

Simultaneous capability building

MMV's sustained capacity building has resulted in fully-upgraded laboratory facilities and clinical trial capacity at recipient sites, but more significantly, some sites, where necessary, have received simultaneous capacity building – whereby support is provided to improve the capacity of both personnel and facilities. The PI and local staff at each site are given GCP training in partnership with a recognized institution (accredited certificate), as well as microscopy and protocol-specific training, and training in good laboratory practices (GLP). Each site is closely followed-up, on at least two separate occasions, by a Quality Control (QC) monitor, who ensures that the training provided is being applied. Corrective action is taken when necessary.

Training is a sustainable form of capacity building and results in an increased pool of highly-qualified staff that can participate in GCP clinical trials in the future and an increased capacity to be involved in more diverse activities (targeting other diseases, doing their own research etc.). Staff can then go on to further train local clinicians, researchers, nurses and technicians. In addition, MMV supports the increased visibility and international recognition of clinical investigators at these sites via publications. This has allowed the PIs to:

- Apply for international grants to sustain their research
- Offer skills and clinical/laboratory facilities to other clinical research initiatives
- Become high-level advisors to national health authorities.

MMV works closely with the Swiss Tropical Institute and the Malaria Clinical Trials Alliance. These organizations provide training and technical assistance as well as infrastructural help to malaria research centres, such as those developed by MMV. We are also proud to support the African Network of Drugs and Diagnostics Innovation, started recently by WHO/TDR² and is dedicated to improving Africa's capacity to produce new medicines and diagnostics. Working closely with other groups who build capacity is an essential part of our mission.



▲ Training in progress in Lambaréné, Gabon.

Medicines for Malaria Venture (MMV) is a not-for-profit organization created to discover, develop and deliver effective and affordable antimalarial drugs through public-private partnerships. Our vision is a world in which these innovative medicines will cure and protect the millions at risk of malaria and help to ultimately eradicate this terrible disease.

Medicines for Malaria Venture International Centre Cointrin
Route de Pré-Bois 20 PO Box 1826 1215 Geneva 15 Switzerland
Tel. +41 22 799 40 60 Fax +41 22 799 40 61
www.mmv.org communications@mmv.org

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Benefit to countries

MMV's capacity building at clinical trial sites has greatly benefited the countries where the sites are located. It has:

- Created new buildings, transformed/refurbished existing facilities, painted/redesigned rooms, installed air conditioners and generators, and supplied other essential equipment.
- Enlarged the network of centres capable of running clinical studies to an international standard.
- Increased standards of research from in-country scientific teams (better diagnosis, rigorous collection and capture of data etc.).
- Enhanced international recognition and competitiveness of participating teams.
- Allowed collection of high-quality data to inform in-country decisions on malaria treatment protocols.
- Improved the ability of trial sites to support their own funding in the future.

What lies ahead?

MMV has accomplished much over the past 10 years in terms of capacity building. It is clear that the return on an investment of 2% of the 2005–2008 R&D project spend has been considerable.

In an ideal world, MMV would like to ensure the continued use of the laboratory and clinical facilities it has helped to set-up and refurbish, for example, for conducting further MMV-supported Phase IV post-registration studies. Both malaria research and countries where trial sites are located could benefit from not only the continued training and transfer of skills from one generation of trained laboratory staff to the next, but also the refurbishment of centres to a higher level in order to be able to run crucial clinical trials that will enable the validation of new generations of treatment.

African researchers and scientists are a rich resource and MMV is proud to have been able to contribute to their research environment and continued training. But much more needs to be done in terms of health systems strengthening to make real impact. As Kevin Marsh, Director of the Kemri-Wellcome Trust programme in Kilifi, Kenya, said in *The Guardian*, 12 May 2009, "People have thought that building capacity means training PhDs. But it doesn't matter how many PhDs you've got, if you release them into a failed system they will sink without a trace."

1. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use.
2. WHO Special Programme for Research and Training in Tropical Diseases.

Editors: Elizabeth Poll and Jaya Banerji, MMV. Photos: courtesy of our clinical trial site partners.
Designer: phg-Pascal Henridor.

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MMV capacity building

Building capacity to run high-quality clinical trials

MMV's primary roles are to discover, develop and deliver new, effective and affordable drugs to treat malaria. At each step of the research and development process the projects have to undergo a series of trials – early-stage projects are tested in laboratories while those that have reached the clinical development phase are tested at clinical trial sites in malaria-endemic countries in Africa and SE Asia. The capacity and functionality of these trial sites vary enormously, posing considerable but surmountable challenges for the MMV clinical development team. More often than not, in order to ensure the trial sites are fully functional and up to internationally accepted Good Clinical Practice standards, MMV has to upgrade, refurbish, renovate, re-staff and re-equip them.

Meeting varying trial-site needs

MMV has been coordinating clinical trials since 2005. Between 2005 and 2008, 2% of the total research and development (R&D) project spend has been invested in capacity building (Figure 1). This investment in equipment, infrastructure and training has helped MMV conduct 38 clinical trials and has resulted in the launch of the first MMV-supported product (Coartem® Dispersible). Furthermore, the submission for registration of two further artemisinin combination therapies (ACTs) is imminent.

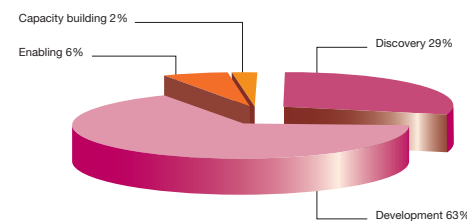
MMV conducts its clinical trials to internationally-recognized stringent regulations at trial sites that are compliant with Good Clinical Practice (GCP). Without GCP-standard trial sites MMV's work in clinical development would come to a halt. In the past 10 years MMV has built up a significant network of over 55 clinical trial sites in 24 countries in order to facilitate 38 clinical trials in the development of high-quality, effective antimalarials.

The standard of available trial-site facilities, and therefore the level of support required, varies considerably. Of the 55 clinical trial sites, which enrolled approximately 11,500 patients in total, 39 required some degree of support from MMV in terms of capacity building (see Figure 2, page 2).

The clinical trial sites initially encountered by MMV can be categorized into three types: clinical research centres that are GCP-compliant; those that are not GCP-compliant; and those with basic facilities that have little or no research capacity.



▲ The Pyramax® clinical development team, Dakar, Senegal.



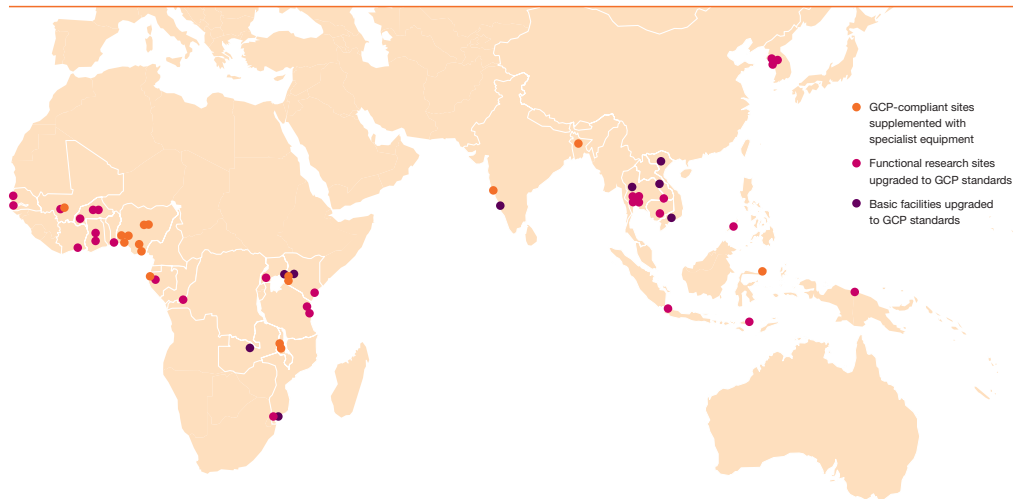
▲ Figure 1. MMV R&D project expenditure 2005–2008.



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▲ MMV clinical trial sites and the varying degrees of capacity building support required for GCP-compliance.

● GCP-compliant sites supplemented with specialist equipment

To enable Phase III clinical trials to be carried out, GCP-compliant research centres are upgraded with specialist equipment for patients suffering from specific clinical symptoms of severe malaria (e.g., cerebral malaria). A sterling example is the Medical Research Unit (MRU) of the Albert Schweitzer Hospital in Lambaréné, Gabon.

The MRU was established in 1992 with Prof. Peter G. Kremsner, MD, FRCP, as its Head. In 2006, an international team of about 50 staff were employed at the MRU with a particular focus on malaria research – clinical aspects, chemotherapy and prophylaxis. The centre also developed a clinical research training programme for African scientists and built a new high-tech laboratory. Clinical research projects have been conducted at the MRU for more than a decade – to ICH¹ GCP standards, as far as local capacity allowed. However, the scope of malaria clinical research was limited to uncomplicated malaria due to the lack of adequate facilities to care for patients suffering from severe falciparum malaria.

With support from the Dutch government, MMV was able to help refurbish the MRU and convert it into a high-quality facility, able to perform clinical trials on patients with complications, who required hospitalization and continuous monitoring.

MMV's main objectives at this site were to:

- Upgrade, extend and construct additional infrastructure
- Set-up facilities for inpatient care, including monitoring of participants in Phase I trials
- Relocate the laboratory to obtain space for a fully-equipped clinical research ward
- Furnish the routine laboratory and provide molecular biology equipment.



▲ Equipment supplied to the MRU at the Albert Schweitzer Hospital, Gabon, included beds; diagnostic and therapeutic bedside-equipment; computer-assisted monitoring of cardiac function, respiratory rate, blood oxygenation and body temperature; technology for resuscitation; and laboratory equipment.

● Functional research sites upgraded to GCP standards

Some centres, although operational, do not meet GCP requirements and must therefore be upgraded to international standards with additional infrastructure, scientific equipment and essential materials before MMV can conduct a clinical trial. The principal investigator (PI) and his or her local staff are also provided with training to enhance their skills to GCP levels.

For example, to strengthen clinical research in Central Africa, MMV has helped to upgrade clinical research facilities in the School of Public Health, Faculty of Medicine, University of Kinshasa, Democratic Republic of Congo (DRC). Since then, the facility has been selected to be part of a newly created alliance to conduct clinical research in DRC – the Alliance pour la Recherche Clinique et l'Épidémiologie Clinique au DR Congo.



▲ Professor Antoinette Tshetu and her students in their laboratory in Kinshasa, DRC.

● Basic facilities upgraded to GCP standards



▲ A new pre-fabricated pod was constructed for use as a laboratory in Chokwe, Mozambique.



Some clinical research centres are well-located but need to be substantially upgraded before MMV can use them as a site for GCP clinical trials. These facilities are renovated or sometimes rebuilt to the extent that new laboratories, wards and outpatient areas are constructed and furnished with essential equipment. Sometimes, to save time, giant pre-fabricated structures are bought and used to house laboratories or clinical areas, as occurred in Chokwe, Mozambique.

In 2006, the Centro de Investigação e Treino em Saúde de Chokwe (Chokwe Health Research and Training Centre), Chokwe, Mozambique, did not conduct any type of research. Following MMV-supported capacity building, the site now has a full suite of clinical and behavioral science facilities, a web-based data entry system, two five-bed patient wards and an on-site laboratory. Currently, a new structure is being built to be able to accommodate larger research activities and further expand clinical trial capacity.



Equipment supplied by MMV to its clinical trial sites:

- Laboratory equipment, such as biochemistry and haematology analyzers, microscopes, electrocardiograms, refrigerators and deep freezers;
- Furniture, such as beds, filing cabinets (water and fire proof) and lockable pharmacy cabinets, as well as generators and air conditioning units;
- Cars or motorbikes;
- Communication equipment, for example, satellite internet connection and mobile phones;
- Data management tools and office supplies including computers, scanners and photocopiers.