Malaria Research & Development
An Assessment of Global Investment

Malaria R&D Alliance

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November 2005

This report was prepared by The Malaria R&D Alliance with significant funding from The PATH Malaria Vaccine Initiative (MVI) and contributions from Medicines for Malaria Venture (MMV) and the Gates Malaria Partnership of the London School of Hygiene and Tropical Medicine (LSHTM).

The **Malaria R&D Alliance** is an alliance of malaria research and development (R&D) organizations jointly advocating for global commitment for increased and sustained resources for malaria R&D. Goals of the Alliance are to raise awareness about malaria and the critical need for R&D to combat the disease. The Multilateral Initiative on Malaria (MIM) is the current convenor of the Alliance. Member of the Malaria R&D Alliance working group, charged with developing Alliance activities, include: Sarah Ewart of MVI, Mary Galinski of Malaria Foundation International (MFI) and Emory University; Jamie Guth of Special Programme for Research and Training in Tropical Diseases (TDR); Andreas Heddini of the MIM; Carol Hooks of MVI; Jane Kengeya-Kayondo of TDR; Wilfred Mbacham of MIM; Heather Naylor of the LSHTM and Anna Wang of MMV.

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FOREWORD

In sub-Saharan Africa, one in five children will die before they reach age five. All too often, they die of a preventable and curable disease - malaria.

Thankfully, today there is an increasing recognition of this crisis and an increasing conviction in the international community that we can defeat malaria. We now possess powerful interventions: insecticide treated bednets, indoor insecticide applications, and combination antimalarial drugs. They must be deployed quickly, widely, and wisely. If this effort is to succeed, it must avoid a critical but easy mistake: thinking that we have all we need to defeat malaria globally. Ultimately, we will need new and better tools. Painful lessons from malaria history have taught us that what works today may not be effective in the future and that success in malaria control requires careful attention to emerging challenges that must be tackled with innovative solutions.

In the recent past, we have seen estimates of total annual funding for malaria research and development (R&D) that vary by hundreds of millions of dollars due to the absence of systematic data. This uncertainty has made it difficult to effectively advocate for appropriate levels of sustained investment for malaria R&D.

We, in the malaria community, believe that there is gross under-investment. However, until now, we didn't have the data to confirm our conviction and better understand the funding situation. The Malaria R&D Alliance has undertaken a study to establish a baseline of current global investment for malaria R&D. The Alliance surveyed organizations around the world to compile the figures presented in this report. Their efforts and the high recognition of the need for good data resulted in excellent participation from some 80 funders and R&D entities. This report presents a credible estimate of 2004 global funding of malaria R&D. It is the most comprehensive study of its kind and provides critical information for funders and researchers alike. It answers our questions: who funds malaria R&D, what do they fund, and where does the funding go?

Although malaria R&D funding has risen over the past decade, research continues to be woefully under-funded compared to the disease burden caused by malaria. The report clearly shows that more must be done. Despite limited resources, we are seeing groundbreaking advances. Thousands of researchers in labs, clinics, and research centers around the world need increased funding in order to develop life-saving interventions. It is time to redouble our efforts and accelerate the development, availability, and accessibility of these tools.

We are finally coming together as a world community committed to turning the tide against malaria. It would be an unspeakable tragedy to make great progress, only to see that progress erased because of our failure to anticipate new challenges and invest in finding ways to respond to them.

If we are to succeed in defeating malaria, we must fully deploy the tools we have today and invest in superior ones for tomorrow.

Dr. N. Regina Rabinovich
Director, Infectious Diseases
Bill & Melinda Gates Foundation
Seattle, Washington, USA

Prof. Fred Binka
Director
INDEPTH Network
Accra, Ghana

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ABBREVIATIONS

ACTs	Artemisinin-based combination therapies
AMANET	African Malaria Network Trust
BMGF	Bill & Melinda Gates Foundation
DALY	Disability-adjusted life-year
DFID	UK Department for International Development
DoD	US Department of Defense
EC	European Commission
FDA	Food and Drug Administration
GDP	Gross domestic product
GFHR	Global Forum for Health Research
GSK	GlaxoSmithKline
HIV	Human Immunodeficiency Virus
IDRC	International Development Research Center
KEMRI	Kenya Medical Research Institute
LSHTM	London School of Hygiene & Tropical Medicine
MIDRP	Military Infectious Disease Research Program
MIM	Multilateral Initiative on Malaria
MMV	Medicines for Malaria Venture
MRC	Medical Research Council
MVI	PATH Malaria Vaccine Initiative
NCE	New chemical entity
NCRR	National Center for Research Resources
NGO	Nongovernmental organization
NHLBI	National Heart, Lung, and Blood Institute
NIAID	National Institute of Allergy and Infectious Diseases
NICHD	National Institute of Child Health & Human Development
NIH	National Institutes of Health
NIMR	National Institute for Medical Research (UK)
OECD	Organization for Economic Co-operation and Development
PPP	Public-private partnership
R&D	Research and development
SDC	Swiss Agency for Development & Cooperation
SAMRC	South African Medical Research Council
TDR	Special Programme for Research & Training in Tropical Diseases
USAID	US Agency for International Development
WHO	World Health Organization
WRAIR	Walter Reed Army Institute of Research

EXECUTIVE SUMMARY

Malaria causes more than one million deaths each year and exerts an enormous health and economic toll on developing nations. The estimated cost to Africa alone is more than $12 billion per year in lost (GDP)[1]. As malaria-related deaths rose in the 1990s, so did calls for more funding to fight the disease. Despite the historic and continuously high disease burden malaria imposes, little has been known about the amount of funding dedicated globally to research and development (R&D) of new tools to prevent and treat malaria. In 2005, the Malaria R&D Alliance, a global coalition of research and development organizations working to find new and improved solutions to combat malaria, conducted a survey of malaria R&D investment, the results of which are presented in this study.

Detailed financial information relating to disbursement of funds for malaria R&D was collected from approximately 80 organizations through an online survey. The presumed largest global funders of malaria R&D, a total of 14, completed the survey; the aggregate response rate from the 50 contributors believed to invest at least one million dollars annually in malaria R&D was 92%.

Survey respondents reported that $323 million was invested in malaria R&D in 2004.

Who invested in R&D?

Investment was heavily concentrated, with 12 survey entities contributing 88% of total funding. The two largest contributors, the US National Institute of Allergy and Infectious Diseases (NIAID) and the Bill & Melinda Gates Foundation, provided 49% of the total.

The public sector, comprised predominantly of government and multilateral funding agencies, provided $181 million of the 2004 investment or 56% of the total. The largest public sector contributor, the US government, invested $129 million in 2004 through four departments and agencies (more than 70% of total public sector support and almost 40% of the total investment).

European governments and the European Commission (EC) provided $36.1 million (20% of total public sector support and 11% of the total investment), led by Switzerland, the United Kingdom, and the Netherlands at $12.2, $9.8, and $7.0 million, respectively.

The not-for-profit sector invested $103 million (32%) in 2004. Private philanthropic organizations accounted for $95 million (92%) of not-for-profit contributions.

2004 Investment: $323 million

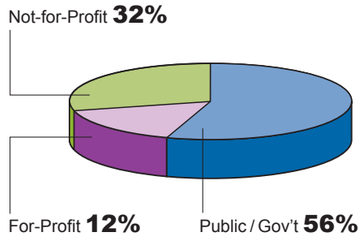

Figure A: 2004 Investment by Sector

The for-profit (industry) sector invested $39 million (12%) of total 2004 funding. The vast majority of this funding came in the form of intramural (internal) research and development by pharmaceutical and biotechnology companies.

1 Roll Back Malaria Infosheet, *Malaria in Africa*, **http://rbm.who.int/cmc_upload/0/000/015/370/RBMInfosheet_3.htm**, accessed on October 3, 2005

Who Received R&D Funds?

More than one-quarter of the total investment (27% or $88 million) was intramural funding to support research conducted by the funding entities themselves. The remaining $235 million (73% of total investment) was in the form of extramural funding, or grants made from one organization to a separate research entity.

Two-thirds of the extramural funding ($156 million) was granted directly to researchers and developers, while the balance ($79 million) was channeled through funding managers, such as nongovernmental organizations (NGOs), public-private partnerships (PPPs), and programs such as the Special Programme for Research and Training in Tropical Diseases (TDR). Funding managers support the research of numerous R&D entities; many apply a portfolio approach to product development to increase the chances of success and accelerate the overall product development process.

How Were R&D Funds Used?

Survey data indicate few organizations equally support both R&D and prevention and control; most focus on one area or the other. Sixty percent of respondents (45 organizations) stated that all or almost all of their malaria funding is directed toward R&D.

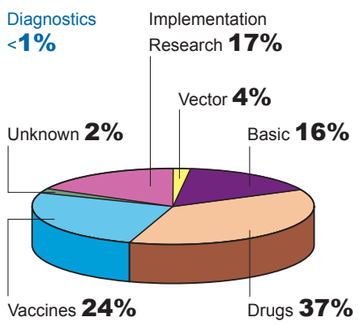

Figure B: Allocation by R&D Category

Respondents allocated malaria R&D investments to six categories. *Antimalarial drug discovery and development* received $120 million (37%) of the 2004 total investment. *Vaccine development and vaccine trials* was the next highest funded R&D category, at $79 million (24%), followed by *implementation research* at $55 million (17%) and *basic research* at $51 million (16%). *Vector control research* received $12 million (4%), and *development of malaria diagnostics* received the least investment, at $700,000 (<1%).

$156 million was granted directly to researchers and developers while $79 million was channeled through funding managers such as public-private patnerships.

Extramural funding was distributed fairly evenly across the three larger R&D areas, with antimalarial drug discovery and development receiving 27% of the total 2004 extramural funding, vaccine development and vaccine trials receiving 25%, and implementation research receiving 23%. Basic research, vector control research and development of malaria diagnostics figures remain largely consistent with total investment percentages at 18%, 4% and less than 1%, respectively.

Trends in Funding

In order to determine if malaria R&D funding has grown over time, the findings from this survey were compared to those reported in a 1996 study published by the Wellcome Trust. After accounting for inflation, indications are that there has been real growth of more than $166 million in spending on malaria R&D investment between 1993 and 2004. More than 80% of the real growth in investment is attributed to the increased contributions of two organizations: the Bill & Melinda Gates Foundation and NIAID.

Despite this growth, investment in malaria R&D is low relative to its disease burden. Malaria R&D investment represents approximately 0.3% of total health-related R&D investment. Yet malaria's impact on humanity is roughly 10 times that amount, accounting for 3.1% of global disease burden. Were malaria research funded at the average rate for all medical conditions, it would receive more than $3.3 billion in annual R&D funding.

Full use of the tools that exist today would greatly decrease the malaria burden, but new generations of tools and new methods in implementing these tools are needed to control malaria effectively.

Were malaria research funded at the average rate for all medical conditions, it would receive more than $3 billion in annual R&D funding.

Survey respondents overwhelmingly (88%) reported that they believed malaria R&D is under-funded. Determining an appropriate level of malaria R&D investment is an important challenge that lies ahead.

I INTRODUCTION

The Importance of Research and Development to Combat Malaria

Malaria causes more than one million deaths each year and exerts an enormous health and economic toll on developing nations. Despite the historic and continuously high disease burden that malaria imposes, little has been known about the amount of funding dedicated globally to the research and development of new tools and strategies for malaria prevention, control and treatment. In 2005, the Malaria R&D Alliance, a global coalition of research and development organizations working to find new and improved solutions to combat malaria, conducted a survey of malaria R&D investment, the results of which are presented in this report.

The seriousness of the malaria problem is reflected in the UN Millennium Development Goals. Halting and reversing the spread of malaria is an explicit target.[2] In its *Global Strategic Plan 2005-2015*, the Roll Back Malaria Partnership highlights research and development as a top priority; more than 20 key R&D milestones are listed in the strategic plan, including the development of new drugs, novel insecticides, and effective vaccines.[3]

A Public Health Crisis

Estimating malaria deaths and episodes has always been challenging because of inadequate health reporting systems, the co-incidence of malaria and other diseases, and the similarities of symptoms with those of other diseases. As of late 2004, the World Health Organization (WHO) reported that 3.2 billion people living in 107 countries were at risk of contracting malaria. WHO estimates 300 million to 500 million new infections occur per year, resulting in more than 1.2 million deaths annually.[4] Recent publications suggest that the number of infections with *P. falciparum*, the most deadly malaria parasite, may even be higher, accounting for up to 660 million infections worldwide.[5]

Malaria accounts for approximately 11% of the disease burden in sub-Saharan Africa, where almost 90% of global malaria deaths occur.[6] The overwhelming majority of malaria fatalities occur in children. Malaria is the number one cause of death in children under age five in Africa, accounting for 20% of mortality for this age group. Globally, more than 10 million children die each year, and malaria is a key factor, accounting for approximately 9% of these deaths.[7]

The disease attacks children in several ways:[8]

- Acute infections before children's immune systems have fully developed can lead to seizures, coma, and too often death;
- Repeated infections throughout the early years can lead to severe anemia and death;
- Infections during pregnancy can result in low birth weight or premature delivery, which are significant contributors to infant mortality.

In addition, non-fatal malaria weakens children and makes them more vulnerable to other common childhood illnesses, contributing to increased mortality.

2 United Nations website, **http://www.un.org/millenniumgoals/**, accessed on August 18, 2005
3 Roll Back Malaria Partnership, *Global Strategic Plan 2005-2015*, pp. 6, 34-36
4 WHO, *World Malaria Report 2005*, p. 11
5 Snow et al (2005) "The global distribution of clinical episodes of *Plasmodium falciparum* malaria". *Nature* 434; 214-217
6 *World Health Report 2004;* 2002 disease burden statistics based on DALY analysis
7 Black, R., Morris, S. and Bryce, J., 2003, "Child Survival I: Where and why are 10 million children dying every year?" *The Lancet*, Vol. 361, pp. 2226-2230.
8 World Health Organization/UNICEF, *The Africa Malaria Report 2003*, pp. 18-19

In a 2004 study, the Global Forum for Health Research calculated the trend in cause of death for children under five in the low- and middle-income countries. Their findings demonstrated that the child death rate from malaria approximately doubled between 1990 and 2002.[9]

Without the widespread implementation of effective control measures, it is estimated that the number of malaria cases will double over the next 20 years.[10]

In low- and middle-income countries, the under-five child death rate from malaria approximately doubled between 1990 and 2002.

The Economic Impact of Malaria

Malaria is inexorably linked to poverty. Gallup and Sachs write, "The geographical specificity of malaria, the wide biological variation in the capacity of mosquito vectors, the inability to control malaria in Africa under experimental conditions, and the persistence of fatal blood diseases as a defense all point to a causation from malaria to poverty, not vice versa."[11] The implications are profound on both the micro- and macroeconomic levels.

Malaria imposes a steep economic burden on the poor, not only as direct healthcare expenses but also as lost wages from illness and caring for the sick. The World Health Organization estimates that a poor family in Africa can spend 25% of its income on malaria prevention and treatment.[12]

In endemic countries, malaria caused a reduction in annual economic growth of 1.3% between 1965 and 1990. The long-term effect of retarded growth translates to a 50% reduction in GNP over the period.[13] Malaria accounts for 25%-35% of outpatient visits and 25%-40% of hospital admissions in endemic African countries, imposing a steep economic and human resource burden on already stretched public health systems.[14]

A Neglected Disease

Malaria is a classic neglected disease, characterized by a high disease burden in the developing world, a low disease burden in high-income nations, and a low level of funding in relation to the disease burden. As with other neglected diseases, the perceived lack of a lucrative consumer market for antimalarial products is used to explain the relatively low rate of R&D investment by the private sector and why government support has historically formed the cornerstone of malaria R&D funding.

Until recently, decades had passed without the development of major medical breakthroughs against malaria. In the 25 years between 1975 and 1999, only four of the 1,394 new drugs developed around the world were antimalarials, and all of these were supported with some degree of public funding.[15]

9 Global Forum for Health Research, *Monitoring Financial Flows for Health Research*: 2004, p. 59; analysis based on WHO source data
10 Breman, J., 2001, "The Ears of the Hippopotamus: Manifestations, Determinants, and Estimates of the Malaria Burden," *American Journal of Tropical Medicine and Hygiene* 64(1,2) S, pp. 6-7
11 Gallup, J. and Sachs, J., 2001, "The Economic Burden of Malaria," *American Journal of Tropical Medicine and Hygiene*, 64 (1, 2) S., p. 90
12 Kindhauser, M. (ed.), 2003, *Communicable Diseases 2002: Global defense against the infectious disease threat*, WHO: Geneva, p. 176
13 Sachs, J. and Malaney, P., 2002, "The Economic and Social Burden of Malaria," *Nature* Vol. 415, pp. 680-685.
14 WHO, *World Malaria Report 2005*, p. xvii
15 Trouiller, P. et al, 2002, "Drug development for neglected diseases; a deficient market and a public-health policy failure," *The Lancet*, Vol. 359, pp. 2188-2194.

The under-funding of research in neglected diseases has come to be known as the "10/90 gap" – referring to estimates that less than 10% of global health R&D expenditures are devoted to the diseases and conditions associated with 90% of the world's health problems.[16]

Objectives and Key Methodological Elements of the Study

The Malaria R&D Alliance's motivation for conducting this study was to establish an understanding of current global investment in research and development to combat malaria. Findings from the last major study with a similar goal were published in the Wellcome Trust's report, *Malaria Research: An Audit of International Activity*. The authors estimated 1993 global expenditures on malaria research to be approximately $84 million.[17]

In the last few years, there have been widely divergent estimates of annual malaria R&D funding, varying by hundreds of millions of dollars.[18] In order to determine an appropriate level of malaria R&D resources, credible, comprehensive and updated data are essential.

Accordingly, the Malaria R&D Alliance undertook a survey to determine the global level of funding for malaria R&D, with a focus on 2004, the most recent year for which complete data were available. Numerous analyses have been performed on the data submitted for 2004 and previous years, in order to develop a more complete picture of the global investment of R&D to combat malaria.

Global investment refers to original source funds disbursed by the donor and funding community, including funding of intramural research (e.g. by the National Institutes of Health [NIH] and the private sector). In order to avoid double-counting, funds received by a wide variety of funding managers were not counted in the annual global investment figure. They were tracked for cross-referencing and data integrity purposes, and to assist in determining investment categorization.

This study has several key elements and methodological points to highlight, including:

- **Broad involvement by those in the malaria R&D community**

The survey instrument was designed based on the input of many experts in the fields of malaria R&D and resource tracking, and information gathered through an extensive literature review. Members of a project advisory committee were involved in the testing of the survey instrument and in the review of this report. Early involvement of and regular contact with survey participants helped contribute to a 92% response rate from the presumed 50 largest contributors to malaria R&D.

16 See Global Forum for Health Research, *10/90 Report on Health Research 2003-2004*, for more discussion
17 Anderson, J., MacLean, M., and Davies, C., 1996, *Malaria Research: An Audit of International Activity*, Wellcome Trust: London
18 For example, see: WHO Commission on Macroeconomics and Health, December 2001, *Macroeconomics and Health: Investing in Health for Economic Development*, p. 79, ("Malaria research outlays are perhaps $100 million"). For a high estimate, see: WHO, 2003, *Communicable Diseases 2002*: Global defense against the infectious disease threat, p. 174 ("Worldwide spending on malaria research, estimated at US$ 84 million in 1998, has soared to over US$ 1 billion…")

- **A focus exclusively on malaria research and development investment**

Annual funding in the form of disbursements[19] was measured, as it was deemed that disbursements give the most accurate picture of actual funds made available to conduct malaria R&D in any given year. While commitments are also valuable to track, they provide different information, as they often span many years, may not be disbursed as originally planned.

- **Capturing funding data from beyond the donor community**

Three categories of organizations were surveyed: 1) donors and funders; 2) funding managers; and 3) researchers and developers. Surveying different types of organizations makes it possible to capture investment data thoroughly and accurately, while cross-referencing survey submissions helps to avoid double-counting.

- **Electronically capturing current data**

An online survey instrument was developed for data collection. Financial data from 2002 through 2006 were requested. As expected, financial submissions from 2004 represent the most current complete year available, hence 2004 is the focus of data analyses.

- **Treatment of data from pharmaceutical and biotechnology companies**

To encourage pharmaceutical and biotechnology companies to participate in the study and submit data, a policy was adopted to aggregate their responses for reporting purposes and not to share any individual company's financial data. Accordingly, survey contributions from pharmaceutical and biotechnology companies will be considered as one source of malaria R&D investment.

- **Capturing data at a detailed level**

In addition to determining total investment in malaria R&D in 2004, additional data were collected and catalogued. Total investment can be examined in numerous ways, including by the type of organization supplying the funding (e.g. government versus private philanthropy), and by the areas in which the money is invested. Funding is allocated to six R&D categories:

- *Basic research*
- *Antimalarial drug discovery and development*
- *Vaccine development and vaccine trials*
- *Vector control research*
- *Development of malaria diagnostics*,
- *Implementation research*

For a more detailed discussion of the six R&D categories and 16 sub-categories, please see the *Definitions of Malaria R&D* in the next section and Appendix E.

See Appendix A for a more detailed explanation of methodology, including limitations of the study.

19 Because of information or accounting system limitations, a few organizations could not provide actual disbursement data. These organizations generally provided budget data instead of disbursements. In most such cases, verification was received that budget data were a good proxy for actual disbursements.

Survey Administration and Response

The online survey instrument was emailed to a distribution list of more than 150 organizations in May 2005. The list encompassed donors, a variety of funding managers and private companies, and a sample of large and small research entities.

Survey responses were accepted for nine weeks, until July 2005. Securing responses required significant follow-up, with most efforts focused on a group considered to be the largest contributors to malaria R&D. This group included all the presumed major donors, as well as funding managers and R&D entities believed to be involved in more than $1 million of malaria R&D funding per year. Of the 50 organizations identified in this category, 46 responded to the survey, yielding a response rate of 92%.

Responses were received from nearly 80 organizations based in 20 countries on six continents, as well as from numerous multilateral entities.

Fourteen of these organizations were deemed as particularly important to a successful survey outcome, due to their multi-million-dollar annual investment in malaria R&D. This group included major government donors, large philanthropic organizations, private companies, and major research institutions. A 100% response rate was secured from this group.

In addition to the 46 large contributors, 33 other organizations responded to the survey. The majority of these organizations were recipients of funding, and their responses enabled the survey team to cross-reference data and develop a better understanding of the overall flow of funds. Responses were received from organizations based in 20 countries on six continents as well as from numerous multilateral entities.

For a complete list of survey respondents, please see Appendix B.

Roles and Involvement in Malaria R&D Funding and Investment

Many types of groups are involved in malaria R&D, with some playing multiple roles in the funding process. Traditionally, funding has flowed from donors to researchers and developers, but increasingly funding managers play catalytic roles in securing and managing funds. A significant amount of research is also being self-funded by the healthcare industry and government research institutions. This table illustrates the different roles survey entities play. The sum of annual funding in tan boxes (Government Agency, Multilateral Budgetary Funds, Private Philanthropic and R&D Entity-Self Funded) equals annual global investment.

Table 1: Roles and Involvement in Malaria R&D Funding and Investment

Role in Funding	Type of Organization	Role in Malaria R&D	Examples
Donors & Funders (Funding Sources)	Government Agency	Government agencies providing original source funding to other organizations to support malaria R&D.	DfID, SDC, USAID
	Multilateral: Budgetary Funds	International financial institutions, UN agencies, or multi-country entities funded by contributions from member governments, which utilize these budgeted funds to support malaria R&D.	EC, World Bank
	Private Philanthropic	Private entities, including trusts, foundations, corporations and individuals, providing original source funding to others to support and carry out malaria R&D.	Gates Foundation, Rockefeller Foundation, Wellcome Trust
Funding Managers (Facilitators)	Public-Private Partnership or NGO	Groups playing a key role in the targeted distribution, management, and monitoring of funds from donors to R&D entities.	AMANET, MIM, MMV, MVI
	Multilateral: Extrabudgetary Funds	UN agencies or affiliates and sponsored entities, that receive extrabudgetary funding from donors, and which utilize these funds to support malaria R&D.	TDR
Researchers & Developers (End Users)	R&D Entity: Self Funded	Government research institutions, private companies and publicly traded corporations that conduct malaria R&D with their own funding (not received from others)	GSK, NIH Intramural, Pfizer
	R&D Entity: Externally Funded	Research institutions and universities that conduct malaria R&D with funding provided by donors or funding managers.	LSHTM, Swiss Tropical Institute

II SURVEY FINDINGS: MALARIA R&D INVESTMENT

Who Invested?

Donor Investment in Malaria R&D in 2004

Reported global investment for research and development to combat malaria totaled $323 million in 2004. This investment is the sum of original source funding disbursed to support malaria R&D. The majority of this funding was contributed by donors to other organizations in the form of extramural grants, and the balance was intramural (internal) funding.

Investment was heavily concentrated. Two organizations, the US National Institute of Allergy and Infectious Diseases (NIAID) and the Bill & Melinda Gates Foundation, provided 49% of total malaria R&D investment in 2004 ($80.2 million and $77.6 million respectively). Pharmaceutical and biotechnology company respondents in aggregate contributed more than $38 million in R&D funding, and the US Department of Defense invested $25.6 million.

The top 12 survey entities contributed more than $283 million in malaria R&D funding, representing 88% of 2004 total investment.

The Wellcome Trust continued its long history of malaria R&D support, providing $13.5 million in 2004. Several other European organizations were large donors, including the Swiss Agency for Development & Cooperation ($10 million), the Netherlands Ministry for Development Cooperation ($7 million); the UK Medical Research Council (MRC) ($6.4 million); and the European Commission ($6.0 million).

Other large donors include the US Agency for International Development ($9.7 million), the US Centers for Disease Control and Prevention ($5.9 million), and the UK Department for International Development ($3.4 million).

The top 12 survey entities contributed more than $283 million in malaria R&D funding, which represents 88% of 2004 total investment.

These respondents reported investments ranging between $3.4 and $80.2 million, as shown in Figure C.

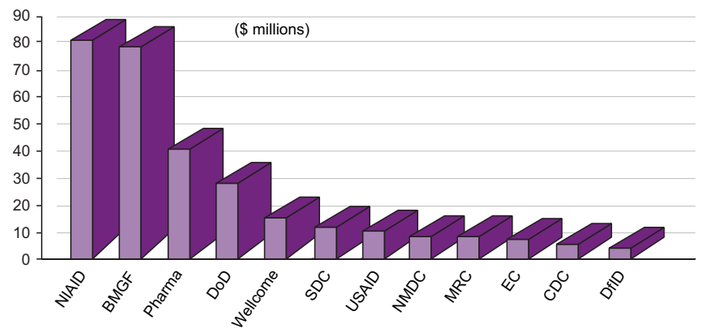

Figure C: 2004 Funders with Investment > $3 million

Table 2 displays total funding from those entities that reported more than $3 million of original source investment for malaria R&D in 2004.

Table 2: 2004 Malaria R&D Investment by Largest Funders (>$3 million)

Survey Entity	Total Funding $
US National Institute of Allergy and Infectious Diseases	80,238,125
Bill & Melinda Gates Foundation	77,550,637
Pharmaceutical and Biotechnology Company Respondents [a]	38,108,877
US Department of Defense [b]	25,633,821
Wellcome Trust	13,514,165
Swiss Agency for Development & Cooperation	9,971,854
US Agency for International Development	9,657,000
Netherlands Ministry for Development Cooperation	6,951,131
Medical Research Council [c]	6,407,909
European Commission [d]	6,030,228
US Centers for Disease Control and Prevention	5,861,000
UK Department for International Development	3,363,237
Subtotal	283,287,984
Other Sources	40,152,273
Total	**323,440,257**

Notes:
a Financial information aggregated for all pharmaceutical and biotechnology company respondents
b Survey submitted by Military Infectious Disease Research Program (MIDRP), which encompasses the Walter Reed Army Institute of Research (WRAIR), the Naval Medical Research Center (NMRC), and the Army and Navy overseas labs in Indonesia, Thailand, Kenya and Peru and the US Army Medical Materiel and Development Agency (USAMMDA). This figure does not include salaries of uniformed active duty personnel who work exclusively in malaria.
c Includes UK National Institute of Medical Research funding
d The European Commission figure encompasses EC disbursements reported by the Europe AID Cooperation Office, as well as 2004 receipts credited to the EC by other survey respondents. The survey received from the European Commission's General Directorate Research office noted 2004 commitments of €37.25 million. Most of this funding has not been included in the 2004 investment figure, as all survey calculations are based on disbursements.

Type of Funding: Definitions

Intramural funding	Funding that originates within an organization for activities carried out within the bounds of the organization. Sometimes referred to as self-funding or internal funding.
Extramural funding	Funds provided to another organization for activities carried out outside the bounds of the funding organization. Sometimes referred to as external funding.

Spotlight on Specific Donor Organizations

Additional information follows on several of the surveyed large donors.

- **NIH and NIAID**

With funding appropriated by the US Congress, NIH, comprised of 27 institutes and centers, invests more than $27 billion annually in medical research. Five NIH entities that fund malaria R&D responded to the survey:

- The National Institute of Allergy and Infectious Diseases (NIAID)
- The Fogarty International Center
- The National Center for Research Resources (NCRR)
- The National Institute of Child Health & Human Development (NICHD), and
- The National Heart, Lung, and Blood Institute (NHLBI)

Malaria R&D investment by these five agencies of NIH totaled $87.7 million in 2004, with NIAID accounting for 92% of the funding.[20] NIAID's mission is to conduct and support "basic and applied research to better understand, treat, and ultimately prevent infectious, immunologic, and allergic diseases."[21] In 2004, NIAID funded more than $20 million of malaria research in its labs, more than half of which ($10.5 million) was devoted to vaccine research.

NIAID funded the largest number of grantees in 2004; and was the only organization to provide funding to all six R&D categories.

NIAID also provided almost $60 million to other R&D entities. Of all survey respondents, NIAID funded the largest number of grantees (the NIAID survey submission listed more than 150 principal investigators) in 2004, and was the only organization to provide funding to all six R&D categories. *Vaccine development and vaccine trials* received the largest share of total NIAID investment, followed by *antimalarial drug discovery and development* and *basic research* (at 36%, 26% and 23% of total NIAID funding, respectively). NIAID was the largest investor in the categories of *basic research*, *vaccine development*, and *vector control research*.

Funding from Fogarty, NCRR, NICHD and NHLBI totaled $7.5 million in 2004. This funding was largely extramural (91%) and chiefly supported basic research.

- **The Bill & Melinda Gates Foundation**

The Bill & Melinda Gates Foundation is the world's largest private philanthropic organization, with an endowment of approximately $28.8 billion. The mission of the Gates Foundation's Global Health program "is to ensure that people in the developing world have the same chance for good health as people in the developed world,"[22] and it funds a variety of malaria R&D initiatives.

The number of Gates Foundation grantees and its total annual giving have been rapidly increasing. In 2002, three organizations were funded at a total of $20.2 million. By 2004, 11 organizations received a total of $77.6 million to support malaria R&D. More than 60% of 2004 investment went to public-private partnerships.

20 "Editor's note: In reviewing a late draft of this report, NIH reported that two additional NIH entities together funded approximately $800k of malaria research in 2004, namely the National Cancer Institute and the National Institute of Environmental Health Sciences."
21 NIAID website: **http://www3.niaid.nih.gov/about/overview/niaid_overview.htm**, accessed on August 15, 2005
22 Bill & Melinda Gates Foundation website: **http://www.gatesfoundation.org/GlobalHealth/**, accessed on August 26, 2005

In 2004, the Gates Foundation's investment in malaria R&D was distributed across four categories of R&D. *Drug development, vaccine development*, and *implementation research* were funded at similar levels (36%, 32%, and 31% of the total, respectively). The balance of funding was invested in *vector control research*. The Gates Foundation is the largest investor in *implementation research*.

- **The Wellcome Trust**

The Wellcome Trust, based in the United Kingdom, was established in 1936 and has an endowment of approximately £11.5 billion (US $20 billion). It is an independent charity with a mission "to foster and promote research with the aim of improving human and animal health."[23] The Wellcome Trust has a long history of supporting malaria R&D.

In 2004, the Wellcome Trust provided more than $13.5 million to support more than 40 malaria R&D initiatives, many of which were in malaria-endemic countries. In this particular year, 64% of its funding supported *basic research*, with *drug development* accounting for 17% of investment, followed by *implementation research* at 9%. Grants provided by the Wellcome Trust vary in scale and often span a number of years; therefore, its funding may vary considerably from one year to another. In 2000, it reported nearly $45 million in malaria R&D funding and its commitment for 2005 is estimated at $64 million. Between 2000 and 2004, Wellcome Trust funded a yearly average of $31.5 million in malaria R&D.

- **Pharmaceutical and Biotechnology Company Respondents**

A number of pharmaceutical and biotechnology companies responded to the survey. Since private-sector companies often are reluctant to report internal financial data, the companies responses have been aggregated to maintain confidentiality.

Pharmaceutical and biotechnology company respondents funded a total of $38.1 million of intramural malaria R&D in 2004. This represents 12% of total 2004 investment, and was entirely allocated to *drug development*. Given the lack of previous data from industry, it cannot be determined if this level of investment is representative or has been consistent over time. At present, several major pharmaceutical and biotechnology companies are engaged meaningfully in malaria R&D, generally in collaboration with public-private partnerships.

Other Large Donors

Thirteen additional organizations, each of which invested more than $1 million in malaria R&D in 2004, are listed in the following table. These organizations are of two types:

- Surveyed organizations that contributed between $1 million and $3 million of original source funding;
- Organizations that did not complete the survey, but were identified in recipient surveys as having funded more than $1 million of malaria R&D.

Please see Appendix C for a consolidated list of donors identified in survey responses.

23 Wellcome Trust website: **http://www.wellcome.ac.uk/aboutus/whatwedo/**, accessed August 26, 2005

Table 3: 2004 Malaria R&D Investment by Other Significant Donors

Survey Entity	Total Funding $
Anonymous Donor [a]	5,000,000
Global Fund to Fight AIDS, Tuberculosis and Malaria [b]	4,170,523
Fogarty International Center	2,801,497
World Bank	2,289,880
National Center for Research Resources	2,162,934
Ellison Medical Foundation	1,811,986
Swiss Government – Ministry of Interior [c]	1,809,409
National Institute of Child Health & Human Development	1,261,697
Médecins Sans Frontières [d]	1,208,967
National Heart, Lung, and Blood Institute	1,206,000
Government of Australia [e] 1,191,352	
Business Trust of South Africa [f]	1,137,882
Rockefeller Foundation	1,000,000
Total	**27,052,127**

Notes:
a Johns Hopkins Malaria Research Institute reported receipt of this anonymous donation to support malaria research
b South African Medical Research Council reported receipt of this funding for implementation research
c Swiss Tropical Institute reported receipt of this funding
d The Drugs for Neglected Disease Initiative reported receipt of this funding
e The Australian Army Malaria Institute reported receipt of this funding
f South African Medical Research Council reported receipt of this funding

The 25 donors and funders listed in Tables 2 and 3 account for 96% of total investment for malaria R&D in 2004.

Flow of Funds from Donor Organizations in 2004

Approximately one-half ($156 million) of the total investment flowed from funders directly to R&D entities conducting research. Another one-quarter ($79 million) of total investment was granted to funding managers-organizations that foster collaboration with R&D entities, disburse research funding, and manage research activities among numerous organizations working in a particular area of focus.

Total Investment: $323 million

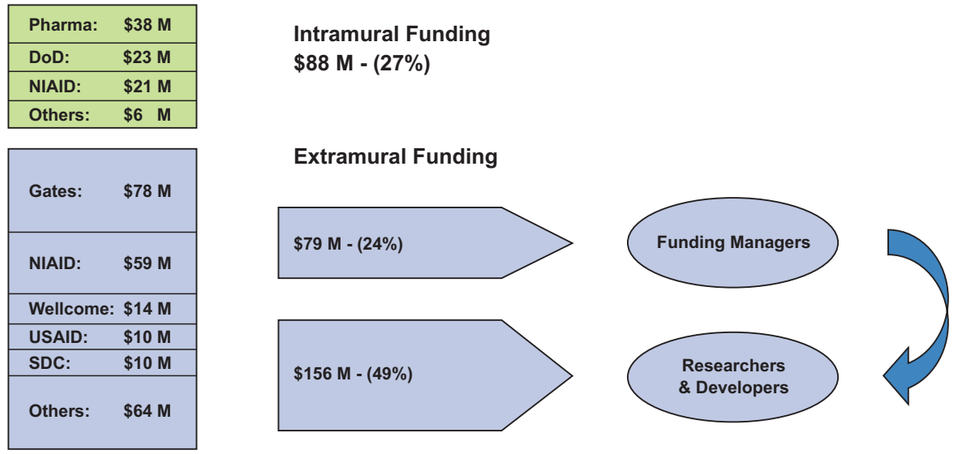

Figure D: Funding Flow of Donor 2004 Malaria R&D Investment ($ millions)

This diagram depicts the flow of malaria R&D funds from donor and funding organizations in 2004. Intramural funding represented 27% ($88 million) of total investment; extramural grants accounted for the remaining 73% ($235 million); details are discussed in the following sections.

Who Received Funding?

Funding Managers

Funding managers play a central role in the targeted distribution, management and monitoring of funds from donors to R&D entities. These organizations exist in a variety of forms: nongovernmental organizations (NGOs), public-private partnerships (PPPs), and special programs such as TDR.

Bringing together expertise and resources from multiple stakeholders, several funding managers are building and managing a large pipeline of new pharmaceutical products. By leveraging investments and managing projects with a focus on the public good, funding managers aim to accelerate the overall product development process by funding, partnering with, and fostering relationships among pharmaceutical and biotechnology companies, government agencies, and academic or other research institutions. Several funding managers like MIM and AMANET focus more on scientific capacity building than on product development.

Funding managers are generally not the originators of funds, and hence have not appeared in the tables of top malaria R&D investors. That stated, significant levels of funding are received and disbursed by these organizations. The table below highlights funding manager survey participants and their 2004 receipts.

Table 4: Funding Managers and 2004 Funding Received

Survey Entity	Total Received $
Medicines for Malaria Venture	27,844,413
PATH Malaria Vaccine Initiative	24,831,823
TDR	13,372,128
Multilateral Initiative on Malaria	3,990,000
Africa Malaria Network Trust	2,710,947
Drugs for Neglected Diseases Initiative	2,115,741
European Malaria Vaccine Development Consortium	1,614,105
Institute for OneWorld Health	1,429,611
WHO Initiative for Vaccine Research	502,500
European & Developing Countries Clinical Trials Partnership	496,648
Total	**78,907,916**

With aggregate receipts of almost $79 million, this group managed 24% of total 2004 malaria R&D investment and received 34% of the total extramural funding.

Private philanthropic organizations provided the majority of funds ($47.4 million or 60%) to funding managers in 2004. The Gates Foundation contributed 95% of private philanthropic funding to this group ($45.1 million), followed by the Rockefeller Foundation and the Wellcome Trust.

Many funding managers came into existence within the past six years, and their involvement in research funding continues to grow. The five funding managers with the highest receipts in 2004 (representing 92% of total funding manager receipts) also submitted survey data for the years 2002 and 2003. The compound annual growth rate of funding received by this group during this period is greater than 31%. Seventy-five percent of this growth was fueled by increased support from the Gates Foundation. A significant amount of the increase in malaria R&D funding in the last decade can be attributed to funds generated by this group.

Public Private Partnerships

Public-private partnerships (PPPs) in the field of healthcare product development represent a new type of not-for-profit organization that became prevalent in the late 1990s. Many PPPs are aligned with a specific disease or product area, and play a catalytic role in addressing an identified health inequity.

Several factors contributed to the recent emergence of these product development PPPs, including:[24]

- The highlighting of diseases of poverty through the systematic analysis of disease burden;
- Private industry's continued lack of R&D investment in neglected diseases;
- The growing recognition, fostered by the HIV/AIDS pandemic, that more must be done to address the health needs of developing nations;
- An improved understanding of industry motivations and expertise by the public health community;
- The financial and organizational support provided by private philanthropic organizations;
- The growing recognition that healthcare product development requires involvement of multiple stakeholders and effective partnerships between the public and private sectors.

Spotlight on Specific Funding Managers

Additional information follows on several of the surveyed funding managers.

- **UNICEF/UNDP/World Bank/WHO Special Programme for Research & Training in Tropical Diseases (TDR):**

TDR is funded by four UN co-sponsoring organizations, 23 governments, and nine other sources (e.g. philanthropic organizations and corporations). TDR's mission is "to help coordinate, support, and influence global efforts to combat a portfolio of major diseases of the poor and disadvantaged,"[25] including malaria.

Total TDR funding associated with malaria R&D in 2004 was $13.4 million. A significant portion of this funding was reported in donor surveys, and as such was attributed to the original donors to avoid double counting. Forty-nine percent of TDR funding ($6.5 million) was allocated to *antimalarial drug discovery and development* in 2004. *Implementation research* was the next largest categorization at 32% ($4.2 million), followed by *basic research* at 8% ($1 million). TDR dedicated $1.6 million in 2004 to capacity building, a key area of its work.

- **Medicines for Malaria Venture (MMV):**

MMV was launched in November 1999 with a mission "to bring public, private and philanthropic sector partners together to fund and manage the discovery, development and delivery of new medicines for the treatment and prevention of malaria in disease-endemic countries."[26] MMV has made significant progress toward its mission, managing a portfolio of more than 20 projects – believed to be the largest antimalarial drug research portfolio ever pursued. All of MMV's funding in 2004 was devoted to *antimalarial drug discovery and development*. Indicative of many other funding managers, the majority (80%) of MMV's funding came from private philanthropic sources, with the Gates Foundation contributing more than 70% of its total 2004 funding.

24 Adapted from Widdus, R., and White, K., 2004, *Combating Diseases Associated with Poverty: Financing Strategies for Product Development and the Potential Role of Public-Private Partnerships*, Initiative on Public-Private Partnerships for Health: Geneva, pp. 1-6
25 TDR website: **http://www.who.int/tdr/about/mission.htm**, accessed August 29, 2005
26 MMV website: **http://www.mmv.org/rubrique.php3?id_rubrique=38**, accessed August 18, 2005

- **Africa Malaria Network Trust (AMANET):**
Initially launched to plan, build capacity for, and conduct malaria vaccine trials in Africa, the role of AMANET was expanded in 2002 to focus on a broader, integrated approach to fight malaria. AMANET's mission is to "promote capacity strengthening and networking of malaria research and development in Africa."[27] All of AMANET's funding in 2004 was allocated to *vaccine development and vaccine trials* to support existing clinical trials and to develop capacity for future ones.

Researchers & Developers

Given its primary focus on sources of investment in malaria R&D, this study did not attempt to survey every recipient of funding dedicated to malaria research. However, the study team did engage a broad sampling of research and development entities to participate in the survey, including many major government research institutions, pharmaceutical and biotechnology companies, universities, and other externally funded research entities. In total, this group reported receiving $156 million of funding in 2004 to support malaria research and development.

Forty-four percent of this $156 million supported research activities in government research institutes. Four US government entities accounted for 77% of the total for this group: the US Department of Defense (DoD), NIAID, Centers for Disease Control and Prevention, and NICHD. The majority of investment supporting government research institutes was intramural funding.

2004 Sample Size: $156 million

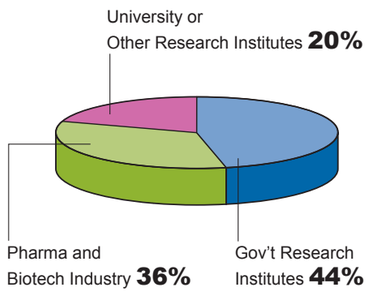

Figure E:
2004 Funding by Type of Research Entity

Pharmaceutical and biotechnology industry respondents reported more than $55 million of investments in research. The majority of the investment (69%) came in the form of intramural or in-house research and development by pharmaceutical and biotechnology companies, with the balance represented by research grants received from donors and funding managers. So while industry is receiving considerable funding to conduct malaria research and development (e.g. from public-private partnerships), it is also making significant internal investments.

Other research institutions, primarily universities, accounted for 20% of all reported funding to research entities. There is considerable variation in the size of the research programs. The London School of Hygiene & Tropical Medicine was funded for $6.9 million of malaria research, while several other entities were funded at less than $100,000. On average, surveyed universities and other externally funded research institutes received about $1.8 million of funding.

There was also variation in the categories of research funded at the different types of research institutions in this sample. Government research institutes were most heavily funded for *vaccine development*, with *drug development* being the next highest funded area. The pharmaceutical and biotechnology respondents were heavily focused on *drug development*. University and other externally funded research institutes were most heavily focused on *basic research*, to which almost 50% of their funding was allocated.

27 AMANET website: **http://www.amanet-trust.org/**, accessed August 29, 2005

Spotlight on Specific Research Institutions

Transforming donor funding into scientific advances is the work of the malaria research community. Scientists in basic research labs are investigating the genetics of *Plasmodium*; medical practitioners are conducting drug and vaccine clinical trials; field researchers are striving to improve interventional strategies through implementation research.

- **Department of Defense's (DoD) Walter Reed Army Institute of Research (WRAIR) and Naval Medical Research Center (NMRC):**
Department of Defense facilities were funded to conduct almost $30 million (including external funding) of malaria R&D in their labs in 2004. WRAIR and NMRC combined form DoD's largest biomedical research laboratory, with decades of experience in a broad spectrum of malaria research.

WRAIR was instrumental in the development and testing of drugs such as mefloquine, halofantrine, and tafenoquine, and has been involved in the clinical trials and FDA approval for prophylaxis of numerous others (e.g. Fansidar, and Chloroquine-primaquine combination treatments). Among WRAIR's current areas of focus is the development of an intravenous artesunate drug to treat severe, drug-resistant malaria. WRAIR is developing several malaria vaccines and is in the final stages of FDA approval of a new malaria diagnostic device it has been developing since 2000.

Forty-six percent of DoD's funding supports *drug development*, with 38% allocated to *vaccine development* and 9% *to basic research*.

- **South African Medical Research Council (SAMRC):**
SAMRC's mission is "to improve the nation's health status and quality of life through relevant and excellent health research aimed at promoting equity and development."[28] SAMRC was funded to conduct more than $7 million of malaria R&D in 2004 in the categories of *basic research*, *drug development*, and *implementation research*. The largest component of funding was devoted to *implementation research* (83%) to maximize the effectiveness of indoor residual spraying and ACT implementation over a 100,000-km^2 region of southern Africa. Before program implementation in 2000, this high-transmission region accounted for more than 400,000 cases of malaria per year. Post implementation results in Kwa-Zulu Natal and Mpumalanga provinces recorded 96% and 75% reductions in malaria cases between 2000 and 2003. Funding for this program was initially provided entirely by the private sector and over time grew to include support from the Global Fund to Fight AIDS, Tuberculosis and Malaria and the governments of South Africa and Mozambique.

- **London School of Hygiene & Tropical Medicine (LSHTM):**
LSHTM's mission is "to contribute to the improvement of health worldwide through the pursuit of excellence in research, postgraduate teaching, and advanced training in national and international public health and tropical medicine, and through informing policy and practice in these areas."[29] In support of its mission, LSHTM was funded to conduct almost $7 million of malaria R&D in 2004, with the Gates Foundation and the Gates Malaria Partnership contributing 41% percent of the total. Funding was primarily allocated to the categories of *drug discovery and development* (35%); *basic research* (24%); *implementation research* (22%); and the *development of malaria diagnostics* (13%). In 1998 the school established the Malaria Centre; currently about 70 LSHTM staff work partially or wholly on malaria, as do many students.

28 SAMRC website: **http://www.mrc.ac.za/about/about.html**, accessed on August 15, 2005
29 LSHTM website: **http://www.lshtm.ac.uk/aboutus/mission.html**, accessed on August 15, 2005

Funding of R&D Relative to Prevention and Control

Data from this study indicate that few organizations equally support both R&D and prevention and control, but rather focus on one area or the other.

N = 75 Respondents

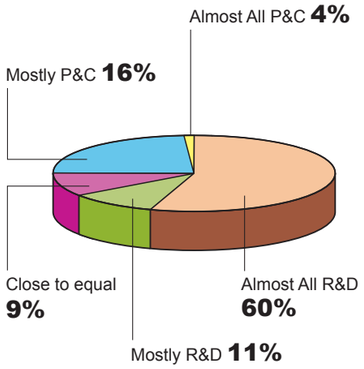

Figure F: Funding of R&D Relative to Prevention and Control

Sixty percent of survey respondents (45 organizations) stated that all or almost all of their malaria funding is directed toward R&D. Specific respondents in this group included NIAID, Wellcome Trust, and the US Department of Defense.

Eight organizations, including the Gates Foundation and MRC, characterized their malaria funding as mostly R&D (>75%). Seven organizations, including the EC, the US Centers for Disease Control and Prevention, and the London School of Hygiene & Tropical Medicine, devote roughly equal funding to malaria R&D and prevention and control.

Among the 12 respondents who fund mostly prevention and control activities are the Netherlands Ministry for Development Cooperation, the UK Department for International Development (DfID), and the World Bank. Three survey respondents indicated that almost all of their funding is for malaria prevention and control. This group includes the Roll Back Malaria Partnership and the Swiss Agency for Development & Cooperation.

How Was the Funding Allocated?

Categorization of Investment in Malaria R&D

Malaria R&D investment in 2004 can be examined from many perspectives. Of particular interest are investment by sector, by geography for government giving, by type of research activity (e.g. *basic research* versus *drug development*), and by type of funding (extramural versus intramural).

2004 Investment: $323 million

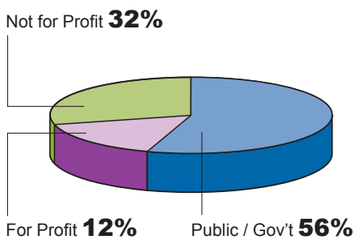

Figure G: Investment by Sector

The public sector, comprised predominantly of government and multilateral funding agencies, is the largest investor in malaria R&D, providing $181.4 million (56%) of the $323 million total in 2004.

The not-for-profit sector contributed $102.5 million (32%) of total investment in 2004. Private philanthropic organizations reported donations of $95.4 million in 2004, and university research labs and other not-for-profit organizations accounted for an additional $7.1 million.

Investment by the for-profit sector was $39.5 million (12% of the total). The vast majority of this funding (96%) was in the form of intramural research and development by pharmaceutical and biotechnology companies, with the balance being comprised of corporate donations. In this study, ExxonMobil Foundation and BHP Billiton were the only two for-profit companies or company foundations contributing to malaria R&D outside of the pharmaceutical sector.

Geographical Breakdown of Public Sector Investment

The US government invested $128.8 million in malaria R&D in 2004 (more than 70% of total public-sector support and 39.8% of total investment). European governments and the European Commission (EC) provided $36.1 million of funding (20% of total public-sector support and 11% of total investment), led by Switzerland, the UK, and the Netherlands at $12.2, $9.8, and $7.0 million, respectively.

Funding by the United Nations and multilateral organizations ($7.2 million) includes $4.2 million from the Global Fund to Fight AIDS, Tuberculosis and Malaria to support *implementation research*, and World Bank funding of $2.3 million.

Several governments in endemic countries, including South Africa Mozambique, and India, invested in malaria R&D.

Contributions from many donor governments have been captured through the survey submission of TDR. A significant portion of TDR's funding has been geographically linked back to the contributing governments, but some remains in the "not classified" category.

2004 Total Government Investment: $182.5 million

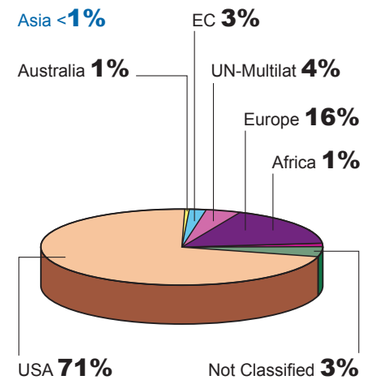

Figure H: Government Investment by Region

Definitions of Malaria R&D

For the purposes of this study, malaria R&D includes all activities using scientific approaches to further advance the understanding of the malaria disease, parasites, and vectors, and research on turning this knowledge into innovations and control measures. Research and development is required to develop much-needed drugs, vaccines, diagnostics, and insecticides, and to discover and apply new knowledge for malaria control.

The categories used in this global survey are based largely on the 1996 Wellcome Trust report, *Malaria Research: an Audit of International Activity*.[30] The Wellcome Trust team reviewed different types of malaria research and divided them into eight major categories and 14 subfields.

Because of scientific advances over the past decade, some changes have been made to the categorization system. For example, under *basic research*, bioinformatics and proteomics have been added. Survey respondents were asked to classify funding into six general categories, which were further broken down into 16 subfields for informational purposes. For additional details on the categories and subfields, please see Appendix E.

Six general categories of research for the malaria R&D funding study are:

1. *Basic research*
2. *Antimalarial drug discovery and development*
3. *Vaccine development and vaccine trials*
4. *Vector control research*
5. *Development of malaria diagnostics*
6. *Implementation research*

30 Anderson, J., MacLean, M., and Davies, C., 1996, *Malaria Research: An Audit of International Activity*, The Wellcome Trust: London. See Box 4.1, pp. 44-45

Investment by R&D Category

Survey participants were requested to allocate funding to six categories of malaria R&D. All but 2% of the funding reported for 2004 was allocated to R&D categories.

2004 Investment: $323 million

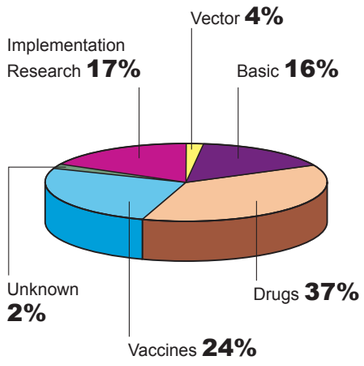

Figure I: Allocation of 2004 Funding by R&D Category

Antimalarial drug discovery and development received the largest amount of investment in 2004: $120.2 million (37% of the total). The largest sources of this investment were the pharmaceutical and biotechnology company respondents at $38.1 million, followed by the Gates Foundation at $28.2 million, NIAID at $21.2 million, and DoD at $11.7 million.

Vaccine development and vaccine trials was the next highest funded category, at $78.7 million (24% of the total). NIAID was the top investor in this category, with 2004 funding of $29.2 million, followed by the Gates Foundation at $24.8 million and DoD at $9.6 million.

Implementation research investment totaled $54.6 million in 2004. The Gates Foundation was the largest investor at $24.4 million, followed by the Swiss Agency for Development & Cooperation (SDC) at $8.0 million, and the Global Fund at $4.2 million.

Basic research investment totaled $50.8 million in 2004. Three organizations contributed 67% of total basic research funding. NIAID was the largest investor at $18.8 million, followed by the Wellcome Trust at $8.7 million and MRC at $6.4 million.

Vector control research totaled $11.9 million. The majority of this funding (64% or $7.6 million) was contributed by NIAID, followed by DoD at $1.9 million and the Wellcome Trust at $1 million.

Development of malaria diagnostics received the lowest level of investment, at $718,000. Funds contributed ($200,000) by an anonymous donor to the Johns Hopkins Malaria Research Institute made up the largest component of funding, followed by contributions from the Swiss Government's Interior Ministry ($161,000).

Implementation Research

Implementation research examines the application of R&D outputs in the field in order to maximize their effectiveness. It is closely linked to prevention and control, so at times there is a fine line between R&D and prevention and control activities.

In the 1996 Wellcome Trust study, the research area that was cited most frequently as likely to benefit from increased resources was research into the implementation of control measures. In that study, publications on implementation research only represented 6% of the total malaria research publications. In and of itself, this is not the indicative of the amount of funding, but it seems likely that investment in implementation research, which accounted for 17% of the total investment in 2004, has risen in the past decade. Two of the largest funders of implementation research, the Gates Foundation and the Global Fund, are new funders created since the Wellcome Trust report.

In this study, *implementation research* specifically included:

- Trials to test commercially available measures for the control of mosquito vectors (such as bednets, environmental and biological control measures, and insecticides) and to test other interventions for the control of malaria morbidity and mortality in communities (e.g. drug treatment and prophylaxis);
- Design of treatment and control programs appropriate to local prevailing conditions;
- Implementation and evaluation of large-scale malaria treatment and control programs operated through health care services, government ministries, nongovernmental organizations, and others.

Intramural versus Extramural Funding

Seventy-three percent of the investment in malaria R&D in 2004 ($235 million) was in the form of extramural funding - or grants made by one organization to another. The balance (27% or $88 million) was reported as intramural funding (internal or self-funding), and was heavily concentrated in three survey entities: pharmaceutical and biotechnology company respondents, NIAID, and the US DoD. This group accounted for more than $81 million of 2004 intramural funding (92% of the total).

Pharmaceutical and biotechnology company respondents reported conducting more than $38 million of intramural R&D in 2004. Funding by the companies that responded amounted to 12% of the total investment in malaria R&D in 2004. The US DoD and NIAID, respectively, reported $22.9 and $20.7 million of intramural research in 2004. Together, these three entities funded 93% of all intramural investment.

Table 5: 2004 Malaria R&D Intramural Investment (>$1 million)

Survey Entity	Intramural Funding $
Pharmaceutical and Biotechnology Company Respondents [a]	38,108,877
US Department of Defense	22,867,367
National Institute of Allergy and Infectious Diseases	20,691,546
Medical Research Council [b]	2,929,330
US Centers for Disease Control and Prevention	1,227,500
Subtotal	85,824,620
Other Sources	2,594,531
Total	**88,419,151**

Notes:
a Financial information aggregated for all pharmaceutical and biotechnology company respondents
b Includes National Institute of Medical Research funding

2004 Intramural Investment: $88 million

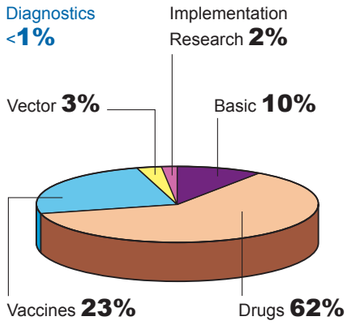

Figure J: Categorization of 2004 Intramural Investment

Allocation of the $88 million of intramural funding by R&D category produces a different result from the categorization of the total $323 million investment.

Because of a high level of investment in drugs by the pharmaceutical and biotechnology respondents, the percentage of investment categorized as *drug discovery and development* is significantly larger in the intramural categorization than in the total funding (62% of intramural versus 37% of total investment; see *Figures J* and *I*). Offsetting decreases are recorded in *implementation research* (2% versus 17%) and *basic research* (10% versus 16%).

2004 Extramural Investment: $235 Million

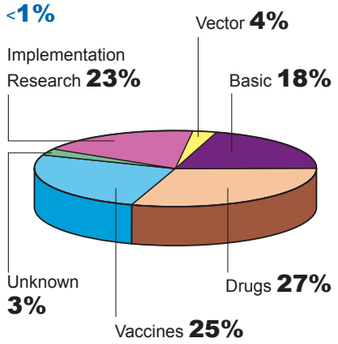

Figure K: Categorization of 2004 Extramural Investment

The distribution of extramural funding is more even across R&D categories. *Drug discovery and development* remains the largest categorization but decreases to 27% (from 37% of the total investment). *Vaccine development and vaccine trials* is the next largest category, at 25% (versus 24% in the total investment allocation). The percentage of extramural investment categorized as *implementation research* is 23% (versus 17% of total investment). Little change was observed in the other categories.

Funding for Capacity Building

Building local capacity to conduct research in malaria-endemic countries has become a new focus of funding over the past decade. Improving human resources and institutional capacity to conduct research in the countries most affected by malaria is believed to help advance R&D.

Because capacity building cuts across the various areas of research, it was not included as a separate category in the survey. However, respondents were asked to indicate how much of their reported malaria R&D funding was specifically dedicated to capacity building. Survey respondents reported malaria R&D capacity building funding of $12.4 million[31] in 2004. This represents 3.8% of total 2004 investment. The Swiss Agency for Development & Cooperation reported the highest capacity building investment at $3.2 million, followed by Fogarty International Center ($1.9 million), the Netherlands Ministry for Development Cooperation ($1.9 million), and TDR ($1.6 million).

Perceptions of Funding Levels

Survey respondents overwhelmingly reported that they believed malaria R&D is underfunded. Only four of 74 respondents thought that malaria R&D was appropriately funded. Three-quarters of respondents believed that *antimalarial drug discovery and development, vector control research, and implementation research* were significantly or somewhat under-funded.

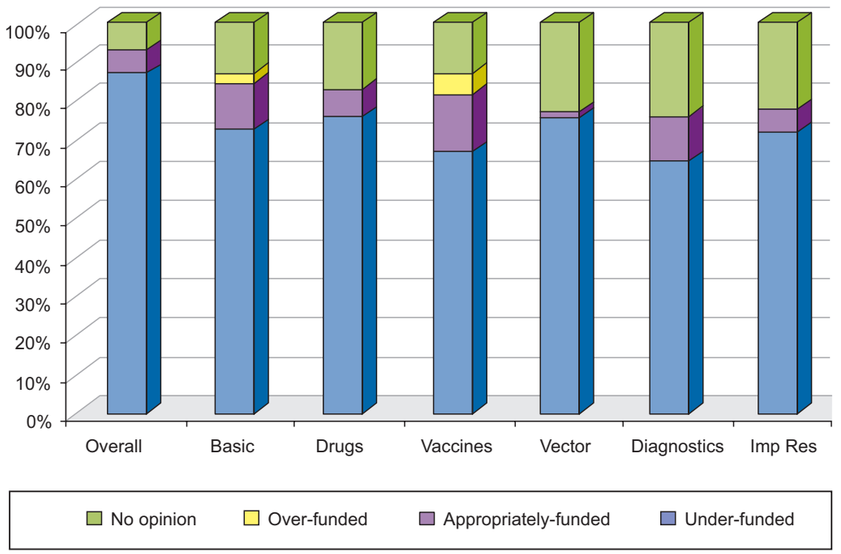

Figure L: Perceptions of Funding Levels

31 This total does not include major infrastructure projects, as they were specifically excluded from the survey

III MALARIA R&D INVESTMENT IN CONTEXT

Current Funding Compared to Past Funding

This study calculates the investment in malaria R&D in 2004 to be $323 million.

In its 1996 study, *Malaria Research: An Audit of International Activity*, the Wellcome Trust reported that "total identifiable global expenditure on malaria research in 1993 was approximately $84 million."[32] Adjusting this figure for biomedical R&D inflation yields $119.1 million in 2004 dollars.[33]

The Wellcome Trust study primarily identified extramural support, and the authors noted that data from the pharmaceutical industry could not be obtained. Subtracting pharmaceutical and biotechnology industry respondent investment from the present study's findings yields $285.3 million, which can be compared to the inflation-adjusted Wellcome Trust figure of $119.1 million.

Using these data, it can be inferred that real funding for malaria R&D has increased by an estimated $166 million between 1993 and 2004, with real growth at 8.3% per year, after accounting for biomedical R&D inflation.

What has driven this growth?

New donors and new means for donors to use their resources efficiently, have both contributed to increases in funding. A significant component of the increased funding can be attributed to specific new donors, like the Gates Foundation. NIAID funding also increased well above the inflation rate, from $13.1 million reported by the Wellcome Trust to $80.2 million in 2004. Funding provided by these two organizations accounts for over 80% of the identified non-inflationary growth in investment between 1993 and 2004.

New public-private partnerships have provided foundations, governments, and industry a transparent conduit for increased investment and are another likely reason for increased resources devoted to malaria R&D.

Is malaria R&D funded at an appropriate level?

One way to address this question is to assess the burden that malaria and other diseases impose on global health, and compare malaria R&D funding with that of other diseases.

Malaria's Share of R&D Funding

For 2001, the most recent year for which data are available, total global spending on all health-related R&D was estimated at $105.9 billion by the Global Forum for Health Research (GFHR). The vast majority of these funds originated in high-income countries and was spent in high-income countries on illnesses affecting their citizens.[34]

32 Anderson, J., MacLean, M., and Davies, C., 1996, *Malaria Research: An Audit of International Activity*, The Wellcome Trust: London, p. 7. This figure was expressed in 1992 dollars

33 The Bureau of Economic Analysis of the US Department of Commerce publishes a biomedical research and development price index based on NIH data. See **http://ospp.od.nih.gov/ecostudies/BRD_Distrib_2005**, accessed on September 7, 2005

34 Global Forum for Health Research, *Monitoring Financial Flows for Health Research*: 2004, pp. 13-14

The private, for-profit sector was the largest source of health R&D funds, accounting for 48% of funding. The public sector was the next largest source, contributing 44% of funding. The remaining 8% of funding came from the private, not-for-profit sector. This is in sharp contrast to funding for malaria R&D in 2004, of which the private, for-profit sector contributed 12% of funds, the public sector 56%, and the private not-for-profit sector 32%.

Table 6: Comparison of Total Health R&D and Malaria R&D Funding by Sector

Sector	All Health-Related R&D [a]	Malaria R&D [b]
For-Profit	48%	12%
Public	44%	56%
Not-For-Profit	8%	32%

a From GFHR's Monitoring Financial Flows for Health Research 2004, p. 15
b Calculated from survey data

Malaria R&D investment in 2001 was estimated at approximately $288 million in a paper prepared for GFHR's Forum 8 in Mexico City.[35] The authors employed a bibliometric approach[36] to determine R&D investment for eight disease areas. Investment in malaria R&D represented less than 0.3% of global R&D investment in 2001. Yet malaria's impact on humanity is roughly 10 times that amount, accounting for 3.1% of the global disease burden and overwhelmingly occurring in poor countries.

Comparing Disease Burden and Funding Levels

Disease burden - the impact of a disease on people - is tracked by WHO in terms of disability-adjusted life-years (DALYs). "The disability-adjusted life year is an indicator of the time lived with a disability and the time lost due to premature mortality"[37] and is a common unit of disease burden measurement in the public health community.

Cardiovascular diseases are the leading cause of death in the world and afflict rich and poor alike (cardiovascular diseases account for 38.1% of deaths in high-income countries and 27.9% of deaths in low- and middle-income countries[38]). Tuberculosis and dengue fever primarily afflict developing nations, so these also make interesting comparators, as does HIV/AIDS. The death toll from diabetes and malaria are somewhat similar, so diabetes has also been included in the comparison. Examining these conditions, as well as all medical conditions, helps put malaria R&D funding in perspective.

35 Lewison, G., Rippon, I., de Francisco, A., and Lipworth, S., 2004, "Outputs and Expenditures on Health Research in Eight Disease Areas, 1996-2001," GFHR Forum 8, Mexico City, November 2004

36 The authors describe the approach on p. 1 of their paper: "The method involved identification and analysis of research outputs – papers in the serial literature and indexed in the Science Citation Index – and their multiplication by the estimated cost per paper, determined from questionnaires sent to leading researchers."

37 Homedes, N., "The Disability-Adjusted Life Year (DALY) Definition, Measurement and Potential Use," from **http://www.worldbank.org/html/extdr/hnp/hddflash/workp/wp_00068.html#TofC1**, accessed on July 20, 2005

38 GFHR, *Monitoring Financial Flows for Health Research*: 2004, p. 58. Disease and death figures are 2002 data from *The World Health Report 2004*

Table 7: Disease Burden and Funding Comparison, 2001-2002 data

Condition	Global Disease Burden [a] (million) DALYs	Total Global Disease Burden	Deaths [a] (millions)	Total Global Deaths	R&D Funding (millions) $	R&D Funding per DALY $
Cardiovascular	148.190	9.9%	16.733	29.3%	9,402[b]	**63.45**
HIV/AIDS	84.458	5.7%	2.777	4.9%	2,049[b]	**24.26**
Malaria	**46.486**	**3.1%**	**1.272**	**2.2%**	**288[b]**	**6.20**
Tuberculosis	34.736	2.3%	1.566	2.7%	378[b]	**10.88**
Diabetes	16.194	1.1%	0.988	1.7%	1,653[b]	**102.07**
Dengue	0.616	0.00%	0.019	0.0%	58[b]	**94.16**

a DALY and death statistics are 2002 data, from WHO, *World Health Report 2004*
b Estimate for 2001-2002 funding from Lewison, G., et al., 2004, "Outputs and Expenditures on Health Research in Eight Disease Areas, 1996-2001," GFHR Forum 8, Mexico City, November 2004. The authors use a bibliometric approach to estimate R&D funding and the paper has not been published in a peer review journal. For the sake of data consistency, GFHR figures are taken for malaria R&D because the year for the other diseases are taken from the same year.

R&D funding per DALY is $6.20 for malaria, whereas R&D funding average for all conditions is $71.07 per DALY.[39] Cardiovascular diseases and diabetes are funded at $63.45 and $102.07 per DALY, respectively. Were malaria funded at the average rate for all conditions, it would receive over $3.3 billion in annual R&D funding; it currently receives about 9% of that amount.

Were malaria research funded at the average rate for all medical conditions, it would receive more than $3 billion in annual R&D funding.

Note, also, that in percentage terms, malaria ranks relatively higher in disease burden compared to deaths, while the opposite is true for many diseases, especially cardiovascular diseases. This is an indication that malaria disproportionately strikes the young, as the death of a child accounts for many more lost years of productive life than the death of an elderly individual. Viewed another way, R&D expenditures aimed at addressing malaria will yield tens of millions of additional years of productive life when compared to treatments primarily affecting older adults.

Copenhagen Consensus 2004
The Copenhagen Consensus project convened a panel of experts to set priorities in confronting some of the globe's most pressing problems. Specifically, the group was asked: "What would be the best ways of advancing global welfare, and particularly the welfare of developing countries, supposing that an additional $50 billion of resources were at governments' disposal?"[40]

39 The average for all conditions calculation is based on GFHR's $105.9 billion estimate of 2001 health-related R&D spending divided by WHO's 1.49 billion estimate of 2002 total disease burden in DALYs
40 See **http://www.copenhagenconsensus.com/Files/Filer/CC/Press/UK/copenhagen_consensus_result_FINAL.pdf**, accessed on June 8, 2005. Also see: Mills, A., and Shillcutt, S., 2004, "Challenge Paper on Communicable Diseases," **http://www.copenhagenconsensus.com/Files/Filer/CC/Papers/sammendrag/Accepted_Communicable_Diseases_160404.pdf**, accessed on June 8, 2005

The panel of eight distinguished economists, including four Nobel laureates, reviewed dozens of expert proposals addressing a wide set of global issues: civil conflict, climate change, communicable diseases, education, financial stability, governance, hunger and malnutrition, migration, trade reform, and water and sanitation.

Projects were ranked in terms of costs and benefits to answer the question of how the money should be invested to do the most good. Among the results: "New measures for the control and treatment of malaria" was ranked fourth, appearing in the highest rated category of projects.

Low Funding Results in Few Scientific Breakthroughs
Low R&D investment is reflected in limited drug development, as evidenced by Trouiller and colleagues in a 2002 study. His team found that between 1975 and 1999, only four drugs were developed to combat malaria and three for tuberculosis, while 89 were developed for respiratory illnesses and 179 for cardiovascular diseases. Drug development follows perceptions of lucrative market segments. Cardiovascular drugs represented almost 20% of the $204 billion drug market in 1999, and respiratory drugs accounted for 9.3% of the market. By contrast, malaria drug sales represented 0.1% of the worldwide total. On a sales per DALY basis, cardiovascular and respiratory drugs brought in $283 and $307 per DALY respectively, while malaria drug sales were $5 per DALY.[41]

Table 8: New Chemical Entities (NCEs) Approved Between 1975-1999 by Therapeutic Area, Disease Burden, and Sales; from Trouiller et al.

Therapeutic Area	Approved NCEs 1975 – 1999		NCEs per million DALYs[a]	Drug Sales per DALY[a]
	#	% of total		
Total for All Therapeutic Areas	1,393	100%	1.01	$148
Tuberculosis	3	0.2%	0.11	$11
Malaria	**4**	**0.3%**	**0.10**	**$5**
HIV/AIDS	26	1.9%	0.37	$44
Respiratory (non-infectious)	89	6.4%	1.44	$307
Cardiovascular	179	12.8%	1.25	$283

a Trouiller cites DALY data from WHO *World Health Report 1999*, and 1999 drug sales data

The private sector is motivated primarily to pursue profitable market opportunities. The development of new drugs and vaccines is very expensive, costing hundreds of millions of dollars. Given the perception of low return on investment, private sector R&D expenditures on malaria are very low. To address this "market failure," continued and increased support from the public and not-for-profit sectors will be required to finance malaria R&D. Although malaria R&D is expensive, the return on investment is far more dramatic than perceived, not only in lives saved but also in economic returns in the disease-endemic countries.

41 Trouiller, P. et al, 2002, "Drug Development for neglected diseases: a deficient market and a public-health policy failure," *The Lancet*, Vol. 359, pp. 2188-2194

What Malaria R&D Funding Can Buy

As noted, malaria R&D receives about 0.3% of global medical R&D spending, or roughly one-tenth of the amount suggested by its 3.1% share of global disease burden. The $323 million of investment identified through this survey is funding an array of highly complex research activities across six categories of R&D. As a general rule, progress in research is linked to funding. While determining appropriate funding for malaria R&D requires further study, survey respondents and the published literature have provided some perspective on R&D costs and what malaria funding can buy.

The cost of developing new drugs has been estimated in a number of studies, including several by the Tufts Center for the Study of Drug Development. In a 2003 study, Tuft's DiMasi surveyed 10 pharmaceutical firms and examined the R&D costs for 68 randomly selected new drugs. Including the cost of drug candidates abandoned during testing and the opportunity cost of capital, he arrived at a development cost of over $800 million for a new drug.[42] MMV estimates that its costs will be significantly lower although the total cost, including cost of failures, to develop new combination antimalarial drugs cannot be credibly calculated until a new drug has been developed. According to a recent study by the London School of Economics, dramatic reduction in drug development cost for neglected diseases is due to various advantages of operating as a public-private partnership. They include: significant in-kind contributions from research partners; reduced project risk and cost through a portfolio approach; and "piggy-backing" on existing research and knowledge in the public and commercial sector.[43]

Vaccine development is even more complex and costly, especially when dealing with parasitic diseases like malaria as opposed to viruses such as flu or measles. In its 2003 report *State of the World's Vaccines and Immunization*, WHO referenced "approximately $600 million a year invested in HIV vaccine research," a figure corroborated by a recent *HIV Vaccines and Microbicides Resource Tracking Working Group* report.[45] In the case of malaria, the formidable opponent is a complex parasite that is incredibly innovative in the face of assault.

Descriptions of malaria-specific research activities conducted by survey respondents, along with the associated costs, have been summarized as illustrative examples in the following table.

42 DiMasi, J., Hansen, R., Grabowski, H., 2003, "The price of innovation: new estimates of drug development costs," *Journal of Health Economics* 22(2), 151-185
43 Moran, M., et al, 2005 "The new landscape of neglected disease drug research and development," London School of Economics, pp. 54.
44 World Health Organization, 2003, *State of the world's vaccines and immunizations. – Rev. ed.*, Geneva, pp. 9-10
45 Preventive HIV vaccine investment was estimated at ~$682 million for the year 2004; see: Lamourelle, G., et al., 2005, "Tracking Funding For Preventive HIV Vaccine Research & Development: Estimates of Annual Investments and Expenditures 2000 to 2005," HIV Vaccines and Microbicides Resource Tracking Working Group

Table 9: Illustrative Costs of Malaria R&D Activities [a]

R&D Category	Activity	Description	Cost
Basic Research	Immunology	A study was conducted in a malaria-endemic country over a 60-month period, to characterize the natural responses to block transmission of *Plasmodium vivax*.	$413,000 *including personnel, supplies and travel costs*
	Genetics	A study was conducted in a malaria-endemic country over a 36-month period, to analyze the genetics of the human malaria parasite *Plasmodium falciparum* to determine the nature of the parasite's resistance to the drug chloroquine and its accelerated resistance to other antimalarial drugs.	$987,486 *including personnel, supplies, travel, and technical support*
Drug Discovery and Development	Phase 1 clinical trial	A Phase 1 clinical trial for an antimalarial drug candidate was conducted in the UK over 10 months. The trial included four studies involving 92 subjects.	$2,750,000 *including personnel, equipment, and insurance costs*
	Phase 3 clinical trial	A Phase 3 clinical trial for an antimalarial drug will involve 2,550 patients in eight countries in Africa and Asia. The trial will last approximately 15 months, and the patient follow-up time will be approximately 50 days.	$10,250,000 *including personnel, equipment and insurance costs*
Vaccine Development and Vaccine Trials	Pre-clinical	A pre-clinical evaluation of an experimental vaccine was conducted in a malaria-endemic country over a 24-month period. The research focused on determining the immunogenicity and protective efficacy of the recombinant protein 200L of *Plasmodium vivax* in *Aotus* monkeys.	$308,900 *including personnel, equipment, travel and technical support*
	Phase 1 clinical trials	Two Phase 1 clinical trials of potential malaria vaccine candidates were conducted over a 12-month period and involved 50 volunteers. The project also includes: * production of sufficient quantities of material to evaluate in preclinical studies in animals to determine immunogenicity and toxicity; * cGMP grade production and release of the malaria antigen and the individual vaccine formulations so that they are acceptable for testing in humans.	$2,925,000 *including personnel and supply costs*
	Phase 2b clinical trials	A Phase 2b clinical trial in a malaria-endemic country in sub-Saharan Africa involved 400 children, aged one to three years, over a 2.5-year period.	$2,850,000 *including some site infrastructure costs*
Implementation Research	Intervention trials and health services research	An integrated malaria control and evaluation program was launched in 2000 in a highly malarious region of Africa. The program initially involved indoor residual spraying and was expanded to include ACT implementation. The program included training of local health personnel and ongoing scientific monitoring.	$6,000,000 *including personnel and supplies (such as insecticide, equipment, and drugs).*

a Illustrative R&D activity descriptions and the associated cost information was provided as supplemental information by survey respondents in interviews and follow-up communications.

When analyzing R&D expenditures, it should be kept in mind that many unsuccessful candidates must be funded on the route to approved products, and that these failed products factor into the costs. A report of a conference convened by the Association of American Medical Colleges and the US Food and Drug Administration noted that "most experts agree that less than 10% of drug candidates entering clinical development ever become marketed products. Especially distressing is the fact that up to 30%-50% of drugs in Phase 3 studies fail to provide supporting evidence for regulatory approval, and the attrition rate is even higher for novel, first-in-class drug candidates."[46]

The most expensive activity, a Phase 3 trial for malaria vaccines, may cost $50 million-$100 million or more, but the social and financial return on investment in a licensed vaccine would be significant. The failure rate for anti-parasitic vaccines is unknown, as none are yet commercially available. This is because parasites are highly complex organisms, often having hundreds of times the antigenic targets[47] of viral and bacterial organisms against which vaccines have been successfully developed.

These examples illustrate not only malaria-specific research costs, but also that progress is being made. Malaria research is a complex field, and the speed and success rate of scientific advances are largely dependent on available funding.

46 Korn, D., and Stanski, D., eds.,"Drug Development Science - Obstacles and Opportunities for Collaboration Among Academia, Industry and Government," Center for Drug Development Science at UCSF, 2005.
47 Hooks, C., 2004, "Clinical Trials: Crucial Steps on the Road to a Malaria Vaccine," Malaria Vaccine Initiative

IV GLOBAL COMMITMENT TO COMBATING MALARIA

A child dies from malaria every thirty seconds, and malaria fatalities increased in the last two decades of the 20th century. A variety of factors has driven the growing burden of malaria, including increased resistance to once-effective drugs and insecticides, and poor or deteriorating public health systems in many nations.

The international community has repeatedly emphasized that addressing malaria is essential to African and global development, as evidenced by:

- Adoption of a UN Millennium Development Goal to halt and begin to reverse the incidence of malaria and other major diseases by 2015;
- Formation of the Roll Back Malaria Partnership to halve the burden of malaria by 2010;
- Creation of the Global Fund to Fight AIDS, Tuberculosis and Malaria, with promises of hundreds of millions of dollars per year to implement existing malaria interventions;
- Establishment of the Multilateral Initiative on Malaria to raise the profile of malaria, particularly the need for research capacity building and increased malaria R&D.

Without a doubt, there is great demand for improved malaria control—from better use of existing tools to the creation and effective implementation of new ones. This report estimates that annual investment across all areas of malaria R&D totaled $323 million in 2004. It goes on to suggest that this amount is perhaps one-tenth what it should be relative to disease burden. The international community will need to increase funding significantly if it is to live up to its commitments and meet the challenge of malaria.

Fortunately public and private investments are increasing, which along with creative financing mechanisms should assist the international community in meeting its commitments. Evidence of increases in investments include the following:

- Public-private partnerships focused on malaria R&D have been formed and are playing catalytic roles in securing and managing funds while taking a portfolio approach to product development;
- Governments are committing new resources to malaria R&D, with the United States continuing to provide a large share of intramural and extramural funding;
- The Bill & Melinda Gates Foundation has become a significant donor in malaria R&D, disbursing over $77 million in 2004;
- New financing mechanisms are being explored, including the creation of a research fund for neglected diseases and advance-purchase commitments to guarantee the purchase of needed products when developed.

And there is evidence that the R&D pipeline will produce the tools it promises, including long-term solutions for combating malaria:

- The WHO Initiative for Vaccine Research listed 23 types of malaria vaccines in various stages of development in its April 2005 vaccine R&D status report;[48] and an MVI-supported clinical trial in Mozambique demonstrated that a malaria vaccine can reduce the risk and severity of malaria in young children;[49]
- MMV reported that it has over 20 drug discovery and development projects in its portfolio as of 2005,[50] and the Drugs for Neglected Diseases Initiative (DNDi) has two fixed-dose Artemisinin-based Combination Therapies in Phase 3 clinical studies;

48 WHO Initiative for Vaccine Research website, **http://www.who.int/vaccine_research/documents/en/Status_Table_April05.pdf**, accessed August 18, 2005
49 Alonso P, Sacarlal J, Aponte J et al. Efficacy of the RTS,S/AS02A vaccine against Plasmodium falciparum infection and disease in young African children: randomised controlled trial. Lancet. 2004; 364: 1411-20.
50 **Medicines for Malaria Venture website, http://www.mmv.org/rubrique.php3?id_rubrique=11**, accessed August 18, 200551

- NetMark, a USAID-funded PPP, partnered with industry to develop a process for the mass treatment of bednets with long-lasting insecticide at the factory instead of by the end-user.[51]
- More convenient and rapid diagnostic tests are becoming commercially available, and their use is steadily increasing. Improved diagnostic tests contribute toward drug conservation and appropriate treatment, and can therefore curb the growth of resistance.

These and other advances in malaria R&D represent real progress, but their momentum and prospects for ultimate success will be undercut without adequate financial resources to support them. Despite its impact on life, health, and economic development, malaria has long been a neglected disease. While further study is needed to reasonably estimate how much malaria R&D funding is needed, it is clear that current funding is not in line with the size of the problem, and that significantly more support will be required.

51 **http://www.netmarkafrica.org/news/New%20LLIN%20Tech.html**, accessed October 7, 2005

APPENDIX A: METHODOLOGICAL DETAILS

The challenges of tracking the investments made across the globe in malaria research and development include: identifying the proper parties to contact; defining what is meant by malaria R&D; clearly defining terms and data requirements (e.g. disbursements versus commitments); securing responses; reconciling different fiscal years and multiple currencies, and avoiding double-counting. Specific details on the study methodology follow.

Conducting the Survey

The survey was administered online, with web links and unique identification codes e-mailed to more than 150 organizations in May 2005. The survey response period lasted nine weeks. Securing responses required significant follow-up, with most efforts focused on 50 entities presumed to be large contributors to malaria R&D.

The survey contact list was initially created by the Malaria R&D Alliance, and refined through literature review, interviews with experts in the field, and contact tracing. Many organizations were called to secure current contact information for potential survey respondents. An iterative process was followed to refine the list.

Analyzing the Results

Data were rigorously checked for accuracy throughout the survey administration and analysis. Any issues were highlighted to respondents, in order to resolve questions and ensure accurate data capture. A number of topics pertaining to data analysis are highlighted below.

- **Fiscal Years**

Organizations employ different fiscal years, so it was necessary to adopt a standard convention to address this issue. Survey respondents generally submitted data based on the fiscal year of their organization, rather than the calendar year. For such organizations, the data were grouped into the calendar year with which it shared the most months. For example, the fiscal year FY ‘04 running from October 31, 2003 to September 1, 2004 is associated with 2004 for this survey.

- **Fiscal Data**

Annual investment refers to original source funds disbursed by the donor and funding community, including self-funding of intramural research (e.g. by NIH and the private sector). In order to avoid double-counting, funds received by a wide variety of funding managers and R&D organizations were not counted in the annual global investment figure. They were tracked for cross-referencing and data integrity purposes, and to assist in determining investment categorization.

Occasionally, survey respondents reported receiving significant funding from donor organizations that did not respond to the survey. When such funding exceeded $250,000, the funds were classified as original funding and were included in the total investment figure.

Annual investment is calculated from the perspective of the original funding organizations. For example, a grant disbursed by a donor in 2004 is included in total 2004 annual investment, even if the recipient organization did not fully utilize the funds in 2004.

Disbursement data were requested of all donor and funder organizations, as disbursements give the most accurate picture of actual funds made available to conduct malaria R&D in any given year. The survey team worked closely with organizations to secure disbursement data whenever possible.

Because of information or accounting system limitations, some organizations could not provide actual disbursement data. These organizations generally provided budget data instead of disbursements. In most such cases, verification was received that budget data were a good proxy for actual disbursements.

Financial Terms Definitions

Disbursement [52]	The release of funds to, or the purchase of goods or services for a recipient; by extension, the amount thus spent. Disbursements record the actual transfer of financial resources, or of goods or services valued at the cost of the donor.
Commitment	A firm obligation, expressed in writing and backed by the necessary funds, to provide specified assistance to a recipient. Commitments are generally recorded in the full amount of expected transfer, irrespective of the time required for the completion of disbursements.
Budget	A detailed financial plan of activities and programs expressed in terms of assets, liabilities, revenues and expenses, for a specific period.
Receipts	The funding actually received from another organization. A disbursement by a grantor should correspond with a receipt by a grantee.

Of the 79 survey respondents, only three made final submissions of 2004 commitment data, and only one of these three contributed original source funding (the European Commission). Financial commitments are valuable to track, but provide different information than was sought in this survey, as they are often disbursed over many years, and at times are not fully disbursed as originally planned. For these reasons, commitment data are not included in total R&D investment calculations.

All funding attributed to the EC in the surveys of recipients was counted in total investment calculations. The EC total investment figure encompasses disbursements reported by the EuropeAID Cooperation Office, as well as 2004 receipts credited to the EC by other survey respondents.

- **Data Adjustments**

Foreign currencies were converted to US dollars based on the 2002, 2003, and 2004 average annual exchange rates as reported in the *World Factbook 2005*.[53] To compare R&D funding across years in terms of constant dollars, the US Department of Commerce's biomedical research and development price index was employed. This index is based on NIH data, and was used in making annual inflation adjustments. The Bureau of Economic Analysis of the US Department of Commerce developed and maintains the index, which is available through the NIH website.[54]

52 Disbursement and commitment definitions adapted from OECD glossary, see: **http://www.oecd.org/glossary/0,2586,en_2649_33721_1965693_1_1_1_1,00.html#a**, accessed on August 5, 2005

Limitations of the Study

Potential limitations associated with the survey and data include:

- **Non-response:**

Some malaria R&D funding may not have been captured, either because organizations were not included in the survey distribution list or because completed surveys were not received from organizations. The study did not secure participation from several notable organizations that may be funding malaria R&D including government and research agencies in France and Australia.

- **Double-counting:**

Every effort has been made to avoid double-counting, but given the complex funding flow in malaria R&D, the possibility remains that some funds were attributed to more than one organization.

- **Incorrectly reported data:**

Organizations could have made errors compiling data or entering information in the survey instrument. The survey team reviewed and analyzed all data, and some items were clarified or corrected through dialogue with respondents. Ultimately though, the only data analyzed and included in the survey results were the data received from respondents.

- **Inconsistently classified data:**

A glossary of terms and detailed instructions were included in the survey instrument, but terms and instructions could still be misinterpreted, leading to the possibility of misclassified data. Difficulty also could arise in assigning malaria versus non-malaria research, especially where multiple diseases are studied or basic or fundamental research is the focus.

- **Type of financial data provided:**

In order to estimate annual investment in malaria R&D, disbursement data were requested, and disbursement data were generally provided. Some organizations provided budget data as a proxy for disbursement data, and the possibility exists that deviations from the budget occurred. Only one donor organization submitted 2004 commitment data. Funds submitted as commitments were only included in total investment calculations when actual disbursement of the funds was verified through recipient surveys, although this could result in the undercounting of some actual disbursements.

- **Confidentiality concerns:**

Private sector companies do not often report internal financial data, and some organizations may not have responded because of concerns about data confidentiality. To encourage pharmaceutical and biotechnology companies to submit data, a policy was adopted of aggregating their responses for reporting purposes; no individual company financial data will be shared.

- **Valuation of in-kind and intramural contributions:**

In-kind contributions are the donation of goods and services, rather than cash. Intramural funding originates within an organization for activities carried out within the bounds of the organization. Such contributions can be challenging to consistently value. When disbursement data for such contributions could not be provided, survey respondents were instructed to value goods at the fully allocated budgeted expense of such goods, and to

53 Central Intelligence Agency, *The World Factbook 2005*, **http://www.cia.gov/cia/publications/factbook/index.html**, accessed on August 3, 2005

54 See NIH Office of Science Policy & Planning website, **http://ospp.od.nih.gov/ecostudies/brdpi.asp**, accessed September 7, 2005

value personnel services based on the number of full-time equivalent workers multiplied by an average wage-plus-benefits figure.

- **Fiscal year differences:**
Categorizing fiscal year data into the calendar year with which it shares the most months is common practice but can create some data anomalies. For example, it is theoretically possible that a disbursement on a particular date by a donor could be recorded as a receipt by an R&D organization on the same date, but in a different fiscal year.

- **Time lags in the funding process:**
Given the complex funding flow in malaria R&D, it cannot be expected that a donor's grant will always be recorded as a receipt by an R&D entity in the same fiscal year, a factor that make complete cross-referencing of annual data challenging. Many donors make large grants to funding managers, who in turn make grants to multiple R&D entities; hence, months can elapse between original donor disbursement of funds and receipt by R&D organizations.

- **Limitations of using data primarily from one year:**
Analyzing multiple years of data, when possible, is preferable to reviewing a single year's information, as considerable variation in funding and R&D categorization is possible across years.

- **A first snapshot in time:**
The malaria R&D funding survey is a new instrument. The Malaria R&D Alliance recognizes that such an effort can increase in accuracy through future iterations.

APPENDIX B: SURVEY RESPONDENT LIST

The following organizations responded to the 2005 Malaria R&D Funding Survey:

- Africa Malaria Network Trust, Tanzania
- Albert Einstein College of Medicine, USA
- Amani Medical Research Centre, Tanzania
- Australian Army Malaria Institute
- BHP Billiton, Australia
- Bill & Melinda Gates Foundation, USA
- Biotechnology Center, University of Yaoundé, Cameroon
- CSL Limited, Australia
- Drugs for Neglected Diseases Initiative, Switzerland
- Ellison Medical Foundation, USA
- EuropeAID Cooperation Office
- European & Developing Countries Clinical Trials Partnership, the Netherlands
- European Commission, Belgium
- European Malaria Vaccine Development Consortium
- European Malaria Vaccine Initiative
- ExxonMobil Foundation, USA
- Fogarty International Center, USA
- Foundation for Innovative New Diagnostics, Switzerland
- Foundation for the National Institutes of Health, USA
- Genvec, USA
- GlaxoSmithKline, UK
- Howard Hughes Medical Institute, USA
- Institute for OneWorld Health, USA
- Institute of Tropical Medicine, Belgium
- Institute of Tropical Medicine, Brazil
- International Clinical Epidemiology Network
- John D. and Catherine T. MacArthur Foundation, USA
- Johns Hopkins Malaria Research Institute, USA
- Kenya Medical Research Institute
- Kintampo Health Research Center, Ghana
- London School of Hygiene & Tropical Medicine, UK
- Malaria Research Center, India
- Malaria Vaccine and Drug Testing Center, Colombia
- Maxygen, USA
- Medical Research Council, UK
- Medicines for Malaria Venture, Switzerland
- Multilateral Initiative on Malaria, Sweden
- National Center for Research Resources, USA
- National Heart, Lung, and Blood Institute, USA
- National Institute For Medical Research, Tanzania
- National Institute For Medical Research, UK
- National Institute of Allergy and Infectious Diseases, USA
- National Institute of Child Health & Human Development, USA
- National Science and Technology Development Agency, USA
- Netherlands Ministry for Development Cooperation
- Pan American Health Organization
- PATH Malaria Vaccine Initiative, USA
- Pfizer, USA
- Research Initiative on Traditional Antimalarial Methods, UK
- Rockefeller Foundation, USA
- Roll Back Malaria Partnership
- Royal Tropical Institute, the Netherlands
- Sir Dorabji Tata Centre for Research in Tropical Diseases, India
- South African Medical Research Council
- Special Programme for Research and Training in Tropical Diseases, Switzerland
- St. George's Hospital Medical Schools, UK
- Sudanese Environment Conservation Society
- Swedish Research Council
- Swiss Agency for Development & Cooperation
- Swiss Tropical Institute
- Tropical Diseases Research Center, Zambia
- Tropical Medical Research Institute, Sudan
- United Kingdom Department for International Development
- United States Agency for International Development
- United States Centers for Disease Control and Prevention
- United States Department of Defense Military Infectious Disease Research Program
- University of Buea Faculty of Health Sciences, Cameroon
- University of Ibadan College of Medicine, Nigeria
- University of Khartoum, Institute of Endemic Diseases, Sudan
- University of Mississippi, USA
- University of Nebraska, USA
- University of North Carolina, USA
- University of Pennsylvania, USA
- University of Washington, USA
- Walter Reed Army Institute of Research, USA
- Wanxing Biopharmaceuticals, China
- Wellcome Trust, UK
- World Bank
- World Health Organization: Initiative for Vaccine Research
- World Health Organization: Roll Back Malaria Department
- Yale University, USA

APPENDIX C:
ADDITIONAL DONORS IDENTIFIED IN SURVEYS

The following organizations were not survey respondents but were identified in recipient surveys as having provided over $250,000 of 2004 malaria R&D funding. Such funds were counted in the 2004 total investment calculation. The contributing organizations are listed below:

- Anonymous Supporter of Johns Hopkins Malaria Research Institute
- Australian Government
- Belgian Ministry of Development Cooperation
- Business Trust of South Africa
- Department of Health of South Africa
- Global Fund to Fight AIDS, Tuberculosis and Malaria
- UK Health Protection Agency
- Médecins Sans Frontières
- Ministry of Foreign Affairs of Denmark
- Ministry of Health of Mozambique
- Ministry of Interior of Switzerland
- Miscellaneous Contributors to TDR
- Swiss National Science Foundation

APPENDIX D:
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APPENDIX E:
DETAILED EXPLANATION OF R&D FUNDING CATEGORIZATION

For the purposes of this study, malaria R&D includes all activities using scientific approaches to further advance the understanding of the malaria disease, parasites, and vectors, and research on how to turn this knowledge into innovations and control measures. Survey respondents have been asked to classify funding into six general categories, which have been further broken down into 16 subfields for informational purposes.

Detailed descriptions of the subfields comprising the categorization system are provided below.

I Basic Research

1 Immunology
- Signaling pathways of immune function (cellular immunity – cytokines and T-cell receptors).
- Determining interaction and impact of the signaling pathways with the malaria parasite, and develop assays potentially useful for vaccine development. Identification of correlates of protection. This includes in vivo and in vitro studies on the protective immune response (cellular and humoral) of the mammalian response to malaria by investigating the immune response to particular antigens, population studies of human immunity to malaria and the effects of antimalarial drug treatment on immune status.
- Studies on the genetics of the immune response to malaria.

Excluding: Vaccine development and Human vaccine trials (see III). Epidemiology studies of the effects of specific host genotypes on malaria transmission and prevalence (see VI). Biochemical characterization of vaccine candidate proteins (see III).

2 Biology of Plasmodium
- Structure and morphology of different developmental stages. Host–parasite interactions. Biology of invasion of host cells. Localization of parasite proteins or antigens.
- Culture of parasites.
- Purification of parasites or parasite stages.
- Descriptions of species of *Plasmodium* and characterization of malaria strains in animal models (course of infection, susceptibility of different hosts).
- Studies on rosetting, sequestration and adhesion of infected erythrocytes in which pathological consequences are not examined.
- In vitro studies of interactions between *Plasmodium* and other infectious agents (e.g. EBV).

3 Biochemistry of Plasmodium
- Metabolism and nutrition.
- Enzymology.
- Translation, processing and export of proteins.
- Protein sequences, protein and enzyme characterization (including antigen analysis).
- Glycosylation, GPI anchors, transporters, ion channels, mitochondrial metabolism, electrophysiology studies. Influence of parasite on host-cell biochemistry.
- Characterization of antigen/protein diversity in strains of *Plasmodium*.
- Characterization of proteins involved in sequestration and rosetting of infected erythrocytes and of molecular basis for host-cell invasion.

4 Genetics of Plasmodium
- Studies on chromosomes. Genomic maps.
- Genetic crosses.
- Cloning and sequencing of genes/cDNAs for functional Plasmodial proteins (including drug targets and vaccine candidates).
- Expression of proteins from cloned genes. RNA analyses.
- Control and timing of expression of genes.
- Post-transcriptional processing.
- Genetics of antigenic variability.
- Techniques for the genetic transformation of *Plasmodium*.
- Studies of genetic diversity and phylogeny.
- Tests for genotyping *Plasmodium*.

Excluding: Epidemiology of antigenic variability (see VI). Diagnostic tests for detection of malarial parasites (see V).

5 Bioinformatics and proteomics related to malaria
- Microarray analysis.
- Genome annotation – gene predictions.
- Comparative genomics.
- Variation (SNPs).
- Database applications.
- Data mining tools – improve the interface for the community.
- Structural and functional genomics.
- Proteome analysis.
- Structural and functional proteomics.

6 Pathophysiology and disease symptoms of malaria
- Clinical diagnosis of malaria and clinical observations of the disease presentation and pathophysiology of malaria in humans and in animals (e.g. observations on cerebral malaria, malaria during pregnancy, mild malaria).
- Interactions between malaria and other concurrent infections.
- The role of nutritional status in determining disease severity.
- Histopathology of malaria in humans and in animals.
- The mechanisms of pathology in malaria, including the role of the host immune system, expression of adhesion molecules etc.
- Studies of the mechanisms by which particular susceptible/resistant mammalian host genotypes exert their effect.
- Research on anemia.
- Neurological effects of malaria.

Excluding: Epidemiological studies of malaria prevalence in relation to human genotype (see VI).

II Antimalarial Drug Discovery and Development

7 Antimalarial drug discovery and development in vitro and in animal models
- Target identification.
- Measurement of the activity of potential antimalarial drugs in animal models and in vitro models of malaria.
- Antimalarial drug pharmacokinetic, toxicity and metabolism studies in vitro and in animal models.
- Chemistry and synthesis of antimalarial drugs.
- Analytical tests for assaying antimalarial drugs.
- High throughput screening.
- Research on drugs from Natural Products.

Excluding: Effects of drugs on immune status (see I).

8 Mechanisms of drug action

- The biochemistry of drug action on *Plasmodium*.
- The mechanisms of parasite resistance to antimalarial drugs.
- Analysis of genes involved in drug resistance.
- Characterization of drug-resistant strains of *Plasmodium*.
- Tests for drug susceptibility of parasites.

Excluding: Epidemiology of drug resistance (see VI).

9 Clinical management of malaria and antimalarial drug trials

- Antimalarial drug pharmacokinetic, toxicity and metabolism studies in humans.
- Trials of antimalarial drugs and combinations of drugs in human malaria patients to establish efficacy.
- Drug treatment and prophylaxis recommendations.
- Development of drug treatment regimens for particular clinical presentations of malaria (e.g. severe malaria, cerebral malaria or malaria during pregnancy, drug-resistant malaria).
- Development of intermittent preventative treatment
- Case history reports and studies of antimalarial drug side effects.

Excluding: Studies of social factors influencing drug treatment and compliance. Assessment of long-term prophylaxis in communities in endemic areas. Health service research (see VI). Studies on drug-resistant strains of *Plasmodium* (see VI).

III Vaccine Development and Vaccine Trials

10 Vaccine Development

- Studies of specific antigens proposed as vaccine candidates, manufacturing scale-up and consistency of manufacture.
- Pre-clinical safety and immunogenicity studies with candidate vaccines, including use of functional assays.
- Pre-clinical challenge models.
- Effect of antigen polymorphism – genotyping of breakthrough parasites from field studies.
- Studies of adjuvants or carrier systems for malaria vaccines, and studies on the genetics of the immune response to selected antigens as malaria vaccine candidates.
- Trials of antimalarial vaccines in humans to establish safety and efficacy.
- Reviews on the status of antimalarial vaccine development.

Excluding: Immunology research that is potentially useful for vaccine development (see I).

11 Human vaccine trials

- Clinical development: Phase 1a safety/dosing/immunogenicity in less than 100 volunteers(cumulative); Phase 1b safety/dosing/immunogenicity in a malaria-exposed population Phase 2a challenge studies; Phase 2b for preliminary efficacy in a malaria-exposed population in several hundred volunteers; Phase 3 for expanded efficacy, effectiveness and safety studies in thousands of volunteers, depending on multiple factors.

Excluding: Preliminary studies of malaria morbidity and mortality in vaccine study area (see VI).

IV Vector Control Research

12 Vector biology, biochemistry and genetics.

- Studies of vector susceptibility to infection by *Plasmodium*, genetic transformation of vectors, insect transposable elements, genetics of insecticide resistance, tests for vector identification, taxonomy and systematics.
- Development of tests for the identification of *Plasmodium*-infected mosquitoes.
- Characterization of mosquito behavior and ecology.
- Studies of parasites and pathogens of mosquitoes, including those which might be applied as biological control agents.

Excluding: Studies primarily on biology of parasite interaction with mosquito host (see I). Studies in which the epidemiology and behavior of vectors is specifically related to the transmission of malaria (see VI). Field testing of mosquito control measures (see VI).

13 Vector Control Product Development

- Development of products in controlling mosquito populations including insecticides and insecticide related products.
- Development of products that prevent mosquitoes contact with human.
- Development of products that control the mosquito population.

V Development of Malaria Diagnostics

14 Diagnostic tests for the detection and identification of malarial parasites in humans

- ELISAs.
- DNA probes.
- PCR tests.
- Novel microscopy tests.

Excluding: Application of these tests in epidemiology studies (see VI). Tests for genotyping parasites (see I).

VI Implementation Research

15 Epidemiology of malaria prevalence and severity, and mathematical modeling

- Epidemiology of the distribution of species of malarial parasites and mosquito vectors, and of the prevalence of morbidity and mortality due to malaria.
- Studies of the biological, environmental, social and economic determinants of malaria transmission dynamics and of malaria prevalence (e.g. roles of human behavior; vector behavior, ecology and epidemiology; inoculation rates, host genetic factors, *Plasmodium* strain variation etc.).
- Epidemiological studies of genetic factors influencing the prevalence of malaria, including sickle cell genes, thalassaemia, HLA type etc.
- The impact of malaria on selection for particular host genotypes.
- Epidemiology of resistant/susceptible strains of *Plasmodium* to antimalarial drugs and of mosquito vectors to insecticides.
- Mathematical modeling of malaria (e.g. of malaria transmission and of human immune response to malaria).

Excluding: Studies on the mechanisms by which specific mammalian host genotypes influence host immunity or pathology (see I). Studies of vector ecology and behavior which are not in the context of transmission (see IV).

16 Intervention trials and health services research

- Trials to test commercially available measures for the control of mosquito vectors (bednets, environmental and biological control measures, insecticides etc.) and to test other interventions, administered through health care services etc., for the control of malaria morbidity and mortality in communities (e.g. drug treatment and prophylaxis).
- Studies of community attitudes, knowledge and practice in relation to malaria treatment and control programs.
- Health care service studies in relation to delivery of malaria treatment and control measures.
- Design of treatment and control programs appropriate to local prevailing conditions.
- Implementation and evaluation of large-scale malaria treatment and control programs operated through health care services, government ministries, nongovernmental organizations etc.
- Operational research.
- Economic impact of malaria morbidity and mortality on communities and the economics of malaria control measures.

Excluding: Clinical trials of drugs or vaccines to establish safety and efficacy (see II or III).

Capacity Building for Malaria Research and Development in Malaria-Endemic Countries

Capacity Building

- Building academic research capacity.
- Improving existing academic capacity.
- Providing training opportunities.
- Strengthening R&D institutional capacity.
- Preparing existing and future sites for clinical trials for product development.
- Ensure that research findings are translated and applied.

Excluding: Major infrastructure development

A definition for capacity building for research has been included, but this is not one of the six general categories. Capacity building is not research in itself, yet capacity building in malaria endemic-countries is important and has become a new focus of funds over the past decade. These funds aim to promote human resources and institutional capacity in the countries most affected by malaria to ensure that research results can be translated into policies and practices. In the survey, respondents were asked to allocate malaria R&D capacity building funds into whichever of the general categories best describes the research use of those funds. In addition, respondents were also asked to indicate how much of their total malaria R&D funding was dedicated to capacity building for malaria R&D.

Malaria R&D Alliance is an alliance of malaria research and development organizations jointly advocating for global commitment for increased and sustained investment for malaria R&D. Goals of the alliance are to raise awareness about malaria and the critical need for R&D to combat the disease.

www.MalariaAlliance.org

Malaria R&D Alliance