1. NACCAP project APRIORI (Tanzania)
   African Poverty-Related Infection Oriented Research Initiative

2. NACCAP project CoMMAL (Malawi)
   College of Medicine, Malawi-Amsterdam-Liverpool partnership for Research Capacity Development

3. NACCAP project INTERACT (Uganda and Rwanda)
   Infectious diseases network for Treatment and Research in Africa

4. NACCAP project ART-A (South Africa)
   Affordable Resistance Tests for Africa

5. EDCTP project VITA (Tanzania and Zambia)
   Improving the balance between efficacy and the development of resistance in women receiving single-dose nevirapine for the prevention of mother-to-child transmission of HIV/AIDS

6. EDCTP project PanACEA
   Pan-African Consortium for the Evaluation of Anti-Tuberculosis Antibiotics

7. EDCTP project TB (Kenya)
   A prospective epidemiological study on the prevalence and incidence of TB infection and TB disease in adolescents in the Karemo division

8. EDCTP network CANTAM (Congo-Brazzaville, Cameroon and Gabon)
   The Central African Network on TB, HIV/AIDS and malaria

9. EDCTP network EACCR (Kenya, Uganda, Tanzania, Ethiopia, Sudan)
   East Africa Consortium for Clinical Research

10. EDCTP network WANETAM (Senegal, Nigeria, Gambia, Burkina Faso, Mali, Ghana, Guinea-Bissau)
    The West African Network of Excellence for TB, AIDS and Malaria
Foreword

In sub-Saharan Africa, the poverty-related diseases of HIV/AIDS, tuberculosis and malaria pose major problems. Many of the countries affected by these diseases lack the research capacities to develop African solutions to tackle these problems. It is for this reason that NACCAP has set ambitious goals to help make a change on the lives of millions of people dealing with these diseases every day to contribute to the development of new interventions against poverty-related diseases and to contribute to sustainable development of African research capacity. This booklet will introduce you to the projects in Africa that are funded by NACCAP. It will illustrate the approach taken by NACCAP, highlighting what these projects have accomplished and, importantly, identifying what can be learned from them.

The overall mission of NACCAP is to foster the developmental of African-owned research centers capable of carrying out clinical testing of new interventions against poverty-related diseases. In addition, NACCAP aims to stimulate networking between R&D institutions in Africa to help ensure collaboration and complementarity. Such ambitious goals cannot be met without facing real challenges. Available funds and influence need to be used strategically, a coherent approach needs to be developed and lessons have to be learned during the process.

In order to reach its goals, NACCAP launched two open calls for proposals for research and capacity strengthening. Through these calls, four African-European partnership projects were funded: INTERACT, CoMMAL, APRIORI and ART-A. These partnerships were selected based on their quality and their relevance to the aims of NACCAP. You can read about these partnership projects in this booklet.

Following the start of EDCTP, NACCAP became an active partner in the EDCTP collaboration. As a partner, NACCAP contributed to EDCTP calls through joint development as well as by providing co-funding. Almost half of the total NACCAP budget was allocated through EDCTP. Information about these projects is also presented in this booklet.

The focus of this booklet is on best practices and the lessons that can be learned. NACCAP is convinced that understanding whether or not, and why, a certain approach is successful is key knowledge that can be used to shape and optimize future funding. It is anticipated that this knowledge will be valuable to researchers, policy makers, stakeholders, and others involved in capacity strengthening for clinical trials. We hope that this knowledge will also be valuable to you.

The principle of mutual partnership is also demonstrated through the proactive empowerment of the researchers from sub-Saharan Africa. This enables them to propose research to solve their own problems as well as to lead research projects. This empowerment can be seen in almost all of the research projects supported by NACCAP, but an exemplary illustration is the ART-A project. This project has contributed to the development of an affordable test for viral load and resistance to antiretroviral therapy through appropriate technology that can be adapted to suit the African environment.

An everlasting principle of all NACCAP and EDCTP capacity development projects is to ensure that clinical trials are carried out using best practices and that the developed capacity will be maintained to guarantee this in a sustainable manner. This is underpinned in the practice of funding capacity development activities as part of the research projects so that researchers are trained in the technologies that are required for their research, while actually doing the research in question. This process is called “learning by doing” or “learning while you learn”. In this way, the capacity that is developed is immediately utilized to provide successful outcomes, while at the same time encouraging retention of the gained capacity. This approach has been effective in many of the projects that have been funded by NACCAP, such as the INTERACT and APRIORI networks.

Research capacity strengthening is a long-term undertaking that needs sustained input from both partners. For the efforts of NACCAP and EDCTP to be long-lasting, a continuous commitment and investment from the funders and the partners from sub-Saharan Africa will be required.

Charles S. Mgone
Executive Director EDCTP

Chairman of the NACCAP Programme Committee

The European and Developing Countries Clinical Trials Partnership (EDCTP) was founded in 2003 in response to the overwhelming burden of the poverty-related diseases of HIV/AIDS, tuberculosis and malaria. It is a partnership of European member states and sub-Saharan African countries with the objective of accelerating the research and development of tools and capacity to fight these diseases. To complement these efforts, the Dutch government has established NACCAP, the Netherlands–African Partnership for Capacity Development and Clinical Interventions against Poverty-Related Diseases, with the goal of combining scientific research with sustained investment in research and development (R&D) capacity in Africa. The two programmes have worked very well together to create a synergy that has allowed capacity development to go hand-in-hand with the conducting of clinical research using best practices.

When well planned, research capacity strengthening can be very effective and capable of yielding significant results even after only a short period of time. To attain this, the investment in capacity building must be purposeful and tightly linked to the objectives of genuine partnership. The targeted partners who are to benefit from the developed capacity must be fully engaged in the process and must take charge of the capacity, including taking ownership of the process through which capacity is developed. This is the case with the initiative for developing and promoting clinical research capacity in sub-Saharan Africa. A good illustration of this is the experience of Makerere University College of Medicine. Here, through the identified needs of the college, the NACCAP project has contributed positively to the improvement of research and financial management by supporting the college’s Research Support Centre that centrally administers research projects. This is an example to be emulated by other institutions in Africa where lack of sound research management is a major setback in attaining best practice when conducting research.

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Prof. Willy Spaan
Chairman of the NACCAP Steering Committee

Prof. Joost Ruitenberg
Chairman of the NACCAP Programme Committee

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What is NACCAP?

The Netherlands–Africa Partnership for Capacity Development and Clinical Interventions of Poverty-related Diseases (NACCAP) is a partnership between the Netherlands and southern African countries that aims to strengthen the capacity of African research institutions to conduct medical research that meets international regulatory standards, and encourages them to shape local research agendas.

Projects funded by NACCAP

APRIOIRI – Moshi, Tanzania (page 9)

The African Poverty-related Infection Oriented Research Initiative (APRIOIRI) has two main objectives: to set up a state-of-the-art clinical research institute in Tanzania and to strengthen South–South cooperation. The purpose-built Kilimanjaro Christian Research Institute (KCI) now coordinates all of the research projects at the hospital and enables Tanzania to determine its own research priorities and function as equal partners in dialogue with their Western counterparts. The project also aims to invest in future research of a high international standard by training MSC and PhD students. Furthermore, through APRIOIRI, scientific research is performed with the aim of developing future malaria vaccines and shorter TB treatment regimens.

CoMIMAL - Blantyre, Malawi (page 15)

CoMIMAL is a partnership project for research capacity development involving Malawi’s College of Medicine, the Emma Children’s Hospital in Amsterdam and...
European context

EDCTP has embarked on its new strategy for 2014-2020. This includes a greater focus on population health, an emphasis on strengthening health systems, and a greater focus on the management of chronic diseases. EDCTP continues to play a key role in addressing the global health challenges of infectious diseases and non-communicable diseases.

Clinical trials

Testing medicines by means of clinical trials involves elaborate procedures. A good understanding of the objectives, the design, and the necessary steps to be taken before the four phases of a clinical trial can begin.

During phase I, the safety of a new medicine is tested on healthy volunteers. In phase II, the medicine is tested on patients with the disease for the first time. In phase III, the medicine is tested on a larger group of patients to determine its efficacy compared to existing treatments.

The Liverpool School of Tropical Medicine. One of the project’s most important goals was to set up a Research Support Centre (RSC) in order to raise the standard of Malian research. The idea is that ultimately the RSC will be self-sustaining. Now that NACCAP funding has been extended for another year, this goal seems to be within reach.

Furthermore, the Research Support Centre has successfully pursued an active re-entry policy for Malian researchers working abroad. Developing the Centre has also enabled Malians to influence the research agenda, which would otherwise still be governed mainly by donors. The Centre raises its own funds for research and sets its own research priorities. The CoM/MAL project has funded two clinical trials. The first involved research on a therapy to prevent anemia in young children as a result of malaria. The second trial was related to HIV and examined the safety of treatment with nevirapine and efavirenz in HIV-positive children. Iron supplements are used to treat patients who have contracted anaemia, but in HIV-infected children, these supplements can increase their susceptibility to other infectious diseases.

INTERACT – Kampala, Uganda, and Kigali, Rwanda (page 28)

The Infectious Diseases Network for Treatment and Research in Africa (INTERACT) project aims to increase the capacity of researchers to conduct independent clinical trials that comply with international regulatory standards. The project has provided training for researchers, and for more than 600 hospital staff in Good Clinical Practice. The project has also funded seven PhD students in Rwanda and Uganda. This led to a blossoming collaboration between their respective institutions that is highly appreciated in both countries.

One key objective was to increase the number of clinical trials conducted in Africa, to make the efficacy of placebos available.

ART-A – Johannesburg, South Africa (page 34)

The Affordable Resistance Test for Africa (ART-A) project has worked to develop a more affordable alternative to existing tests to detect resistance against HIV/AIDS. ART-A was awarded funding as a result of the second NACCAP call, which was specifically intended to encourage the involvement of private sector partners in research consortia. It is the only project funded by NACCAP that involves private partners, and they have shared valuable technical knowledge with the consortium’s public partners. The ART-A project has organized several workshops for Southern partners on HIV diagnostics, treatment and resistance, and has conducted clinical tests to detect the presence of HIV/AIDS.

EDCTP projects co-funded by NACCAP

As soon as the EDCTP strategy had been developed, NACCAP began contributing its resources to EDCTP projects by encouraging researchers from its partnership projects to respond to EDCTP calls for research proposals. NACCAP has contributed to EDCTP by co-funding the following projects:

- A project on the prevention of mother-to-child transmission of HIV/AIDS (through a joint call):
  - Improving the balance between efficacy and the development of resistance in women receiving single-dose nevirapine to prevent the mother-to-child transmission of HIV (the VITA studies, in Tanzania and Zambia) – page 19.

- Three EDCTP networks of excellence:
  - The establishment of CANTAM, the Central African Network on Tuberculosis, HIV/AIDS and Malaria for the conduct of clinical trials (a Central African network, coordinated in Cameroon and Congo-Brazzaville) – page 21.
  - Capacity building to prepare West African sites for clinical trials (WANETAM, a West African network, coordinated in Senegal, Mali and Côte d’Ivoire) – page 27.

- Support for a large collaboration on tuberculosis treatments, and a study of tuberculosis in neonates:
  - Prospective epidemiological studies of tuberculosis in neonates and adolescents in preparation for future vaccine trials (at York) – page 23.

NACCAP has also co-funded two calls initiated by EU member states on the impact of clinical trials and on tuberculosis: placebos by contributing to a common pot of funding. Furthermore, NACCAP contributed to several commissioned projects, including training workshops, to the mapping of research systems in Tanzania, as well as networking and communication activities.

APRIOIRI

Sub-projects

- Capacity building to establish Kilimanjaro Clinical Research Centre
- Phase I and II testing of malaria vaccines
- Capacity building and establishment of clinical trial centre to test new tuberculosis vaccines (phases I/IIa) and tuberculosis drug interventions in the conduct of HIV in Africa
- Concurrent treatments for tuberculosis and HIV coinfection
- Development of drug regimens to shorten treatment times for tuberculosis

Success stories

- The Kilimanjaro Clinical Research Institute was established
- APRIOIRI funding acted as a stimulus to attract other sources of funding for the institute
- The improved research environment has led to better research and outcomes that benefit the local population
- Research activities at the Kilimanjaro Christian Medical Centre are well coordinated and sustained
- An MSc programme in clinical research has been initiated

Lessons learned

- Four years is not enough to build up the infrastructure necessary to conduct independent clinical trials
- The Kilimanjaro Clinical Research Institute was established
- An MSc programme in clinical research has been initiated

Main applicant

Radboud University Nijmegen Medical Centre (the Netherlands)

Partners

Tansania, Kilimanjaro Christian Medical Centre, Malta, Malawian Research and Training Centre (MRTC), Ethiopian Harvard Research Institute (AHRM), Netherlands: London Medical University Centre, University, KNCV Tuberculosis Foundation, Erasmus University, Maastricht University, National Institute for Public Health and the Environment (RIVM), Wageningen University, ENCO Tuberculosis Foundation, Enschede, University Medical Center Groningen, Rotterdam, United Kingdom: London School of Hygiene and Tropical Medicine, Denmark: Statens Serum Institute

Running time

15 August 2006 – 14 August 2010

Budget

€ 2,251,000
It sounds logical: encourage sustainable science not only by educating a new generation of scientists, but also by investing in physical infrastructure and training for research staff. In Tanzania, APRIORI has made both these initiatives a priority, thereby setting in motion the crucial process of capacity building.

The university in Nijmegen and the Kilimanjaro Christian Medical Centre (KCMC) in Tanzania have been working together for quite some time, says Professor Van der Ven. ‘We have been working together for quite some time. There is a library where students can use computers, and a conference room equipped for global teleconferencing. Although the ground floor is not in use yet, everything is ready for the first clinical trials. Such infrastructure is hugely important for conducting scientific research, says Kibiki. But it is not always something that can be taken for granted. ‘To be honest, sometimes there are contradictions in the demands made by research funding programmes. Almost all funders agree that the problem in Africa is a lack of qualified staff and a lack of infrastructure. But once they grant funding, they often only support research projects and staff training. They pay no attention to physical infrastructure, such as a research institute and the facilities required for thorough research. Physical infrastructure is like an engine. You need it if you want to move forward.’

This has major consequences, according to Kibiki. ‘You can give people good education, but without the right infrastructure, it will ultimately leave one feeling as if they have a better chance of keeping scientists if we offer them a good environment in which they can do the work they want to do. The reverse is equally true: you cannot maintain a research project for long if the facilities are good but no one knows how to use them. Unlike some other funding projects, APRIORI provides the opportunity and the budget to meet both these needs.’ Van der Ven is enthusiastic about this combination. ‘It’s learning by doing practice, and at the same time you build your capacities. This has made Tanzanians owners of the project.’

A Tanzanian research agenda

Much has changed with the founding of KCRI, says Kibiki. ‘This research institute is now officially the third pillar of KCMC, next to patient care and education, which were the initial impetus to ensure that Tanzanians also undertake research on their own priorities. That is extremely important. They are now equal partners in dialogue rather than spokespersons for research ideas conceived abroad.’

Kibiki agrees. ‘At first, we didn’t have the infrastructure, so we had to start from scratch with a European partner institute. But organizing the logistics of the

We have a better chance of keeping scientists here if we offer them a good environment in which they can do the work they are trained to do.”
Several measures were taken following the evaluation, says Kibiki. ‘In the end, sub-project 2 did get off the ground and a TB team was trained, although there are still problems getting the necessary materials for research. Sub-projects 3 and 4 proceeded under the auspices of the EDCTP’s Pan-African Consortium for the Evaluation of Anti-tuberculosis Antibiotics (PanACEA), which is co-funded by NACCAP and aims to simplify and reduce the length of TB treatments. Since November 2010, we are officially an institute of the Good Samaritan Foundation, the founder and owner of KCMC, and we fall under their management.’

Core funding is still a problem, however. Although the Kilimanjaro Clinical Research Institute is part of Good Samaritan Foundation, financial arrangements have not yet been made. KCMC receives a budget from the Tanzanian government, but it doesn’t cover all the hospital’s expenditures. So it is already having a difficult time. But a request for core funding for KCI has been submitted to the government, and we hope that KCMC will be able to allocate a percentage of their budget to us.’

Now that APRIORI has ended, and there is as yet no certainty about core funding, KCI will remain independent of the various research projects in order to keep the institute operational. ICMC can support some of our staff, and at the moment we have a number of ongoing research projects, such as EDCTP’s PanACEA and a few projects funded by the National Institutes of Health in the United States, so we can continue our research. We are also a partner of the East African Consortium for Clinical Research and a member of the Malaria Capacity Development Consortium.’

An important lesson

Even though there are enough projects to keep the institute more or less operational, it is felt that four years was too short a time both to set up the institute and to hand over financial management to a local partner. The idea behind APRIORI, namely that local stakeholders ultimately take it over, was brilliant’, says Kibiki. ‘But I think the most important lesson has been that four years was not enough to achieve both goals, especially in a setting that lacked infrastructure.’

Van der Ven agrees that four years was not enough. APRIORI has a very good formula, but of course you have to discover a number of things for the first time yourself. You can’t set up a site for conducting clinical trials within just four years in Nijmegen either.’ Nevertheless, Kibiki would not characterize APRIORI as overly ambitious. ‘It’s true that it is difficult to set priorities in our situation, because there are so many problems. But you have to start somewhere. So he is not pessimistic about the future. ‘It’s important to have core funding and not be overly dependent on interim projects. But we will continue writing proposals to try to secure funding.’ APRIORI has achieved a great deal. ‘Thanks to APRIORI, we have been able to raise other funds and launch other initiatives. We have laid the foundation and set a process in motion. That process won’t end once subsidies end.’

Research centres around Africa strive to develop clinical interventions to disease that are safe and effective for use in Africa. To conduct such research in accordance with recognised international quality standards requires a strong foundation of high-quality health research. Providing this foundation necessarily requires long-term capacity strengthening. It is for this reason that NACCAP has focussed on capacity strengthening in the research projects it has funded. NACCAP has focused on three levels of capacity strengthening: individual, institutional and environmental. The three levels are also used in the ESSENCE Framework for capacity building efforts in health research that is proposed by the ESSENCE group of funders.

Three levels

Individual capacity strengthening, first of all, involves the capacity of individual researchers to acquire, manage, and apply the results of their research. In promoting individual capacity strengthening, NACCAP has employed a ‘learning-by-doing’ approach, whereby MSc and PhD researchers are trained on the job. Additional training courses targeting specific skills to improve research practices have also been developed, for example to educate researchers in Good Clinical Research Practice and Good Laboratory Practice. Through their partnership projects, NACCAP has supported the training of many researchers and technicians and has developed a number of training courses. For example, eight students are expected to obtain their PhD through the INTERACT project. Each PhD student is jointly supervised by two senior researchers, one from the African research centre and one from the European partner institute. Similarly, many researchers, clinicians and other health

Capacity Strengthening:

A multi-level approach

Dr. Andrew Kitua, former Director General of the National Institute of Medical Research in Tanzania and currently leader of the Malawi Research Unit at TDR, discusses the lessons that can be learned from NACCAP, multi-level approach to capacity strengthening.

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Secondly, institutional capacity strengthening refers to improving the capacity of research institutes, for example in terms of infrastructure, staffing, curricula, acquisition of funds, and external contacts. NACCAP has explicitly allowed partners to reserve a portion of their budget for this purpose.

For example, the CoMMAL project in Malawi has helped develop a special Research Support Centre which provides the infrastructure for institutional research. The Centre comprises an excellent training facility that provides consultation, training and support for clinical researchers. It has succeeded in attracting large follow-up grants and recognition. For more, see the report from the Wellcome Trust and the College of Medicine at the University of Malawi, its home institute. This has enabled effective coordination of research grants and activities leading to sustainable growth. A further example is provided by APRIORI, which used funds from NACCAP and EDCTP to develop the Kilimanjaro Clinical Research Institute. The Institute is now established as the research arm of the Kilimanjaro Christian Medical Centre, a large referral hospital in the north of Tanzania.

And thirdly, capacity is strengthened on an environmental level. This relates to issues such as government commitment to research at financing and policy levels. The aim of this capacity strengthening is to increase commitment to promote research capacity, to ensure sufficient standards are set and to maintain the necessary links between policy, research and practice. Maintaining close ties to policy makers, both at national and regional levels, is important to ensure government commitment to NACCAP’s projects.

To promote environmental capacity strengthening, 'Implementing projects on the back of long-established collaborations has made capacity building easier and more effective'
NACCAP has involved public health policy makers by encouraging all projects to establish and maintain close links with the relevant Ministries and other policy making organisations. For example, the Research Support Centre developed through the CoMMLAL project has forged strong contacts with the ministries of Health and Education and the Pharmacy, Medicines & Persons Board in Malawi.

South—South networking

NACCAP has promoted inter-country ties to promote mutual learning between institutions on different countries. For example, the INTERACT project has linked health institutions in Rwanda and Uganda in order to develop a network in which the Rwandan network can function as a main applicant and by setting clear, high targets for the percentage of funding for Africa. These deliberate steps have helped strengthen the capacities of weaker African partners by reducing the need for negotiation. National policies to assist students should also exist. For example, allowing students to retain their institutional positions to return to work after their studies provides a clearer career path. Policies that preferentially support students from weaker institutions as a means to bridge the imbalance in human resource capacities should also be considered.

NACCAP has also emphasized the importance of effective institutional policy to support students. PhD students should be provided with sufficient time to conduct their research. Mechanisms that allow smooth running of routine clinical work would enable this. This could be facilitated by ensuring that research is closely related to clinical work. Funding organisations could also consider supporting the salaries of the students, at least to cover their clinical work. In order to remain competitive and strengthen their positions as an equal partner in research, home institutions should provide a strong training environment to attract both young and senior researchers.

NACCAP’s projects have led to numerous successes in capacity strengthening within sub-Saharan Africa. In order to be successful, however, it has been necessary to learn from mistakes. Future programmes would benefit from the key lessons that can be learned from NACCAP to provide a strong foundation for continued success in the future.

Dr Andrew Klaus is Leader of the Malaria Research Unit at the Thelwall Institute, University of Malawi.

Lessons learned

• Allowances must be made for adequate buy-in from existing structures.

• It is crucial that sufficient logistical support exists in resource-poor nations.

• Key local personnel should be involved at a management level from the beginning.

• Capacity building should always be balanced with the needs of the institution.

• The Research Support Centre must work more closely with the Ministries of Health and Education to assist roll-out of state policies.

CoMMLAL

Sub-projects

1. Development of a Research Support Centre within the Post-Graduate Institute of the College of Medicine, University of Malawi

2. Intervention Preventing Therapy post-discharge: an innovative approach in the prevention of rebound severe malaria anaemia in young children

3. Randomized controlled trials of iron supplementation in HIV infected children: iron safe and beneficial

4. The effect of iron supplementation on maternal morbidity in HIV-infected pregnant women (in cooperation with Fogarty/NIH)

Goals

• Establish a Malawian owned, internationally recognized Research Support Centre to assist local researchers in the design and conduct of clinical research

• Introduce Global Clinical Practice quality standards as set out by the International Conference on Harmonisation

• Develop a training programme focusing on research methodology

• Reduce drain and encourage talented Malawian post-graduates and senior scientists to return to Malawi to work

Budget

£ 1,650,000

Main applicant

Dr M. Bande van Hensbroek, Academic Medical Centre – Emma Children’s Hospital, Amsterdam, the Netherlands

Partners

Malawi: University of Malawi, United Kingdom: University of London, School of Tropical Medicine

Country of execution

Malawi

Running time

15 December 2005 - 15 August 2010

(Note: This project was granted a one-year extension, with additional funding.)
Malawi is one of the world’s most densely populated countries, yet least developed countries. Its economy is heavily dependent on agricultural exports and substantial foreign economic aid. A chronic shortage of foreign exchange over many years has weakened Malawi’s ability to help itself. Meanwhile, HIV/AIDS, tuberculosis and malaria all pose a serious threat to the country’s primarily rural population. In a bid to fight these killers, while also reducing reliance on foreign aid, scientists at the University of Malawi’s College of Medicine have set up the CoMMAL project, to address some of the country’s health challenges from within.

The University of Malawi’s College of Medicine (CoM), based in Malawi’s second largest city Blantyre, is Malawi’s only medical school. For many years, it has attracted medical and scientific researchers specializing in tropical diseases and AIDS. There was concern from the University board and Malawian scientists, like Dr Victor Mwapasa and Dr Kamija Phiri, however, that Malawi’s indigenous research capabilities were not being developed. There was an imperative to find a solution to the urgent health needs of the country and a desire to find a solution from within.

To address these challenges, Mwapasa and Phiri joined forces with Dr Michael Esan, a Liverpool School of Tropical Medicine. This study was set up to test whether iron supplements can safely be used to treat anaemia in HIV-infected children, because iron supplements that are used to treat anaemia may also increase a child’s susceptibility to other infectious diseases. Dr Esan was able to benefit from the work of Dr Phiri in setting up the first clinical trial through the RSC.

The RSC is the first trial to be run through the RSC, focusing on anaemia in HIV-infected children, was run by Dr Michael Esan, a Nigerian doctor working at the Liverpool School of Tropical Medicine. This study was set up to test whether iron supplements can safely be used to treat anaemia in HIV-infected children, because iron supplements that are used to treat anaemia may also increase a child’s susceptibility to other infectious diseases. Dr Esan was able to benefit from the work of Dr Phiri in setting up the first clinical trial through the RSC.

In a situation oddly reminiscent of the one previously faced by Dr Phiri, Dr Esan’s team had to address the issue’s research priorities and therefore influence the research agenda. The two clinical trials that had been funded and developed by the RSC were chosen because they addressed the most pressing needs of the Malawian population. The first trial concerned a therapy to prevent anaemia in young children as a result of malaria. The second was a malaria study and examined the safety and efficacy of treatment of anaemia with iron in HIV-positive children.

The first trial looked at severe anaemia, which often occurs in children as a result of malaria infection. The trial was successful in several aspects: the trials were successful in several aspects: the trials were successful in recruiting enough suitable candidates for a meaningful trial.
The Research Support Centre is being used as a model in other African countries

international standards of GCP. ‘We have run several courses for GCP to enable researchers to carry out their work following international standards, as well as to protect the integrity of the data and the integrity of individual,’ says Mwapasa. ‘We have also introduced courses on advanced GCP for managers, coordinators, lead nurses and lead clinicians and courses in advanced methodology targeted at the writers of the research.’

To achieve the second goal, it was essential to strengthen the brand of the College of Medicine within Malawi. Malawian graduates had to see CoM as a purveyor of research, not just a recipient of northern expertise. Mwapasa believes that the RSC has created confidence for Malawians to carry out research, as well as created an institution with the right environment to facilitate this research. It has thus been successful in achieving both its goals for capacity building.

Self-sufficient funding

In order to address the issues of funding, it has been necessary to first gain a better understanding and control of the different research projects being undertaken by the CoM. Mwapasa muses, ‘Research at CoM was rather uncoordinated and the college had challenges knowing what type of research was being done, or what the focal areas were, or what research income was generated and how many projects were running. Prior to 2006, there was no office responsible for coordinating the research grant awards.’

Much of the medical and scientific research done under the auspices of the CoM is run through affiliate research centres. These are semi-autonomous entities working under the legal framework of the university. The research grant applications usually stipulate that about 8 to 10% of the grant should go to the University for administration and overhead costs. For a variety of reasons, this administration fee has rarely been paid, instead going towards further research.

‘In the US and internationally, 40% of grant money is supposed to pay an overhead fee to the institution for administration and overhead costs. For a variety of reasons, this administration fee has rarely been paid, instead going towards further research. By January 2011, the RSC finally had an almost complete database of all research being conducted at the University and by its affiliates. Going forward, this database will help avoid duplication of research as all proposals will go through the RSC. ‘For a country that is as poor as Malawi, research is not a good place for many doctors, nurses or lab technicians around. It is therefore necessary that their work contributes to finding solutions to health problems in an efficient way.’

The database has also allowed the CoM to calculate how much money they were due from unpaid research income. It was envisaged that CoM would pick up the entire tab at the end of three years, but this has not happened. ‘Was it an oversight in the three-year projection? Sometimes you only know how a car drives after you have driven it!’ Mwapasa quips. ‘I am more confident now than three months ago. It is looking good, though not yet perfect. Give us another year and we will walk on our own two feet.’

This massive step forward will certainly help put the RSC on a sustainable footing. It was envisaged that CoM would pick up the entire tab at the end of three years, but this has not happened. ‘Was it an oversight in the three-year projection? Sometimes you only know how a car drives after you have driven it!’ Mwapasa quips. ‘I am more confident now than three months ago. It is looking good, though not yet perfect. Give us another year and we will walk on our own two feet.’

In the long term, the objectives of the project are vast and long-reaching. Mwapasa explains, ‘We want to train Malawians to compete at the same level, for the same money, with their international colleagues. After all, international funders do not care if the principal reviewers are, they do not care if the principal researcher is Malawian; they are looking at the quality of the science.’

As director of the RSC, Mwapasa was prepared to take the risk of upsetting them. A critical part of ensuring the success of the RSC was to create a database of all grants and funds coming through the CoM. ‘We wanted a complete database of all the research projects happening at CoM. It sounds simple, but it has taken us a long time. We underestimated how long it would take to change the mindset.’

Projects aimed at preventing mother-to-child transmission of HIV were set up in Tanzania and Zambia at the end of 2007. Called the VITA Studies, their aim was to improve the balance between efficacy and the development of resistance in women receiving single-dose nevirapine for the prevention of mother-to-child transmission of HIV. Put simply, these studies carried out tests to see if resistance to nevirapine could be reduced in mothers taking the medication. Two clinical trials were set up, and 200,000 euros were made available to expand the Kilimanjaro Clinical Research Institute in Moshi, Tanzania. Building capacity by educating people is an important element of the VITA project. ‘Once you have the infrastructure, the lab and the building, you suspect that people to work there,’ says Elton Kisanga, project coordinator at the Kilimanjaro Medical Centre. ‘EDCTP enabled us to attract PhD candidates and Master’s students from Tanzania and the Netherlands, and the development of resistance in women receiving single-dose nevirapine for the prevention of mother-to-child transmission of HIV/AIDS. The Kilimanjaro Medical Centre in Moshi has the infrastructure, the laboratories and the human capacity to conduct high-quality research. The teams have been given an additional year’s funding to conduct the VITA2 trial, which will end in March 2012. ‘EDCTP advocates empowering the Southern partner by offering high-quality training, including PhD courses,’ says Kisanga. ‘But a three-year grant may not be enough to support research-based PhD training. However, the good news is that EDCTP allows one-year no-cost extensions, to enable us to finish what we have started.’

The VITA clinical trials were set up with partners from the Netherlands, Tanzania, Kenya and Zambia. ‘This is extremely satisfying with this North-South and South-South cooperation,’ says Zawadzki. ‘We are blessed to have a highly experienced international team. Each of us has our own strengths. The Medical Research Council (MRC) Clinical Trials Unit from the United Kingdom has over 20 years of expertise in conducting field studies and clinical trials in the developing world. The two Dutch partners, Radboud University Nijmegen and Utrecht University, have vast experience with clinical data management and have developed analytical methods for pharmacokinetics and resistance assays. The Zambia team from the University Teaching Hospital in Lusaka has extensive experience in conducting paediatric HIV studies, which have changed the standard of care for children infected with HIV/AIDS. The Kilimanjaro Medical Centre in Moshi has the infrastructure, the laboratories and the human capacity to conduct high-quality research.’

The transmission of HIV from mother to child, and resistance to certain drugs are still huge medical challenges for Africa. A high-quality international effort is underway at the Kilimanjaro Clinical Research Institute in Tanzania to develop effective methods of prevention.

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PanACEA
‘Resist needless bureaucracy’

Three major studies aim to produce new medicines that will shorten tuberculosis treatment. It is a slow and costly process, but the African institutions that are part of the PanACEA consortium have a great deal to gain from it.

With current tuberculosis (TB) treatment, patients are required to take medication for at least six months. Many patients find it difficult to adhere to such a long treatment plan – especially because they often start to feel better after the first few weeks. As a result of not seeing the treatment through to the end, TB often comes back, which causes patients to become resistant to the drugs. A great deal is being invested in improving compliance by advising and supervising patients. And at the same time, the Pan-African Consortium for the Evaluation of Anti-Tuberculosis Antibiotics (PanACEA) has been developing drugs that can make the TB treatment period shorter.

The PanACEA project has a 27 million euro budget, one-third of which is donated by NACCAP. The project has three distinct sub-projects, which liaise to make the research more efficient. One of the sub-projects – led by lung specialist Martin Boeree from Radboud UMC in Nijmegen – is to test the efficacy of administering a higher dosage of the anti-TB drug rifampicin, to reduce the length of treatment plans. This is taking place in three separate clinical trials.

The second sub-project tests an antibiotic called moxifloxacin, in combination with other drugs. This is taking place in three separate clinical trials. The third sub-project tests a combination of SQ109, an entirely new antibiotic (PanACEA) study. This enables us to test several drugs in one period shorter.

Boeree is adamant that both the PanACEA idea and its structure are good, but points out that the speed at which research is taking place is still too slow. GCP standards require that research proposals are assessed by local and national ethics committees. This is one of the reasons why trial preparations can take a year or more. There is a lot of bureaucracy in Africa, but at EDCTP and NACCAP we are guilty of this too.

The lesson that Boeree would like everyone concerned to learn from this is that the pursuit of responsibility, and thus accountability, can be taken too far. ‘We are noticing it with the proposal for follow-up studies, for example. I understand that accountability is necessary, for example when setting up a study, but sometimes it verges on suspicion. If everything has to be justified, then creativity and productivity can be compromised.’

Encouraging openness

One of the main issues that NACCAP, as well as other funding institutions, is still grappling with is the fair use of funding. Stronger partners are more likely to have the infrastructure to absorb the developed capacity compared to a weaker partner and, as such, may be more ready to conduct the actual research. Furthermore, ambitious plans for capacity strengthening may not always be achieved due to reasonable scientific and political factors. A monitoring and mentoring system is important to detect this problem as soon as it occurs, so that potential solutions may be sought.

It will be important for NACCAP and other funders to foster and encourage openness with the recipients of grants within the partnerships, to allow upfront discussions of some of the potential problems and to allow possible brainstorming on solutions before they become issues. NACCAP and other funding bodies like EDCTP will need to develop more stringent oversight bodies or mechanisms to help monitor and provide assistance. Having said this, EDCTP and NACCAP are not always the only funders of projects and in some cases not the largest funders. Harmonization amongst
1. **Fair partnerships**

**The sharing of data**

Within NACCAP-funded partnerships, data generated during the projects belongs to the inventors. When a medical device, drug or vaccine is developed, in most cases the inventors and/or the developers have intellectual property rights to the product based on agreements outside of the funded partnership. However, when new interventions have been tested and approved, they should be made available for the general population as soon as possible. A commitment to make the product available to the country’s Southern partner is required and is considered a reasonable benefit. It may, however, be difficult for donors to insist on the above commitments or to monitor that this is carried out, especially given that the budget invested by donors is usually not compared to the overall cost of the developed product.

Effective sharing of knowledge through scientific publications and data sharing is encouraged. Good examples of this are the development of standard operating procedures and other learning modules by ART-A, which are freely available on the web, as well as numerous publications by the different partnerships. For publications following from partnerships, an agreement on authorship of publications based on credible assessment is encouraged following international guidelines, such as those of the International Committee of Medical Journal Editors.

**Flexibility and versatility**

Successful and fair partnerships are built on partners being upfront and transparent, outlining expectations and ambitions from the outset. In partnerships there will always be stronger and weaker partners. Therefore, a monitoring and mentoring system is important. This should ensure that the NACCAP objectives of fair and equitable partnership are met, and that they are shared with other potential partners in venues such as the EDCTP forum. The success of NACCAP to date has in part been due to its small size and relative lack of bureaucracy in its administration and funding processes. This flexibility allows NACCAP to be effective in allocating funding, allowing it to evolve to meet new challenges and to discard processes that have not been successful. Given the successes of the past, I look forward to seeing the direction the “new” NACCAP will take in the future.

Dr. Opaluku Ojjo-Aryehim is a Senior Manager of Clinical Development at GlaxoSmithKline Biologicals and a member of the NACCAP Programme Committee.

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**A targeted approach to funding**

EDCTP remains NACCAP’s main partner and NACCAP preferentially supports EDCTP-funded projects. This is important because, although there has been an increase in funding for research into HIV, tuberculosis and malaria, the budget currently available is still insufficient for the needs of the researchers. EDCTP and NACCAP have been able to take complementary approaches and NACCAP provides co-financing for several EDCTP calls and projects. EDCTP and NACCAP will continue to work hand-in-hand.

NACCAP’s strategy has been to focus on development within a limited number of consortia, for example INTERACT, CoMMAAL, APIORII and ART-A, located mostly in Eastern and Southern Africa. Some may ask if this approach is fair and equitable, leading to the diseases that are mainly funded by NACCAP are also found in other parts of Africa. The benefits of such an approach, however, are to ensure that the funding is focused and not fragmented, leading to more tangible research benefits.

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**Tuberculosis (TB)**

TB is very prevalent in rural western Kenya, a region that suffers from a great deal of poverty. The TB problem in the area is further exacerbated by the fact that some 15% of the population is HIV positive, which makes them more susceptible than normal to TB infection.

For a long time, there has been an urgent need for a better vaccine against TB, but until recently, no research into this was being carried out in developing countries. Such research requires large-scale clinical trials involving thousands of patients – a daunting undertaking in countries where resources are few and experience is often lacking. In 2007, a special research project on TB vaccines was launched by KEMRI in cooperation with the US Center for Disease Control and Prevention (CDC).

The goal of the project was to start a phase II clinical trial on a new TB vaccine for children. The lesson that Van’t Hoog believes can be learned from this is that the development of African-senior researcher is important. Many research institutes in Africa can now request and conduct a clinical trial themselves, she says. ‘But it’s also important that Africans help to formulate the ideas that lead up to clinical trials and the products that underlie them. Often, these are still determined by the sponsor and the manufacturer of the product, in our case, Aeras Global TB Vaccine Foundation. We must give more thought to the role of PhD students in researching these projects, because they are the senior researchers of the future.’

And that is why Van’t Hoog is happy that NACCAP insisted on creating three PhD positions, even though finding candidates was not always easy. ‘I would like to spend more money and time on scientific research and PhD supervision. In the Netherlands, assistant research fellows are full-time researchers. But in Africa, people are often doctors or heads of a unit while they are studying for their PhDs. It’s important that enough scientists are educated in Africa – otherwise, African research institutes will become little more than data factories.’
Networks of excellence

To strengthen South–South cooperation, NACCAP supports both individual research projects and three EDCTP projects aimed at regional networks. These networks of excellence unite research institutes in West Africa, Central Africa and East Africa.

If Africa is to develop new medicines, treatment methods and vaccines, it needs more trained researchers placed in strong research institutes who conduct their own clinical trials in adherence with international standards. However, in most parts of sub-Saharan Africa, there are not enough researchers, not enough funds allocated to research, and research facilities are inadequate. To compound this, many researchers work in isolated environments, and facilities and knowledge are not often shared.

To help change this situation, NACCAP, the Netherlands–Africa Partnership for Capacity Development and Clinical Interventions of Poverty-related Diseases, supports three regional networks in different corners of the continent. Within each network of excellence, the partner institutes work together, pooling their individual strengths and forming networks to share their knowledge and experience. They do this by organizing joint training sessions and sharing the findings of their research.

Weaker institutes, who have less experience available to them, strengthen their capacity by networking with more established institutes. The networks also work with other initiatives, such as the World Health Organization’s centres of excellence, to ensure that research is not duplicated. Moreover, the networks look to African national governments and local donors for political goodwill and financial support.

Broad capacity building

Looking at the networks and the way they work, one conclusion that can be reached is that institutes learn a great deal from each other – regional cooperation pays dividends. As well as exchanging technical knowledge and expertise during training sessions, capacity is also built in other fields such as financial administration, internet and communications technology, and project management. And the networking of institutes also facilitates the drawing up of ethical guidelines for use during clinical trials.

Broad capacity building allows the networked institutes to apply for grants themselves to fund research projects and clinical trials. This strengthens their position at an environmental level. The capacity to secure additional funds is seen as an important mark of quality in the world of science, and network coordinators are very aware that new-funding is sorely needed. Investing in regional networks of excellence develops a capacity that other donors can rely on.

What coordinators have learned from this process is that they are able to build a successful network, but that there are often insufficient funding to then carry out substantial joint research projects. That is a shame, because the coordinators have confirmed that ‘learning by doing’, or building capacity by conducting research together, is highly effective. In short, a solid foundation has been laid for the future, but this will need to be built upon in order to take full advantage of the potential of the networks.

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CANTAM, Building trust through transparency

‘Creating an international network of research institutions is of vital importance for resolving public health issues in Africa’, says Professor Francine Ntoumi, molecular biologist and coordinator of CANTAM, the Central African Network on TB, HIV/AIDS and malaria. ‘However’, she warns, ‘you need to make sure that, from the start, everyone is clear about what they want to contribute to and gain from the network.’

Ntoumi also considers that African ownership of the network is very important. ‘This network is fully African-driven. This has helped to generate local funds from the oil company Total and the national government, since a healthy population is important for them. The visibility of the laboratory convinced Total and the national government that Congolese researchers were able to find their own solutions to important problems.’

Ntoumi believes that the success of CANTAM stems from the fact that all partners where clear from the outset about the opportunities available to them. ‘Through the network we can share our resources, which are otherwise very limited. We need each other to learn from each other, to share experiences and to apply for international grants together’, she says. ‘When setting up a network like this, you need to make sure that all partners are fully engaged. We have always made clear what we put on the table, and what we plan to get from the table. If not, we risk an artificial network and we should absolutely avoid that.’

The CANTAM network has been limited to seven institutions in three countries. Starting with only a few partners has proved beneficial. ‘There were more at the beginning’, Ntoumi says, ‘but it was not clear what they wanted to contribute. Now that we have developed a strong base, we are ready to expand the network.’

Photo: A droplet of blood is taken from a baby to test for HIV infection

Title:
The Central African Network on TB, HIV/AIDS and malaria (CANTAM)
Where:
Congo-Brazzaville, Cameroon and Gabon
Started:
19 December 2008
Budget:
€ 0.5 million
Funds from NACCAP:
€ 0.5 million
Website:
www.cantam.org
The East Africa Consortium for Clinical Research (EACCR) brings together a wide variety of research institutes, some of which have never previously collaborated with each other. According to Professor Pontiano Kaleebu, project coordinator and director of the Medical Research Council at the Uganda Virus Research Institute, a lot has been achieved for improved clinical trials but there are still challenges ahead.

The EACCR is a large network of six Northern partners and 24 African institutions. Half of the African institutions are established regional centres, while the other half are weaker in terms of clinical research in all or one of the major diseases of HIV/AIDS, TB and malaria. ‘Bringing together researchers in the three disease areas from a wide range of institutions brings strength. However, the size of the network also brings its challenges,’ says Kaleebu.

The activities of EACCR are all aimed at enabling more research institutes to perform clinical research according Good Clinical Practice (GCP) standards. They include running short-term training events in key areas such as diagnostics, as well as funding master’s degree students and post-doctorate positions at partner institutions. An interactive website has been set up, together with regional databases with clinical trial and disease-specific information for TB and malaria. The physical infrastructure and equipment at various institutions have also been improved. Clinical trials require thorough record-keeping and monitoring to ensure adherence to Good Clinical Practice, for example when recruiting participants, which can be very expensive. To address this, the EACCR has created a reciprocal monitoring scheme to create a pool of well-trained and experienced clinical trial monitors who will be available within the network to provide reciprocal monitoring as an in-house capacity. Hands-on training in management and financial administration has also improved capacity to deal with larger projects.

‘The African ownership of this project is essential, because it teaches institutes how to run large grants. The cross-cutting South-South cooperation is also an important asset,’ says Kaleebu. ‘In the past, researchers working on HIV, TB or malaria in East Africa were mostly focused on their specific disease area. We can now learn from each other as we all need to carry out good population studies, investigate disease burdens and work under GCP-conditions. There are challenges as well,’ says Kaleebu. ‘One of those is the size of the network. It took us quite some time to get all the institutions on board. Another challenge is how to become sustainable after the funding ends. The foundation has been laid and we are now writing joint grant applications. It is clear that more funds are needed for the future. The budget for this network did not allow for much specific research. Going forward, we need to continue setting up clinical trials that allow us to build capacity for the future through hands-on research.’

Facing the challenges of a large network

The East Africa Network of Excellence for TB, AIDS and Malaria (WANETAM) was set up in 2009. The aim of the network is to facilitate capacity building, technology transfer and scientific exchange in order to develop more West African sites for the successful conduct of clinical trials.

‘This project distinguishes itself from others in that it brings together institutions in three different languages,’ says Mr. Souleymane Mboup, a professor of virology at the Aristide Le Dantec Hospital in Dakar and coordinator of the WANETAM project. Researchers from fourteen research institutions in seven West African countries – speaking English, French and Portuguese – work together in the network. ‘In the past, research institutes in this region have always worked in isolation. As a result, it took us the entire first year of the project to build the network. Activities like training and capacity building have only started this year.

Nevertheless, the project has already reached 175 scientists and laboratory assistants at various institutions through hands-on trainings and cross-cutting trainings. Baseline studies on drug susceptibility for TB and drug resistance monitoring for HIV have started. Through the training associated with these studies, the capacity of researchers is being built. Most of the training events organised by WANETAM, however, are not aimed at a particular disease or a particular region that will be held. The network includes, for example, training on ethics in research and Good Clinical Practice according to international standards. Additionally, each institution was assessed to determine what upgrades were required to allow each centre to carry out the biochemical and haematological tests used in clinical routine care. Research buildings were restored and equipment was acquired, including biochemical and haematological robots and four MGIT machines, an automated system that detects mycobacteria. The Bambol Health Project in Guinea-Bissau was also upgraded to enable detection of different strains of TB including drug resistant strains. ‘With these training programmes and improvements, more researchers are able to perform good clinical tests,’ says Mboup. ‘Then again, that is not enough. We also need good managers and administrators, as well as cooperation among all. Other capacity building activities have, therefore, focused on project and financial management. For example, a web-based platform has been created to manage the project, monitor its activities and facilitate data exchange, while a new telecommunication system for video-conferencing has also been introduced. In addition to improving capacity to conduct clinical trials, the network is importantly opening new funding opportunities for the West African institutions involved. As Mboup explains, ‘English is the most important language in the international research community. With our trilingual network, the French and Portuguese speaking institutions have an increased chance in the competition for scientific research funds, because they cooperate with English-speaking institutions. As a network, we can apply for grants we couldn’t apply for before. This has already allowed us to become involved in new partnerships and follow-up projects such as WAPHR and WANETAM Plus.’
INTERACT

Sub-projects

A. Building sustainable clinical trial capacity
B. Building and implementing high-quality data systems
C. Implementation research: operational aspects of the diagnosis and treatment of HIV infection and tuberculosis (TB) at the district level
D. Assessing the impact of HAART (Highly Active Antiretroviral Therapy) on the reproductive health of Rwandan women
E. Incidence of and risk factors for selected adverse effects of HAART treatment in HIV-1 infected adults where there is no clinical suspicion of TB co-infection
F. Immune reconstitution inflammatory syndrome (IRIS) and other selected adverse effects of therapy on TB-HIV co-infected patients commencing HAART
G. Surveillance of HIV-1 drug resistance in patients treated with HAART and in the general population
H. Malarias treatment and intermittent preventive treatment in pregnancy, with and without HIV infection
I. The optimization of chemotherapy for HIV/AIDS, malaria and TB
J. Incidence of and risk factors for selected adverse effects
K. The degree of adherence to TB treatment, with and without HIV co-infection
L. Malaria treatment and intermittent preventive treatment in pregnancy, with and without HIV infection
M. The degree of adherence to TB treatment, with and without HIV co-infection
N. The degree of adherence to TB treatment, with and without HIV co-infection

GOALS

A. To establish and consolidate the infrastructure for conducting clinical and experimental research in HIV/AIDS, malaria and TB
B. To accelerate the development of clinical interventions for HIV/AIDS, malaria and TB
C. To determine the overall impact of these diseases

SUCCESSES

A. Conducting many training courses, for example the Good Clinical Practice (GCP) courses, which were completed by 340 people in Uganda and 263 in Rwanda
B. The organisation of ACREM (Applied Clinical Research and Evidence-based Medicine) courses in both Rwanda and Uganda, and the request by the Rwandan Ministry of Health to continue the courses
C. The conduct of seven PhD tracks, four in Rwanda and three in Uganda
D. The strengthening of clinical research environment and the establishment of a clinical research data and monitoring unit
E. Improved and upgraded health care and laboratory services as a result of infrastructure strengthening, implementation of operational research results and GCP training
F. Strong collaboration with partners in Uganda and Rwanda

LESSONS LEARNT

A. Five or perhaps six years is a more realistic time frame for a project with such broad objectives, because the start-up period for capacity strengthening and clinical research will take more time than initially anticipated
B. Choosing the right partners to work with is essential and depends on the national context
C. Other demands do not suit every context
D. It is important to develop specializations in order to stand out

MAIN APPLICANT

Academic Medical Center Amsterdam and the Center for Tropical and Emerging Infectious Diseases (CTED), the Netherlands

PARTNERS

Uganda: Makerere University, Infectious Diseases Institute. Rwanda: The Ministry of Health and the Treatment and Research for AIDS Center (TRAC Plus)

RUNNING TIME


BUDGET

€4,793,000

WE HAVE FOUND OUR NICHE

For a long time, African research institutes collaborated mainly with researchers from Europe and the United States. African clinics supplied data, which was then analyzed at Western universities. But INTERACT did things differently, and it laid the foundation for fruitful research contacts between Uganda and Rwanda. ‘We can use this cooperation to develop ourselves,’ says principal investigator of INTERACT Elly Kabatira, who is also the first African representative to hold the position of president of the International AIDS Society.

‘We were aware that a lot of research had been conducted on tuberculosis (TB) and HIV,’ says Elly Kabatira, professor at Makerere University and principal investigator of the Infectious Diseases Network for Treatment and Research in Africa (INTERACT). ‘But we wanted to do something that was sustainable, something that trained people. These skills will result in better health care for patients, even after the project has ended. All too often, projects do good work while they are running, but once the paper has been submitted, that’s it. The person who benefits most is the PhD student who conducted the research. But in the workplace, life tends to go on as before.’

Nadine Pakker, country director of INTERACT in Uganda explains what the network was trying to achieve: ‘The goal was to build and strengthen clinical trial capacity in Rwanda and Uganda,’ she explains. ‘Exactly what shape clinical trial capacity building’ should take was not clear to the participants at the beginning. ‘It took some time to develop the right approach with the partner institutes.’

The first to get underway in Uganda were three PhD programmes. ‘Specifically, our partners convinced us that INTERACT to be pampered,’ says Pakker. ‘For example, the director of the Infectious Diseases Institute at the time thought that 5 million euros to fund a PhD students was way over the top. They were agreed with the PhD students was way over the top. We explained that a substantial part of the budget was earmarked for capacity building, training and infrastructure, and that the 5 million would be spread across two countries over a four-year period – which was ultimately extended to five years.

This makes INTERACT unique, according to Pakker. ‘In the end, we succeeded together with our partner institutes, in setting up a sustainable and well-structured clinical research unit that would also support future clinical research activities. It is relatively easy to set up a clinical trial research team and collect data in Africa. But a recurring flaw is that people are not trained in a responsible, internationally accepted manner to be able to independently conduct and lead research. This problem is being solved by investing in ACREM (Applied Clinical Research and Evidence-based Medicine) and Good Clinical Practice training courses – as INTERACT is doing.’

Elly Kabatira is also very pleased with the results achieved by INTERACT in Uganda. ‘More than six hundred people have received Good Clinical Practice training,’ he says. ‘Our three PhD students will be awarded their doctorates at the end of 2011, and our master’s students have already graduated.’

A number of publications contributed to the output of Makerere University as well as the Kampala Capital City Authority Clinics, because one of the PhD students worked there in Kampala. As a result, scientific research has been put on the Kampala city council’s agenda. ‘The service we deliver to our patients has improved too,’ says Kabatira. ‘There was a budget to build three health units. These were containers with enough space and the necessities to conduct thorough research.’

CHANGING BEHAVIOUR

The fact that the research project had a budget for physical infrastructure is a break with the past, according to Kabatira. ‘In order to be eligible for funding, you have to meet the donor’s requirements. In the past, when we wanted to conduct a study with a

NADACAP

39

INTERACT

39
North American university, for example, and the study was funded by the United States, then we wouldn’t have the part of the research budget required to research facilities at Makerere University or the Kampaal Capital City Authority Clinics. The money went primarily to the American university, and we hereby supplemented data.

This has changed. ‘Instead of money sitting with a partner in the United States or Europe, the university is now with us,’ says Katahe. ‘We can use this cooperation to develop our own capacity.’

Ibrahim Sedaghe is a PhD student affiliated with the Kampaal Capital City Authority, and he has noticed the difference. The construction of additional office space in the form of modified containers at the three health units where INTERACT’s research has led to a change in behaviour, ‘he explains. ‘At first, no one wanted to work with INTERACT and there was no privacy and no infection control. These patients, who were often coughing, were always treated last. But now that we have a separate, well-equipped place for them, they have become priority patients.’

The health units are only one aspect of what INTERACT does. ‘In Uganda we can now offer a high-quality PhD education,’ says Harriet Mayanja-Kizza, head of the department at the Faculty of Medicine at Makerere University. ‘That’s something we had little expertise in. We also had to learn how to work together with an African country. Rwanda. I had never worked with Rwandans before and the academic interaction we had with them opened my eyes. We should work more with neighbouring countries instead of getting stuck in the old idea of seeing each other in Europe. We have to interact more among ourselves, share experiences and training, share capacities and capabilities so that we can develop as a region.’

Katahe is very positive about the South-South cooperation, which was a demand set by NACCAP from the very beginning. ‘South-South cooperation was not always treated last. But now that we have a separate, well-equipped place for them, they have become priority patients.’

Nevertheless, this approach does create dilemmas. ‘While the importance of capacity building is emphasized, by the United States on the one hand, the research results have to be produced at the same time. The different objectives sometimes have conflicting timelines,’ says Frank Cobelens, science coordinator at INTERACT. ‘A project that had to happen over a four-year period: we had to build the capacity to conduct research, and this project, and also fund PhDs at the end of the ride. So we had to start the research at an early stage, because our capacity was lower than is about more than just intellectual capacities – we also needed things to be in place, like the lab. That made it difficult at times.’

Pauline Byasika, a PhD student in Uganda, experienced exactly this while researching the interaction between anti-malaria drugs and HIV. ‘There was no local capacity in Uganda for testing one of the three medicines we were investigating,’ she explains. ‘I was facing strict deadlines and had to ship my samples to Bangkok. If I hadn’t had the pressure of a deadline, I could have devoted my time to building the capacity of the laboratory in Uganda.

Trendy terms

Four years for such a widely conceived project as INTERACT is too short, according to Boer. ‘If you really want to achieve something, you then have to give a project more time. A project like this needs a long-start-up phase. We found our niche only during the second half of the project, which is when it took on importance. We sorely needed the one-year extension to ensure that we could hand over the training to our partners – so that it wasn’t all left to the last minute. You need at least five or six years if you want trendy terms like sustainability, fair partnership and capacity building to really pay off. ‘I am surprised that INTERACT has grown as the project progressed. We have found that grew with time,’ she says. ‘The INTERACT team itself grew as the project progressed. We have seen that you need your own niche and your own kind of trademark. People respect INTERACT now for that reason.’

This respect is evident from the fact that the Infectious Diseases Institute is sending its staff to INTERACT’s training courses, says Pakker. INTERACT is genuinely appreciated for the impetus it gave to clinical research to the University of Makerere. ‘We had been asking with data management and a database building in Tanzania and other countries as well. Moreover, the national ethical committee had granted INTERACT to see what we can learn from each other.’

Positive response

Deep ties have developed with our Ugandan partners, halfway through the project, INTERACT was criticized for being insufficiently embedded in the local government structure. Embedding in the local government and institutional context are demands that you have to meet. European donors like to use this term, but in Uganda’s case university and government embedding are relatively disinterested, ‘said Boer. ‘In order to gain funding in Uganda and Rwanda was a huge learning experience. Everything goes through the Ministry in Rwanda. They want to be closely involved. The Ugandan Ministry, on the other hand, has little business to do with these kinds of projects. If we had consciously pushed our project in Uganda with the Ministry of Health, it probably would have impeded it. It is also important to recognize that the different countries and partners have different needs, in Rwanda INTERACT concentrates more on research methods academic training, whilst in Uganda we focus more on CCP and data management.

Now that the project is coming to an end, Pakker has noticed that INTERACT is seen more in the African context by other research groups too. ‘That’s really something that grew with time,’ she says. ‘The INTERACT team itself grew as the project progressed. We have seen that you need your own niche.’ A Good Clinical Practice, data management and training cooperation to develop our own capacity.’

According to Boer, the Rwanda example shows that choosing the partners you are going to work with is crucial. ‘This is where the major differences lay between Rwanda and Uganda. INTERACT in Uganda had mostly short lines of communication with the School of Public Health of Makerere University, the Infectious Diseases Institute and Kampaal Capital City Authority.

The Ugandan Ministry, on the other hand, has little to show for being insufficiently embedded in the local government structure. Embedding in the local government and institutional context are demands that you have to meet. ‘For many of the academic courses, working directly with Rwandan partners, or even with a Rwandan partner in the United States or Europe, the advantage is that you have to meet. European donors like to use this term, but in Uganda’s case university and government embedding are relatively disinterested, says Boer. ‘During our partnership, TRAC Plus was of the opinion that a larger project with disease surveillance and public health policy and operational research. Moreover, we would have been more satisfied if we had been able to get a longer extension like now. In Rwanda, INTERACT is considered an entity that is not incorporated into the existing structures.’

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Ensuring sustainability for future growth

Professor Irene Agyepong shares her views on the importance of ensuring that capacity building is sustainable for the future growth of research in Africa:

‘One of the biggest challenges with building capacity is to not create empty capacity. Lack of integration and contextual aspects, such as how researchers and their profession are perceived, or the process of “brain drain”, can result in the loss of built capacity. The ultimate goal of NACCAP has therefore been to strengthen the Research & Development capacity of multiple, locally-owned health research centres in Sub-Saharan Africa that are contributing to the EDCP objectives, and to do so in a sustainable way. NACCAP has aimed to provide a stronger research environment in which researchers can organise, prioritise and conduct research according to international quality and ethical standards. The centres should function independently as centres of knowledge and capacity building in their region and be able to contribute to the national research agenda for health. This objective can only be achieved when the centres are independent of their donor’s agendas and can independently decide what their research priorities are.

To achieve these arms, capacity building has been an integral part of NACCAP’s projects from the start. NACCAP has approached capacity building from a conceptual point of view, distinguishing three levels: individual, institutional and environmental. Capacity building needs to be carried out synergistically at all levels. Only then can capacity of individuals is built within the context of the research institutions in which they work. Institutional and environmental capacity needs to be developed alongside individual capacity to ensure the right work environment exists to support individual productivity and then to channel this towards sustainable new disease control interventions.

Successfully fighting the ‘brain drain’

The loss of expertise from African countries, the so-called brain drain, is one of the reasons why interventions targeted at capacity retention as well as capacity building are so important. Brain drain is not only a consequence of the potentially very large salary differences between countries, but also of the way that individual capacity is often built without developing institutional and environmental capacity to support and retain the expert individuals.

NACCAP’s project in Malawi has achieved remarkable results in addressing these aspects of the brain drain problem, even managing to reverse the brain drain, by developing a special Research Support Centre to invest in institutional capacity to support and retain Malawian researchers. This has involved training excellent Malawian researchers abroad and convincing them to return to Malawi to work in the Research Support Centre of the College of Medicine. Many were successfully convinced to return when they realised that their concerns about supportive institutional and wider environment issues had been addressed, for example, housing, transport and education for their children. This approach has also been adopted in Zimbabwe where brain drain is also successfully being reversed.

Ghana – a model of sustainability

Despite these inspiring examples, it is too early to determine whether the investments of NACCAP in capacity building will lead to sustainable results. A programme was started in Ghana in 1989, long before NACCAP began, to develop research capacity in a supportive institutional environment, while building individual capacity for health care systems research. The programme was initially supported by the British Department for International Development. From a small-scale programme aimed at capacity building for health systems research, consisting only of the Director for Research and a handful of staff, there is now a Research & Development Department within the Ghana Health Service with field research stations. The position of Research Officer, which did not exist before this initiative, is now an established position in the Ghana Health Service. As well as there being minimal brain drain of researchers, staffing, capacity and outputs have also continued to grow. Health systems research is now an institutionalised part of the health system, closely linked to the School of Public Health of the University of Ghana. Since the School of Public Health runs several projects involved in training future generations of researchers, this link represents an important contribution to sustainable capacity building. The ambitions of trainee researchers no longer seems to be to relocate to more developed countries after training, but rather to find their niche within Ghana.

It will be very interesting to see if NACCAP can achieve the same results elsewhere as those achieved in Ghana, where investments in capacity building have led to excellent research and researchers, and a positive perception of research within the health system. The potential to succeed exists, however, this will require dynamic and engaged leadership within the supported research institution together with a commitment to research on a national level. A major challenge for NACCAP in its final stages will thus be how to further support leadership development on institutional as well as national levels.

Diversifying the skill-set

A real challenge for environmental capacity building is the development of national health research systems that adequately support institutions and the individuals within these institutions. This effort requires relevant policy making on a national level, together with strong leadership, management and advocacy skills.

Unfortunately, such skills are not yet a part of the routine training of PhD level researchers. Likewise, the development of these skills has also not been part of NACCAP. Our work has shown us that most African researchers, like most other people, are not necessarily naturally blessed with skills such as advocacy. Specific training and development in these areas is therefore required. To address this, sub-projects should be introduced to train researchers in communication skills such as advocacy to strengthen their ability to lobby, network and impact on policy makers. Such expertise is required for environmental capacity building to support institutions in the long term.

Personally, I find NACCAP particularly interesting because of the linking of individual and institutional capacity development, which is not always the case with other donor-funded research programmes. The frequent and short-term exchange of researchers between partner institutions is another positive aspect of NACCAP. Often when people have had to live for several years in the North to obtain the required training, they experience difficulties when they subsequently try to re-adjust and re-establish themselves in their home country. The result is that they often choose not to return. NACCAP has addressed this issue by providing short-term exchanges of only a few months. In this way, a fruitful exchange between researchers from both worlds has been achieved while at the same time ensuring researchers have not become estranged from their country of origin. This has proven to be a very successful formula to prevent brain drain and to secure and maintain the enthusiastic, long-term involvement of partners.

Professor Irene Agyepong is Regional Director of the Ghana Health Service and a member of the NACCAP Programme Committee.

‘Success will require dynamic and engaged leadership within the supported research institutes, together with a commitment to research on a national level’
ART-A

Sub-projects
1. Development of a convenient sample collection device suitable for use in Africa, together with an affordable, easy to use viral load and sequencing protocol
2. Development of affordable genotypic applications
3. Implementation and optimization of genotypic interpretation software
4. Creation of automated sequence analysis software that is freely available online
5. Improve technology transfer by means of a Training Work Package
6. Improve dissemination of information and communication to help build research capacity

Goals
1. Development of a convenient sample collection and kit to enable it to be positioned as a cheap, transferable kit, to capacitate countries to produce the new lab tests to measure HIV viral load as well as drug resistance suitable for use in Africa and drug resistance test suitable for use in Africa
2. Development of affordable, easy to use viral load and sequencing protocol
3. Implementation and optimization of genotypic interpretation software
4. Creation of automated sequence analysis software that is freely available online
5. Improve technology transfer by means of a Training Work Package
6. Improve dissemination of information and communication to help build research capacity

Success stories
- Algorithms were developed, including several new lab tests to measure HIV viral load as well as drug resistance test suitable for use in Africa and drug resistance test suitable for use in Africa
- The ART-A algorithms have been successfully transferred for local applications in Uganda and South Africa, and the ART-A tests have been submitted for provisional patenting in South Africa
- A unique cooperation was established between academic, not-for-profit, and commercial partners to develop the best possible kits to deliver the stated goals

Lessons learned
- Allow for more time to deal with the logistical and legal delays that are unavoidable when dealing with multiple countries
- Conduct more thorough costings. Financial constraints resulted in the number of countries planned for the trials to be cut from five to two
- Ensure that the budgets of donors and state projects in Africa allow for viral load and resistance testing. In view of the increasing prevalence of drug resistance in sub-Saharan Africa, this should be done without reducing the market for the ART-A kit

Main applicant
The Center for Poverty related Communicable Diseases (CPCD) through the PharmAccess Foundation, Amsterdam, the Netherlands

Public Partners
The Netherlands: Dept. of Molecular Medicine and Hematology (CPCD) through the PharmAccess Foundation, Amsterdam, the Netherlands
Belgium: VIRCO, Mechelen, South Africa: Contract Laboratory Services (CLS), Uganda: Joint Clinical Research Centre (JCRC)
Luxemburg: Centre Utrecht (UMCU), Utrecht
The Netherlands: Centre de Recherche Public de la Santé (CRP Santé), South Africa: Dept. of Molecular Medicine and Hematothogy, WitsvanderZee University (Wits), Johannesburg
Private Partners
Belgium: VIRCO, Mechelen, South Africa: Contract Laboratory Services (CLS), Uganda: Joint Clinical Research Centre (JCRC)

Running time
1 October 2008 – 30 September 2010 (budget-neutral extension until 31 December 2011)

Budget
NACCAP: 3,000,000, CLS: 500,000 (in kind), VIRCO 2,500,000 (in kind)

Professor Tobias Rinke de Wit, director of the ART-A (Affordable Resistance Test for Africa) project, holds a grudging respect for the virus he is trying so hard to fight. He explains, ‘HIV is one of the most remarkable organisms we have to deal with. First of all, it uses the power of numbers. In an HIV patient who is not on treatment, more than 10 billion viruses are generated every day. On top of this, the virus is extremely variable, it changes every day. High numbers combined with high mutation speed is a deadly combination: the virus basically creates every possible mutation. Resistance is extremely difficult to fight such a virus, whether it is with drugs or by developing a vaccine.’

HIV is normally treated using a combination of drugs with the aim to keep the numbers of viruses in the body as low as possible. Reducing the viral count will avoid the weakening of the immune system. This will allow the immune system to recover from the damage already caused by HIV and allow it to better fight any secondary disease.

The drugs can provide a valuable lifetime to someone infected with the virus. However, they need to be taken every day for the rest of a person’s life. ‘If you reduce or interrupt the drugs for any reason – perhaps due to forgetfulness or because the drugs are finished at the clinic, then the virus will start to replicate again. This will allow the virus to mutate and develop resistance to the drugs. The only way to keep the patient safe, and drug resistance down, is to keep the numbers of viruses down,’ says Rinke de Wit.

At the beginning of treatment, the combination of drugs that a person is given is called first line therapy. If the virus becomes resistant to these drugs after a while, or because the side effects are particularly bad, then a change to second line therapy can be made.

Second line therapy involves administering a new combination of drugs. Unfortunately these second line drugs are five to ten times more expensive.

One of the primary researchers working on the ART-A project is South African scientist Michelle Bronze. She explains the implications of HIV treatment in Africa. ‘Before patients initiate any therapy, a drug resistance test should ideally be performed. This will establish if the virus transmitted to the patient is a resistant strain and will help determine the best combination of first line drugs to take. Here in Africa, we can’t afford such tests, so a standard first line therapy is given. There is generally a choice of three first line treatments, regardless of the subtype of HIV contracted or whether the HIV is resistant to any of the drugs.’

If a patient fails to adhere to therapy or if the therapy is not as effective as it should be, the viral load in a patient will increase. When a patient has a viral load of more than 5,000 copies per ml of virus, the standard treatment is to prescribe second line therapy. Again, this is given ‘blindly’, without initial resistance test.

The choice of second line drugs may also not be correct or the patient may not actually need second line therapy at all.

Currently, 5 to 7% of patients in sub-Saharan Africa, and 12% in Uganda, are infected with a drug-resistant HIV. For those patients who are infected with a drug-resistant HIV, the treatment is not effective and the patient will fail to respond to therapy.

Chasing the elusive virus

HIV remains one of the biggest killers in Africa, due in no small part to the virus’s remarkable ability to mutate. This ability allows it to build resistance against known drugs for HIV and renders finding a cure or long-lasting treatment almost impossible. The ART-A project was set up to develop an affordable HIV drug resistance test for Africa to help ensure that the treatment received by patients is effective, while reducing the proliferation of drug resistant strains of the virus. It is the first project funded by NACCAP that brings together public and private partners.

Their joint expertise enables them to make important strides in the African fight against HIV.
Similarities of this case with the ART-A project draws in a consortium of international partners so that these can share their information can be uploaded to a secure site and the resultant data can be used to test representative samples of HIV patients at key locations in Africa. The health policy makers would benefit from knowing which type of drug resistance, if any, is circulating in their country. This information would help them to make the right decisions when choosing the drugs for HIV treatment. A greater number of patients would benefit from this test in a timely manner, and patients would be able to understand the repercussions of not taking their pills. This was not the case.

Bronze's experience underscores why the ART-A project is so important. If, a scientific discovery translates into real life, it can provide generic software for interpreting the results, and so we miniaturized the test, thereby effectively reducing the volumes for manufacture, transport costs and so on. The project aims to develop an algorithm capable of translating genotypic data into a phenotypic analysis. The project aimed to develop the ART-A viral load test with a targeted cost of between $10 and $15, depending on variable costs within each country. In practice, the developed and tested system is much more cost-effective than those in current use. In Uganda, the average cost saving is 56% and in South Africa it is 63%.

The result is that clinics can have a testing facility where a nurse can initiate the testing by taking a sample and making dried blood spot samples. These can easily be sent to a reference lab for testing. Even with a slow internet connection, the resultant information can be uploaded to a secure site and the resultant data can be used to test representative samples of HIV patients at key locations in Africa. The health policy makers would benefit from knowing which type of drug resistance, if any, is circulating in their country. This information would help them to make the right decisions when choosing the drugs for HIV treatment. A greater number of patients would benefit from this test in a timely manner, and patients would be able to understand the repercussions of not taking their pills. This was not the case.

The experience also motivated Bronze to seize the opportunity the project offered in terms of empowering African scientists. Not only has she been working in a haematology lab so had immediate access to philoviral antiretroviral treatment.

The main motivation for the ART-A research was to find a way to allow more patients in resource poor countries to access better, safer healthcare. At first, this was not the case. The project is currently undergoing clinical evaluation. The best way for ART-A tests to be used is for key locations in Africa. The health policy makers would benefit from knowing which type of drug resistance, if any, is circulating in their country. This information would help them to make the right decisions when choosing the drugs for HIV treatment. A greater number of patients would benefit from this test in a timely manner, and patients would be able to understand the repercussions of not taking their pills. This was not the case.

In 2007, shortly before beginning work on the ART-A project, Bronze was working in a haematology lab so had immediate access to phylloviral antiretroviral treatment. From the position of a detached, scientific observer, Bronze suddenly found herself in the world of people on antiretroviral treatment, the very people her research was aiming to help. She was able to understand first-hand how it felt. It was horrible, she explains. You have a constant headache and feel like your brain is going to burst out of your head as I realized I had forgotten to take my last pill.

Bronze entered the experience of adherence. A first-hand account

The importance of strict adherence to treatment, day after day, was emotionally brought home to Bronze in a way she would never have expected. This experience completely changed the way she viewed her work and the lives of those around her.

Adherence? A first-hand account

Security

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The final words of the NACCAP programme committee are as follows:

The NACCAP Programme Committee is the scientific organ, established and mandated by the Steering Committee to develop work plans for new funding activities and actively monitor the progress of ongoing activities performed under NACCAP.

**Chair**
Prof. E. Joost Rutenber
Professor of Immunology, Chair for International Public Health, Free University of Amsterdam, the Netherlands

**Members** (alphabetical order, from 1 January 2009)
- Irene A. Agyepong
  District Director of Health Services, Ghana Health Service, Ghana
- James G. Hakim
  Chair of Department of Medicine, Zimbabwe University, Harare, Zimbabwe
- Andy I.M. Hoepelman
  Head Department of Internal Medicine & Infectious Diseases, University Medical Center, Utrecht, the Netherlands
- Opoloa Ofori-Ayim
  Senior Manager Clinical Development, Ciba-Geigy, Belgium
- Prof. Andy I.M. Hoepelman
  Head Department of Internal Medicine & Infectious Diseases, University Medical Center, Utrecht, the Netherlands
- Dr Els Borst-Eilers
  Professor of Immunology, Chair for International Public Health, Free University of Amsterdam, the Netherlands
- Prof. E. Joost Ruitenberg
  Chair for International Public Health, University Medical Center, and CEO of Jeroen Bosch hospital, Den Bosch, the Netherlands
- Dr Els Borst-Eilers
  Professor of Immunology, Chair for International Public Health, Free University of Amsterdam, the Netherlands
- Prof. Irene A. Agyepong
  Chair of Department of Medicine, Zimbabwe University, Harare, Zimbabwe
- Prof. Andy I.M. Hoepelman
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For the mid-term reviews of the NACCAP project, ad hoc external MTR committees were established. These MTR committees were chaired by Prof. Agyepong of the Secretariat (NWO-WOTRO office).

Dr Judith F.E.M. de Krom
Senior Programme Coordinator NACCAP

Dr Els Borst-Eilers
Professor of Immunology, Chair for International Public Health, Free University of Amsterdam, the Netherlands

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Dr Judith F.E.M. de Krom
Senior Programme Coordinator NACCAP

Dr Els Borst-Eilers
Senior Programme Coordinator NACCAP
Colophon

This booklet is a publication of
NWO–WOTRO Science for Global Development
Laan van Nieuw Oost-Indië 300
2593 CE The Hague
Netherlands
Tel.: + 31 (0)70 344 0763
Fax: + 31 (0)70 381 9874
E-mail: wotro@nwo.nl
Website: www.wotro.nl

Concept
Lokaalmondiaal

Production and Coordination
Selma Zijlstra

Texts
Irene Agyepong
Janneke Juffermans
Andrew Kitua
Greg Marinovich
Opokua Ofori-Anyinam
Joris Tielen
Ilse Zeemeijer

Photography
Jimmy Adriko
Geoffrey Kamali
Charles Kimani
Greg Marinovich
Djibril Sy

Editing
Sanne de Boer and
Nerissa Lonergan

Translation
Contactivity

Graphic Design
SAZZA, Amsterdam,
www.sazza.nl

ESSENCE on Health Research
members Professor Hannah
Akuffo (Swedish International
Development Agency and
chairperson of EDCTP’s General
Assembly), Dr Val Snewin
(Wellcome Trust) and Dr Linda
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[Photo (right): Charles Kimani
Photo front cover: Jimmy Adriko]