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กระทรวงสาธารณสุข
ถนนติวานนท์ จังหวัดนนทบุรี 11000

19 กันยายน 2550

เรื่อง การสนับสนุนงบประมาณให้กับองค์กร Medicines for Malaria Venture (MMV)

เรียน เลขาธิการคณะรัฐมนตรี

สิ่งที่ส่งมาด้วย สำเนาเอกสารข้อเสนอโครงการต่อประเทศไทยขององค์กร Medicines for Malaria Venture (MMV) จำนวน 70 ชุด

ตามที่องค์กร Medicines for Malaria Venture (MMV) มีหนังสือขอเงินสนับสนุนจากรัฐบาลไทย เพื่อการวิจัยและการพัฒนายาชนิดใหม่สำหรับโรคมาลาเรีย รวมถึงการเข้าถึงและการจัดส่งยา ใน 30 ประเทศทั่วโลก ทั้งในทวีปยุโรป อเมริกา เอเชีย และแอฟริกา จำนวนเงินปีละ 500,000 ดอลลาร์สหรัฐฯ เป็นระยะเวลา 5 ปี ตั้งแต่ปี พ.ศ. 2551 - 2555 (2008 - 2012) รวมเป็นจำนวนเงินทั้งสิ้น 2.5 ล้านดอลลาร์สหรัฐฯ องค์กร MMV เป็นองค์กรที่ไม่หวังผลกำไร ก่อตั้งเมื่อปี พ.ศ.2548 (1999) เพื่อทำการพัฒนายาต้านมาลาเรีย และก่อสร้างระบบการจัดส่งยาที่ยั่งยืนในประเทศที่โรคมาลาเรียระบาด ซึ่งการเข้าถึงการรักษาในประเทศเหล่านั้นเป็นไปอย่างอยากลำบาก โดยตั้งเป้าหมายหลัก ดังนี้ (1) ลดค่ารักษาโรคมาลาเรียให้เหลือ 1 ดอลลาร์สหรัฐฯ หรือน้อยกว่านั้น เพื่อให้มั่นใจว่าประชากรในประเทศที่โรคมาลาเรียระบาดจะเข้าถึงการรักษา (2) พัฒนายาที่มีความเสี่ยงต่อเด็กและสตรีมีครรภ์ และ (3) นานาชาติให้การอนุมัติ artemisinin-based combination therapies (ACTs) ตัวใหม่อย่างน้อย 3 ตัว ภายในปี พ.ศ. 2553 (2010) โดยยาตัวแรกจะสามารถใช้ได้ในปี พ.ศ. 2551 (2008) ทั้งนี้ ได้ประสานให้กรมควบคุมโรค และกรมวิทยาศาสตร์การแพทย์พิจารณาให้ความเห็นในเรื่องดังกล่าวด้วยแล้ว นั้น

การนี้ กระทรวงสาธารณสุขพิจารณาแล้ว เห็นสมควรให้การสนับสนุนเงินแก่องค์กรดังกล่าว เนื่องจากประเทศไทยจะได้รับผลประโยชน์โดยตรง เนื่องจากไทยเป็นแหล่งเกิดเชื้อดื้อยามาลาเรียที่สำคัญ ซึ่งการศึกษาวิจัย จะเป็นการเตรียมความพร้อมเพื่อรับมือกับปัญหาดังกล่าว ซึ่งต้องใช้งบประมาณและบุคลากรสาธารณสุขเป็นจำนวนมาก นอกจากนี้ จะเป็นการแสดงจุดยืนของประเทศไทยในการสนับสนุนการวิจัยด้านมาลาเรียในระดับโลก จึงเห็นควรพิจารณาให้เงินสนับสนุนองค์กรดังกล่าวเป็นจำนวนเงิน 100,000 ดอลลาร์สหรัฐฯ

จึงเรียนมาเพื่อโปรดพิจารณา หากเห็นชอบ ขอได้โปรดนำเสนอเข้าที่ประชุมคณะรัฐมนตรีเพื่อพิจารณาให้ความเห็นชอบในการให้เงินสนับสนุนแก่ Medicines for Malaria Venture (MMV) จำนวน 100,000 เหรียญสหรัฐฯ โดยใช้งบประมาณกระทรวงสาธารณสุข จะเป็นพระคุณ

ขอแสดงความนับถือ

(นายมงคล ณ สงขลา)
รัฐมนตรีว่าการกระทรวงสาธารณสุข

สำนักงานปลัดกระทรวงสาธารณสุข
สำนักการสาธารณสุขระหว่างประเทศ
โทร 0 2590 1366
โทรสาร 0 2590 1374, 0 2591 8562

MMV Proposal to the Government of Thailand

Grant title	For research and development of new medicines in the domain of malaria, and the facilitation of their access and delivery
Proposal Date	25/06/2007
Project Title	New Antimalarial Drug Research & Development Portfolio
Organization Name	MMV - Medicines for Malaria Venture
Project Dates	2008 - 2012
Project Duration	60 months
Proposal	$ 500'000 per annum $2.5 Million over 5 years: Drug R&D Portfolio with Access & Delivery
Geographic Locations	Switzerland, USA, UK, S. Korea, India, Australia, Spain, Italy, Canada, Belgium, France, Colombia, Thailand, China, Laos, Cambodia, Indonesia, Singapore, S. Africa, Tanzania, Zanzibar, Cameroon, The Gambia, Malawi, Mozambique, Uganda, Kenya, Senegal, Burkina Faso, Zambia

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Proposal prepared by Peter Potter-Lesage **Date Submitted:** *25/06/2007*

Medicines for Malaria Venture

CONTENTS

1. Executive Summary

Today, more people are dying of malaria than a decade ago. Malaria's burden persists primarily in Africa where nearly 90% of the estimated 1-3 million annual deaths occur. Children and pregnant women are most vulnerable. In fact, malaria is the biggest killer of children under five - one child dies every 30 seconds. Of the 3.2 billion people at risk worldwide from this deadly disease 300-600 million are infected every year. Malaria is also returning to many regions, such as Yemen and the former Soviet countries of central Asia. Malaria perpetuates a cycle of poverty costing more than $12 billion annually in lost GDP in Africa alone.

Numerous vector control initiatives focus on the prevention of malaria through, for instance, indoor residual spraying and the use of long-lasting insecticide-treated bed nets. Each of these prevention measures is proven, relatively affordable, and increasingly available. But these tools will not always work. Both the parasite and the mosquito that transmits it have adapted rapidly to new technologies.

Over the last 50 years, the malaria parasite has gradually grown resistant to widely-used drugs, such as chloroquine, that had effectively treated the disease for decades. As a result, malaria continues to afflict millions. In Africa, the death toll continues to rise because effective drugs are inaccessible due to cost, poor health systems, inadequate distribution networks, and policy challenges.

Today, the most effective cure for malaria is artemisinin-based combination therapies (ACTs). However, with a price 10 to 30 times that of older drugs, ACTs are beyond the means of the most vulnerable families.

Continuous research and development (R&D) for new diagnostics, medicines, vector control methods and an effective vaccine for malaria are urgently needed, but this critical area has been left to generous philanthropists. Large global agencies such as the Global Fund for HIV/AIDS, TB and malaria (GFATM), and the recently created President's Malaria Initiative do not fund R&D of new health tools. They are, however, extremely effective at providing funding for vector control measures and the procurement of antimalarials. Unless public funding directed at drug research is radically increased, these global agencies will not have new drugs to distribute to malaria-endemic countries.

Medicines for Malaria Venture (MMV), a not-for-profit organization, was created in 1999 to discover, develop, and deliver safe, effective, and affordable antimalarial drugs. With the largest-ever portfolio of antimalarials drugs in development, MMV ensures that its products are developed and delivered as "public goods" to enable the greatest possible public health impact in disease-endemic countries. Effective management of resources includes negotiation around intellectual property rights (IPR). MMV wishes IP to be a driver of the drug R&D process for malaria rather than a hindrance. Moreover, each contract is signed with a provision for eventual royalties to be re-injected into the MMV's core work in research and development.

To achieve its vision, MMV will need to drive forward the discovery and development of new drugs to cure malaria and help facilitate the creation of sustainable systems to deliver them to where they are most needed –vulnerable populations in malaria-endemic countries that currently have the least access to treatment and care.

Sustained fundraising efforts have enabled MMV to raise over USD 270 million during its first 7 years of existence. A significant portion of this is in the form of bilateral support from European countries such as the UK, Ireland and the Netherlands. To achieve its vision, however, it is estimated that MMV's R&D activities still need additional commitments for 2007 to 2010 as well as considerable supplementary funding for scale-up, launch and 'access' activities. MMV's total funding gap stands at around USD 150 Million.

A contribution from the Government of Thailand in the form of non-specific core funding to MMV would help ensure the continued R&D of antimalarials. This is an opportunity for Thailand to join a group of international governmental and philanthropic funding entities in the global R&D action against malaria.

2. Overview of Medicines for Malaria Venture (MMV)

Medicines for Malaria Venture is a not-for-profit public-private product development partnership (PDP) created in November 1999. Its mission is to discover, develop and deliver new affordable antimalarial drugs through effective public-private partnerships. The long-range goal is to provide significant health and development impact in malaria-endemic countries.

MMV's goal is to

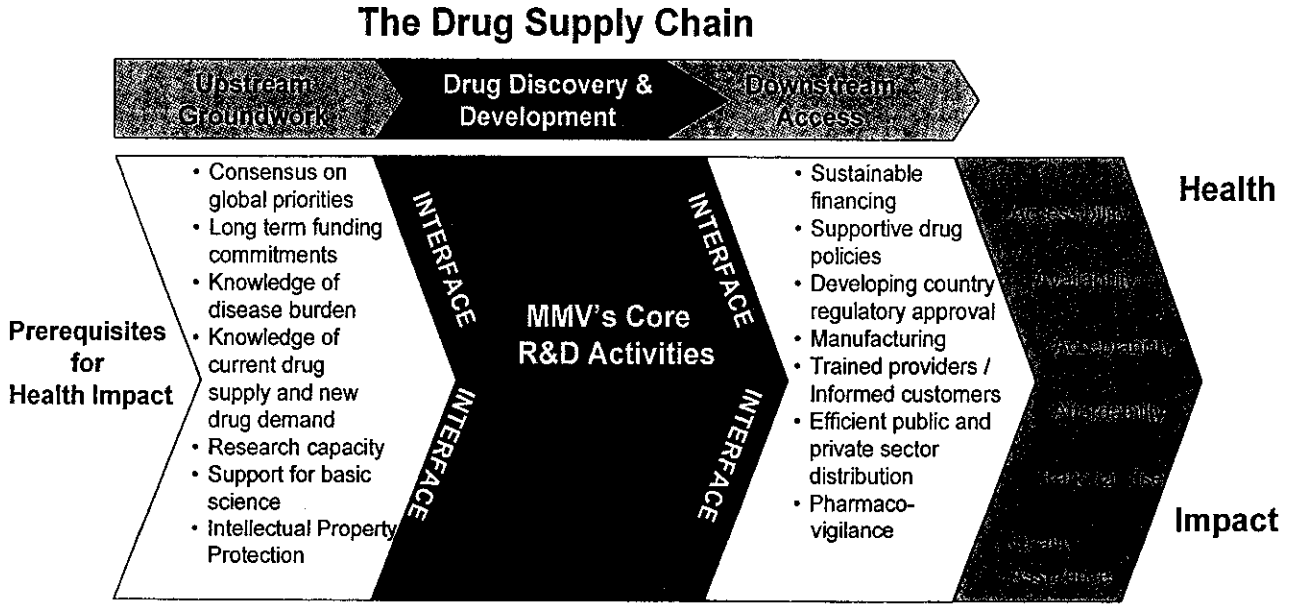
- **Develop antimalarial treatments that cost $1 or less and ensure that they reach the most vulnerable populations in malaria endemic regions**
- **Develop drugs for high risk groups such as children and pregnant women**
- **Gain international regulatory approval of at least three new ACTs before 2010. The first drug could be available for widespread use by 2008.**

MMV's ultimate goal is a one-dose cure.

MMV's Strategic Planning

MMV's initial strategy was laid out in its original 'Business Plan 2000' and then a subsequent updated version: Business Plan 2003 – 2007. The directives for MMV were as follows:

- Found a new public-private partnership to re-create a viable pipeline of new antimalarial drugs
- Apply criteria of stringent regulatory oversight and ICH guidelines
- Create a business model and philosophy akin to the commercial sector
- Engage the collaboration and support of academic and commercial pharmaceutical partners
- Hire staff, create infrastructure and forge partnerships
- Engage new stakeholders and raise funds to attain sustainability
- Grow and manage the pipeline
- Interact with global players
- Discover, develop and facilitate delivery of new drugs
- Initial expectation of one single drug (no mention of combination therapy) registered by 2010
- Initially for a total operational cost of USD 250 million over 10 years

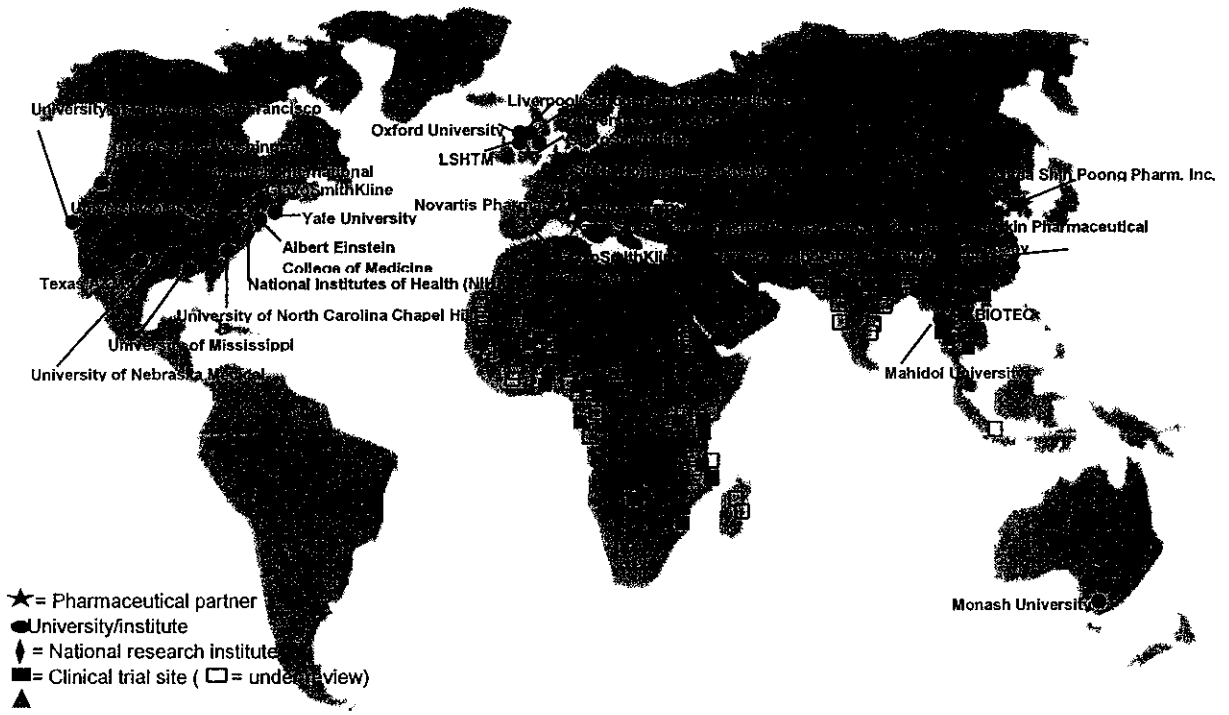


This plan has been largely executed by MMV's experienced management team. Plans however cannot always predict a changing regulatory, policy and 'best practice' environment, and several additional changes have been adopted by MMV's Executive Management Team and Board of Directors. Thus the World Health Organization's (WHO) recent recommendation of artemisinin combination therapy as the treatment of choice has been accepted and embraced, as have additional indications such as intermittent preventive treatment in early infancy (IPTi), *P.Vivax* malaria or emergency treatments. MMV is also now involved in supporting enabling technologies such attempts to improve yield from *Artemisia annua* through mutagenesis and selection – a project that recently gained its host University (York) a 'Queens Anniversary Award' as part of the National Honours system in the UK .

More important than the breadth and scope of its activities, however, is MMV's ability to execute this activity efficiently. The organisation underwent a very positive evaluation by the 'Donor Coordination Group' during 2005. The *'Independent Review of Medicines for Malaria Venture'* was commissioned jointly by the following entities: the UK Department for International Development (DFID), the Wellcome Trust, the World Bank, the Swiss Agency for Development and Cooperation, the Bill and Melinda Gates Foundation and the Netherlands Ministry for Foreign Affairs.

Working with Partners

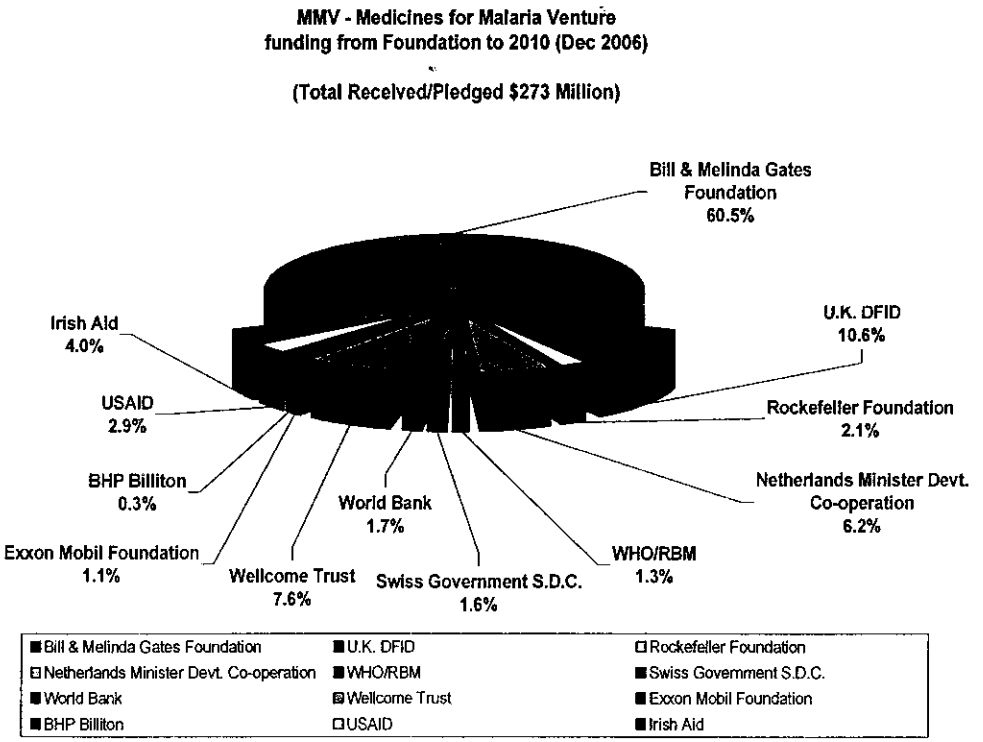
After seven years of operations MMV, together with its many partners, manages the world's largest antimalarial R&D portfolio covering the innovation spectrum from basic drug target discovery and validation projects through to advanced formulations of existing drugs.



Contractual partners in MMV's projects for 2007 include around 80 leading-edge research entities across the globe, including universities and non-profit organizations, as well as pharmaceutical/ biotech company laboratories based in India, Europe, South Korea, and North & South America.

MMV Donor Support

Unusually for a PDP, MMV has a relatively broad and credible stakeholder base. Support has been generated from 12 major governmental and philanthropic funding agencies, as can be seen in the pie chart below. Since its foundation MMV has been granted multi-year pledges of funding notably from the Bill & Melinda Gates Foundation, the United Kingdom Department for International Development, the Swiss Agency for Development and Cooperation, the Rockefeller Foundation, USAID, Irish Aid, the ExxonMobil Foundation, BHP Billiton and the Wellcome Trust with additional annual commitments from the Netherlands Minister for Development Cooperation, the World Bank.



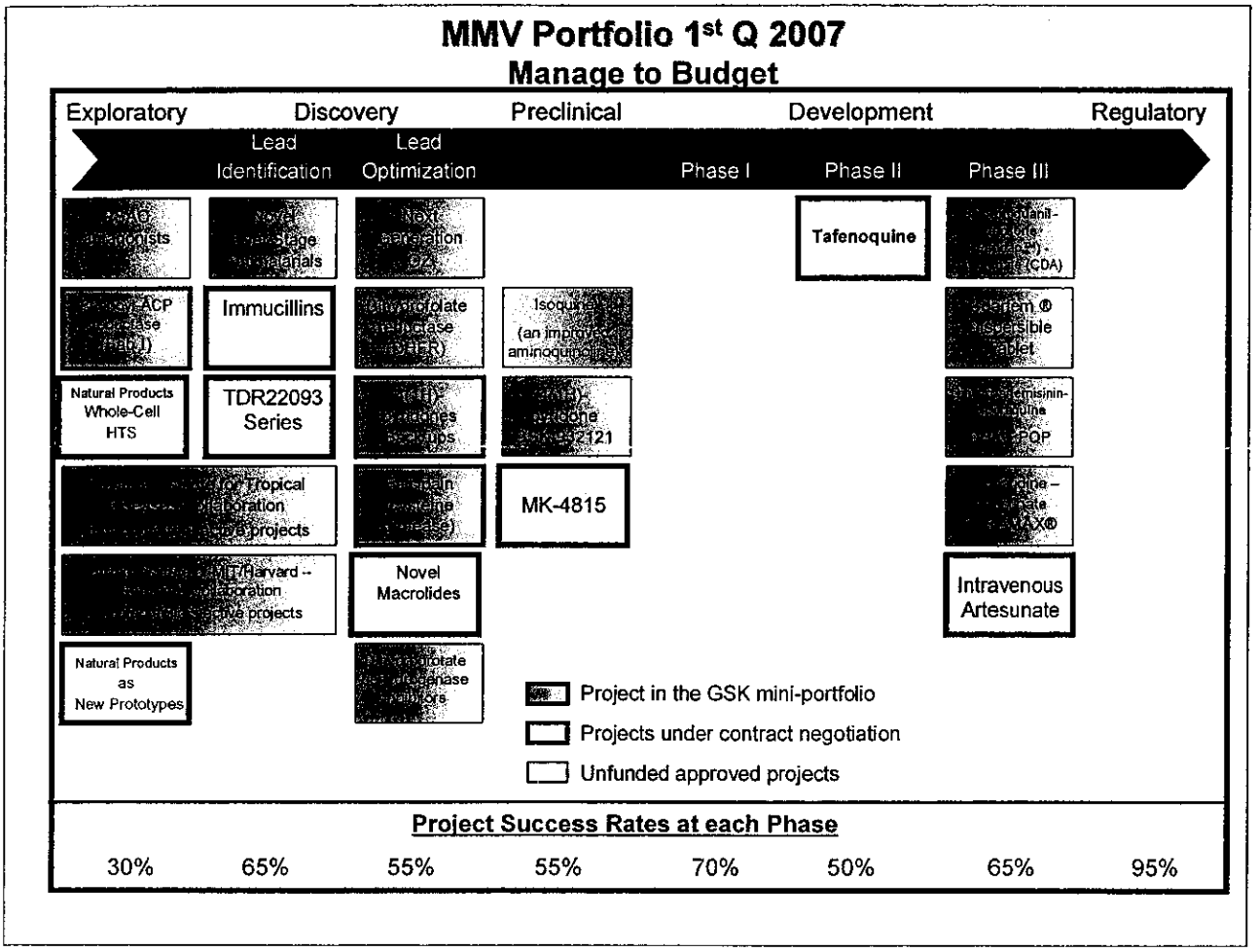
MMV's links to the WHO are strong. WHO maintains its role as an advisor to MMV, which has high regard for WHO's drug pre-qualification status. Currently, MMV is seeking and receiving valuable advice on how to conduct access and delivery activities, and the head of Roll Back Malaria-Global Malaria Partnership (RBM-GMP) is Chair of MMV's Access and Delivery Committee. The WHO, in turn, considers MMV as *"the premier public-private partnership for developing new malaria drugs."*

MMV has been fortunate that to date the funds needed to advance the portfolio have thus been made available. These grants have helped to make the MMV one of the most successful public private partnerships. MMV understands that funding is dependent on maintaining the trust of donors in our ability to produce results.

MMV manages its projects carefully to ensure adequate funds to progress them to their goals. There are, however, specific targeted actions, particularly in the areas of making funds available earlier, which will help to accelerate these projects.

Research & Development Portfolio Overview

The MMV portfolio has grown from 3 initial discovery projects in 2000 to a dynamically managed portfolio of 35 projects, including 3 mini-portfolios, and 6 projects in clinical development. (See chart below). Since the year 2000, 54 projects have been added and 19 terminated, all for scientific, financial or contractual reasons.



The present portfolio is largely directed at the priority goal of developing drugs for uncomplicated *P.falciparum* malaria with one project focused on providing a new treatment for complicated severe malaria and several others for *P.vivax* malaria. As the portfolio matures, we will need to expand our vision to better reflect the essential needs of malaria-endemic countries. This will be achieved by a much more indication-specific approach to the discovery and development of second generation drugs - for example, innovative drugs for intermittent preventive treatment for pregnant women (IPTp) or in infants (IPTi), or the highly desirable 'one dose cures' or transmission blocking drugs which, if widely used, could act at a population level.

MMV's decision to advance a project through the portfolio is based on the advice of the MMV Expert Scientific Advisory Committee (ESAC). ESAC members participate in an annual review of all projects, and make recommendations to the MMV Board concerning the continuation of funding. They also assist in reviewing and short-listing proposals when MMV has a Call for Letters of Interest.

Several drugs are currently in advanced development (See table on page 8). The first 2 dossiers will be submitted for registration by end 2007. The public sector target price for a full course of treatment with these innovative new combination therapies is 1 US dollar or less. We also hope to achieve the lowest possible private sector prices. To enable such low prices to be sustained, product competition is needed and we are poised to deliver 2 or 3 potential new combination antimalarial drugs by 2010, beginning as early as 2008.

MMV Product Profile: Anti-Malarials in Phase III Clinical Development

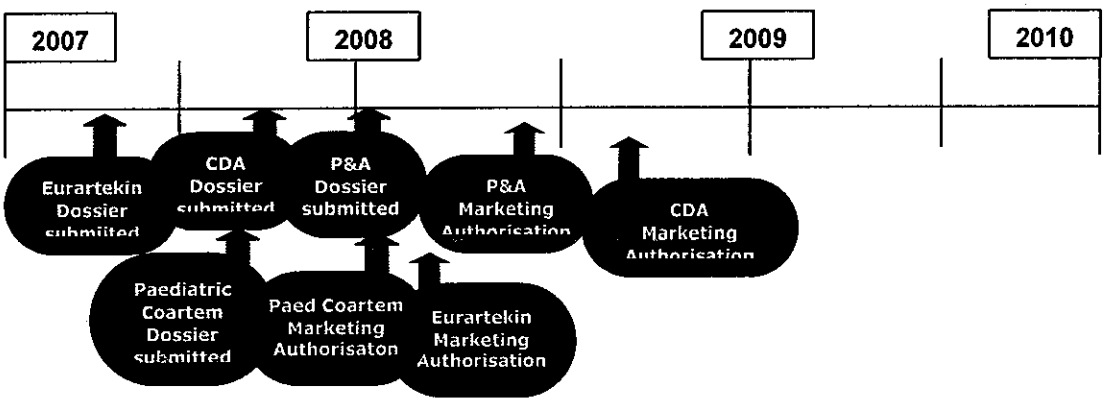
	• Should meet MMVs guidelines for Cost • ACT with a different pharmacophor	• Should meet MMVs guidelines for Cost • Potentially first drug to complete MMV pipeline	• Indicated for both *P. vivax* and *P. falciparum* • Pediatric formulation • Longer shelf life • Lower propensity for resistance	• Use for children above 5 kg • Coartem on essential drugs list • First mover advantage
	Fixed-ratio combination of chlorproguanil-dapsone (Lapdap™) with artesunate	Fixed-ratio combination of dihydroartemisinin and piperaquine	Fixed-ratio combination of pyronaridine and artesunate	Fixed-ratio combination of artemether and lumefantrine
	Uncomplicated *P. falciparum* malaria	Uncomplicated *P. falciparum* malaria	Uncomplicated *P. falciparum* and *P. vivax* malaria	Uncomplicated *P. falciparum* malaria
	Adults and children	Adults and children	Adults and children	Infants and children
	Pregnancy	Pregnancy	Pregnancy	Pregnancy
	Tablets: for adult and children and infants	Tablets: for adult and children and infants	Tablets: for adults and children Pediatric Granules: for infants	Dispersible tablet: for small children and infants
	Oral, once daily for three days	Oral, once daily for three days	Oral, once daily for three days	Oral, twice daily for three days
	Pricing depends on many factors and it cannot be known at this stage. MMV's current price guideline is that cost ≤ $1.00 per adult treatment and ≤$0.50 for a child			
	≥ 95%	≥ 95%	≥ 95%	≥ 95%
	Lapdap™ resistance in Southeast Asia	Piperaquine history in China	None	Lumefantrine in SEA
	Potential hemotoxicity (Lapdap™)	None known	None known	Artemether - hearing complications. Lumefantrine - cardiac complications
	Probably ≥2 Years	Possibly ≥2 Years	3 Years	2 Years
	UK MAA to be submitted – Q12008. Approval expected – Q1 2009. Projected launch - 2009	Planned submission to the Italian Medicines Agency – Q4 2007. Approval expected – Q2 2008. National approvals expected - Q4 2008	To be submitted to the Korea FDA and the EMEA – Q1 2008. KFDA and EMEA approval expected – Q4 2008	To be submitted to Swissmedic - 2007. Approval expected - Q1 2008.
	Phase III trials are in Burkina Faso, Cameroon, Gambia, Ghana, Kenya, Nigeria and Tanzania.	Pharmacokinetic trials in Africa. Phase III trials completed in Burkina Faso, Kenya, Mozambique, Uganda, Tanzania, Ongoing in India, Laos, and Thailand	Phase III trials initiated Senegal, Gambia, Ghana, Mozambique, Kenya, Mali, DRC, Cambodia, Indonesia, India, South Korea, Philippines, Thailand and Vietnam	Phase III trials are in Kenya, Mali, Tanzania, Zambia, and Cambodia completed 19 Jan 2007.
	GSK, Liverpool School of Tropical Medicine, LSHTM, TDR	Holley Pharmaceutical, Oxford U., Sigma-Tau	Shin Poong Pharma.	Novartis Pharma.

MMV's New Drugs in Late-stage Development

MMV's four new fixed-dose artemisinin-based combination therapies (ACTs) in Phase III clinical development are anticipated by end 2008 beginning of 2009, and aim to address a number of country-critical requirements:

- Low cost of goods: basic cost of treatment = <US$1.00 per adult, ~US$0.5 per child
- Faster cure rate: within 3 days
- Improved shelf life: up to 3 years or more
- Simplified dosing regimen (once/day)
- Paediatric formulations: safe in infants of less than 6 months
- Low propensity to generate rapid resistance

Estimated* Timeline for Registration and Use of New Products



* Timelines indicated are dependent on a number of factors and may be subject to change

All MMV development projects are executed to international Good Clinical Practices (GCP) standards as defined, for example, by the European Agency for the Evaluation of Medicinal Products (EMEA) or the United States Food and Drug Administration (FDA). Equally, all drugs are produced to Good Manufacturing Practices (GMP) standards as promulgated under European Directive 2003/94/EC or equivalent.

Public implementation in key countries will take 2-3 years due to the rather lengthy and stringent international regulatory process outlined above, as well as the time needed to meet global (WHO) policy and local policy requirements, manufacture the drug, secure finances, and ensure distribution.

MMV's Focus on Access

'Discover, Develop, Deliver' are the stated objectives of MMV. It is, however, clear that the original goal of drug registration is but the first step to ensuring 'delivery'. There are many more steps to go before we can achieve the underlying imperative of our mission, namely 'health impact'. MMV now fully accepts it will need to participate actively, on a case-by-case basis, in launch, 'marketing' and Phase IV (public health utility) trials with its partners. Moreover, these are real challenges for all the partners involved, including RBM-GMP, who have never before been faced with this potential breadth of drug choice or massive opportunity for delivery.

MMV's priorities regarding access & delivery are to improve understanding of the antimalarials market and prepare endemic countries to facilitate rapid uptake of our new ACTs. These include the following areas of work:

1. **Accelerating Product Uptake:** Understanding the market dynamics for antimalarials; country situation analysis: preparing for launch of late stage products
2. **Shaping the Debate:** Understanding decision framework for new product adoption; Phase IV consensus meeting; deepening distribution outlets.
3. **Achieving Health Impact:** Proof-of-principle activities to assess best method for ensuring maximum availability of high quality, low price ACTs through all outlets.

MMV is targeting highly impoverished malaria-endemic populations in Sub-Saharan Africa, Asia and South America. Access to treatment will be through both the public and private market sectors depending on the health-seeking behaviour of differing populations. Specific countries are currently being identified as part of 'global access plans' for each late stage development project taking particular account of the existing distribution networks of MMV's various pharmaceutical partners.

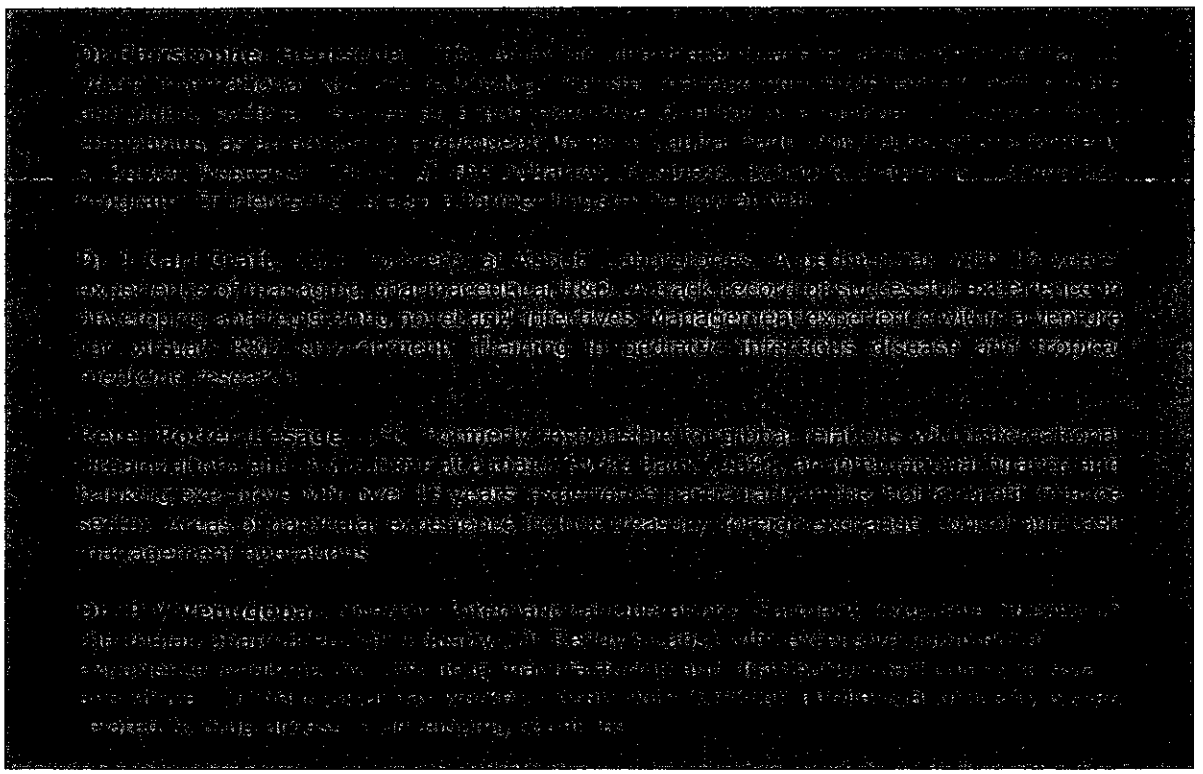
The ultimate impact will depend on uptake of the new drugs, which will in turn depend on the scale-up, launch and 'marketing' or 'access' activities that MMV will undertake together with its current pharma partners and new potential partners such as GFATM, UNICEF, MSH (Management Sciences for Health), and Population Services International (PSI - a non-profit organization established in 1970 that delivers subsidised products and services to save lives in the field of malaria and other areas of public health). MMV has just completed a consultancy process entitled 'Planning for Success' together with the Gates Foundation and the Boston Consulting Group where demand and access issues were examined.

MMV's Management Arrangements

Although it is a not-for-profit foundation, MMV's business model and its leadership style and culture are similar to that of a biotech or small commercial company. The Chief Executive Officer is assisted in his management duties by an Executive Management Team (See box below). External, independent scientific advice and support are provided by ESAC, and oversight is provided by the Board of Directors chaired by Baroness Lynda Chalker.

MMV's stakeholders, Board of Directors, Expert Scientific Advisory Committee (ESAC) and research partners are highly knowledgeable representatives from leading academic, governmental, industry and international organizations worldwide concerned with malaria research and drug development. Among other luminaries, the Board includes the former Prime Minister of Mozambique Pascoal Mocumbi and the former Director General of the Association of the British Pharmaceutical Industry. While the ESAC has included Dr Kitima Yuthavong, Vice President , Thailand Centre of Excellence for Life Sciences for a term of two years. The Executive Management Team is small enough to keep indirect spending down, but expert and dedicated enough to manage in a complex multi-partner environment.

MMV's Executive Team

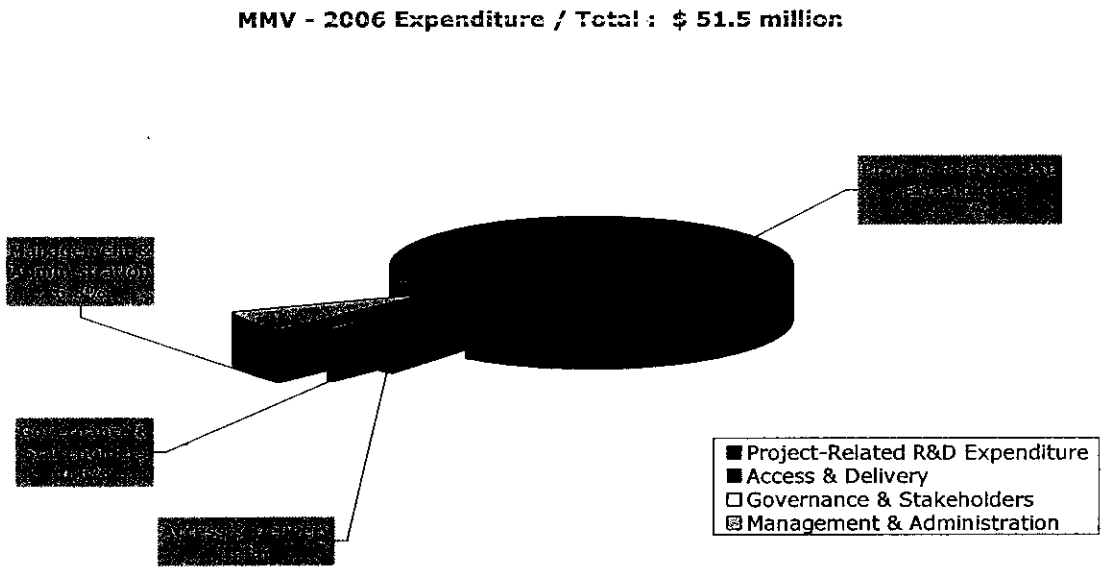


The organisation was designed to be lean, effective and efficient, while conserving robust, transparent control mechanisms. Quick decision making, implementation and flexibility are central to the organisational culture and have been instrumental in the successful start-up and progress of what is often referred to as a 'virtual pharma company'.

Compared to most not-for-profit organisations, MMV is unusual in that almost all staff have considerable private sector experience, for the most part in the pharmaceutical industry.

The organisation has remained faithful to the staffing principle of its original business plan: 'a small, highly-qualified staff'. Since its foundation, MMV has grown from a staff of one person in temporary offices to 21 people in rented office accommodation near Geneva airport (2006), and a target of 25 by late 2007. The majority of the 3-4 staff hires expected this year will be in the area of phase III/IV clinical trial expertise, delivery and access. Supplementary office space adjacent to the current rented accommodation is now in use since January 2006 to accommodate the new staff members.

Accountability and Transparency



Each year, MMV's financial statements are published under International Financing Reporting Standards (IFRS) in the Annual Report. The accounts are also presented to the Board twice a year and at the annual Stakeholders meeting. Our auditors are KPMG.

The organization promotes a culture of 'value for money' as witnessed in the pie chart above. MMV's expenditure on its core business (R&D) is over 90% while at 6.8% its management and administration costs are well below the average for similar ventures.

For legal, IPR and liability issues, MMV is advised by CMS Cameron McKenna, London, UK and Sidley, Austin, Brown & Wood LLP, Washington, DC, USA.

3. Proposal to Government of Thailand for 5-year Grant Support: 2008-2012

As an independent Product Development Public Private Partnership (PDP) in Geneva, Switzerland, with strong links to the WHO, MMV collaborates with over 80 public and private entities globally, including the Mahidol University and Hospital for Tropical Diseases and Thailand's cutting-edge National Centre for Genetic Engineering and Biotechnology (BIOTEC).

MMV receives bilateral support from several countries, philanthropic foundations and corporate foundations (see page 6). Sustained fundraising efforts have enabled MMV to raise over USD 273 Million during its first 7 years of existence but a funding gap of around USD 150 Million still exists.

To achieve its vision, it is estimated that MMV's R&D activities need additional commitments for 2008 to 2012 as well as considerable supplementary funding for scale-up, launch and 'access' activities. Only then will it be able to fully contribute to the achievement of the Millennium Development Goals.

Meeting the MDGs

Malaria constitutes a major challenge in international health. Currently available public health measures, from bed nets to indoor residual spraying, are failing to bring the disease under control. New and improved technologies and drugs are urgently needed if the Millennium Development Goals (MDGs) are to be achieved by 2015.

Malaria keeps poor people poor; new antimalarials will mean a healthier workforce which will help eradicate poverty and hunger (Goal 1). New malaria medicines for children, the population most affected by this disease, will allow them to go to school (Goal 2) and reduce child mortality (Goal 4). Maternal health will improve (Goal 5) and the spread of HIV/AIDS and malaria will ultimately be halted and reversed (Goal 6). And the drugs will be developed and produced with the help of PDPs, in cooperation with pharmaceutical companies (Goal 8). MMV's mission and work will contribute to the achievement of six of the eight MDGs.

In this context, in 2005 the UK government (through DFID) with the Wellcome Trust, explained its commitment to achieving the MDGs by its additional support to MMV, as well as its G8 commitment to encourage the development of new drugs for malaria via PDPs.

MMV's aims and aspirations are aligned with Prince Mahidol's ambitious vision in public health. By supporting MMV's work, Thailand will not only strengthen its commitment to fight malaria and demonstrate to the world its commitment to research and development, but also clear the current misconception that Thailand is not committed to Pharmaceutical Innovation. Most of Thailand's contribution will be re-invested in Thailand itself, and will also benefit the underprivileged in developing nations.

MMV Investments in Thai Organizations 2003 – 2007: USD 2,472,236

Protocol	Currency	Total USD	Site
Pyramax Phase II (conducted by Dr. Somchai - payment through CRO Fulcrum))			
	USD	323,083	per original CTA (80 patients)
	USD	371,159	per amendment (additional 120 patients)
Pyramax Phase III, for information (on going - payment through CRO Fulcrum))			
	USD	264,500	Mae Sot
	USD	106,350	Mae Sot vivax
	USD	271,250	Mae Lamad
	USD	106,350	Mae Lamad vivax
Artekin (payment through CRO MDS)			
	USD	198,450	CTA Thailand
Total through Contract Research Organisations		1,641,143	

COUNTERPART	YEAR	USD	Purpose
MAHIDOL UNIVERSITY Bangkok			
Pyramax	2007	7,403	Site initiation microscope training
	Total 2007	**7,403**	
Pyramax	2006	4,970	Prof Somchai expenses to ASTMH Atlanta
RBx11160		711	Exp. S Looaresuwan Site visit in Thailand
RBx11160		1,047	Exp. S Looaresuwan trip to Dehli
RBx11160		45,055	Study Title: An Open Label, Bioavailability Study of 100 mg orally administered RBx11160, one a day for 7 consecutive days in Patients with Acute Uncomplicated Plasmodium falciparum Malaria
RBx11160		48,938	Study Title: A single-dose, open label, randomized, two-period, crossover bioavailability study on RBx11160 to assess the effect of posture and time of dosing in healthy, adult, Thai subjects under fasting conditions
Pyramax		4,740	Papron Wilairat expenses to ASTMH Atlanta
	Total 2006	**105,460**	
Others	2005	3,011	Travel and accommodation Combin. Meeting Jan 2005
RBx11160		8,285	Travel expenses investigator meeting
RBx11160		13,498	Purchase of two ECG Machines
RBx11160		209	Piperaquine P K study
RBx11160		726	Travel to Mae Sot
RBx11160		4,500	P Vivax studies Kesinee Chotinavich
Others		5,000	Expenses related to board and stakeholders meeting in Bangkok
RBx11160		2,955	Prof Somchai travel OZ/PDT meeting July 2005
Others		6,448	Travel costs to Washington re meetings Panda/OZ/DB289
	Total 2005	**44,632**	
RBx11160	2004	955	Dr Krudsood (Advisor) travel expenses to OZ Meeting
	Total 2004	**955**	
TOTAL 2004 - 2007	**USD**	**158,450**	

BIOTEC Pathumthani, Thailand			
	2007	185,000	Renewal of MMV support for 2007
	2006	159,446	Renewal of MMV support for 2006
	2005	32,500	Supplementary funding Oct to Dec 2005
	2004	122,697	Renewal of MMV support
	2003	173,000	MMV Support (1st year)
TOTAL 2003 - 2007	USD	672,643	
Total MMV Investments in Thai Organizations 2003 - 2007		2,472,236	

Proposal to the Government of Thailand

The Government of Thailand will join a group of international governmental and philanthropic funding entities that all provide non-specific core funding to MMV. Some of these organisations are more interested in the R&D components of MMV's activities, others in downstream activities and potential health impact. We would welcome input on R&D and any support to inform delivery strategies, in-country effectiveness studies, modest capacity building, and help in building relationships with developing country governments.

The proposal listed below is for an initial 5 years, from 2008 to 2012.

$2.5 Million - New Drug R&D Portfolio + Access & Delivery of New Antimalarials

Drug Research and Development is the core function of MMV and the major driver for spending. Direct R&D portfolio project partner-support stood at over USD 43 Million in 2006. Moreover, as is well-established in industry, the volatility and magnitude of R&D costs increase significantly in the clinical development phases I, II, and particularly phase III.

The recent extension of the mission to the facilitation of Access and Delivery has increased the global project cost and human resource requirements considerably, as compared to earlier projections. However, the work planned for this enhanced mission will ensure that the new drugs emerging from the MMV pipeline do not simply 'sit on the shelf', but are distributed, affordable, used appropriately and begin to ensure tangible health-impact as soon as possible.

The dossiers of the first 2 new ACTs will be submitted for registration by end 2007 and MMV expects to launch between 3 and 4 important new antimalarial drugs before 2010. Adding Phase IV trials (safety, tolerance and acceptability) and other post-registration activities while facilitating access to both the public and non-premium private sector will ramp up costs significantly.

MMV proposes that the Government of Thailand supports research and development of the full portfolio of new antimalarial combination drugs from discovery through to registration, on to access and delivery into the hands of those most affected by the disease, mainly small children and pregnant women in Sub-Saharan Africa and Asia, and also potentially in South America.

Output/Performance Indicators

Key indicators are:

- Ability of MMV to continue to fill (particularly with innovative discovery projects) and progress projects through the pipeline;
- Ability of current projects to meet milestones;
- Effective registration of new drugs;
- Engagement of new partners in access and delivery;
- Engagement with international and developing country regulatory authorities to hasten uptake as first line treatment;
- Engagement with WHO to obtain inclusion on the Essential Drugs list and to interact with RBM;
- Facilitation of launch and 'access' activities;
- Organisation of Phase IV type implementation studies;
- Engagement with partners such as the Global Fund, the UN Millennium Project, UNICEF, UNDP, MSH and PSI to ensure all this leads to health and development impact.

Monitoring/Review Arrangements

Internal monitoring, evaluation and quality management are carried out by the management team through annual individual objectives and performance appraisals. This in-house system is subject to oversight by the Board and is tied to the work of the Board Remuneration Committee. Weekly scientific meetings, headed by the CSO, and bi-annual review by ESAC provide scientific monitoring. A monthly financial report is provided by the CFO to the management team, the board, and staff.

Reporting to donors is through the statutory Annual Report, the annual Stakeholders' meeting at which MMV's Executive Officers give presentations on the overall progress of the organisation, and the audited financial statements (auditor KPMG).The accounts and financial situation are presented to the full Board by the CFO twice a year and also at the annual spring Stakeholders meeting. Over and above the Annual Report, MMV provides specific annual scientific and financial reporting to a number of its donors. Internal regulations governing financial management are contained in the MMV Financial & Accounting Rules and Procedures Manual, comprising Financial Regulations, Investment Guidelines and Financial & Accounting Rules and Procedures.

Cost Implications/Budget

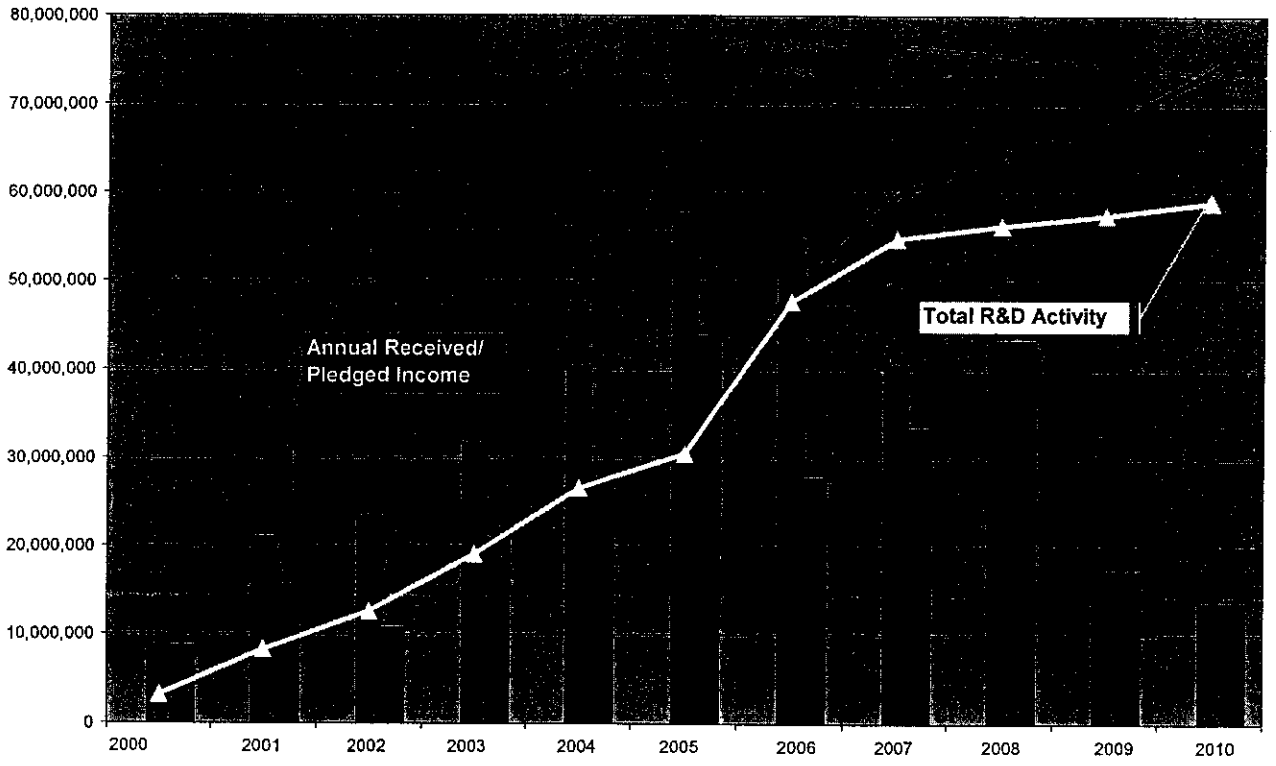
Medicines for Malaria Venture:
Funds Received / Pledged from Foundation (November 1999) to date (Dec 2006)

Donor		2000-2003	2004	2005						Total
Governments:										
Swiss Government (DEZA/SDC)	$	1,823,945	798,340							4,596,545
U.K Government (DFID)	$	5,926,209	1,793,000	1,803,000						9,522,209
U.K Government (DFID)	$									18,025,100
USAID	$									6,500,000
Netherlands Government	$	2,183,544								3,344,965
Netherlands Government (Tran)	$									11,694,087
Irish Aid	$									11,028,000
	Total	9,933,698	4,679,781	4,879,963	12,797,857	13,219,607	11,500,000			
U.N. Agencies:										
World Bank/Global Forum Health	$	2,500,000								5,500,000
WHO/Roll Back Malaria ...	$	3,500,000								3,500,000
	Total	6,000,000	750,000	750,000	750,000	750,000	0			
Foundations:										
Bill & Melinda Gates Foundation	$	20,000,000	5,000,000							25,000,000
Bill & Melinda Gates Foundation	$	10,000,000								40,000,000
Bill & Melinda Gates Foundation	$									100,000,000
BHP Billiton	$	0								750,000
Exxon Mobil Foundation	$	400,000								2,900,000
Rockefeller Foundation	$	4,300,000		0						5,750,000
Wellcome Trust	$	1,162,872								3,137,904
Wellcome Trust	$									18,086,100
Individual Donors	$	221		5,804	12,279					18,304
	Total	35,863,093	22,414,632	38,125,004	15,639,579	24,100,000	34,100,000			
Foundation capital:										
Netherlands 1999 / (TDR)	$	2,309,741								2,309,741
DFID U.K Govt. 1999 (TDR)	$	1,197,619								1,197,619
DFID U.K Govt. 1999 (TDR)	$	439,299								439,299
DFID U.K Govt. 2003		53,341								53,341
	Total	4,000,000								
		2000-2003	2004	2005						Total
			83,641,204	127,396,171	156,583,606	194,653,213				

Sectoral percentages include Foundation capital

The **'Funding Gap'** 2007-2010 is equivalent to USD 147 million, according to current budget projections (see below). This represents the total projected cost of our Access/Delivery activities over the five-year period. As can be seen in the financial modelling graph below, our current funding pledges are probably insufficient only to cover our planned R&D activity to end 2007, leaving the additional 'health impact' aspect of our extended mission completely unfunded.

	2006	2007	2008	2009	2010	2011	2012	
Annual Received/Pledged	30.6	38	45.5	19.5	13.6	-	-	
Available Income	60	60	45.5	19.5	13.5	-	-	
Scientific R&D	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	
R&D related expenditure	3.3	4.5	5.5	6	7	8	9	
Management & Admin.	3.5	5.3	6	7	7.5	8	8.5	
Expenditure: R&D Activity	60.2	60.5	57.1	60	65.5	79.8	77.5	
Access/Delivery	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	
Total R&D + Access	60.9	65.5	65.1	70	80.5	94.8	92.5	
Surplus/(gap)	[illegible]	(16)	(20)	(51)	(67)	(95)	(93)	(340)



The post-2006 figures are management's best estimates of future income and expenditure according to current information. Budgets and programmes are adapted on an ongoing basis as significant changes in scientific, material and financial circumstances may occur.

4. Conclusion

This proposal aims to address Prince Mahidol's vision of the advancement of public health, emphasising humanitarian action, and contributing to the global movement to achieve the MDGs by 2015.

By providing non-specific core funding to MMV, the Government of Thailand will join a group of European and international governmental and philanthropic funding entities that support its not-for-profit mission to discover, develop and facilitate the delivery of new, effective and affordable antimalarials to poor, populations in malaria-endemic regions in the developing world.

MMV has translated the vision of its public founding stakeholders (WHO, UK DFID, World Bank, Governments of Switzerland and the Netherlands) and those from the private sector (International Federation of Pharmaceutical Manufacturers and Associations IFPMA) into a tangible reality. Imagined initially as a 'social venture capital fund', MMV has assumed greater ownership and management than expected of the individual partnership projects within its portfolio to become what could be called a 'virtual pharma company'.

MMV management, with the support of the Board, its Stakeholders, and invaluable advice from its independent Expert Scientific Advisory Committee, has assembled a portfolio of over 35 antimalarial drug R&D projects. Scientific project selection is through a robust, open procedure of a public call for letters of interests, with internal and external ESAC review. Contract negotiation including intellectual property issues is competently managed. Scientific management of partnerships comprising academic, pharma and other partners around the world is well-structured and targeted specifically with the aim of obtaining appropriate, affordable, new combination therapies for malaria endemic populations. Projects which after internal and independent ESAC review do not meet milestones, have undesirable characteristics, or do not meet affordability criteria, are no longer supported. Financial management is effective and transparent.

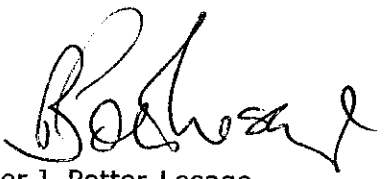
Value for money is the fundamental principle. The accounts have been produced to International Financial Reporting Standards (IFRS), from 2005. The management team and small staff in Geneva have created and implemented efficient procedures and controls. Moreover, they have effectively translated the initial vision into tangible, measurable action. Going forward, the challenge will be to manage change while growing the organisation to meet the needs of facilitation of access and delivery in endemic countries.

5. Final Declaration

Medicines for Malaria Venture, a not-for-profit Swiss foundation, declares that all funding received is used exclusively for its charitable purpose: to discover, develop and facilitate the delivery of new, appropriate, affordable antimalarials for poor populations in endemic countries.

Geneva, 25 June 2007

Dr Christopher C. Hentschel
Chief Executive Officer
Medicines for Malaria Venture



Peter J. Potter-Lesage
Chief Financial Officer
Medicines for Malaria Venture

Acronyms	
ACTs	Artemisinin-based combination therapies
AECI	Spanish Agency for International Cooperation
DFID	UK Department for International Development
EMEA	European Agency for the Evaluation of Medicinal Products
ESAC	MMV Expert Scientific Advisory Committee
FDA	United States Food and Drug Administration
GCP	Good Clinical Practices
GFATM	Global Fund for HIV/AIDS, TB and malaria
GMP	Good Manufacturing Practices
IFRS	International Financing Reporting Standards
IPR	Intellectual property rights
IPTi	Intermittent preventive treatment in early infancy
IPTp	Intermittent preventive treatment for pregnant women
MDGs	Millennium Development Goals
MMV	Medicines for Malaria Venture
MSH	Management Sciences for Health
PDP	Public-private product development partnership
R&D	Research and development
RBM-GMP	Roll Back Malaria-Global Malaria Partnership