by the broadly relevant scientific insights malaria contributes to the understanding of host-pathogen interactions and immunity, in addition to the desire to tackle a clinical problem responsible for considerable morbidity and mortality, especially in young children. Some of this has been driven by the increase in general public interest in developing countries and in Africa, and an awareness of the disparities in global health which has encouraged the research community to address the scientific challenges of neglected diseases, and by the commitment of a group of very special people who have been in positions of leadership in the universities and research and funding organizations in industrialized countries, no longer directly affected by malaria.

Malaria research in Africa has made considerable progress over the last three decades, particularly during the last ten years, due to external and now increasing internal investments in people and institutions. The maturation of senior African scientific leadership, and the recognition of their contributions to knowledge generation, has placed them in the center of research planning and progress. These achievements have involved combined investments by major bilateral and multilateral donors, philanthropy, malaria endemic countries, affected communities, R&D institutions, and industry. With the growth in the number of African scientists working on malaria and increased administrative capacity to support them, they are likely to increasingly compete successfully for available new sources of funding and generate new knowledge that ultimately will lead to major reductions in the burden of illness due to malaria.

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<sup>9</sup> Review of the Multilateral Initiative on Malaria, MIM  
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