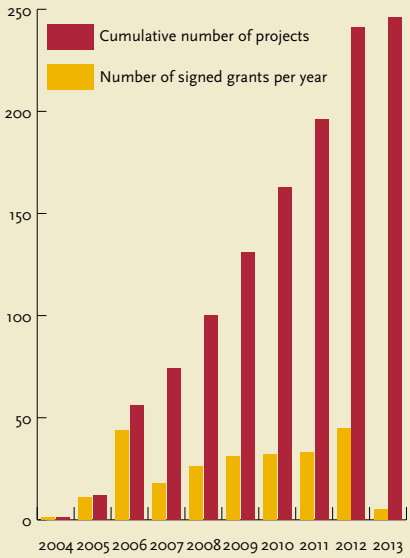
EDCTP

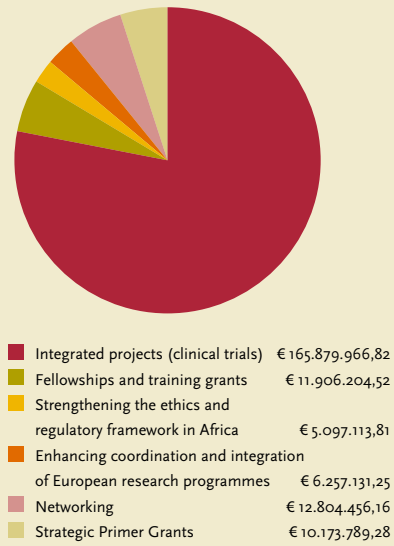
European & Developing Countries Clinical Trials Partnership

Annual Report 2013

The first decade

Key performance indicators 2003-2013

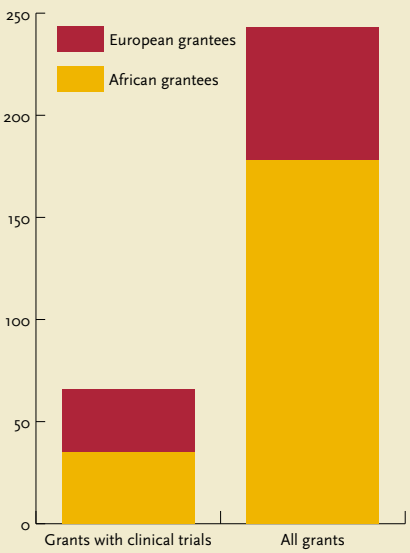


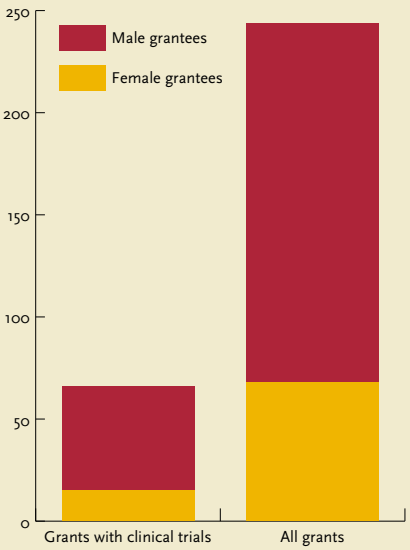


EDCTP grant giving activities

Since 2003, EDCTP has launched 65 calls for proposals and funded 246 grants with a total signed value of € 212.12 million. The main EDCTP funding schemes are:

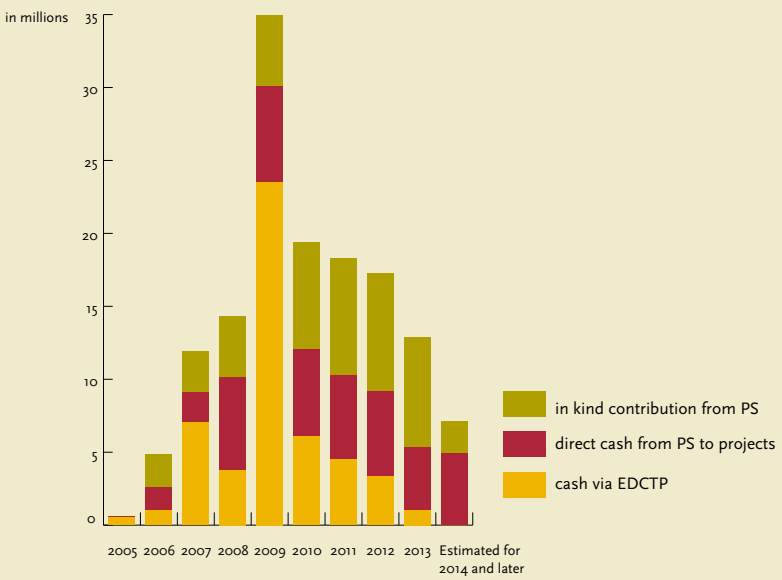
- Integrated Projects (clinical trials as the core activity with associated capacity building and networking activities)
- Ethics (establishing, strengthening and mapping of national ethics committees and institutional review boards)
- Fellowships (personal awards to African researchers, with a focus on Senior Fellowship awards to develop African research leaders and building research teams)
- Member States Initiated projects (enhancing integration and coordination of European member states' research projects)
- Regional Networks of Excellence for conducting clinical trials (collaborative support for regional consortia)
- Joint Call by Member States (thematic research projects funded through pooled funds from several EDCTP Participating States)
- Strategic Primer Grants (short-term awards that provide seed funding for researchers to explore novel and innovative lines of research that may lead to the development and testing of new or improved clinical interventions).





Profile of EDCTP grantees

EDCTP promotes African leadership in the conduct of clinical trials as part of its strategy to build sustainable research capacity in Africa. Seventy-two percent of EDCTP projects are led by researchers employed at African institutions. Recognising that women are under-represented in research, particularly in Africa, EDCTP aims to achieve a gender balance by actively encouraging female applicants to its schemes and by promoting gender balance in the composition of consortia. Twenty-eight percent (28%) of all EDCTP grants are led by female researchers. It is encouraging to note that 40% of PhD students and 42% of Master's students supported on EDCTP grants are African women.



Annual cofunding contribution from EDCTP Participating States to EDCTP activities

The amount of cofunding from EDCTP Participating States (PS) to the EDCTP programme was € 141.62 million by the end of 2013. The contributions from the Participating States are made in cash or other resources required for the successful conduct of the project. Cofunding can be given via EDCTP, directly to the project and in kind.

Contents

Message from the Executive Director

In 2013, EDCTP celebrated its tenth anniversary marking a decade of partnership. This was a remarkable year in many ways, especially because commitments and decisions to continue and expand the programme were taken. Following the decision of EDCTP Participating States and the European Union (EU) not only to continue with the programme, but also to expand it, earnest preparations started to outline the new programme. To ensure there was no loss of momentum, EDCTP organised a series of stakeholder meetings on various themes to gather input on what the new programme should look like. To complement this, various mapping exercises were conducted to gather data on the research activities of the prospective Participating States within the scope of the EDCTP programme– neglected infectious diseases and implementation research included – from both Africa and Europe. The aim of the mapping exercises was to identify not only gaps and specific needs, but also areas of strength and where activities could be coordinated to enhance synergy.

Other undertakings to ensure readiness for the second EDCTP programme included continued capacity strengthening activities such as supporting 24 clinical laboratories in sub-Saharan Africa in their development towards accreditation. Furthermore, EDCTP launched a call for proposals in epidemiology and medical statistics in view of the current lack of capacity in this field. The call was received well and resulted in 52 eligible applications.

In order to consolidate what had been achieved to date, and to expand its activities, EDCTP reached out to potential new members in Europe and Africa. Advocacy and information dissemination visits were made to European Union Member States that were not part of EDCTP. Following these visits, expressions of interest have come from some countries, among which Finland and Latvia. EDCTP organised a high-level meeting in Dakar, Senegal, that brought together several African government ministers and high-level officials representing health research funding institutions in sub-Saharan Africa. At the meeting, several African governments showed their willingness to join EDCTP as members. EDCTP followed up with measures to change its legal implementation structure from a European Economic Interest Group to an Association under Dutch law. Such a structure allows African countries and non-EU countries that are associated to the European Union Framework Programme Horizon 2020, to join the organisation as members.

Other improvements in EDCTP's governance included the streamlining of the advisory structure. In 2012, the Partnership Board and the Developing Countries Coordinating Committee were merged to form the Interim Strategic Advisory Committee and in 2013 this was replaced by the Scientific Advisory Committee. The Scientific Advisory Committee will serve both the current and the new programme on scientific and strategic matters.

All of these preparatory activities took place on the background of continuing monitoring and supporting of many ongoing EDCTP-funded projects. By the end of its first decade, EDCTP had launched 65 calls and supported 246 projects with a total value of € 212.12 million; 106 of these were still ongoing. All of this could not have happened without the strong support of our stakeholders: research volunteers and their communities, especially from sub-Saharan Africa; the research community; international development partners; scientific peer reviewers; EDCTP advisory bodies; the European Union; our General Assembly members and many others. Special thanks go to our Secretariat, which has worked tirelessly and diligently over the past decade.

Charles S Mgone
Executive Director

A decade of partnership

The European & Developing Countries Clinical Trials Partnership (EDCTP) was created in 2003 as a European response to the global health crisis caused by HIV/AIDS, tuberculosis and malaria. Its first objective was to accelerate the development of new or improved interventions towards prevention and treatment of these three major poverty-related diseases especially by supporting clinical trials. Its second objective was to facilitate cooperation and integration of relevant European national research programmes and activities. These two objectives were to be accomplished through working in partnership with sub-Saharan African countries and like-minded organisations.

The partnership

EDCTP was devised as an initiative based on Article 185 (ex-Art. 169) of the Treaty on the Functioning of the European Union, which allows the EU to participate in research programmes undertaken by several EU Member States. The EDCTP partnership currently comprises 16 European Participating States (14 EU Member States and 2 associated European countries) and sub-Saharan African countries.

With support of the EU, the EDCTP programme brought together the combined strengths of its European Participating States with those of their sub-Saharan African counterparts and interested third parties in order to address the global challenge of fighting poverty-related infectious diseases, which is beyond the capacity of individual countries. It facilitated cross-border research in Europe and sub-Saharan Africa and contributed to the development of the European Research Area. The programme also promoted sustainability and African ownership through support of capacity building in sub-Saharan African countries. Through EDCTP, European countries had a coherent and coordinated voice internationally and a common strategy for clinical research to fight poverty-related infectious diseases.

Integrated projects for sustainable research

EDCTP has developed a programmatic funding approach that focuses on clinical trials as the core activity and supports networking and capacity development integrated with the clinical trials.

Targeting HIV/AIDS, tuberculosis and malaria, EDCTP has funded clinical trials on treatment drugs, vaccines, microbicides and diagnostics. Through its funding instruments, it has contributed to the coordination and integration of national research programmes. Results from various trials have informed national and international policies such as the WHO policy on the prevention of mother-to-child transmission of HIV and the registration of a paediatric formulation of an antiretroviral product (Pedimune) in several African countries. Furthermore, in its first decade, EDCTP provided professional training to 514 African scientists and medical doctors, including 56 Career and Senior Fellows as well as more than 406 Master's and PhD students.

Overall, EDCTP represents a flagship programme for conducting sound multi-country clinical trials in sub-Saharan Africa, building a true partnership between Europe and Africa, and fostering African leadership in scientific research. Europe's strong commitment to partnership is reflected in the fact that 74% of EDCTP funding was invested into activities implemented by African research institutions and 72% of all EDCTP-funded projects were led by African researchers.

The EDCTP programme also contributed to networking African research which resulted in the launch of four African Regional Networks of Excellence for clinical trials. Moreover, the ethics and regulatory environment has been improved by strengthening ethics review capacity and national regulatory authorities in many African countries. EDCTP was the main funder of the African initiative to establish the Pan African Clinical Trials Registry (PACTR, www.pactr.org), which is now an official WHO Primary Clinical Trials Registry.

Towards EDCTP2

Based on the progress so far, the second EDCTP programme (EDCTP2) will be implemented from 2014 to 2024 as part of the next European Framework Programme for Research and Innovation - Horizon 2020. Its scope is based on the current objectives and achievements and will be expanded to include all clinical trial phases (I-IV); neglected infectious diseases (NIDs)[1]; diagnostic tools; and health services optimisation research. The new programme will also see a stronger partnership, with more European and African countries participating, and increased collaboration with the pharmaceutical industry, product development partnerships, philanthropic organisations and development agencies. As global efforts are required to address poverty-related and neglected infectious diseases, partnerships and synergy with other funders which support research outside sub-Saharan Africa, will be necessary.

EDCTP aims to integrate and align national programmes and projects into one strategically coherent Joint Programme. The current Participating States, with the exception of Belgium, expressed the political will to support EDCTP2. New European countries, including Finland and Latvia, as well as several African countries, expressed interest to join EDCTP2 as members of its new legal framework. By the end of 2013, the total financial commitment to the second programme was an estimated € 1.366 billion. The expanded scope of EDCTP will transform the initiative into a major global player in product development for poverty-related and neglected infectious diseases as it will have increased financial resources to provide leadership in funding clinical testing and developing safe and efficacious products for poverty-related and neglected infectious diseases. EDCTP is expected to move from a collaborative research programme to a programme that will contribute to the long-term sustainable development of sub-Saharan Africa.

[1] The NIDs that will be covered by EDCTP2 are those in the WHO-TDR list of Neglected Tropical Diseases (www.who.int/neglected_diseases/diseases, except Chagas disease) in addition to diarrhoeal and respiratory infections.

EDCTP timeline 2003-2013

2003

In September 2003, 14 European Union Member States and Norway established EDCTP with support of the European Union. The programme was formed to pool resources, funds and activities to achieve a greater impact against HIV/AIDS, tuberculosis and malaria in sub-Saharan Africa. The initial intended duration of the programme was five years with a budget of € 400 million. EDCTP was the first programme created under the umbrella of the Article 185 (ex-Article 169) of the Treaty on the Functioning of the European Union and was set up under the Sixth Framework Programme (FP6) for Research and Technological Development.

2004

Hosted by the Netherlands Organisation for Scientific Research (NWO), the EDCTP Europe Office in The Hague was officially opened on 4 February 2004. A few months later, on 26 July 2004, the EDCTP Africa Office, hosted by the Medical Research Council (MRC) of South Africa, was launched in Cape Town.

Six calls for proposals on HIV/AIDS, tuberculosis and malaria were launched in two rounds (February 2004 and June 2004). In May 2004, EDCTP launched the first Senior Fellowships call for proposals.

2005

A new set of calls for proposals was launched. These regarded site development for phase III trials on tuberculosis vaccines; site development for phase I/II and phase III trials of microbicides against HIV; treatment of HIV/TB co-infection; networking grants; strengthening research ethics review; and proposals for Senior Fellowships, Career Development Fellowships, PhD scholarships and MSc studentships. The calls for proposals amounted to more than € 20 million. It was the first time that EDCTP Participating States' cofunding was introduced for large capacity building and clinical trials.

2006

New calls to support the prevention of HIV/AIDS in Africa were launched. The call for proposals for the prevention of mother-to-child transmission of HIV with a total budget of € 6.1 million was published in July 2006. On World AIDS day 2006, EDCTP together with EDCTP Participating States and the Bill & Melinda Gates Foundation, launched a € 20 million grant to support capacity development to prepare for phase II clinical trials of HIV preventive vaccines.

2007

The Integrated Projects grant scheme that combines clinical trials as a core component with networking and capacity strengthening activities, was established. For the first time, EDCTP initiated thematic stakeholders meetings prior to the launch of calls. Representatives from the EDCTP Participating States, pharmaceutical industry, other product developing partners and scientific experts participated. These meetings informed EDCTP of current and future research developments in the field of HIV/AIDS, tuberculosis and malaria, and provided recommendations for research strategies and implementing partners.

2008

In January 2008, a consortium of TB research groups started to draft a proposal to shorten and simplify first-line treatment of TB. It was the beginning of the Pan African Consortium for the Evaluation of Antituberculosis Antibiotics (PanACEA). The consortium started to conduct a coordinated series of clinical trials to evaluate different combinations involving three new drugs, moxifloxacin, rifampicin and SQ109, for treatment of drug-sensitive tuberculosis.

In December 2008, a grant was signed for the first EDCTP-funded Network of Excellence for the conduct of clinical trials, the Central African Network on Tuberculosis, HIV/AIDS and Malaria (CANTAM).

2009

In September 2009, the World Health Organization (WHO) conferred on the EDCTP-funded Pan African Clinical Trials Registry (PACTR) the status of primary registry, the only such registry in Africa. PACTR now feeds data into the global WHO International Clinical Trials Registry Platform facilitating African representation in the global overview of planned, ongoing and completed clinical trials.

The first EDCTP Awards for Outstanding African Scientist were given to Dr Alexis Nzila (Republic of Congo) and Dr Dominique Pepper (South Africa). The award ceremony took place at the Fifth EDCTP Forum in Arusha, Tanzania, on 14 October 2009. These awards are given to mid-career and senior researchers in sub-Saharan Africa with significant achievements in their fields. Since 2009, these awards are given biennially.

2010

The European Commission (EC) carried out an assessment of EDCTP's impact, consisting of a public consultation of all EDCTP stakeholders and an analysis by an EC expert panel. It was agreed that EDCTP should continue and that its impact could be maximised by expanding its scope to phase I and IV clinical trials and to other neglected infectious diseases. In September 2010, representatives from the Participating States organised a meeting under the Belgian EU Presidency to seek agreement on a proposal for a second programme of EDCTP to the European Council and the European Parliament.

2011

A Strategic Business Plan for a second EDCTP programme was drafted. The plan provided the foundation for the legislative process for approval of continuation and expansion of the EDCTP programme by the European Parliament and the Council.

EDCTP held its Sixth Forum in Addis Ababa, Ethiopia, on 9-12 October 2011. It was the largest EDCTP Forum to date. The Forum showed the maturation of the EDCTP programme as evidenced by 265 presentations (including 138 posters); more than 60% of these were from EDCTP-funded projects.

2012

In March 2012, EDCTP received an EC Coordination and Support Action (CSA) grant. The EDCTP-Plus activities supported by this CSA grant are to consolidate the achievements of the first EDCTP programme and lay the foundation for the second programme.

National representatives from current and prospective Participating States of EDCTP convened in Copenhagen, Denmark on 15 May 2012 with the support of the Danish EU Presidency. The goal was to begin the process of expanding European membership of the second EDCTP programme.

A high-level meeting to consult African and international stakeholders was hosted by the South African government, the European Commission and EDCTP, in Cape Town on 5 November 2012. The objective was to discuss the needs and expectations from African, European and global partners. The meeting was attended by ministers and senior representatives from African and European governments, product development partners, the research community and civil society representatives. At the meeting, several African and European governments expressed a clear commitment to EDCTP2.

2013

In 2013, the 10th year of the EDCTP programme, the focus of activities was on preparations for the second EDCTP programme. The EDCTP2 proposal of the European Commission was discussed in the European Parliament and the Council.

Five stakeholder meetings were held on six thematic areas: neglected infectious diseases, HIV, malaria, tuberculosis, and a joint meeting on research ethics review and regulatory affairs.

A second high-level meeting on EDCTP2 took place in Dakar, Senegal, on 21 October 2013. High-level representatives from African countries, European Participating States reaffirmed their commitment to the second EDCTP programme.

2013 in a nutshell

In 2013, the 10th year of the EDCTP programme, the focus of activities was on management of active grants and preparations for the second EDCTP programme (EDCTP2). These preparations were part of the EDCTP-Plus project funded by the Coordination and Support Action grant (304786) from the European Commission. Funding from two of its Participating States (Sweden and United Kingdom) enabled EDCTP to launch a call for applications in August 2013. The Master's Fellowships in Epidemiology and Medical Statistics aim to support the training and career development of junior researchers.

Five stakeholder meetings were held on neglected infectious diseases, HIV/AIDS, malaria, tuberculosis and other mycobacterial infections, as well as on research ethics review and regulatory affairs. The recommendations from the meetings contributed to EDCTP's strategy and funding approaches for the second programme.

A second high-level meeting on EDCTP2 took place in Dakar, Senegal on 21 October 2013. High-level representatives from African countries, European Participating States as well as current and potential partners were brought together to reaffirm their commitment to the second EDCTP programme. The Seventh EDCTP Forum which was planned to take place in Dakar from 22-24 October 2013 had to be cancelled due to the necessity for the Senegalese government to host the ECOWAS Heads of State summit in the Forum venue during the scheduled dates.

EDCTP Awards

Every two years EDCTP confers awards for scientific excellence to African scientists. In November 2013, Prof. Glenda Gray (University of Witwatersrand and Medical Research Council, South Africa) received the EDCTP Outstanding African Scientist Award. The achievements of Dr Graeme Meintjes (University of Cape Town, South Africa) were recognised with the EDCTP Rising Star African Scientist Award. The awards consist of a recognition trophy and a cash prize of € 20,000 and € 10,000 respectively. The awards aim to further the research programmes of the winners.

Prof. Glenda Gray is one of the world's foremost authorities on the HIV epidemic in sub-Saharan Africa. Her work on the epidemiology and biology of HIV and advocacy for improving the care of HIV-infected individuals are well recognised. She is also the recipient of the Nelson Mandela Award for Health and Human Rights for her instrumental work in reducing mother-to-child transmission of HIV-1. Prof. Gray is the founding Executive Director of the Perinatal HIV Research Unit in Cape Town, South Africa. She aims to use the prize to support two PhD projects led by young women scientists: "By supporting cutting edge research and early stage investigators, I am committed to developing African scientists of the future".

Dr Graeme Meintjes is an Associate Professor of Medicine at the University of Cape Town (UCT). He was a Wellcome Trust Training Fellow from 2007 until 2011 and was awarded a 5-year Wellcome Trust Intermediate Fellowship in Public Health and Tropical Medicine in 2012. He jointly established and ran the Infectious Diseases Unit at GF Jooste Hospital in Cape Town from 2004. In 2012 he became a full member of the Institute of Infectious Disease and Molecular Medicine at UCT. Dr Meintjes will continue to develop his research on HIV-TB co-infection and TB treatment.

Prof. Glenda Gray, Dr Michael Makanga and Dr Graeme Meintjes at the EDCTP Awards ceremony in Cape Town, South Africa

Second high-level meeting on EDCTP2

The second high-level meeting on EDCTP2 took place in Dakar, Senegal on 21 October 2013. The meeting was hosted by the Ministry of Health of Senegal, the European Commission and EDCTP. It followed up on the first high-level meeting in Cape Town, South Africa that took place on 5 November 2012. High-level representatives from African countries, delegates from European EDCTP member countries and other current or potential partners participated to reaffirm their commitment to EDCTP2. The objective of the meeting was to discuss practical ways to ensure active and direct involvement of African countries in the EDCTP programme and governance.

The meeting was attended by government ministers and their delegations from the The Gambia, Republic of Congo, Senegal, South Africa, Uganda and Zambia, while other countries were represented by senior officials, including Burkina Faso, Cameroon, Gabon, Kenya, Mali, Mozambique, Niger and Tanzania. This high-level representation was a clear indication of the continued commitment of African governments to EDCTP. The European Commission as well as the African Union Commission of Social Affairs, the New African Partnership

Dr Matshidiso Moeti, Mr Victor Madeira dos Santos, Prof. Charles Mgone, Prof. Hannah Akuffo, Hon. Prof. Awa Marie Coll-Seck, Hon. Adv. Tshililo Michael Masutha, Hon. Prof. Nkandu Luo and Dr Pascoal Mocumbi at the opening session

for Economic Development (NEPAD) and the World Health Organization Regional Office for Africa (WHO-AFRO) had high-level representation.

At the meeting, representatives of the governments of Senegal, South Africa, Tanzania and Uganda indicated preference to join EDCTP as individual countries, while others favoured regional and sub-regional representation. The challenge of finding a way of representing the interests of the countries not directly involved in the General Assembly was recognised and national and sub-regional representations were not considered to be mutually exclusive concepts. While there were different views on the mechanism of representation, the strong willingness of African countries to be represented on the EDCTP General Assembly was abundantly clear.

Stakeholder meetings

A series of thematic stakeholder meetings in preparation for the second EDCTP programme was successfully completed in 2013. Meetings on neglected infectious diseases (The Hague), HIV/AIDS (Lisbon), malaria (Vienna), tuberculosis and other mycobacterial infections (Paris), as well as meetings on health research ethics review and regulatory affairs (Antwerp) brought together experts from research institutions, policymaker and representatives of product development partnerships, pharmaceutical industry and international organisations. A stakeholder meeting on capacity development will be held on 3 July 2014 in Berlin, Germany.

These meetings aimed to:

- Identify and review the current research issues, interventions, products in development and key players in the field
- Ensure that EDCTP remains focused on the most pressing research needs, the most promising opportunities, and aligns its strategic planning and funding approaches accordingly
- Identify priority areas for future calls for proposals
- Identify interested and potential partners to collaborate with in the execution of future EDCTP activities
- Harness the efforts of EDCTP stakeholders in order to promote integration of national programmes of EDCTP European Participating States and strengthen the partnership with African researchers.

The recommendations from these meetings will further inform EDCTP's strategic planning and operational workplans for the second programme.

Mapping research

A comprehensive analysis of relevant European and African national research programmes, partnerships, activities and capacities was conducted as part of the EDCTP-Plus project. The mapping project consisted of several studies.

The Secretariat conducted a desk review of European Member States' research programmes and, as part of the preparation for the annual workplan, liaised in 2013 with EDCTP Participating States to collect information on activities within the scope of EDCTP and identify opportunities for synergy between different countries. Secondly, in 2012 the Secretariat commissioned a bibliometric analysis of African and European research programmes, partnerships, activities and capacities in the fields of HIV/AIDS, tuberculosis, malaria and neglected infectious diseases over the period 2003-2011. The report was finalised in 2013 and included a supplementary analysis of intra-European research collaboration in each of the disease areas, an evaluation of the impact of EDCTP-funded research and an overview of leading sub-Saharan African researchers based on research outputs and citations. Lastly, a second study commissioned under EDCTP-Plus mapped sub-Saharan African health research activities and capacities in the relevant areas and analysed how these relate to national funding commitments, health research policies and the mission of EDCTP.

Evaluation of EDCTP ethics grants programme

A comprehensive evaluation of the EDCTP grants programme for strengthening research ethics review in sub-Saharan Africa and all 75 EDCTP funded ethics projects were analysed. This evaluation – based on desktop review, interviews and on-site visits - was part of the EDCTP-Plus project.

The evaluation focused on each of the three EDCTP funding areas: the mapping of ethics review and clinical trial regulatory capacity in sub-Saharan Africa (MARC); establishment and strengthening of National Ethics Committees (NECs) and Institutional Review Boards (IRBs); and training (including the development of online training programmes) for research ethics review.

The MARC project, executed by the Council on Health Research for Development (COHRED), was deemed to be a great success. MARC mapped 166 IRBs in 34 African countries and developed professional social network and discussion functions on the MARC website (www.healthresearchweb.org). Additionally, an online information management system (RHinnO Ethics) was developed. This resource provides IRBs and medicines regulatory authorities with a secure, fully web-based solution for submitting, managing and tracking the process of research applications.

The main purpose of the IRB and NEC-related projects was to enable their operational functioning through support for office infrastructure development, training, development of standard operating procedures and improved quality of protocol review. This funding helped the ethics committees to face considerable challenges. However, limited human resources are still a threat to the sustainability of NECs and IRBs. The evaluation showed that online ethics training activities were the most used and convenient form of training. It provided a good return on investment and reached the highest number of beneficiaries. The data also shows a high level of efficacy in NECs and IRBs and supports the conclusion that ethics has made a solid entrance into research ethics in Africa.

Preparing for laboratory accreditation

In preparation for the second programme, EDCTP initiated a laboratory strengthening project for selected laboratories within its four regional Networks of Excellence (TESA, WANETAM, CANTAM and EACCR). This activity was funded as part of the EDCTP-Plus project and aimed to prepare for the systematic development of 24 clinical research and public health laboratories involved in EDCTP-funded studies towards internationally-recognised accreditation, after performing a baseline gap analysis.

The WHO AFRO Stepwise Laboratory Improvement Process Towards Accreditation (SLIPTA) was used. SLIPTA provides a framework for establishing an effective quality management system for medical laboratory testing. Following assessment, laboratories are graded on a 0 to 5-star scale. Under the second phase of the project, 24 laboratories of the Networks of Excellence in 19 African countries were audited for their initial baseline as regards quality management systems and general laboratory capacity. This audit established the baseline level for 24 laboratories on the SLIPTA scale. All laboratories were informed of non-compliance gaps and the steps required for improving overall quality, management and performance. The audit corroborated the importance of

sustaining continuous activity at the laboratories and continuous employment for laboratory personnel in order to develop and maintain quality standards.

The next phase of this EDCTP initiative will be executed by the African Society for Laboratory Medicine (Ethiopia) and Quintiles Africa (South Africa) in 2014. They will re-audit all 24 laboratories, address the non-compliance gap and prepare each laboratory for accreditation through implementation of mentorship programmes, training schemes and internal quality assessments.

Governance

General Assembly

The EDCTP General Assembly (GA), convened twice in 2013. In May, the GA met in Brussels, Belgium, to discuss the legislative process for the second EDCTP programme, as well as the membership requirements for EDCTP2. It also appointed six experts to the EDCTP interim Scientific Advisory Committee which replaced both the Partnership Board and the Developing Countries Coordinating Committee.

The second meeting took place in The Hague, The Netherlands, on 7-8 November 2013 where the deliberations on the governance, rules and the various funding mechanisms for EDCTP2 were continued. The GA elected Dr Mark Palmer (United Kingdom) as the new Chairperson. Dr Palmer took over from Prof. Hannah Akuffo (Sweden) effective 1 January 2014.

Dr Mark Palmer, EDCTP GA Chairperson

Interim Scientific Advisory Committee

The interim Scientific Advisory Committee (SAC) convened in The Hague, The Netherlands, on 11-12 April and 10-11 October. The discussions focussed on the workplans for 2014-2015 of the Participating States and EDCTP in order to prepare for the start of the second programme.

In March, EDCTP published a call for experts for membership of the full Scientific Advisory Committee. A total of 112 applications were received. A selection panel comprising the EDCTP Executive Director, GA Chair, representative of the EC, the Chair of the interim SAC and an independent expert was convened to select candidates.
A shortlist was presented at the November GA meeting. Subsequent to the meeting, the GA approved by written procedure the appointments of 15 experts. The current SAC comprises 15 members: the Chair, two Vice-Chairs and 12 ordinary members. The mandate of the SAC started on 1 January 2014.

Executive Secretariat

In September 2013, Dr Ole F. Olesen joined EDCTP as Director of North-North Cooperation. Furthermore, EDCTP welcomed several new staff members during 2013. Mariska Louw and Michelle Nderu joined the EDCTP Africa Office in Cape Town as Senior Administrative Officer and Project Officer respectively. The Europe Office welcomed Lara Pandya as North-North Networking Officer. Dr Lidwien van der Valk, long-standing legal advisor to EDCTP, joined EDCTP full-time as Legal Officer. Two temporary staff members, Dr Christy Comeaux and Charlotte Hoekstra, assumed administrative tasks in project document management.

Dr Ole F. Olesen, EDCTP Director of North-North Cooperation

Publications

EDCTP published the following reports and videos in 2013:

- Proceedings of the EDCTP 'Post-Registration Medicinal Products Safety Monitoring in sub-Saharan Africa' meeting (Cape Town, South Africa on 4 November 2012)
- Proceedings of the High-Level Conference on the second EDCTP programme (Cape Town, South Africa, 5 November 2012)
- High-Level Conference on EDCTP2 (video report)
- TB-NEAT: TB diagnostics in low-resource settings (video report)
- Annual Report 2012
- Proceedings of the EDCTP Stakeholder Meeting on Neglected Infectious Diseases (The Hague, The Netherlands, 27-28 June 2013)
- Proceedings of the EDCTP Stakeholder Meeting on Malaria (Vienna, Austria, 19-20 September 2013)
- Proceedings of the Second High-Level Meeting on EDCTP2 (Dakar, Senegal, 21 October 2013).

All publications are available for download in PDF at www.edctp.org. The videos are available on the EDCTP YouTube channel: www.youtube.com/edctpmedia.

EDCTP calls and grants overview

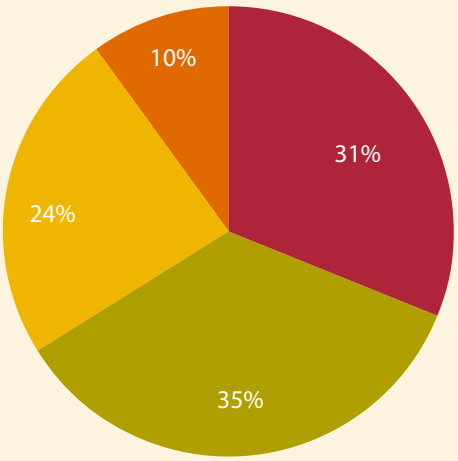
In 2013, one call for proposals was launched, the Master's Fellowships in Epidemiology and Medical Statistics. It aims to build research capacity in sub-Saharan Africa by supporting the training and career development of junior researchers in the fields of epidemiology and medical statistics.

The scheme provides funds for the fellow to undertake a taught master's course in epidemiology or medical statistics at an internationally recognised centre of excellence and to conduct a field study of 6-12 months duration at an institution in sub-Saharan Africa to build practical skills. The maximum duration of the fellowship is two years. The call for proposals was funded by Sweden and the United Kingdom (EDCTP Participating States) and was open from August until November 2013. Fifty-two (52) eligible applications were received. Funding decisions for 5-10 awards will be finalised in 2014.

Since 2003, EDCTP has launched 65 calls for proposals. A total of 246 projects have been funded. Of these, 106 (43%) were active at the end of 2013 and 140 projects grants were completed. The total amount of the 246 projects is € 212.12 million including cofunding via EDCTP. Of these projects, 54 are on HIV/AIDS research, 44 on tuberculosis research and 41 on malaria research, and the remaining 107 projects were non-disease specific.

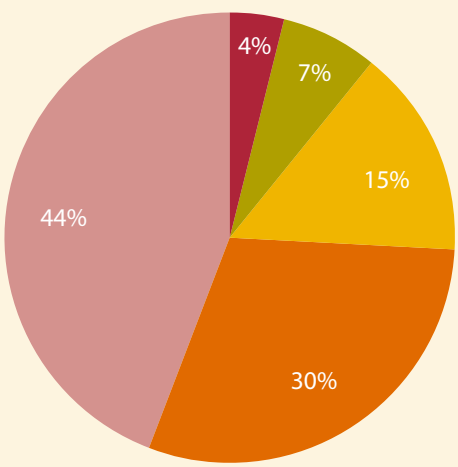
The EDCTP portfolio includes 74 projects with a clinical trial, and 172 projects without a clinical trial. Research into treatments constitutes the majority of projects (60) and share of funding (44% of EDCTP grant funding). EDCTP-funded research on vaccines accounts for a smaller number of projects (26). However, the proportion of funding spent on vaccines represents 30%, reflecting the higher costs involved in vaccine trials. There are 13 diagnostics projects (7% of EDCTP grant funding) and microbicides research accounts for 5 projects (4% of grant funding).

Overview of funding by area 2003-2013 (€ '000)



HIV/AIDS	66,415
Tuberculosis	73,944
Malaria	50,991
Non-disease specific	20,769
Total	212,119

Overview of funding by intervention 2003-2013 (€ '000)



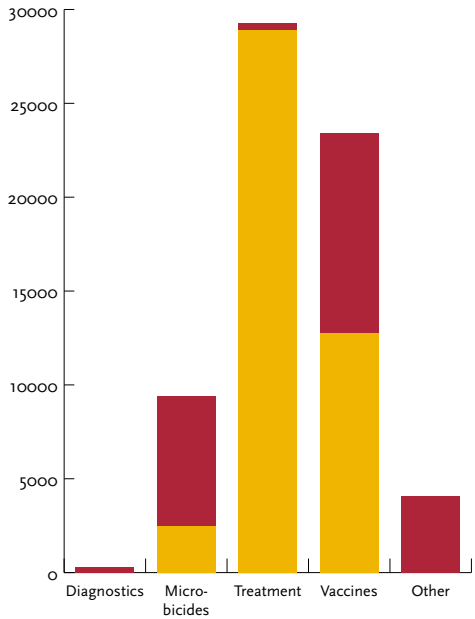
Microbicides	9,387
Diagnostics	14,478
Not-intervention specific	31,663
Vaccines	64,196
Treatment	92,395
Total	212,119


Clean Air
BD

HIV/AIDS

Since 2003, EDCTP has invested € 66.41 million to support 54 research projects on HIV/AIDS, including substantial capacity upgrade at clinical research centres in 23 sub-Saharan Africa countries. The EDCTP portfolio on HIV/AIDS includes 13 treatment trials, second-line therapy and paediatric treatment and studies on HIV/TB co-infection. Six studies focus on the prevention of mother-to-child transmission. Eight vaccine trials have been supported, as well as three trials on microbicides and one trial focused on mechanisms to maximise retention and adherence to treatment.

HIV/AIDS funding of signed grants, 2003-2013 (€ '000)



	Clinical trial	Non trial
Diagnostics	-	€ 291
Microbicides	€ 2,455	€ 6,932
Treatment*	€ 28,880	€ 419
Vaccines	€ 12,753	€ 10,633
Other**	-	€ 4,051
Total	€ 44,088	€ 22,326

*Including € 5.85 million of funding to support projects on prevention of mother-to-child transmission
**Including immunology, epidemiology and cross-cutting issues.

HIV/AIDS treatment

EDCTP funded 17 grants on HIV treatment totalling € 23.44 million. Experts advised that in Africa clinical trials were needed with the following specific aims: to test treatment regimens with lower overall antiretroviral exposure; to investigate the optimal time for initiating treatment; and to investigate the ways to best monitor and manage drug use both in children and in adults. The objectives of these trials were to simplify and standardise antiretroviral regimens in adults and children, and develop new treatment regiments. Two projects addressed issues of HIV and tuberculosis co-infection.

The CHAPAS-1 trial in Zambia started in 2005 and was completed in 2009. Professor Chifumbe Chintu and his team studied the appropriate dosing of and adherence to Triomune Baby/Junior. This is a fixed-dose combination of stavudine (d4T), lamivudine (3TC) and nevirapine (NVP) in a new formulation specifically developed for children. CHAPAS-1 specifically aimed to address the then complete lack of appropriate first-line antiretroviral regimens available for children in developing countries.

The research team shared its preliminary pharmacokinetics data with the USA Food and Drug Authority (FDA) and the data contributed to the approval of Triomune Baby/Junior for use in HIV-infected children in 2007. This approval enabled many HIV-infected children to be placed on treatment in various developing countries. The drug was also made available under programmes such as the US President's Emergency Plan for HIV/AIDS Relief (PEPFAR) and the Clinton HIV/AIDS Initiative (CHAI). The study findings contributed to the WHO recommendations on the optimal drug ratios in fixed-drug combinations and on weight band dosage for antiretroviral in children worldwide. Unfortunately, the stavudine drug, contained in the Triomune fixed-dose combination, turned out to have cumulative toxicity side effects and was discontinued. This necessitated many adults and children on treatment to switch to other antiretroviral drug regimens.

As the number of children under antiretroviral treatment still falls behind that of adults because of the lack of antiretroviral options, the CHAPAS-3 study, led by Dr Veronica Mulenga, followed on CHAPAS-1 to contribute to addressing this gap and increase options of first-line fixed-dose ART for children. CHAPAS-3 evaluates three fixed-dose combination first-line antiretroviral drugs.

Professor Chifumbe Chintu **Dr Veronica Mulenga**

University Teaching Hospital (UTH), Zambia

The availability of fixed-dose combination antiretroviral drugs that can be administered using weight band tables has greatly enabled treatment for a large number of HIV-infected children. Early infant diagnosis using dried blood spots has been another major contribution to diagnosis of many infants and young children and therefore starting them early on treatment. The global movement to mobilise resources for procurement of antiretrovirals, and partnering with pharmaceutical companies to enable price reduction and production of generic drugs, have collectively contributed to the HIV treatment in both children and adults.

EDCTP's support to both CHAPAS-1 and CHAPAS-3 studies has greatly contributed to the current knowledge and practice in the treatment of HIV infection in children. Findings from the CHAPAS-1 trial contributed to the 2010 WHO treatment guidelines at the time and led to the first fixed-dose combination antiretroviral drug being made available for treatment to a large number of HIV-infected children in developing countries. Findings from CHAPAS-3 are eagerly awaited as these data will provide information on the toxicity profiles, appropriate dosing, efficacy and cost effectiveness of other newer first-line fixed-dose combinations.

Nonetheless much more can be done in the coming 10 years. There is a need for simpler and fewer dosing formulations. The links between prevention of mother-to-child transmission and early HIV diagnosis and treatment should be strengthened in order to ensure that HIV-infected infants and children commence treatment at the earliest time. Availability and easy access to improved formulations of second-line and third-line regimens remain a challenge. Novel methods that ensure adherence for sustained viral control need to be evaluated. Better adherence would allow children to stay longer on one regimen before having to change to the next line of antiretrovirals.

The study compares the toxicity, pharmacokinetics, efficacy, adherence and acceptance of two newer fixed-dose combinations of ABC (abacavir) +3TC+NVP/EFZ (efavirenz) and AZT (zidovudine) +3TC+ NVP/EFZ to the first fixed-dose drug Triomune. The study completed recruitment of children in December 2013. The analysis of data has started and will be presented in 2014.

Relevant publications:

1. L'homme, R; Kabamba D; Ewings, FM; Mulenga, V; Kankasa, C; Thomason, MJ; Walker, AS; Chintu, C; Burger, DM; and Gibb, DM. (2008) 'Nevirapine, stavudine and lamivudine pharmacokinetics in African children on paediatric fixed-dose combination tablets'. *AIDS*. 12;22(5):557-65
2. Ryan, M; Griffin, S; Chitah, B; Walker, AS; Mulenga, V; Kalolo, D; Hawkins, N; Merry, C; Barry, MG; Chintu, C; Sculpher, MJ; and Gibb, DM. (2008) 'The cost-effectiveness of cotrimoxazole prophylaxis in HIV-infected children in Zambia'. *AIDS*. 30;22(6):749-57
3. Burger, D; Ewings, F; Kabamba, D; L'homme, R; Mulenga, V; Kankasa, C; Thomason, MJ; Gibb, DM; Chintu, C; and Walker, AS. (2010) 'Limited Sampling Models to Predict the Pharmacokinetics of Nevirapine, Stavudine, and Lamivudine in HIV-Infected Children Treated With Pediatric Fixed-Dose Combination Tablets'. *Therapeutic Drug Monitoring*. 32(3):369-72.
4. Mulenga, V; Cook, A; Walker, AS; Kabamba, D; Chijoka, C; Ferrier, A; Kalengo, C; Kityo, C; Kankasa, C; Burger, D; Thomason, M; Chintu, C; Gibb, DM. (2010) 'Strategies for Nevirapine Initiation in HIV-Infected Children Taking Pediatric Fixed-Dose Combination ""Baby Pills"" in Zambia: A Randomized Controlled Trial'. *Clinical Infectious Diseases*. 51 (9):1081-1089
5. Haberer, JE; Cook, A; Walker, AS; Ngambi, M; Ferrier, A; Mulenga, V; Kityo, C; Thomason, M; Kabamba, D; Chintu, C; Gibb, DM; Bangsberg, DR. (2011) 'Excellent Adherence to Antiretrovirals in HIV plus Zambian Children Is Compromised by Disrupted Routine, HIV Nondisclosure, and Paradoxical Income Effects'. *PLOS ONE*. 21;6(4):e18505
6. Fillekes, Q; Mulenga, V; Kabamba, D; Kankasa, C; Thomason, MJ; Cook, A; Ferrier, A; Chintu, C; Walker, AS; Gibb, DM; Burger, DM. (2012) 'Pharmacokinetics of nevirapine in HIV-infected infants weighing 3 kg to less than 6 kg taking paediatric fixed dose combination tablets'. *AIDS*. 26(14): 1795-1800

Prevention of mother-to-child transmission of HIV

In the area of prevention of mother-to-child transmission of HIV/AIDS EDCTP invested € 5.85 million to fund five projects. Although breastfeeding is essential to prevent malnutrition and infectious diseases in resource-limited settings, it carries a significant risk of transmission of HIV, especially in later stages of infection. The projects aimed to protect the child from being infected with HIV during pregnancy, while making sure that the mother receives proper treatment that is safe for her child. The studies investigate the safety and efficacy of antiretroviral regimens containing drugs such as tenofovir, lamivudine and nevirapine, mostly used in combination to prevent drug resistance.

Professor Marie-Louise Newell of the Africa Centre for Health and Population Studies, South Africa, conducted a study on the impact of Highly Active Anti-Retroviral Therapy (HAART) during pregnancy and breastfeeding on mother-to-child transmission of HIV as part of the WHO-sponsored Kesho Bora study. The aim of the study was to evaluate the use of combination antiretroviral therapy starting in late pregnancy and continued throughout six months of breastfeeding, following the WHO guidelines at the time for HIV-infected mothers in the prevention of postnatal mother-to-child transmission.

Professor Marie-Louise Newell

Africa Centre for Health and Population Studies, South Africa

The confirmation that antiretroviral therapy can virtually eliminate vertically-acquired HIV infection when provided from early pregnancy and continued throughout the breastfeeding period is a major breakthrough. It also serves as a template for the potential elimination of the HIV epidemic among sexually-active adults.

The finding that antiretrovirals given to the mother during the breastfeeding period are safe for the infant has resulted in the revised WHO guidelines on prevention of mother-to-child transmission. The guidelines are now recommended for all HIV-infected mothers under the cover of antiretroviral thus preserving child survival. Further important findings showed that child mortality is substantially reduced among all children born to HIV-infected women that are on antiretroviral for life. Mortality among children of treated HIV-infected women is similar to that of children of uninfected mothers.

EDCTP provided the funding to allow centres in South Africa to participate in this global trial, and provided the necessary laboratory support to the centre in Mombasa, Kenya. The antenatal HIV prevalence is high in South Africa. Thus, it was important for the timely conduct of this WHO-sponsored trial to include South African centres who contributed a substantial number of women to the trial. The trial could not have been able to fully recruit in a timely manner without the support given to the South African sites by EDCTP.

A multicentre randomised controlled trial was set up with two arms: the intervention arm of combination antiretroviral therapy and a control arm of the standard therapy to prevent mother-to-child transmission administered during pregnancy and delivery, but not continued postnatally. Centres in South Africa, Kenya and Burkina Faso were involved in the study.

The study showed the efficacy of maternal combination ART prophylaxis during pregnancy and the breastfeeding period in reducing the risk of HIV-1 transmission to infants. These findings strongly influenced the revision of WHO 2010 guidelines that recommended antiretroviral prophylaxis (either to the mother or to the child) during breastfeeding, in case the mother was not already receiving antiretroviral treatment for her own health. The 2013 WHO guidelines now recommend combination antiretroviral therapy for all HIV-infected women, irrespective of CD4 count, from early pregnancy throughout breastfeeding, and where possible, for life.

Further analyses of the Kesho Bora trial data confirmed that breastfeeding is not associated with disease progression in women. Women benefit from the exposure to combination antiretroviral therapy in terms of delayed HIV disease progression, but only while receiving combination ART. In addition, infants born to HIV-infected mothers on combination ART are not only less likely to become HIV-infected but also benefit from the breastfeeding which results in an improved survival rate.

Relevant publications:

1. The Kesho Bora Study Group (authors include Mepham, S; Naidu, K and Newell, ML). (2011) 'Triple antiretroviral compared with zidovudine and single-dose nevirapine prophylaxis during pregnancy and breastfeeding for prevention of mother-to-child transmission of HIV-1 (Kesho Bora study): a randomised controlled trial'. *Lancet Infectious Diseases*. 11(3): 171-180
2. Bork, K; Cames, C; Cournil, A; Musyoka, F; Ayassou, K; Naidu, K; Mepham, S; Gichuhi, C; Read, JS; Gaillard, P; de Vincenzi, I for the Kesho Bora Study Group. (2013) 'Infant feeding modes and determinants among HIV-1–infected African women in the Kesho Bora Study'. *Journal of Acquired Immune Deficiency Syndromes* 1;62(1):109-18

Preparatory studies for HIV vaccine clinical trials

EDCTP has invested € 23.4 million to support 12 projects for HIV vaccine development. Of these, six projects were funded via the joint call for proposals with the Bill & Melinda Gates Foundation, launched in 2006. The studies aimed to develop capacity to conduct future large phase IIb and III clinical trials of preventive vaccines in Africa according to international regulatory standards.

The SASHA project coordinated by Professor Linda-Gail Bekker of Desmond Tutu HIV Centre, University of Cape Town, South Africa, investigated the feasibility of conducting HIV vaccine prevention trials in South Africa with adolescents, a group that is particularly at risk for HIV infection. Efficient implementation of an adolescent HIV vaccine trial is complex and requires understanding of broader participation issues including clinical, community, ethical, legal and socio-behavioural barriers to trial conduct. The SASHA study aimed to identify and address some of these obstacles and challenges in this vulnerable population.

By using the human papillomavirus (HPV) vaccine as a proxy, the project team showed that it is feasible to conduct multi-site longitudinal biomedical studies with adolescents (12-17 year olds) in South Africa. The recruitment and retention of enrolled participants was high during nine months of follow-up. Understanding of key trial concepts remained throughout study participation. Vaccine uptake and completion rate was remarkably high. This suggests a willingness to engage on the part of the adolescents and also the feasibility to complete an extended vaccine schedule in this group. Self-reported risky sexual behaviour was assessed over the follow-up period. It revealed the adolescent cohort to be at relatively low risk, with condom use improving significantly over the course of the study in the older adolescent participants. This was possibly a result of regular risk reduction counselling, HIV testing and the availability of condoms. However, self-reported risk sexual behaviour remained a challenge across all ages. The high pregnancy rates during the study suggest that it is also a challenge to collect accurate and honest data on risky sexual behaviour in the adolescent population. The project developed an ethical-legal guide for conducting clinical trials with adolescents. All six sites in this study now have the necessary infrastructure for future adolescent vaccine trials.

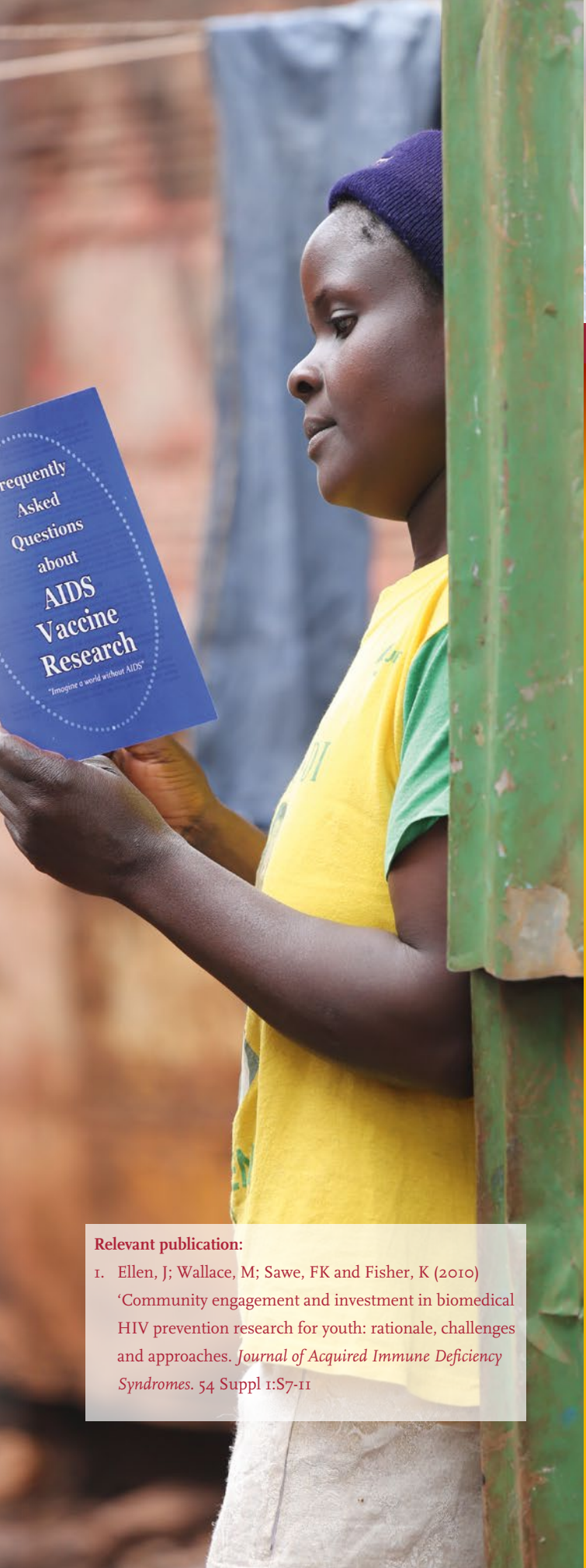
Professor Linda-Gail Bekker

Desmond Tutu HIV Centre, University of Cape Town, South Africa

EDCTP recognised the value of conducting a national, multi-site preparatory study in anticipation of future adolescent HIV vaccine and other biomedical prevention trials and strengthening field site capability. By the completion of the SASHA project, six clinical research sites in South Africa had engaged in adolescent biomedical research, and had engaged with ethics committees and communities in order to do so safely and effectively.

Human efficacy trials of credible vaccine products and vaccine strategies must be implemented urgently since there is no doubt the field moves forward most effectively when immune responses can be linked with outcomes. On-going work in animal models is critical to better understand the role these models can play in vaccine development. We are unlikely to find the most effective vaccine strategy in the first attempts. There also needs to be a robust pipeline of new and innovative products requiring a healthy preclinical and early phase programme.

HIV vaccine and other biomedical trials in adolescent populations are required to ensure that this vulnerable and worthy population is not left behind to biomedical solutions to the HIV epidemic. In order to do this more effectively, a far better understanding of adolescents' thinking, perceptions, decision-making and behaviour is required and this research should be done urgently, in order to develop appropriate biomedical and other prevention tools that adolescents will actually use.



Relevant publication:

1. Ellen, J; Wallace, M; Sawe, FK and Fisher, K (2010) 'Community engagement and investment in biomedical HIV prevention research for youth: rationale, challenges and approaches. *Journal of Acquired Immune Deficiency Syndromes*. 54 Suppl 1:S7-11

Preparatory studies for clinical trials of microbicides

A new approach in the fight against HIV/AIDS is the development of microbicides that can be applied inside the vagina or rectum to prevent infection with HIV through sexual transmission. The availability of non-contraceptive microbicides in the form of a gel, cream, vaginal ring or suppository would greatly empower women to protect themselves and their partners as women could easily control its use.

In 2010, the positive results of the CAPRISA 004 phase IIb microbicide trial suggested the feasibility of such an approach. EDCTP supported five projects that included clinical trials of microbicides, as well as projects that do not include a clinical trial but have a focus on the acceptability of microbicides or support capacity building for microbicides trials. The projects amount to a total funding of € 9.39 million.

One of these projects had the objective to establish HIV microbicide clinical trial capacity in Mozambique and

expand an existing site in South Africa. The project was led by Professor Sheena McCormack of the Medical Research Council, United Kingdom. The microbicide feasibility and pilot study in Mozambique was conducted under the umbrella of the Microbicides Development Programme (MDP). Clinical trial capacity was built at the Reproductive Health and HIV Research Unit (RHRU) in Johannesburg, South Africa.

The project started in 2007 and sought proof of concept for a microbicide containing the drug PRO2000/5 whose mechanism of action *in vitro* was to block the attachment of the HIV protein rgp140 to the human cell receptor. Clinical infrastructure was improved in order to complete this site's targets for the phase III MDP301 microbicide trial exploring the PRO 2000 vaginal gel. Unfortunately, the MDP301 effectiveness trial, which was conducted among almost 9,400 women in four African countries, found no evidence that this microbicide reduced the risk of HIV infection.

The study in Mozambique sought to determine the feasibility of conducting a microbicide trial of a daily vaginal gel and to generate information on the way adherence for microbicides should be assessed. The project was completed in 2010. This feasibility study, which aimed to evaluate the population and study site in the healthcare centres in Mozambique (Mavalane and Manhiça) in preparation for a possible phase III vaginal microbicide trial, provided the first HIV incidence data for the country.

Relevant publication:

1. McCormack, S; Ramjee, G; Kamali, A; Rees, H; Crook, AM; Gafos, M; Jentsch, U; Pool, R; Chisembele, M; Kapiga, S; Mutemwa, R; Vallely, A; Palanee, T; Sookrajh, Y; Lacey, CJ; Darbyshire, J; Grosskurth, H; Profy, A; Nunn, A; Hayes, R; Weber, J. (2010) PRO2000 vaginal gel for prevention of HIV-1 infection (Microbicides Development Programme 301): a phase 3, randomised, double blind, parallel- group trial. *Lancet.* 16;376(9749):1329-37

Professor Sheena McCormack

Medical Research Council, United Kingdom

Microbicides have enormous potential. They allow women to take responsibility for reducing their risk. In contrast to a condom they do not have to be simultaneously contraceptive. The majority of women have expressed other benefits from these vaginal gels including sexual pleasure when used around the time of sex, and a sense of cleanliness. Vaginal rings are an alternative method for delivering product that does not require insertion around the time of sex, and this will appeal to women for different reasons. They also open the door for multi-purpose technologies as contraceptives and antiretroviral drugs can be released from the same ring.

The support from EDCTP allowed us to assess HIV incidence in women in Mozambique and introduce the idea of microbicides to this country for the first time in the Top Up placebo gel study. This ignited political interest and demonstrated the feasibility of conducting future microbicide trials. One of the MDP partners was also able to improve and expand their facilities at the Orange Farm clinic in Johannesburg, South Africa, and this assisted the timely completion of the phase III trial.

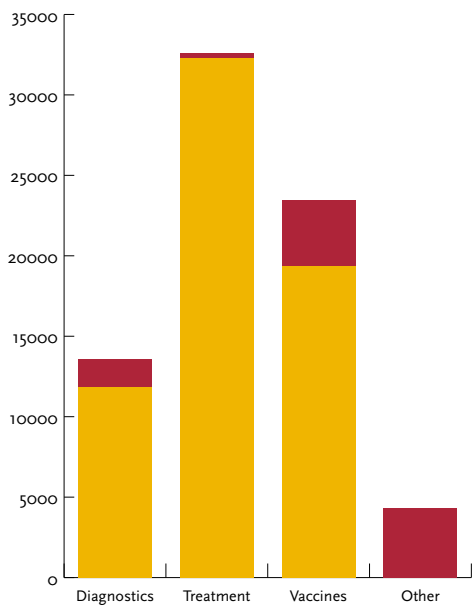
We did not observe any reduction in HIV with PRO2000/5, so there was no benefit from the microbicide itself. However, women gained knowledge by being partners in the research project. This spread beyond the participants to the community organisations and ultimately the broader population in the vicinity of the project. Although the overall result was disappointing, it was only seven months later that CAPRISA 004 reported a significant reduction with tenofovir 1% vaginal gel applied before and after sex, the first proof of concept trial for a microbicide. This provided much needed momentum to the field.

Tuberculosis

EDCTP has supported 44 projects on tuberculosis (TB) research that target the three areas of diagnostics, treatment and vaccines. TB diagnostics must be improved as the standard method is a lengthy process which delays intervention and thereby increases the risk of disease transmission, and makes monitoring of drug resistance more difficult. In addition, the standard method has low sensitivity among HIV co-infected patients. The six month standard treatment for TB is very long and presents an adherence challenge for the patients and increased risk of development of drug-resistant strains of the bacteria. Moreover, HIV co-infection does not just increase TB caseload, but makes combined treatment of both diseases difficult. Options for the prevention of TB are limited as the current vaccine does not protect adults from developing tuberculosis.

The portfolio of EDCTP-funded clinical trials includes 11 projects on diagnostics, 18 treatment trials and 5 projects that focus on phase II vaccine trials. As of 31 December 2013, the total EDCTP funding of TB research amounted to € 73.94 million.

Tuberculosis funding of signed grants, 2003-2013 (€ '000)



	Clinical trial	Non trial
Diagnostics	€ 11,860	€ 1,731
Treatment	€ 32,282	€ 273
Vaccines	€ 19,374	€ 4,077
Other*	-	€ 4,347
Total	€ 63,516	€ 10,428

*Including immunology, epidemiology and cross-cutting issues.

TB treatment

It is generally agreed that the current tuberculosis treatment takes too long to complete. In addition to serious problems of adherence and costs, a significant number of patients are unable to tolerate the current standard drugs combination. The rise of tuberculosis resistance poses a real threat to global health and new challenges of treatment development. EDCTP has supported 16 projects on tuberculosis treatment research with a grant value of € 32.55 million.

EDCTP has granted funding to a consortium of four European universities and 12 African clinical trial centres to provide an overarching structure for three treatment development programmes. This Pan African Consortium for Evaluation of Antituberculosis Antibiotics (PanACEA) explores new drugs that have the potential to shorten TB treatment. The consortium was formed to conduct a series of cooperative clinical trials to evaluate three different drugs (Moxifloxacin, Rifampicin and SQ109) for the treatment of drug-sensitive tuberculosis to simplify and shorten the current regimens. It integrated the clinical studies and the development of the required registration-quality clinical trial capacity at several research centres and sites in sub-Saharan Africa. The long-term goal was to establish a sustainable framework for clinical trials of TB drugs.

The REMoxTB (Rapid Evaluation of Moxifloxacin in the treatment of sputum smear positive tuberculosis) is one of the projects under the umbrella of PanACEA. The study is part of the global REMox clinical trial which aims to establish the efficacy of a possible new drug against tuberculosis in order to reduce treatment time from six to four months. The study is coordinated by Professor Stephen Gillespie of the St. Andrews University, United Kingdom, and sponsored by the TB Alliance. EDCTP funded the part of the REMox study that is conducted in Africa which constitutes approximately 70% of the total number of study patients.

REMoxTB is a three-arm, double-blind phase III study in which moxifloxacin substitutes for two different drugs in the current first-line standard TB therapy, ethambutol and isoniazid, and is administered for a total of four months. REMox has to determine whether either of these two new,

four-month regimens are non-inferior to standard six-month therapy in terms of failure and relapse. As part of the study, the capacity development component for African clinical trial centres to perform studies to the highest international regulatory standards was significantly scaled up for Kenya (Nairobi), Tanzania (Moshi and Mbeya), Zambia (Lusaka) and at several sites in South Africa. The study was completed in 2013 and findings will be published in 2014.

Relevant publications:

1. Singh, KP; Brown, M; Murphy, ME; Gillespie, SH. (2012) 'Moxifloxacin for tuberculosis'. *Lancet Infectious Diseases*. 12(3):176
2. van Ingen, J; Aarnoutse, RE; Donald, PR; Diacon, AH; Dawson, R; Plemper van Balen, G; Gillespie, SH; Boeree, MJ. (2011) 'Why do we use 600 mg of rifampicin in tuberculosis treatment?' *Clinical Infectious Diseases*. 52(9):e194-9
3. Burki, T. (2012) 'PanACEA: a new approach to tuberculosis research'. *Lancet Infectious Diseases*. 12(3):184-5
4. Bryant, JM; Harris, SR; Parkhill, J; Dawson, R; Diacon, AH; van Helden, P; Pym, A; Mahayiddin, AA; Chuchottaworn, C; Sanne, IM; Louw, C; Boeree, MJ; Hoelscher, M; McHugh, TD; Bateson, ALC; Hunt, RD; Mwaigwisya, S; Wright, L; Gillespie, SH; Bentley, SD. (2013) 'Whole-genome sequencing to establish relapse or re-infection with Mycobacterium tuberculosis: a retrospective observational study'. *Lancet Respiratory Medicine*. 1(10):786-92

Professor Stephen Gillespie

REMoxTB Project Coordinator, St. Andrews University, United Kingdom

Timothy McHugh

REMoxTB Project Manager, University College London, United Kingdom

The final data of the study are being analysed. The study has already shown the importance of a standardised approach to tuberculosis clinical trials ensuring high quality data. We also have developed methodologies that are being applied in subsequent clinical trials. For example, a study of recurrence strains indicated the importance of mixed infection in tuberculosis and suggests that in the future, whole genome sequencing will be required to understand the significance of positive cultures in the follow-up period. In partnership with the TB Alliance we have shown what the TB research community can achieve when the key players work together.

The commitment of EDCTP to capacity development has been an important inspiration to the REMoxTB consortium. We have seen a significant increase in the number of sites capable of performing clinical trials to a regulatory standard. This is particularly true of the African laboratories where we have seen EDCTP funds support laboratory development and the teams become familiar with state of the art techniques including mycobacterial growth indicator tube technique and molecular diagnostics.

Although there are now several drugs being evaluated for the treatment of tuberculosis, the challenge of improving treatment both by shortening its duration for susceptible disease and creating more effective regimens for multi-drug-resistant tuberculosis is very great. We need much more resources devoted to finding new and better drugs and to trial these in high-burden countries. To achieve this goal it will be necessary to continue training scientists from across the globe in the latest methodologies that have been developed largely through EDCTP-funded projects.

Van used as a mobile TB diagnostic clinic in Gugulethu, South Africa, part of the EDCTP-funded XACT project

Professor Keertan Dheda

University of Cape Town, South Africa

The TB-NEAT study was fully funded by EDCTP. It enabled training of two Master's students, eight PhD students and five Postdoctoral fellows. In addition, a number of infrastructure upgrades were undertaken at various study sites in South Africa.

The findings of this study have already had several translational impacts. In South Africa, these findings paved the way to install Xpert MTB/RIF machines at TB hotspots such as prisons, mines, and high burden TB clinics with high rates of drug-resistant TB. The Department of Health in South Africa has already outlined plans to make these diagnostic tests available in mines and prisons.

But we still need a low cost point-of-care diagnostic tool suited to TB endemic countries which can provide results to enable onsite treatment for patients. Other aspects of TB diagnostics, such as diagnostics-related research, innovation-led research to develop new antigen targets and detection platforms, harmonisation of regulations relevant to TB diagnostics and their registration, and streamlining of regulatory processes to endorse effective TB tests, should also receive attention and funding support. It is unlikely that we will have a "one-size-fits-all" test for TB and therefore alternative approaches are required for different types of the disease. More attention will also need to be given to research that focus on optimal diagnostic algorithms using different technologies to reduce costs yet retain accuracy and patient retention. I hope this can be achieved in the coming 10 years.

TB diagnostics

Improving the speed and accuracy of the diagnosis of tuberculosis is one of the priorities of the EDCTP programme. Research on diagnostics supported by EDCTP consists of 10 projects with a total grant value of € 13.60 million. Of these, three are large-scale clinical trials that also include capacity building and networking components. The overall objective is to develop simple, cheap, point-of-care TB diagnostics. The remaining diagnostics projects were funded through various EDCTP schemes. Several of these projects focus on testing the performance of the point-of-care Xpert MTB/RIF test for tuberculosis.

Research carried out under Professor Mark Nicol's EDCTP Senior Fellowship contributed to the evaluation trial that showed that Xpert MTB/RIF test can be used effectively in low-resource settings to simplify patients' access to early and accurate diagnosis. The trial findings informed the WHO recommendation that Xpert MTB/RIF should be used as the initial diagnostic test in individuals suspected of MDR-TB or HIV-associated TB.

Since the WHO recommendation, the Xpert MTB/RIF test for tuberculosis continues to being rolled out in many countries. The EDCTP-funded TB-NEAT project, led by Professor Keertan Dheda of the University of Cape Town, South Africa, has been gathering evidence on the implementation of Xpert MTB/RIF and its impact on tuberculosis-related morbidity. The TB-NEAT project consists of several components, but the flagship studies are the Xpert clinical trial and the LAM study, a randomised controlled trial of 2400 patients. The Xpert RCT is the first randomised control trial undertaken of a new diagnostic technology.

The findings of the study showed that it is feasible to place Xpert in a peripheral clinic or health outpost. The Xpert MTB/RIF tool requires only briefly trained healthcare workers to generate accurate results with the same efficiency and accuracy as a fully trained laboratory technician in a centralised laboratory. In addition, when placed in a clinic, the Xpert MTB/RIF tool substantially increases same-day treatment of tuberculosis, reducing by

over 50% the number of patients who were tested TB positive but never initiated treatment.

The study confirmed that patients with drug-resistant TB could be rapidly diagnosed and initiate treatment. It showed that Xpert MTB/RIF sensitivity and negative predictive value in HIV-infected persons is sub-optimal. Thus, a negative result in HIV-infected persons should not rule out alternative investigations of empiric treatment. Overall, introduction of the Xpert MTB/RIF tool resulted in more rapid diagnosis in primary care clinics but did not increase the overall number of patients treated. It did, however, reduce the rate of empiric treatment in the intervention arm.

Relevant publications:

1. Peter, JG; Theron, G; Dheda, K. (2013) 'Can point-of-care urine LAM strip testing for tuberculosis add value to clinical decision making in hospitalised HIV-infected persons?'. *PLOS ONE*. 8(2):e54875.
2. Theron, G; Zijenah, L; Chanda, D; Clowes, P; Rachow, A; Lesosky, M; Bara, W; Mungofa, S, Pai, M, Hoelscher, M, Dowdy, D, Pym, A, Mwaba, P, Mason, P, Peter, J, Dheda, K. (2013) Feasibility, accuracy and clinical impact of point-of-care Xpert MTB/RIF testing for tuberculosis in primary-care settings in Africa: a multicentre, randomised controlled trial. *Lancet*. 2014 Feb 1;383(9915):424-35
3. Peter, J; Theron, G; Pooran, A; Thomas, J; Pascoe, M; Dheda, K. (2013). 'Comparison of two methods for acquisition of sputum samples for diagnosis of suspected tuberculosis in smear-negative or sputum-scarce people: a randomised controlled trial'. *Lancet Respiratory Medicine*. 1(6):471-8
4. Zar, HJ; Workman, L; Isaacs, W; Dheda, K; Zemanay, W; Nicol, MP. (2013). 'Rapid diagnosis of pulmonary tuberculosis in African children in a primary care setting by use of Xpert MTB/RIF on respiratory specimens: a prospective study'. *Lancet Global Health*. 1:e97–104

TB vaccines

The current tuberculosis vaccine BCG shows incomplete and variable efficacy in preventing the disease in infants and children, especially in the immune-compromised populations. Moreover, it does not protect adults from developing tuberculosis. A number of novel candidate TB vaccines have been developed and now have to be tested in phase II and phase III trials over the course of the next decade. To produce robust results, efficacy trials will have to be conducted at multiple sites involving patients from different populations. Each participating site would need to possess or develop regulatory-quality capabilities. Therefore, capacity development is an important part of the EDCTP-funded TB vaccine studies. Since 2003, EDCTP has invested € 23.45 million in TB vaccine research.

Professor Helen McShane from the University of Oxford, United Kingdom, coordinates a study to evaluate whether the new tuberculosis candidate vaccine MVA85A will boost immunity and reduce illness from TB in adults infected with HIV. People infected with HIV are at far greater risk of developing TB disease than HIV-negative people. The candidate vaccine is tested in approximately 1400 adults who are 18-50 years of age.

MVA85A was the first new TB vaccine to enter into clinical testing since BCG was first tested almost a hundred years ago. It entered into clinical testing in Oxford in 2002. Since then the vaccine has been tested in many trials in the South Africa, Senegal and The Gambia, as well as in the United Kingdom. The vaccine was found safe in all of the trials. It also stimulated the type of immune response that is important for protection against TB. The vaccine is now being tested to investigate if it works to stop people getting TB. The results of a recent trial showed that the immune responses in infants in South Africa were very low and MVA85A did not stop those infants from getting TB. The EDCTP-funded trial is testing the vaccine in HIV-infected adults in South Africa and Senegal.

The capacity building component of the project will ensure that two trial sites will be able to participate in similar clinical trials in the future. The site in Dakar, Senegal is managed by the Laboratory for Bacteriology-Virology of University Hospital Centre Aristide Le Dantec, and the site in Khayelitsha, South Africa, is run by the Institute of Infectious Disease and Molecular Medicine of the University of Cape Town. The Scientific Institute of Public Health (WIV-ISP) in Belgium, which first identified the antigen 85A for possible use in a vaccine candidate, is providing in-kind laboratory services for the study.

Relevant publications:

1. Hanekom, WA; Dockrell, HM; Ottenhoff, THM; Doherty, TM; Fletcher, H; McShane, H; Weichold, FF; Hoft, DF; Parida, SK; Fruth, UJ. (2008) 'Immunological outcomes of new tuberculosis vaccine trials: WHO panel recommendations'. *PLOS Medicine*. 1:5(7):e145
2. Rustomjee, R; McClain, B; Brennan, MJ; McLeod, R; Chetty-Makkan, CM; McShane, H; Hanekom, W; Steel, G; Mahomed, H; Ginsberg, AM; Shea, J; Lockhart, S; Self, S; Churchyard, GJ. (2013) 'Designing an adaptive phase II/III trial to evaluate efficacy, safety and immune correlates of new TB vaccines in young adults and adolescents'. *Tuberculosis (Edinb)*. 93(2):136-42.

Professor Helen McShane

University of Oxford, United Kingdom

Ten years ago there were only one or two new TB vaccine candidates that were being tested in clinical trials. We now have over a dozen candidates being tested in clinical trials, and to date all but one of those candidates have been safe and stimulated an immune response. EDCTP has been pivotal in increasing the amount of trial activity in TB high-burden countries and this must continue.

Developing TB vaccines is difficult. We need to try and improve the models with which we select vaccines. The animal models need to be refined and made more representative of human disease. We also need to develop in-vitro *and* in-vivo *human models with which we can test new vaccines. We must take every opportunity to understand more about the immune response in people who do not get TB despite being exposed, and to use samples from clinical efficacy trials where available, so we can use this immunological data to guide vaccine development. We need to do more clinical testing in target populations, as immunogenicity in the developed countries may not predict immunogenicity in the developing world. And as a field we need to be more collaborative as working together will increase the pace of progress.*

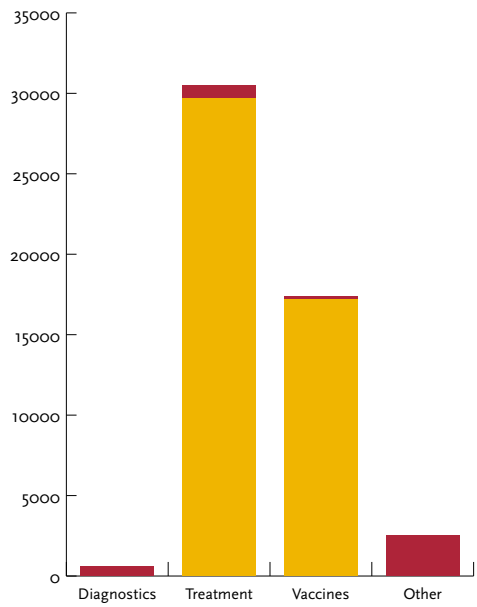
EDCTP is funding and supporting the study in HIV-infected adults in Senegal and South Africa. As part of this trial, we have conducted a substantial amount of capacity building at both trial sites, but particularly at the South African site in Khayelitsha. This is enormously important as it provides a sustainable infrastructure not just for this trial, but as a trial site for many other vaccines in the future.

Malaria

The EDCTP malaria portfolio includes 12 vaccine phase I-II clinical trials evaluating several vaccine candidates, and 22 treatment trials of which 12 are phase IV (post registration) trials, mainly label expansion studies in special or vulnerable groups such as pregnant mothers, very young or malnourished children and people living with HIV. Moreover, the approach adopted in these projects reflects the EDCTP strategy of integrating high quality research with investment in clinical capacity development and expansion of research networks in sub-Saharan Africa.

As of 31 December 2013, the total funding for the 41 malaria research projects supported by EDCTP amounted to € 51 million.

Malaria funding: signed grants 2003-2013 (€ '000)



	Clinical trial	Non trial
Diagnostics	-	€ 595
Treatment*	€ 29,684	€ 857
Vaccines	€ 17,166	€ 192
Other**	-	€ 2,496
Total	€ 46,850	€ 4,140

*Including € 11 million of funding to support studies on malaria in pregnancy
**Including immunology, epidemiology and cross-cutting issues.

Malaria treatment

Malaria remains a major cause of illness and death in developing countries. As resistance of malaria parasites to conventional antimalarial drugs is emerging, it is important to support development of new drugs and combination regimens. EDCTP has provided € 19.53 million to support 19 projects on malaria treatment, which include studies of artemisinin-based combination therapies (ACTs) and non-ACTs. The studies aimed to establish therapies that are safe and highly effective in actual health care situations. Moreover, current studies aim to address the needs of patient groups that need special attention such as infants, malnourished children, HIV/AIDS co-infected individuals and pregnant women.

The Four Artemisinin-Based Combinations (4ABC) study was successfully conducted in seven sub-Saharan African countries at twelve trial centres. The study screened more than 10,000 children between 6 and 59 months old; a total of 4,116 children were included in the study and treated. Three novel artemisinin-based combination drugs were found to be safe and efficacious in treating children with uncomplicated malaria. This study contributed to the evidence on safety and efficacy of dihydroartemsinin plus piperaquine (DHAPQ) for its addition to the list of ACTs options recommended for the treatment of uncomplicated *Plasmodium falciparum* malaria by WHO.

The 4ABC study was coordinated by Professor Umberto D'Alessandro from the Institute for Tropical Medicine, Antwerp, Belgium, currently at the Medical Research Council, The Gambia research unit. It compared artemisinin-based combination treatments of malaria in children between 6 and 59 months old. The group also evaluated the safety and efficacy of repeated treatments. A large multicentre randomised trial was set up to test four different treatments: amodiaquine-artesunate (ASAQ), dihydroartemisinin-piperaquine (DHAPQ), artemether-lumefantrine (AL) and chlorproguanil/dapsone-artesunate (CD+A). Each site tested three of these treatments. Children with uncomplicated malaria were randomised to one of the study treatments, followed up actively until day 28 post-treatment and then passively for the next six months.

The study was completed in 2010. The findings of the 4ABC study were published in *PLOS Medicine* on 8 November 2011.

Relevant publications:

1. D'Alessandro, U. (2010) 'Artemisinin combination therapies (ACTs) for uncomplicated malaria in African children: the 4ABC trial, preliminary results'. *Tropical Medicine and International Health*. 15(8):S13
2. D'Alessandro, U on behalf of The Four Artemisinin-Based Combinations (4ABC) Study Group. (2011) 'A head-to-head comparison of four artemisinin-based combinations for treating uncomplicated malaria in African children: a randomised trial. *PLOS Medicine*. 8(11):e1001119
3. Yeka, A; Tibenderana, J; Achan, J; D'Alessandro, U; Talisuna, AO. (2013) 'Efficacy of quinine, artemether-lumefantrine and dihydroartemisinin-piperaquine as rescue treatment for uncomplicated malaria in Ugandan children'. *PLOS ONE*. 8(1):e53772.

Professor Umberto D'Alessandro

Institute for Tropical Medicine, Belgium and the Medical Research Council unit, The Gambia.

A great achievement in the field of malaria treatment of the past decade is the increase in the number of treatment options currently available and in development. We will have the possibility of choosing the treatment most adequate to the local malaria endemicities.

EDCTP has been essential for the implementation of the important 4ABC trial as it has provided a substantial amount of the resources necessary to carry out the study. In addition, by requesting the collection of high quality data, EDCTP has contributed to the high quality of the study and consequently its credibility.

More needs to be done. We still need to have alternatives to the artemisinin derivatives as resistance seems to have appeared in Asia and may spread to other continents. We also need to have better drugs for interrupting malaria transmission. With the support of EDCTP, we are now carrying out a clinical trial on the treatment of malaria in pregnant women. This will provide a solid basis on which to provide recommendations for this specific population group.

Malaria in pregnancy

In areas where malaria is endemic, pregnant women are at high risk of morbidity and mortality. Malaria infection in pregnancy is associated with increased risk of anaemia in the mother and with low birth weight, which is a major determinant of infant mortality. EDCTP funds three studies with a grant value of € 11 million focusing on malaria in this population which have been implemented by the Malaria in Pregnancy Consortium.

The Malaria in Pregnancy Preventive Alternative Drugs (MiPPAD) is one of the studies under the umbrella of the consortium. The MiPPAD study aims to evaluate the safety, tolerability and efficacy of mefloquine (MQ) as an alternative to the standard drug sulfadoxine-pyrimethamine (SP) used for Intermittent Preventive Treatment in pregnancy (IPTp) in combination with Long Lasting Insecticide Treated Nets (LLITNs). Led by Professor Clara

Menéndez of the Barcelona Centre for International Health Research, Spain, this multicentre randomised clinical trial addresses the critical need for the evaluation of a safe and effective alternative to IPTp-SP in both HIV-negative and HIV-positive women. The MiPPAD study completed enrolment of 4,734 pregnant women in 2012, after screening 17,947 women in Benin (Allada, Sékou and Attogon), Gabon (Fougamou and Lambaréné), Kenya (Kisumu), Mozambique (Manhiça and Maragra), and in Tanzania (Makole and Chambwino). The study has also strengthened capacity development at institutional and individual levels for antimalarial research in all participating sites.

Relevant publications:

1. Ouédraogo, S; Bodeau-Livinec, F; Briand, V; Huynh, BT; Koura, GK; Accrombessi, MM; Fievet, N; Massougbodji, A; Deloron, P; Cot, M. (2012) 'Malaria and gravidity interact to modify maternal haemoglobin concentrations during pregnancy'. *Malaria Journal*. 22;11:348
2. Basra, A; Mombo-Ngoma, G; Capan Melser, M; Akerey Diop, D; Würbel, H; Mackanga, JR; Fürstenau, M; Manego Zoleko, R; Adegnika, AA; Gonzalez, R; Menendez, C; Kremsner, PG; Ramharter, M. (2013) 'Efficacy of mefloquine intermittent preventive treatment in pregnancy against schistosoma haematobium infection in Gabon: a nested randomized controlled assessor-blinded clinical trial'. *Clinical Infectious Diseases*. 56(6):e68-75
3. Schaumburg, F; Alabi, AS; Mombo-Ngoma, G; Kaba, H; Zoleko, RM; Diop, DA; Mackanga, JR; Basra, A; Gonzalez, R; Menendez, C; Grobusch, MP; Kremsner, PG; Köck, R; Peters, G; Ramharter, M; Becker, K. (2013) 'Transmission of Staphylococcus aureus between mothers and infants in an African setting'. *Clinical Microbiology and Infection*. Article first published online : 18 Nov 2013.

Professor Clara Menéndez

Barcelona Centre for International Health Research, Spain

During the last decade there have been significant investments in malaria, along with unprecedented efforts to control this infection. Renewed political and financial commitment has resulted in the creation of new initiatives, such as the Medicines for Malaria Venture (MMV), which is focussed on the discovery of new and more effective antimalarial drugs. The creation of EDCTP allowed, in a quasi-perfect synchrony with MMV, the clinical evaluation of new antimalarials resulting in an increased availability of drugs to treat the infection.

Further research and development is crucial to achieve and sustain malaria control, which should focus not only on Plasmodium falciparum *but also on* Plasmodium vivax. *We urgently need methodologies for estimating and tracking the malaria burden and to measure transmission. We need to know more of the mechanisms and effects of resistance to drugs and insecticides, and we need to have more sensitive point-of-care rapid diagnostic tests for low-density infections.*

With the agenda of malaria eradication in mind, safer and more effective drugs are needed to achieve the radical cure of asymptomatic infections of both P. falciparum *and* P. vivax *in the entire population.*

EDCTP has played a fundamental role in understanding many of the issues that are critical for malaria control in pregnancy in the African region. With regard to the MiPPAD trial, EDCTP funding has provided the study with a framework which goes beyond the - fully supported - pursuit of the scientific objectives. The EDCTP framework is, to my knowledge, one of a kind. It has also promoted and monitored gender awareness, ethics compliance, infrastructure upgrades and capacity development. Therefore, the study's achievements are not only scientific, but have contributed to the longer-term objectives of sustainability and excellence in research.

Malaria vaccines

An effective and highly efficacious malaria vaccine is required to help reduce the burden of malaria in endemic countries. Since 2003, EDCTP has spent € 17.36 million to support six projects that include clinical trials of vaccines and projects that have a focus on immunological responses and capacity building for vaccine trials.

Among these projects are the studies of the Malaria Vectored Vaccine Consortium (MVVC). This consortium was previously led by Dr Babatunde Imoukhuede and now is led by Dr Odile Leroy from the European Vaccine Initiative in Germany. It aims to develop a liver stage malaria vaccine based on the thrombospondin related adhesion protein (TRAP) that is fused to a string of multiple T cell epitopes (ME) administered in two different viral vectors. TRAP is an abundant parasite surface protein that is expressed in the early life cycle stages, the sporozoites and the liver stages. The two viral vectors ChAd63 (a simian adenovirus vector) and MVA (Modified Vaccinia Ankara) both express ME-TRAP and are administered in a prime-boost regimen, which aims at provoking a strong cellular immune response directed against TRAP. Pre-clinical studies, as well as early phase clinical trials, provided evidence that the prime-boost regimen with Chad63 and MVA viral vectors induce strong CD8 T cell responses shown to be protective against malaria in human challenge trials.

An effective vaccine targeting the malaria liver stages can prevent the disease as it would eliminate the parasite before it multiplies in the red blood cells. The prime-boost approach based on viral vectors is targeting the T cell immune pathway, similar to the immune response induced by the pathogen in the human host. With only two doses, the prime-boost approach will also simplify the paediatric vaccine schedule, and could ultimately reduce the costs of malaria vaccination.

The MVVC study showed good safety and immunogenicity in adults in phase Ib clinical trials conducted in The Gambia and in Kenya, as well as in Gambian children and infants. Recently, promising efficacy data was obtained from a phase IIb clinical trial in adults in Kenya. It revealed an adjusted efficacy of 66% against parasitaemia shown by polymerase chain reaction. The data of an additional phase IIb clinical trial in Senegalese adults are currently analysed and publication of the results is being prepared. The first interim results of a phase IIb clinical trial in Burkinabe children aged 5 to 17 months are expected in 2014.

A follow-up study (MVVC2), also supported by EDCTP, selected a second pre-erythrocytic antigen, the circumsporozoite protein (CSP), to be combined with the ChAd63/MVA ME-TRAP vaccine approach. This combination vaccine is expected to result in even higher protection by combining cellular and humoral immune responses.

Relevant publication:

1. Ogwang, C; Afolabi, M; Kimani, D; Jagne, YJ; Sheehy, SH; Bliss, CM; Duncan, CJ; Collins, KA; Garcia Knight, MA; Kimani, E; Anagnostou, NA; Berrie, E; Moyle, S; Gilbert, SC; Spencer, AJ; Soipei, P; Mueller, J; Okebe, J; Colloca, S; Cortese, R; Viebig, NK; Roberts, R; Gantlett, K; Lawrie, AM; Nicosia, A; Imoukhuede, EB; Bejon, P; Urban, BC; Flanagan, KL; Ewer, KJ; Chilengi, R; Hill, AV; Bojang, K. (2013) 'Safety and immunogenicity of heterologous prime-boost immunisation with Plasmodium falciparum malaria candidate vaccines, ChAd63 ME-TRAP and MVA ME-TRAP, in healthy Gambian and Kenyan adults. *PLOS ONE*. 8(3):e57726

Dr Odile Leroy

European Vaccine Initiative, Germany

During the last ten years, the malaria vaccine community has been a pioneer in joining forces in order to address the numerous scientific and technical challenges. It started at funding agency level, when in 2002 the malaria vaccine funders group was constituted with the first task of sharing information and establishing a global portfolio management. It then continued with the endorsement of the malaria vaccine technology roadmap, where priorities were defined.

The results of the MVVC phase Ib and phase IIb clinical trials with ChAd63/MVA ME-TRAP have been very encouraging so far. The promising results of Chad63 vector enabled a collaboration between GlaxoSmithKline and the Jenner Institute to improve the first generation malaria vaccine, the RTS,S.

Up to now, EDCTP contributed to the conduct of seven clinical studies of the project to evaluate the vaccine candidates in different population and age-groups. The funding helped to set up and build capacity in six clinical trial centres of the five African partner institutions. They are now able to perform clinical trials according to international standards. The consortium implemented training on Good Clinical Practices, project management, publication writing and clinical trial protocol development for staff at the five African partner institutions. It also supported the training of three MSc and three PhD students, as well as the research of one Postdoctoral researcher. Thanks to the training received within MVVC, one of the PhD students is now the principal investigator in one of the MVVC2 clinical trials. Through this collaboration, a sustainable network was formed with lively exchanges and ongoing support amongst the junior and senior staff of all partner institutions.

Research capacity

EDCTP adopted a programmatic approach to capacity development. Investments in capacity development and networking activities facilitate the successful undertaking of clinical trials, the partnership's core business. Capacity development, for example through training or infrastructure upgrades of clinical research centres, as well as networking activities are integrated in research projects. By the end of 2013, EDCTP had supported a total of 514 African trainees at various career stages. European researchers are trained as well with EDCTP funding, as many postgraduate students collaborate with African colleagues on integrated clinical trial projects. The majority of EDCTP grants also include budgets for targeted short-term training schemes and workshops, linked to the overall aims of the project.

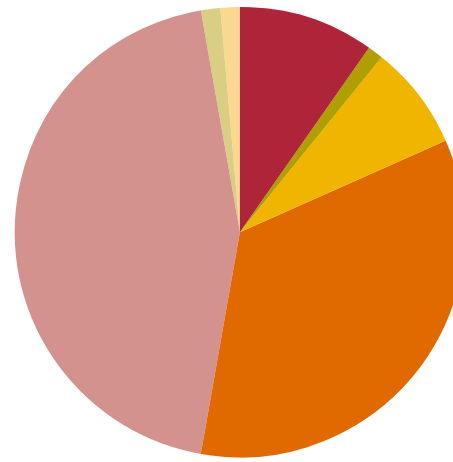
Dr Wendy Burgers

University of Cape Town, South Africa, EDCTP Senior Fellow 2008-2011

The EDCTP Fellowship was the launching pad for my independent research career. Research is driven forward from research findings, following the data, and making new discoveries. The subject of the grant was a new research direction for me, and the fellowship has allowed me to build a research group and research programme around HIV/TB co-infection, because our findings had prompted a range of additional scientific questions to take forward.
We have three publications in preparation on the work we performed and are actively working on a novel TB cell subset that we discovered. My laboratory now has one MSc and three PhD students that I am training, and I am mentoring two postdoctoral fellows as well. My team hails from across the African continent: Botswana, Cameroon, Mauritius, South Africa and Tanzania. Thus, my Fellowship experiences are now being passed on to the next generation of young African researchers.

The project produced a wealth of archived patient clinical material, which we are using to address a range of related scientific questions regarding TB immunity in HIV-infected individuals. I successfully applied for further funding to continue these studies, and was awarded local South African grants, from the Medical Research Council (MRC) and the National Health Laboratory Service (NHLS) Trust. I have submitted an R01 research grant proposal to the National Institutes of Health (United States) using as preliminary data what was generated during this Fellowship. In the final year of the EDCTP grant, I was awarded a 5-year career development Fellowship from the Wellcome Trust, which has allowed me to continue on my trajectory to independence. My team members, whose projects focus on a different aspect of HIV/TB co-infection immunity, have all been awarded prestigious fellowships for their studies.
I hope to repay EDCTP's investment with high quality science, which has a positive impact on global health, and equipping the next generation of young scientists to effectively tackle major public health challenges.

Number of trainees funded by EDCTP (2003-2013)



Career stage	Number of trainees
Senior Fellows	51
Career Development Fellows	5
Postdoctoral researchers on EDCTP grants	39
PhD students	177
Master's students	229
Medical Diploma students	7
Bachelor's students	6
Total	514

Senior Fellowship programme

The Senior Fellowship grant scheme supports the development of African scientific leadership and mentorship. It was instrumental in developing the careers of mid-level to senior African scientists and helping them to become more competitive internationally, to build research teams and to develop the scientific excellence and leadership required for larger grants from EDCTP and other funding sources. A number of Senior Fellows have received prestigious international awards.

Since the inception of this grant scheme in 2004, 10 calls for proposals have been published. A total of 51 Senior Fellows have received this grant support, of which 40 are male and 11 female researchers. Approximately 10% of the Senior Fellows have used this grant scheme to return from academic institutions abroad to research positions in their respective countries. Sixteen of the Fellows conducted

clinical trials as part of their fellowships. The other Senior Fellows focussed on clinical and epidemiological research. Twenty-eight (28) Senior Fellows completed their projects in 2013, 27 of whom continued working in research in sub-Saharan Africa. EDCTP has supported Senior Fellowships in 19 sub-Saharan countries: Botswana, Burkina Faso, Cameroon, Republic of Congo, Cote d'Ivoire, Gabon, The Gambia, Ghana, Guinea, Kenya, Liberia, Malawi, Mali, Nigeria, Senegal, South Africa, Sudan, Uganda and Zimbabwe.

Relevant publications:

1. Djimde, AA; Fofana, B; Sagara, I; Sidibe, B; Toure, S; Dembele, D; Dama, S; Ouologuem, D; Dicko, A; Doumbo, OK. (2008) 'Efficacy, safety, and selection of molecular markers of drug resistance by two ACTs in Mali'. *American Journal of Tropical Medicine and Hygiene*. 78(3):455-61.
2. Tekete, M; Djimde, AA; Beavogui, AH; Maiga, H; Sagara, I; Fofana, B; Ouologuem, D; Dama, S; Kone, A; Dembele, D; Wele, M; Dicko, A; Doumbo, OK. (2009) 'Efficacy of chloroquine, amodiaquine and sulphadoxine-pyrimethamine for the treatment of uncomplicated falciparum malaria: revisiting molecular markers in an area of emerging AQ and SP resistance in Mali'. *Malaria Journal*. 26;8:34
3. Djimde, A; Fofana, B; Sagara, I; Sidibe, B; Toure, S; Dembele, D; Togo, A; Sanogo, K; Dama, S; Dicko, A; Lameyre, V; Plowe, CV; Doumbo, OK. (2012) 'Impact of repeated administration of acts on safety, efficacy and incidence of uncomplicated malaria in Mali'. *American Journal of Tropical Medicine and Hygiene*. 87(1):50-6
4. Zwang, JL; Dorsey, G; Djimde, A; Karema, C; Martensson, A; Ndiaye, JL; Sirima, SB; Olliaro, P. (2012) 'Clinical tolerability of artesunate-amodiaquine versus comparator treatments for uncomplicated falciparum malaria: an individual-patient analysis of eight randomized controlled trials in sub-Saharan Africa'. *Malaria Journal*. 2;11:260.

Associate Professor Abdoulie Djimdé

Malaria Research & Training Center, Mali, EDCTP Senior Fellow 2004-2007, currently Project Coordinator for EDCTP funded integrated project, WANECAM.

The research I conducted with support of EDCTP assessed the public health benefit of the use of artemisinin-based combinations in sub-Saharan Africa. Patients with uncomplicated malaria were randomised to receive artesunate + amodiaquine (AS+AQ; Arsucam®, Sanofi Synthelabo), artesunate + sulfadoxine-pyrimethamine (AS+SP) or artemether-lumefantrine (AL; Coartem®, Novartis). Once subjects had been assigned to a given group, subsequent malaria episodes were treated with the same treatment regimen. Patients were closely followed both clinically and biologically to record any adverse event. Using this novel approach of repetitive treatment over two consecutive transmission seasons and three years, we showed that in this setting of perennial transmission with seasonal peaks, the incidence density of malaria in the AS/SP and AS/AQ arms were reduced as compared to the AL arm. All artemisinin-based combinations maintained acceptable clinical and laboratory safety profiles despite their repetitive usage. Using direct feeding, we showed that all artemisinin-based combinations decreased gametocyte carriage, the impact on gametocyte infectivity to Anopheles mosquitoes varied from one artemisinin-based combination to the other.

Intensive training and capacity development activities were conducted in the context of these studies, leading to the development of an effective team of young scientists, ready to undertake clinical development of antimalarial drugs.

Furthermore, the EDCTP Senior Fellowship allowed me to stay in Mali and continue my work as a starting scientist. Through this experience and funding opportunity, I was able to build a strong team and lay the foundation for the infrastructure required for antimalarial drug trials. This attracted new clinical development activities sponsored by various pharmaceutical groups. Subsequently we received a larger grant from EDCTP for an integrated clinical trial project, the WANECAM project (www.wanecam.org).

Master's in Clinical Trials (Distance Learning)

Between 2007 and 2013, 25 students have received support from EDCTP to undertake the Master's in Clinical Trials (by distance learning) at the London School of Hygiene and Tropical Medicine (LSHTM). Fourteen students received their MSc degree, while eight students are at an advanced stage; for various personal reasons, three students were unable to complete their studies. The Master's course was designed to offer a flexible training schedule that is compatible with working life. Students may complete the Master's training within a period of two to five years at a pace appropriate to their own circumstances and their employing institution's needs. A postgraduate diploma based on completion of four core modules can be awarded after a minimum of one year. Via a second training grant coordinated by LSHTM, EDCTP also provided funding to establish MSc in Clinical Trials courses at the University of Ghana (conducted in English) and at the University of Bobo-Dioulasso in Burkina Faso (conducted in French).

Health research ethics

Since the ethics grant scheme started in 2005, 10 calls for proposals have been launched to strengthen the capacity for ethics review of health research in sub-Saharan Africa. A total of 75 grants have been awarded. Fifty-one (51) projects were successfully completed by 31 December 2013. The aim of the grant scheme is to strengthen the ethics review framework of sub-Saharan institutions and countries. The grants are awarded to develop the appropriate human resource and infrastructure required to achieve functional, competent, independent and sustainable ethics review boards in Africa. Effective ethics review of health research, including clinical trials, is essential for the development of medicines, interventions and medical technologies in and for Africa.

As part of the EDCTP-Plus project, an external evaluation of the ethics capacity development grant scheme was conducted and completed successfully in November 2013. The evaluation highlighted the strategic role of EDCTP in the field of research ethics review. The recommendations from the evaluation were presented at the EDCTP Stakeholder Meeting on Health Research Ethics on 28 November 2013 in Antwerp, Belgium.

The funded projects fall into three categories: training projects, institutional development and networking. The training of members of ethics committees or institutional review boards is supported, for instance through the development of online training programmes. Grants have been awarded to African and European organisations. For example, ERECCA (Enhancing Research Ethics Capacity and Compliance in Africa) offers online courses on Good Clinical Practice and Ethics Research Ethics Review and is led by Professor Keymanthri Moodley (University of Stellenbosch, South Africa).

TRREE for Africa (Training and Resources in Research Ethics Evaluation for Africa) led by Professor Dominique Sprumont (Health Law Institute, Switzerland) offers web-based training and a capacity development programme that provides an introduction to regulations, ethical guidelines and internationally recognised human rights standards relevant to health research as well as access to relevant documentation. The initiative was funded by EDCTP and launched in 2006 by individuals and institutions from Africa, Europe and Canada involved in research ethics. It provides researchers and members of research ethics committees with a high-quality basic education in research ethics.

The TRREE programme is recognised by the World Medical Association and the National Health Research Ethics Committee of Nigeria. Moreover, it is integrated in the education programmes of health professionals in several African universities, most notably in Cameroon. Since its launch, TRREE has involved almost 8,000 participants throughout Africa, including many from francophone countries in central and west Africa.

Relevant publication:

1. Jérome, A; Cédric, B; Ikingura, J; Hirtle, M; Niaré, A; and Sprumont, D. (2009) 'Training needs assessment in research ethics evaluation among research ethics committees members in three African countries: Cameroon, Mali and Tanzania'. *Developing World Bioethics*. 10(2):88-98

Professor Dominique Sprumont

Health Law Institute, Switzerland

EDCTP was the first TRREE funder and has contributed to its first two stages. The first phase from 2006-2009 enabled the needs assessment and the development of the overall structure of the web portal, as well as the first two modules and the national supplements for Mali, Cameroon and Tanzania. In the second phase, from 2009-2012, TRREE added a module on informed consent and national supplements for Senegal, Nigeria and Mozambique.

Thanks to this initial support from EDCTP, TRREE was successful in obtaining additional funding from other funders, including the Swiss National Science Foundation, the Fogarty International Center of the US National Institutes of Health, the South African National Research Foundation and the South African AIDS Vaccines Initiative, as well as other institutions in Europe, Canada and the United States. They allowed us to develop several topic modules and national supplements for several European countries and South Africa.

TRREE has thus become the reference site for the European Network of Research Ethics Committees (EURECNET). From a partnership of Africans, Europeans and Canadians originally focussed on Africa, TRREE now encompasses countries in Europe and Asia and is looking to expand to the Near East and Latin America.

In addition to a financial contributor, EDCTP has also been a valued partner for TRREE in supporting research ethics education in Africa and many other countries.

The second category consists of the grants for the support, establishment and strengthening of ethics capacity at both the institutional and national level. The purpose of these grants is to contribute to the establishment of independent and functional Institutional Review Boards and National Ethics Committees. The EDCTP-funded project towards consolidation of the National Ethic Committees Network in Mozambique is an example of this category of projects. The project promoted training collaboration with African and European networks, which started in 2010 and was led by Dr João Fumane.

With the funding from EDCTP, the Mozambican National Ethics Committee, known as the Comité Nacional de Bioética para Saúde (CNBS), established institutional review boards to create a national network of ethic committees in the country and to strengthen the collaboration with a similar institution in Europe, South America and Africa. The members of the institutional review boards and the members of the existing ethic committees were trained. The training was also extended to researchers, other health professionals, health authorities and students from the medical school. The project has raised ethical review standards and increased awareness of ethical principles in the research community, which has contributed to the protection of study participants.

The objective of the third group of grants was to support the networking and coordination of national initiatives. Examples in this category of ethics grants are the Southern African Research Ethics Network (SAREN) which aims at establishing a network of Chairpersons of sub-Saharan Research Ethics Committees, and the MARC (Mapping African Research Ethics and Drug Regulatory Capacity) project.

The MARC project aimed to create a web-based platform offering an overview of health research ethics review and regulatory activities in sub-Saharan Africa. The project documented Africa's capacity to conduct ethical review of health research (www.researchethicsweb.org). The MARC project has also linked the ethics review capacity development with COHRED's Health Research Web platform (www.healthresearchweb.org) which allows ethics capacity analysis in relation to general research system development and comparisons between countries in and outside Africa. A total of 165 operational research ethics committees were identified in 37 African countries. Moreover, an information management platform was developed with feedback and support from the MARC project. The Research for Health and Innovation Organiser (RHinnO Ethics, www.rhinno.net) facilitates efficient ethical review clearance through a fully web-based system. Since its launch in April 2012, RHInnO Ethics is used by over 50 research ethics committees across seven African countries. The first phase of the MARC project was completed in 2012. In 2013, EDCTP provided additional funding to strengthen and ensure continuation of the MARC project.

Relevant publication:

1. IJsselmuiden, C; Marais, D; Wassenaar, D; Mokgatla-Moipolai, B. (2012) 'Mapping African ethical review committee activity onto capacity needs: The MARC initiative and HRWeb's interactive database of RECs in Africa'. *Developing World Bioethics*. 12(2):74-86.

Dr João Fumane

Ministry of Health/National Institute of Health, Mozambique

EDCTP's support to this project strengthened the National committee for ethics review of health research (CNBS), enabled training of ethics committee members and created an atmosphere of working together and promotion of activities outside the committees. The establishment of rules for the Institutional Review Boards will enable them to operate according to national and international standard guidelines, under close supervision of the CNBS.

The project also enabled the establishment of five new Institutional Review Boards. The ethical standards that were established for the Institutional Review Boards will enable investigators involved in health research in the country to better understand ethical principles. It will also increase the number of protocols submitted to the Institutional Review Boards before implementation of the research. This will be an important contribution to meeting the public health needs in Mozambique.

Professor
Carel IJsselmuiden

Dr Boitumelo
Mokgatla-Moipolai

Council on Health Research for Development (COHRED), Switzerland and Botswana

Through support for the MARC project, EDCTP has substantially contributed to more effective, more efficient and higher quality ethics review of clinical trials and other research that is key to developing medicines, interventions and medical technologies in and for Africa. EDCTP supported the initial goals of the MARC projects (mapping activities) as well as all the innovative ideas and interventions born during the project, including the analysis of the MARC data, development of useful tools such as EthiCALL – a platform for Research Ethics Committees to discuss and address complex ethical issues in research – as well as RHinnO Ethics – a cloud-based ethics review system intended to replace the current complex paper based system widely used by RECs in Africa. We look forward to the continuous growth of MARC through the support of EDCTP.

Clinical trial registry

In 2006, EDCTP established the HIV/AIDS, Tuberculosis and Malaria (ATM) Registry. ATM was operated by the Cochrane Centre at the Medical Research Council in Cape Town, South Africa. It aimed to increase the prospective registration of clinical trials in Africa. In June 2008, the ATM Clinical Trials Registry became the Pan African Clinical Trials Registry (PACTR) following requests from WHO and the African Vaccine Regulatory Forum (AVAREF) for it to register all randomised controlled and controlled clinical trials conducted in Africa regardless of disease. In September 2009, PACTR was officially recognised as a WHO Primary Registry. To date, PACTR remains the only WHO-endorsed primary registry in Africa.

PACTR provides accessible information that describes the scope, location, ethics and funding patterns of trials conducted across the continent. Registration data in the PACTR portal (www.pactr.org) meet the requirements of the International Committee of Medical Journal Editors

(ICMJE) and feed into the WHO International Clinical Trials Registry Platform (ICTRP). The PACTR registry facilitates understanding of regional research patterns, enables the identification of research gaps for future studies, and facilitates the investigation of the scope, quality and funding patterns of African trials. In 2012, the registry received additional support from EDCTP, as part of the EDCTP-Plus activities. The aim was to improve the performance of the registry and to enhance the database to include links to publications related to each trial, as well as geocodes for the clinical trials. By end of 2013, PACTR has received in total 254 trial applications from sub-Saharan Africa.

Relevant publications:

1. Abrams, A; Siegfried, N. (2009) 'Compliance with the WHO minimum data-set in the first Pan African WHO-endorsed Primary Registry'. *Trials*. 10:56
2. Abrams, A; Siegfried, N. Guest Editorial: Maximising the effectiveness of trial registries in resource-constrained settings, *BMJ Clinical Evidence*, 13 July 2009.

Professor Jimmy Volmink

Cochrane Centre, Medical Research Council, South Africa

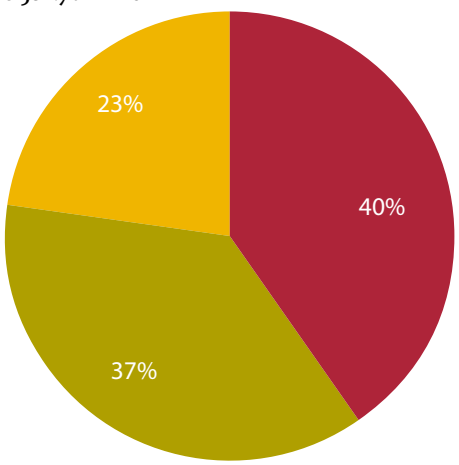
Trial registration is key to tracking information on trials. EDCTP has recognised the importance of ensuring global standards for African clinical trialists by supporting clinical trial registration. The grants from EDCTP provided the start-up funding for the project, and through continued funding have provided for sustained growth of the register. Staff from EDCTP have contributed on the Advisory Board to the vision and strategic development of PACTR, and have ensured that the project remains grounded in its service of researchers in the region. It is worth noting that EDCTP is responsible for funding a large number of the trials that populate the Registry. Of the 254 trials currently registered, 52 are partially or fully funded by EDCTP – this makes EDCTP the largest single contributor to PACTR-registered African clinical trials.

Connecting research

EDCTP has shown that improved coordination of European research as well as collaboration with and among African researchers is of great benefit to all partners and reinforces the impact of the European contribution. Moreover, the programme is one of the few international initiatives to develop a partnership with African scientists by creating opportunities for ownership and leadership by those working on the ground in disease-endemic countries. Through its projects and collaborative approach, EDCTP supports African researchers to establish their own networks. African researchers lead over 72% of all EDCTP-funded activities.

In addition to bringing together European national research programmes and their African partners, EDCTP has maintained and developed links with third parties, including PDPs, multinational pharmaceutical companies, philanthropic organisations, and like-minded organisations contributing to the development of new clinical tools against HIV/AIDS, tuberculosis, malaria.

Funding contribution (expenditures and future commitment) to EDCTP supported projects:
€ 382.70 million



European Commission	€ 154,894,945*
EDCTP Participating States	€ 141,623,498
Third parties	€ 86,179,308**
Total	€ 382,697,751

*This figure includes a € 2.08 million FP7 contribution
**This figure includes a € 14,424 million contribution from African countries

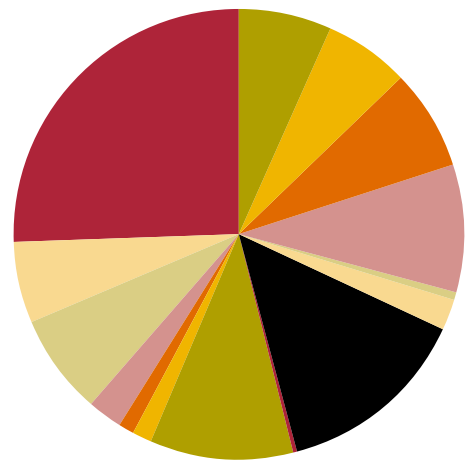
Integrating European research

Before 2005, European Union Member States funded clinical trials on HIV/AIDS, tuberculosis and malaria from their national programmes, in collaboration with historical partners in sub-Saharan Africa, but rarely in collaboration with the national programmes of other EU Member States. Through the activities of EDCTP, this situation has changed notably over the past years. Currently, a large proportion of funding from the European countries that participate in EDCTP for clinical trials on HIV/AIDS, tuberculosis and malaria is coordinated with that of at least one other EU Member State through EDCTP. EDCTP has been successful in integrating the national programmes of EU Member States on these three diseases in jointly funded clinical trials.

By end of 2013, the current EDCTP Participating States had collaborated (two or more countries involved) in 103 EDCTP-funded projects in sub-Saharan Africa. A total of 768 researchers based in Europe participated as collaborators in a total of 170 EDCTP projects, which gives an average of 4 Europe-based researchers per grant. The 76 projects without European investigators are capacity building grants that target African researchers, i.e. ethics grants, Senior Fellowships and studentships.

The signed grant value of all 246 EDCTP projects is € 212.12 million, comprising € 152.82 million EU funding and € 59.30 million cofunding disbursed by EDCTP of which € 50.88 million came from EDCTP Participating States and € 8.42 million from third-party organisations. The strong commitment to partnership is reflected in the 74% of EDCTP funding invested into activities implemented by African research institutions. The total value of all projects, also taking into consideration the cofunding that is contributed directly (i.e. not via EDCTP) to the projects, is € 382.70 million. This represents a substantial investment in research and capacity to tackle the three main poverty-related infectious diseases.

EDCTP Participating States total cofunding for research within the scope of the EDCTP programme, including cofunding of EDCTP projects, 2003-2013 (€ '000)



Austria	1.572
Belgium	54.636
Denmark	53.347
France	60.745
Germany	76.994
Greece	3.455
Ireland	19.983
Italy	115.743
Luxembourg	2.207
Netherlands	87.355
Norway	11.030
Portugal	9.535
Spain	20.755
Sweden	60.663
Switzerland	49.668
United Kingdom	214.416
Total	842.104

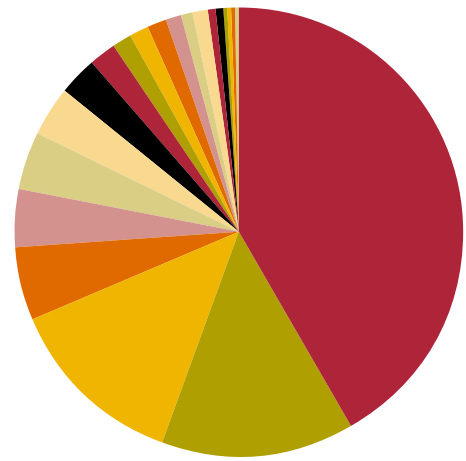
African research

EDCTP encouraged and supported African participation and leadership in the programme with African commitment and ownership both at the political and scientific level. EDCTP proactively engaged with researchers, research managers, heads of institutions and senior government officials in Africa and actively participated in various African forums.

Over the past five years, the number of African principal investigators in EDCTP-funded projects has dramatically increased. Furthermore, the number of institutions participating in EDCTP-funded activities has significantly increased since the inception of the programme. Participation rose from 13 African countries and 20 African institutions in 2005 to 30 countries and 165 institutions by December 2013. Of the 246 EDCTP projects, 239 have one or more researchers based at an institution in Africa. A total of 1,337 African researchers are listed on those projects, resulting in an average of five Africa-based researchers per grant.

By the end of 2013, African cofunding of EDCTP-funded projects had risen to about € 14.2 million which includes both in cash and in-kind. This figure, however, underestimates the African cofunding effort over the full course of the first EDCTP programme as most projects did not specify this cofunding in the past. Most importantly, the majority of the African researchers received their main salary from the hosting institutions or from African governments without it being specified as a contribution to these projects. Moreover, African governments make significant contributions to costs of other personnel, utilities and infrastructure as well as the participation of study volunteers in projects. Nevertheless, this figure demonstrates the European-African partnership that has developed over the course of EDCTP.

African cofunding contributions to EDCTP grants by country, 2003-2013 (€ '000)



South Africa	6,012
Tanzania	2,038
Uganda	1,866
Zimbabwe	763
Gambia	608
Zambia	593
Kenya	507
Ethiopia	412
Rwanda	283
Burkina Faso	207
Gabon	202
Mali	181
Senegal	154
Republic of the Congo	150
Malawi	145
Guinea Conakry	90
Benin	78
Nigeria	43
Mozambique	41
Cameroon	30
Ivory Coast	16
Ghana	5
Total	14,424

Regional Networks of Excellence

The EDCTP-funded Networks of Excellence which connect African academic and research institutions are important as they train a new generation and encourage retention of African scientists. They provide a better environment for research and offer career opportunities in clinical research. The networks improved the balance of clinical research capacity.

EDCTP established four Regional Networks of Excellence for Conducting Clinical Trials (NoE):

- The Central African Network for Tuberculosis, HIV/AIDS and Malaria (CANTAM; established 2008, funding € 2.8 million)
- The East African Consortium for Clinical Research (EACCR; established 2009, funding € 3.46 million)
- The Trials of Excellence for Southern Africa (TESA; established 2009, funding € 2.3 million)
- The West African Network for TB, AIDS and malaria (WANETAM; established 2009, funding € 3.5 million).

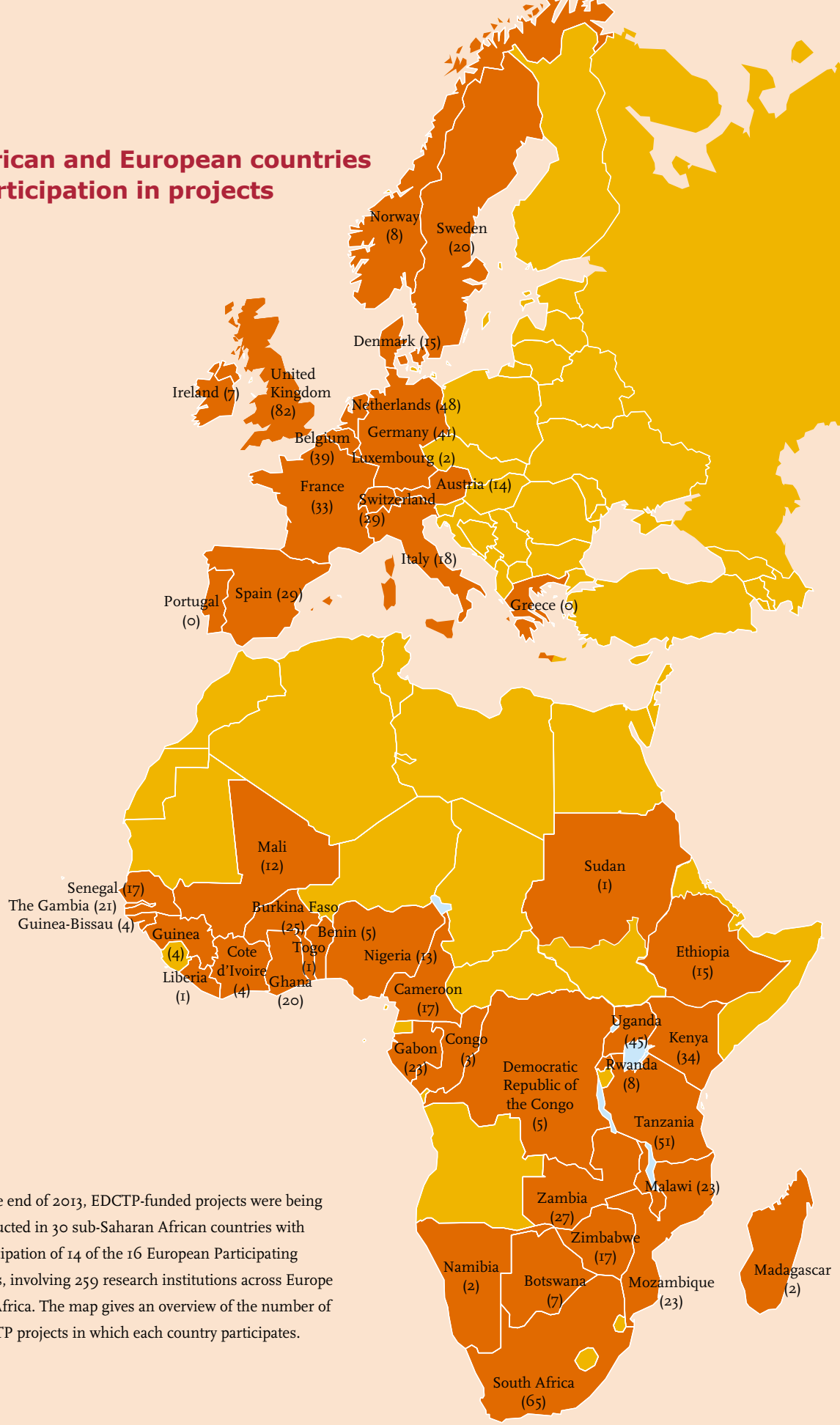
In 2013 the Networks of Excellence published a report on their achievements and challenges, which highlighted that these self-regulating democratic networks with 64 institutions in 21 African countries have trained over 1,000 African scientists, both through short-term and long-term training activities, upgraded 36 sites for clinical trials, leveraged an additional € 24 million of funding and generated 38 peer-reviewed publications (see below: Relevant publications nr. 3).

Furthermore, in 2013 additional funding was approved for each NoE for a period of up to 12 months. This funding aims to facilitate the continuity of their core activities and the completion of current projects by December 2014. As part of the EDCTP-Plus project, a programme of laboratory improvement in view of future accreditation was started at selected laboratories in the networks in 2013 and will continue in 2014.

Relevant publications:

1. Ntoumi, F. (2010) 'Networking and capacity building for health research in Central Africa'. Wien Klin Wochenschr. 122 Suppl 1:23-6.
2. Ntoumi, F. (2011) 'The ant who learned to be an elephant'. *Science*. 30;333 (6051):1824-5
3. Miiro, GM; Ouwe Missi Oukem-Boyer, O; Sarr, O; Rahmani, M; Ntoumi, F; Dheda, K; Pym, A; Mboup, S; Kaleebu, P; and on behalf of the NoEs' programme. (2013) 'EDCTP regional networks of excellence: initial merits for planned clinical trials in Africa'. *BMC Public Health*. 13:258
4. Miiro, G; Ouwe Missi Oukem-Boyer, O; Sarr, O; Rahmani, M; Ntoumi, F; Dheda, K; Pym, A; Mboup, S; Kaleebu, P. (2013) 'EDCTP Regional Networks of Excellence: unprecedented changes in the landscape of clinical trials in Africa'. *BMC Public Health*. 22;13:258

African and European countries participation in projects



At the end of 2013, EDCTP-funded projects were being conducted in 30 sub-Saharan African countries with participation of 14 of the 16 European Participating States, involving 259 research institutions across Europe and Africa. The map gives an overview of the number of EDCTP projects in which each country participates.

International and third-party collaboration

EDCTP collaborated and continues to collaborate with third parties, i.e. pharmaceutical companies, small- and medium-sized enterprises, philanthropic organisations and like-minded organisations, to develop new and improved clinical tools. Examples of effective collaboration are the Malaria in Pregnancy (MiP) Consortium and the Pan-African Consortium for the Evaluation of Antituberculosis Antibiotics (PanACEA).

From the start of the EDCTP programme in 2003 to 31 December 2013, third-party organisations have contributed € 71.75 million to EDCTP grants. The largest third-party funder is the Global TB Alliance. The Global TB Alliance contributed € 16.95 million in cash to EDCTP projects involving research in tuberculosis treatment in sub-Saharan Africa.

However, the overall financial figure underestimates the contributions from third-party organisations to EDCTP projects. Contributions to EDCTP were mainly given via partnerships for individual projects, with several large-scale collaborations (i.e. the EDCTP-Bill & Melinda Gates Foundation joint call for the support of clinical trials, capacity development and networking in HIV/AIDS vaccines). The financial contributions of pharmaceutical companies tend to be underestimated as it is difficult to assign a monetary value to contributions involving the provision of investigational products which are not costed. Nevertheless, EDCTP collaboration with third-party organisations has substantially increased over the years.

Dr François Bompart

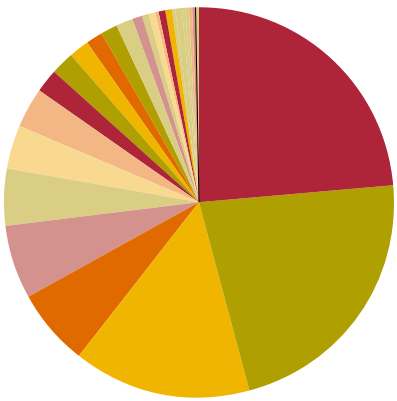
Chairman EFPIA Global Health Initiative; Vice-President, Medical Director and Deputy Head, Access to Medicines, Sanofi, France

As responsible actors in public health, pharmaceutical firms are committed to collaborate with public sector and civil society partners such as EDCTP in the "North" and the "South" to develop the drugs and vaccines that meet the needs of patients, including the most destitute ones. For the industry, specific challenges are posed by diseases which do not offer the prospect of a return on R&D investment. These challenges are best addressed through sustained collaborations between public and private stakeholders. Many examples of successful public-private partnerships set up in the past 10 years attest to the value of this model as an approach to development of new medicines and vaccines for poverty-related and infectious diseases. Success relies upon the combined strengths of the partners, but also on the value of confronting different and sometimes opposed agendas to foster creativity.

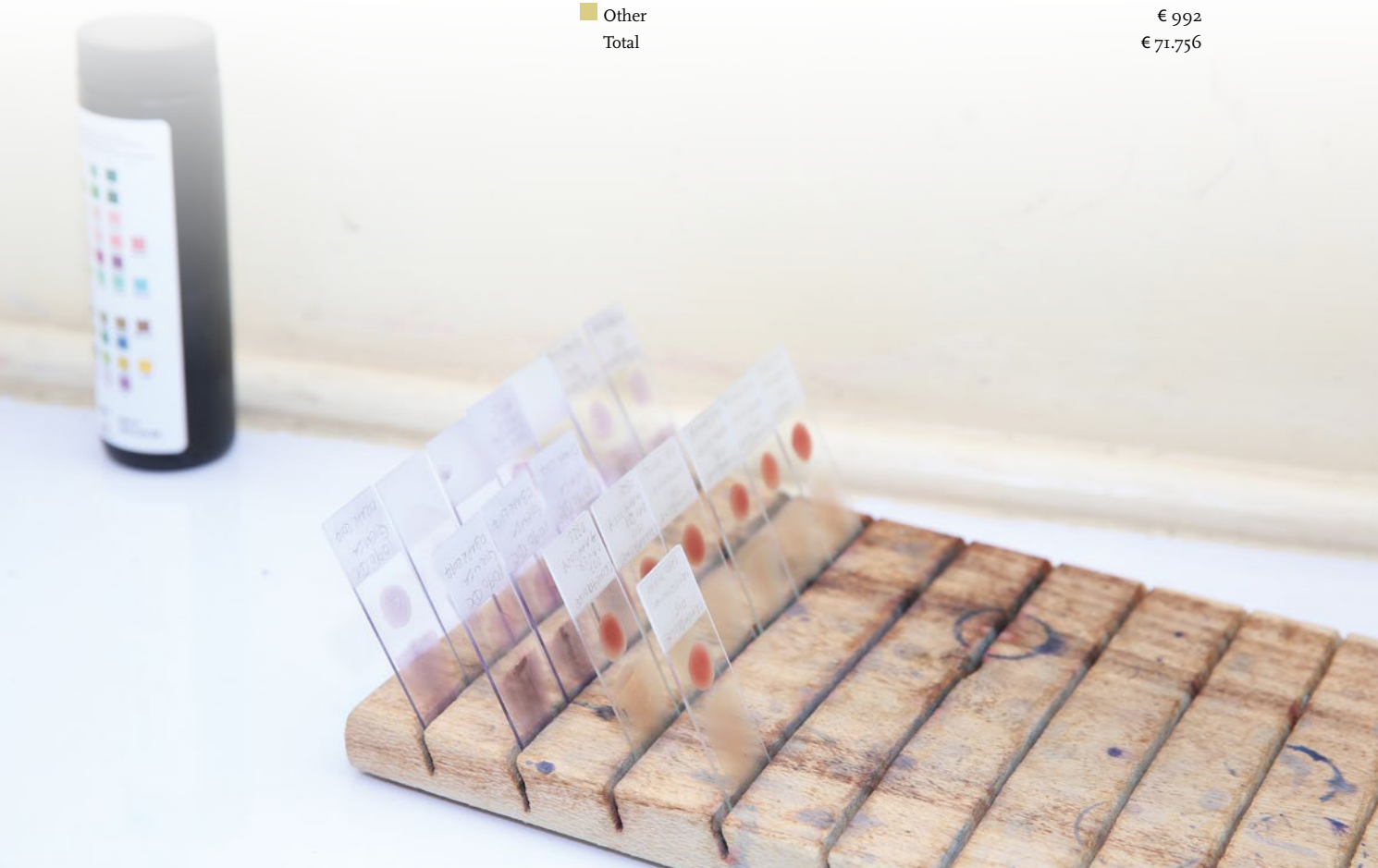
The European Federation of Pharmaceutical Industries and Associations (EFPIA) and EDCTP have worked to strengthen dialogue with the pharmaceutical industry, leading to greater mutual understanding. In 2013, thanks to a discussion forum organized by EDCTP, we set up a joint fellowship programme through which African clinical researchers are offered the possibility of spending 6 to 24 month training periods within pharmaceutical firms to develop specific skills that cannot be gained through academic training or clinical practice in a variety of areas such as biostatistics applied to clinical trials, Good Clinical Practice, pharma-covigilance, regulatory affairs, clinical trials monitoring, auditing, etc. Currently, we are discussing how exchanges between EDCTP and the pharmaceutical industry should be structured under EDCTP2.

Today's investment by EDCTP and its partners in capacity development for poverty-related and infectious diseases will benefit the fight against these diseases but also the research that will be required in years to come to address increasingly important diseases in Africa such as diabetes, cardio-vascular disorders, respiratory diseases and oncology. The involvement of European research-based pharmaceutical companies together with EDCTP and with the stakeholders from African countries is critical to improving access to high-quality healthcare and innovation adapted to the needs of African patients.

Third-party funding to EDCTP grants for all types of contributions 2003-2013 (€ '000)



Global TB Alliance	€ 16.948
Bill & Melinda Gates Foundation	€ 16.030
Aeras Global TB Vaccine Foundation	€ 10.633
Medicines for Malaria Venture (MMV)	€ 4.513
Sequella Incorporated	€ 4.376
European Vaccine Initiative	€ 3.491
Wellcome Trust	€ 2.479
Foundation for Innovative New Diagnostics (FIND)	€ 2.375
International Partnership for Microbicides (IPM)	€ 1.477
World Health Organization	€ 1.330
Bayer AG	€ 1.200
FHI360	€ 1.028
International AIDS Vaccine Initiative (IAVI)	€ 920
Foundation for the National Institutes of Health (FNIH)	€ 641
Sanofi Aventis	€ 375
Sanaria Inc.	€ 369
US National Institutes of Health (for the CHAMPS study)	€ 356
Chiracon GmbH	€ 355
Cipla Ltd.	€ 350
National Institute of Allergy and Infectious Diseases (NIAID)	€ 308
Delft Imaging Systems	€ 300
Vecura Company	€ 200
GlaxoSmithKline	€ 189
Walter Reed Army Institute of Research (WRAIR)	€ 178
International Association of National Public Health Institutes (IANPHI)	€ 178
Heidelberg Pharma GmbH	€ 165
Other	€ 992
Total	€ 71.756



EDCTP Governance

EDCTP General Assembly meeting 7-8 November 2013, The Hague, The Netherlands

General Assembly membership in 2013

Country	Representative	Deputy representative
Austria	Dr Christiane Druml *Vice-Rector for Clinical Affairs* *Medical University of Vienna*	Dr Hemma Bauer *Austrian Federal Ministry of Science and Research*
Belgium	Prof. Bruno Gryseels *Director, Institute for Tropical Medicine*	Ms Margarida Freire MSC *Belgian Science Policy Office*
Denmark	Dr Soren Jepsen succeeded by Mr Mikkel Lyndrup *Statens Serum Institute*	
France	Prof. Patrice Debré *Hôpital Pitié-Salpêtrière*	Dr Bernadette Murgue *INSERM*
Germany	Dr Joachim Klein *Bundesministerium für Bildung und Forschung*	Dr Detlef Böcking *DLR Joint Ventures GmbH*
Greece	Prof. Evangelia Ntzani *University of Ioannina School of Medicine*	Dr Suzanne Kolyva succeeded by Mrs Eleni Stavrianoudaki *General Secretariat for Research & Technology*
Ireland	Dr Teresa Maguire succeeded by Mr Patrick Empey *Irish Aid*	
Italy	Prof. Stefano Vella *Istituto Superiore di Sanità*	Dr Anne-Laure Knellwolf *Istituto Superiore di Sanità*
Luxembourg	Dr Carlo Duprel *Fonds National de la Recherche*	
Netherlands	Ms Marja Esveld MSc (Vice-Chair) *Ministry of Health, Welfare and Sports*	Dr Eva Rijkers *NACCAP-NWO*
Norway	Dr Marit Endresen succeeded by Dr J. Sigurd Røtnes *Norwegian Directorate of Health*	Dr Unni Hirdman Rørslett succeeded by Dr Wenche Dageid *The Research Council of Norway*
Portugal	Dr Paula Elyseu Mesquita *FCT – Foundation for Science and Technology*	Dr Ana Quartin *FCT – Foundation for Science and Technology*
Spain	Dr Rafael De Andrés Medina *Instituto de Salud Carlos III*	Mr Tomas López-Peña Ordoñez *Instituto de Salud Carlos III*
Sweden	Prof. Hannah Akuffo (Chair) *Swedish International Development Agency (Sida)*	Prof. Olle Stendahl *Faculty of Health Sciences, University of Linköping*
Switzerland	Dr Isabella Beretta *State Secretariat for Education,* *Research and Innovation*	
United Kingdom	Dr Mark Palmer (Vice-Chair) *Medical Research Council*	Dr Morven Roberts *Medical Research Council*

African representation at the General Assembly in 2013

The African Union (AU) Commission of Social Affairs
Advocate Bience Gawanas succeeded by Dr Mustapha S. Kaloko
Alternate representative: Dr Olawale Maiyegun, Director for Social Affairs of AU

The East African Community (EAC)
Ambassador Richard Sezibera, Secretary General of EAC
Alternate representative: Dr Stanley Sonoiya, Principal Health Officer of EAC

The Economic Community of Central African States (ECCAS) and the Organisation for the Coordination of the Struggle against Epidemics in Central Africa (OCEAC)
Dr Jean Jacques Moka, Secretary General of OCEAC (left in May 2013)

The African Regional Committee of Health Ministers
Prof. John Gyapong, Pro-Vice-Chancellor (Research Innovation & Development), University of Ghana
Alternate representative: Dr Alasford M. Ngwengwe, School of Natural Sciences, Department of Mathematics and Statistics, Lusaka, Zambia

European Commission representation at the GA

Dr Line Matthiessen-Guyader, Head of Infectious Diseases and Public Health, DG Research & Innovation
Dr Gianpietro van de Goor, Principal Policy Officer for International Cooperation in Health Research, DG Research & Innovation

Observers to the General Assembly

Country / EU	Representative	Alternate representative
Finland	Dr Jarmo Wahlfors *Director, Health Research Unit, Academy of Finland*	Dr Sirpa Nuotio *Senior Science Adviser, Health Research Unit, Academy of Finland*
Latvia	Dr Modra Murovska *Augusta Kirhensteina Microbiology and Virology Institute, Riga Stradins University*	Dr Uldis Berkis *National Contact Person Health, Ministry of Science and Education*
European Commission, DG DEVCO	Dr Walter Seidel *Head of Sector Health Unit B4 EC-DEVCO*	Dr Eric Sattin, *Unit D4 EC-DEVCO* Ms Veronique Lorenzo *Head of Unit B4, EC-DEVCO*

Interim Scientific Advisory Committee in 2013

Prof. Shabbar Jaffar (Chair)	United Kingdom
Dr Abraham Aseffa	Ethiopia
Dr Manica Balasegaram	Switzerland
Dr Philippe Deloron	France
Prof. Alioune Dieye	Senegal
Prof. Alison Elliott	Uganda
Prof. Beate Kampmann	The Gambia
Dr Wilfred Mbacham	Cameroon
Prof. Marie-Louise Newell	United Kingdom
Prof. Gita Ramjee	South Africa
Dr Suzanne Verver	The Netherlands
Dr Dawit Wolday	Ethiopia

EDCTP Secretariat staff in 2013

Prof. Charles Mgone	Executive Director
Abdoulie Barry	Director of Finance and Administration
Dr Michael Makanga	Director of South-South Cooperation and Head of Africa Office
Dr Ole F. Olesen	Director of North-North Cooperation (appointed in September 2013)
Dr Pascoal Mocumbi	High Representative (left in December 2013)
Dr Pauline Beattie	Operations Manager
Dr Gabrielle Breugelmans	North-North Networking Manager
Dr Thomas Nyirenda	South-South Networking and Capacity Development Manager
Hager Bassyouni	Project Officer
Dr Montserrat Blázquez Domingo	Project Officer
Chris Bruinings	Financial Officer
Ana Lúcia Cardoso	North-North Networking Officer
Mary Jane Coloma-Egelink	Grants Financial Assistant
Dr Christy Comeaux	Administrative Assistant (appointed in July 2013)
Lucien de Corte	Information Technology (IT) Officer
Nuraan Fakier	Project Officer
Jean Marie Vianney Habarugira	Project Officer
Charlotte Hoekstra	Administrative Assistant (left in December 2013)
Suzanne Hoogervorst	Travel and Events co-ordinator
Suzanne Ignatia	HR Advisor
Nancy Kensmil	Administrative Officer & HR Assistant
Gert Onne van de Klashorst	Communications Officer
Mariska Louw	Senior Administrative Officer (appointed in July 2013)
Sophie Mathewson	Networking Officer (left in June 2013)
Wendy Morrill	Administrative Officer
Pete Murphy	Project Officer
Michelle Nderu	Project Officer (appointed in October 2013)
Lara Pandya	North-North Networking Officer (appointed in July 2013)
Daniela Pereira-Lengkeek	Assistant Communications & IT Officer
Emma Qi	Grants Financial Assistant
Dr Monique Rijks-Surette	Project Officer
Sayma Siddiqui	Financial Assistant
Dr Michelle Singh	Project Officer (left in July 2013)
Gail Smith	Senior Administrative Officer (left in May 2013)
Rafael Taguas Sánchez	Financial Assistant (left in March 2013)
Dr Lidwien van der Valk	Legal Officer
Jing Zhao	Grants Financial Assistant

Summary financial statements 2013 and Auditor's Report

Statement of comprehensive income for the year ended 31 December 2013

Expressed in thousands ('000) of Euro

	Restricted EC 2013	Restricted Donor 2013	Total 2013	Total 2012
INCOME				
Contributions	14,922	26,690	41,612	34,174
Finance income	147	156	303	631
Total income	15,069	26,846	41,915	34,805
Expenditure				
Grants expenditure	(7,943)	(25,203)	(33,146)	(32,897)
Other expenditure	(6,427)	(364)	(6,791)	(3,656)
Governance expenditure	(152)	(115)	(267)	(302)
Total expenditure	(14,522)	(25,682)	(40,204)	(36,855)
Total comprehensive income for the year	547	1,164	1,711	(2,050)

All income and expenditure relates to continuing activities.

	2013 € 000	2012 € 000
Result attributable to:		
Restricted reserves EC	547	(32)
Restricted reserves Donor	1,164	(2,018)
	1,711	(2,050)

Statement of financial position as at 31 December 2013

Expressed in thousands ('000) of Euro

Assets	31 December 2013	31 December 2012
Non-current assets		
Property Plant & Equipment	–	–
Debtors	–	–
Total non-current assets	–	–
Current assets		
Debtors and other receivables	10 086	16,663
Cash and cash equivalents	18,914	28,919
Total current assets	29,000	45,582
Total assets	29,000	45,582
Equity		
Restricted reserve: EC	308	(239)
Restricted reserve: Donors	3,063	1,899
Total equity	3,371	1,660
Non-current liabilities		
Grant payables	3,819	13,599
Total non-current liabilities	3,819	13,599
Current liabilities		
Grant payables	18,590	29,995
Other payables	3,220	328
Total current liabilities	21,810	30,323
Total equity and liabilities	29,000	45,582

The financial statements were approved by the Executive Secretariat on behalf of the EDCTP-EEIG General Assembly by:

Professor Charles Mgone

Dated 6 May 2014

Statement of Changes in Equity

Expressed in thousands ('000) of Euro

	Restricted reserve: EC	Restricted reserve: Donor	Total
Balance as at 31 December 2012	(239)	1,899	1,660
Total comprehensive income for the year	547	1,164	1,711
Balance as at 31 December 2013	308	3,063	3,371

EDCTP has no unrestricted reserves.

Statement of cash flows for the year ended 31 December 2013

Expressed in thousands ('000) of Euro

	2013	2012
Cash flows from operating activities		
Result for the year	1,711	(2,050)
Adjustment for:		
Finance income	(303)	(631)
Non-cash income	(2,416)	-
(Increase) decrease in debtors and other receivables	6,382	11,967
Increase (decrease) in grant and other payables	(18,693)	(19,544)
Net cash flows from operating activities	(13,319)	(10,258)
Cash flows from investing activities		
Interest received	499	761
Net cash flows from investing activities	499	761
Net increase (decrease) in cash and cash equivalents	(12,820)	(9,497)
Cash and cash equivalents at 1 January	31,734	38,416
Exchange rate effects	-	-
Cash and cash equivalents at 31 December	18,914	28,919

Notes to the summary financial statements

1. Basis of preparation

The summary financial statements, including the 2012 comparative figures, comprising the statement of financial position as at 31 December 2013, the statements of comprehensive income, changes in equity and cash flows for the year then ended, have been extracted from the annual financial statements of EDCTP-EEIG for the year ended 31 December 2013. These financial statements have been prepared in accordance with International Financial Reporting Standards as adopted by the European Union (hereafter EU-IFRS).

2. Accounting policies

The summary financial statements omit the notes comprising the significant accounting policies and other explanatory information as required by EU-IFRS. Therefore, to obtain a full understanding of the financial statements, the summary financial statements should be read in conjunction with the annual financial statements from which the summary financial statements were extracted.

The annual financial statements can be obtained from the EDCTP website (www.edctp.org).

Independent auditor's report

To: The General Assembly of EDCTP-EEIG

The accompanying summary financial statements, which comprise the statement of financial position as at 31 December 2013, the statements of comprehensive income, changes in equity and cash flows for the year then ended, and notes, comprising a summary of the significant accounting policies and other explanatory information, are derived from the audited financial statements of EDCTP-EEIG 2013. We expressed an unqualified audit opinion on those financial statements in our report dated 6 May 2014. Those financial statements, and the summary financial statements, do not reflect the effects of events that occurred subsequent to the date of our report on those financial statements.

The summary financial statements do not contain all the disclosures required by International Financial Reporting Standards as adopted by the European Union. Reading the summary financial statements, therefore, is not a substitute for reading the audited financial statements of EDCTP-EEIG.

Management's responsibility

Management is responsible for the preparation of a summary of the audited financial statements on the basis described in note 1 (Basis of preparation) of the summary financial statements.

Auditor's responsibility

Our responsibility is to express an opinion on the summary financial statements based on our procedures, which were conducted in accordance with Dutch law, including the Dutch Standard on Auditing 810 'Engagements to report on summary financial statements'.

Opinion

In our opinion, the summary financial statements derived from the audited financial statements of EDCTP-EEIG 2013 are consistent, in all material respects, with those financial statements, on the basis described in note 1 (Basis of preparation) of the summary financial statements.

The Hague, 6 June 2014
KPMG Accountants N.V.

C. den Besten RA

Photo acknowledgement

Cover: Dr Sodiomon Sirima and research team at the Regional Hospital of Banfora, Burkina Faso, part of the WANECAM project (led by Prof. Abdoulaye Djimdé)
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Page 7: Beauty and Merel, from the village of Macha in Zambia (2010; photo by EDCTP)
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Page 11: Prof. Glenda Gray, Dr Michael Makanga and Dr Graeme Meintjes at the EDCTP Awards ceremony in Cape Town, South Africa (photo by EDCTP)
Page 12: Dr Matshidiso Moeti, Mr Victor Madeira dos Santos, Prof. Charles Mgone, Prof. Hannah Akuffo, Hon. Prof. Awa Marie Coll-Seck, Hon. Adv. Tshililo Michael Masutha, Hon. Prof. Nkandu Luo and Dr Pascoal Mocumbi at the Second high-level meeting on EDCTP2 (photo by EDCTP)
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Page 21: Laboratory staff at the Charles De Gaulle University Hospital, part of the MONOD project (led by Dr Valériane Leroy)
Page 22: Clinic staff and study volunteer at the Charles De Gaulle University Hospital, in Ouagadougou, Burkina Faso, part of the MONOD project (led by Dr Valériane Leroy)
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