EDCTP

European & Developing Countries Clinical Trials Partnership

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Note from the Executive Director

The countdown towards the EDCTP launch is now in full earnest. The Executive Secretariat of the EDCTP-Association has recently undergone an audit of its preparedness for managing the second phase of the EDCTP programme. It received a clean bill of health certifying it fit for the purpose. A positive outcome was part of the requirements for the European Union and the Association to sign a Delegation Agreement that will entrust the Association with running the programme.
Along with this, the Executive Secretariat has developed the 2014-2015 Annual work plan in consultation with many stakeholders through their contributions at Stakeholder meetings in 2013-2014 and with the input from the interim and the Strategic Advisory Committees. I am glad to inform you that this work plan that details calls for 2014 and tentative calls for 2015 has been peer reviewed by an international panel and approved. The calls are ready to be launched as soon as the Delegation Agreement is signed and the programme officially launched. In the meantime on 31 October, – in a joint venture with WHO TDR – EDCTP launched its first call under the EDCTP2 programme. The call is for Clinical Research and Development Fellowships with a deadline of 30 January 2015.

The official launch of the EDCTP2 programme will take place on 2 December 2014 in Cape Town. This milestone event is jointly organised by the European Commission and EDCTP and will be hosted by the South African Department of Science & Technology. The meeting aims to provide an opportunity to discuss the role and strategic vision of EDCTP2 as well as explore possibilities for synergies with our national and international partners.

Charles S. Mgone

Published

The reports *African Mapping: Current state of health research on poverty-related diseases in sub-Saharan Africa* and the *Proceedings of the EDCTP Stakeholder Meeting on Capacity Development* have been published and are available in English on the website.

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Towards EDCTP2

High-Level Meeting to launch EDCTP2

On 2 December 2014, a high-level event in Cape Town, South Africa, will celebrate the launch of the second programme of EDCTP. Approximately 250 delegates, including African and European government representatives, major research funders, scientists, industry representatives and other experts in the field are expected. The launch meeting is jointly organised by the European Commission and EDCTP, with the South African Department of Science and Technology hosting the event. This milestone meeting will provide an opportunity to discuss the role and strategic vision of the second EDCTP programme as well as explore possibilities for synergy with other national and international players and initiatives.

EDCTP2
With funding of €1.4 billion from the European Union, the Participating States and third parties, EDCTP2 will support all stages of clinical trials, from phase I to IV, on HIV/AIDS, tuberculosis, malaria and neglected infectious diseases. It will also continue to promote collaborative multicentre projects that combine clinical trials; capacity development in sub-Saharan countries; and closer collaboration with industry, like-minded organisations, and funding agencies for research and development cooperation.

Governance
The EDCTP Association, the dedicated implementation structure for the second programme, was established in April 2014. The new legal structure enables European and sub-Saharan countries to become members of the EDCTP Association. The direct and full participation of African countries in the governance and execution of the second programme is a historic step. All Participating States have voting rights in the EDCTP

Towards EDCTP2 (continued from page 1)

General Assembly, the decision-making body of the EDCTP. This reflects EDCTP's commitment to equal partnership built on joint ownership and leadership. Currently, 13 European countries and 11 African countries have already joined the Association in order to participate in EDCTP2.

The 11 African countries that have joined as members of the partnership are: Cameroon, Congo, The Gambia, Ghana, Mozambique, Niger, Senegal, South Africa, Tanzania, Uganda and Zambia. Care will be taken to ensure that the voices of countries that are not directly represented will also be heard. Additionally, the African Union and World Health Organisation African Region, have representatives in the General Assembly with observer status.

Delegation agreement and work plans 2014

After the approval of the second programme and the successful assessment of the EDCTP Secretariat, the final step consists of concluding the delegation agreement between the European Commission and the new EDCTP implementation structure. EDCTP will publish annual work plans as the operational document of the second EDCTP programme. It will include information about activities funded by EDCTP and its participating states, including the calls for proposals. It is anticipated that the EDCTP calls for proposals, included in the work plan for 2014, will address broad topics in clinical research as well as offer various possibilities for capacity development and networking activities.

EDCTP-Plus

Laboratory quality management

EDCTP and Quintiles Laboratories sub-Saharan Africa organised a three-day training workshop on laboratory quality management systems in Pretoria, South Africa, from 8 to 11 September 2014. The training was part of the development of laboratories towards accreditation according to the ISO/IEC 15189 standard, which EDCTP is supporting in consultation with its four Regional Networks of Excellence (NoEs).

The NoEs selected 24 clinical research and public health laboratories actively involved in EDCTP-funded clinical trials in 18 sub-Saharan Africa countries: Burkina Faso, Cameroon, Republic of Congo, Ethiopia, Gabon, The Gambia, Ghana, Kenya, Malawi, Mozambique, Nigeria, Senegal, South Africa, Sudan, Tanzania, Uganda, Zambia and Zimbabwe. Quintiles Laboratories is assisting eight of the 24 laboratories in their progress towards ISO accreditation.
Laboratory and Quality Managers from these eight laboratories attended the workshop. Its objective was to train the managers in designing, drawing up and implementing a laboratory quality management system that is compliant with the ISO/ IEC 15189 standard. The workshop also focused on laboratory quality assurance management. The attendees experienced first-hand the Quintiles CAP 15189 accredited laboratory facility as an essential exercise to enable the attendees work towards systematically improving their own laboratory facilities.
Various department heads within the Quintiles Laboratories Pretoria facility contributed to the training, including the Project Manager, Technical Services Manager, Laboratory Manager and Quality Assurance Manager. The attendees also had an opportunity to give an overview of their laboratory, and share the experiences and challenges they face as they implement a quality management system in their facilities. This training workshop was essential to encourage the exchange of ideas, troubleshoot, and foster networking amongst the laboratories so that they can support and assist each other through the process.

Participants of the workshop on laboratory quality management systems in Pretoria, South Africa

New grant management system

EDCTP implemented a new grants management system 'EDCTPgrants', based on CC Grant Tracker®, a system developed by the company CC Technologies in Glasgow, United Kingdom. The new system went quietly live on 31 October 2014 when EDCTP launched the EDCTP-TDR joint call for applications for the Clinical R&D Fellowships.

The system was implemented with the support of the European Union under the CSA grant (FP7-304786) to prepare for EDCTP2. The system is expected to substantially reduce the administrative complexity of applying for grants, review of proposals as well as reporting by grantees on EDCTP-funded projects.

EDCTP Governance

General Assembly

The General Assembly of EDCTP-EEIG and the EDCTP Association will convene in Cape Town, South Africa on 1 December 2014, the day before the official launch of EDCTP2. The most important topics for the meeting are the adoption of the EDCTP work plan 2014-2015 and deliberation on potential admission of two more African countries, Burkina Faso and Mali, as members of the EDCTP Association.

Scientific Advisory Committee

The Scientific Advisory Committee (SAC) met in The Hague on 2 and 3 October 2014. The committee gave feedback on the individual work plans 2014-2015 of the EDCTP participating states as well as the general EDCTP work plan 2104-2015.

Calls and Grants

First EDCTP-TDR joint call: Clinical R&D Fellowships

On 31 October 2014, EDCTP published the first call under its second programme, a joint call with WHO-TDR. Members of clinical research teams from low- and middle-income countries (LMIC) are invited to apply for the EDCTP-TDR Clinical Research and Development Fellowship scheme. Successful candidates will be placed with leading product development organisations, including pharmaceutical companies and product development partnerships – the 'host organisations' – for a period of up to 24 months. The deadline for applications is 30 January 2015, 16:00 Greenwich Mean Time (GMT). Applications must be submitted online through the EDCTP grants management system accessible at **www.EDCTPgrants.org**.

A total of 25 fellowships are available for this call; 20 product development organisations have offered to host fellows. The host organisations will train individuals to develop specialist product development skills not readily taught in academic or public research institutions.

On returning to their home organisations, the fellows are expected to become an important resource for institutional capacity development to undertake and manage clinical research in accordance with international regulatory requirements and standards.

The EDCTP-TDR partnership includes a joint evaluation and selection process of applications submitted to this call. However, grant awarding and budget management are managed separately by each organisation. Fellows can only be funded once under this grant scheme. Grants awarded are not transferrable from one individual to another. Placements are for a minimum period of 6 months up to a maximum period of 24 months. Fellows must be committed to return to their home organisation for a minimum of two years after completion of the fellowship.

Recently signed grants: Master´s Fellowships

1. **Mr Sungai Tafadzwa Chabata:** 'Estimating the size of hard-to-reach populations – Comparison of three methods of size estimation of sex worker communities in Zimbabwe' (London School of Hygiene & Tropical Medicine (LSHTM), United Kindom) – €119,994.60
2. **Dr Asungushe Bonaventura Kayombo:** 'Access to pre-ART care and treatment, and pre-ART mortality and loss to follow-up among HIV-infected in Kagera' (Kilimanjaro Christian Medical University College (KCMU College, Tanzania) – €40,882
3. **Mr Tumani Nicholas Jackson Kilimba:** 'A validation study of a self-triggered health and demographic surveillance data collection system' (Ifakara Health Institute (IHI), Tanzania) – €49,408.59
4. **Dr Ngozi Moneke-Anyanwoke:** 'The effects of community-based scheduled screening and treatment (CSST) of malaria in pregnancy on infant mortality, malaria parasitaemia and health seeking behaviour' (Medical Research Council, MRC Unit The Gambia) – €119,873.62
5. **Mr Joseph Musaazi:** 'Comparison of tuberculosis (TB) treatment completion in HIV and tuberculosis co-infection patients receiving care from rural and urban health service providers in Uganda' (London School of Hygiene & Tropical Medicine (LSHTM), United Kingdom) – €119,984.70
6. **Ms Patience Nyakato:** 'Sample-based tracing of HIV-positive patients in rural and urban Uganda to estimate linkage to and retention in care before the initiation of antiretroviral therapy' (London School of Hygiene & Tropical Medicine (LSHTM), United Kingdom) – €116,924.50
7. **Dr Phillip O. Owiti:** 'Pre-treatment loss to follow-up in the tuberculosis programme in western Kenya: the burden and determinants' (Moi University College of Health Sciences (MUCHS), Eldoret, Kenya) – €71,748.42
8. **Dr Rovonirina Andry Rakotoarivelo:** 'Study of the prevalence and risk factors associated with Cryptococcus neoformans complex in HIV-infected patients in Antananarivo, Madagascar' (Centre d'infectiologie Charles Merieux (CICM), Madagascar – €72,831

Professor Clara Menéndez, MiPPAD project coordinator

Focus on Projects

Mefloquine not recommended as antimalarial for prevention treatment 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. Finding new antimalarial options for treatment is critical as the malaria parasites are increasingly resistant to sulphadoxine-pyrimethamine (SP), the WHO-recommended treatment for prevention of malaria. Moreover, SP is not recommended in HIV-positive women receiving cotrimoxazole prophylaxis or antiretroviral drugs to avoid any possible increased incidence of adverse drug reactions.

Focus on Research Ethics

Textbook for research ethics committees

The first textbook on research ethics developed by African authors was published in July 2014 and presented at the Seventh EDCTP Forum in Berlin. The aim of the EDCTP-funded project was to develop a resource for African research ethics committees in order to strengthen research ethics review capacity in Africa. The project was developed in response to requests from South African students for research ethics training programmes, but addresses this need in the broader African context.

The publication contains contributions from experienced African researchers and experts. *Research ethics in Africa: a resource for research ethics committees* was edited by Professor Mariana Kruger (Stellenbosch University, South Africa), Dr Paul Ndebele (Director of the Medical Research Council of Zimbabwe) and Dr Lyn Horn (Stellenbosch University, South Africa). Among the wide range of topics discussed in the book are issues crucial to the African as well as general research context, such as vulnerability, especially in research involving vulnerable populations such as children; research and auxiliary care in settings with limited health care services; training in research ethics; evaluation of clinical trials; and tools for use by research ethics committees (e.g. for monitoring research). The book is available in e-format free of charge from the websites of Stellenbosch University, EDCTP, Fogarty International Center (FIC), the South African Research Ethics Initiative (SARETI) and MARC.

EthiCall platform

EthiCall is a collaborative customised web-based platform currently under development by COHRED (Council on Health Research for Development) with coordination of the project supported by EDCTP. It is designed to support a multi-centre ethics review process by research ethics committees (RECs) or institutional review boards (IRBs) worldwide. It will enable researchers to submit a multicentre study to all RECs/IRBs in the respective countries. Involved countries can then conduct a joint review of the study. The system allows discussions of protocols which are under review on the RHInnO Ethics platform, health research ethics review software developed for RECs/IRBs also by COHRED with support from EDCTP.

The overall objective of the EthiCall system is to provide a way for research ethics committees, governments, researchers and medicines regulatory authorities to interact and exchange ideas about ethics reviews. This would contribute to establishing an online community of ethics reviewers and contribute to the collection and dissemination of global information. The online environment allows participants to create ethical review topics and submit questions to the ethical review community.

TRREE: new module on South African research ethics

The Training and Resources in Research Ethics Evaluation (TRREE) programme provides basic online training in ethics and health research regulation. A South African national training module has been developed for the TRREE online platform to provide a resource that contains the essential requirements (i.e. national laws and ethics guidelines) relating to the ethical conduct of research in the South African context.

The South African module was specifically developed for and in partnership with collaborators from African countries. The module was written by Nivedhna Singh of the University of KwaZulu-Natal (UKZN)'s Medical Education Partnership Initiative (MEPI) programme, with expert advice from Dr Ann Strode (UKZN) and Dr Joanna Bourke-Martignoni (University of Neuchâtel, Switzerland). The module provides detailed information on South African research ethics and health guidance as well as legislation.

The TRREE platform was initially sponsored by EDCTP, and has now attracted support from several other international funders, including the European Network of Research Ethics Committees, the Swiss National Science Foundation, the South African National Research Foundation and others. The South African module was sponsored by the Fogarty International Centre of the US National Institutes of Health with a grant to the University of KwaZulu-Natal. The project was led by Prof. U Lalloo.
The module is available free of charge at http://elearning.trree.org/ but (free) registration with TRREE is required. Registration enables free access to all other current and future online TRREE modules.

Mefloquine, a drug for malaria prevention in HIV-negative and HIV-positive pregnant women, was tested in two large randomised controlled trials conducted in Africa. They were part of the EDCTP-funded Malaria in Pregnancy Preventive Alternative Drugs (MiPPAD) study, under the umbrella of the global Malaria in Pregnancy (MiP) Consortium and led by Professor Clara Menéndez (Barcelona Centre for International Health Research, Spain). The results showed that mefloquine could reduce rates of malaria infection and improve maternal health but was not better at preventing low birth weight in new-borns when compared to current WHO-recommended antimalarial regimens. In addition, the drug presented poor tolerability among the trial participants. Based on these findings, the study concluded that MQ cannot be recommended as an alternative to SP in HIV-negative pregnant women nor for malaria prevention during pregnancy in HIV-positive women.

The study was supported by EDCTP, with cofunding from the Institute of Health Carlos III (Spain), the University of Tübingen and German Aerospace Center (Germany); the Institut de Recherche pour le Développement (France); the Austrian Federal Ministry of Science (Austria); and the MiP Consortium, which is funded through a grant from the Bill & Melinda Gates Foundation to the Liverpool School of Tropical Medicine. The trials were conducted in Benin (Allada, Sékou and Attogon), Gabon (Fougamou and Lambaréné), Kenya (Kisumu), Mozambique (Manhiça and Maragra), and in Tanzania (Makole and Chambwino).

Plos Medicine, September 2014, DOI: 10.1371/journal.pmed.1001733 and DOI: 10.1371/journal.pmed.1001735

Focus on Projects (continued from page 4)

TAM-TB: New sputum-independent diagnostic tool for TB in children

An EDCTP-funded project (TB CHILD) has developed a new immunodiagnostic tool that has the potential to improve the diagnosis of TB in children. The sputum-independent T cell activation (TAM-TB) assay is the first immunodiagnostic tool which can detect active tuberculosis disease in children with sensitivity similar to culture and with excellent specificity in a tuberculosis-endemic setting. The TAM-TB assay measures the CD27 phenotype of CD4+ T cells producing IFNg in response to *Mycobacterium tuberculosis*' antigens using a standard intracellular cytokine staining procedure for flow cytometry.

The TAM-TB assay was tested in a proof-of concept study carried out between May 2011 and February 2013 in 290 children that presented symptoms of tuberculosis were recruited and followed-up at the National Institute for Medical Research Medical Research Center in Mbeya and the Ifakara Health Institute in Bagamoyo, Tanzania.

TB CHILD was conducted by research teams headed by Dr Fred Lwilla (Ifakara Health Research and Development Centre, Tanzania) and Dr Klaus Reither (Swiss Tropical and Public Health Institute, Switzerland). The TAM-TB assay was developed by Dr Christof Geldmacher (Ludwig-Maximilians University of Munich, Germany) and jointly evaluated by the Department for Infectious Diseases, Tropical Medicine, University of Munich, Germany; the Swiss Tropical and Public Health Institute, Switzerland; the National Institute for Medical Research – Mbeya Medical Research Center and the Ifakara Health Institute, Tanzania. EDCTP was the main funder of this study which also received funding from Aispo-Nsambya Hospital (Uganda/Italy); Bundesministerium für Bildung und Forschung (BMBF, Germany); FIND (Switzerland); Fondazione Centro San Raffaele del Monte Tabor (Italy); Ministry of Foreign Affairs – Italian Directorate for Development Cooperation (Italy); LMU-Klinikum of the University of Munich (Germany); State Secretariat for Education and Research SER/Swiss National Science Foundation (Switzerland); and the Swiss Agency for Development and Cooperation (SDC, Switzerland).

The Lancet Infectious Diseases, October 2014, DOI:10.1016/S1473-3099(14)70884-9

REMoxTB trial results confirm moxifloxacin safety but not shortened treatment

The results of REMoxTB, a three-arm double-blind phase III global clinical trial of new tuberculosis (TB) drug regimens, were recently published in the *New England Journal of Medicine*. The study showed that replacing one of the drugs in the standard six-month treatment regimen with moxifloxacin did not allow the treatment time for TB patients to be shortened to four months. While the experimental regimens initially killed more TB bacteria than the standard regimen, patients receiving those shortened regimens were more likely to relapse than those taking the standard treatment.

The trial enrolled 1,931 patients at 50 sites in nine countries: China, India, Kenya, Malaysia, Mexico, Tanzania, South Africa, and Zambia. It was led by Prof. Stephen H. Gillespie (St. Andrews University, Scotland) and conducted mainly in Africa (approximately 70% of patients). Prof. Charles Mgone, EDCTP Executive Director commented that although the REMoxTB trial unfortunately did not achieve its main goal, it clearly demonstrates the increased African capacity to undertake trials compliant with regulatory standards.
The study was funded by the Bill & Melinda Gates Foundation, EDCTP, Irish Aid, the Medical Research Council United Kingdom (MRC UK), the United Kingdom Department for International Development (DIFID), and the United States Agency for International Development (USAID). Via EDCTP, contributions were made by the Netherlands-African Partnership for Capacity Development and Clinical Interventions against Poverty-Related Diseases (NACCAP-WOTRO) as well as, again, the Bill & Melinda Gates Foundation and MRC UK. The pharmaceutical companies Bayer Healthcare AG and Sanofi provided the trial drugs and other support. EDCTP has contributed a total of €9.7 million to REMox TB of a total project value of approximately €28 million. The African branch of the REMox TB study is part of the Pan African Consortium for Evaluation of Anti-tuberculosis Antibiotics (PanACEA).

New England Journal of Medicine, October 2014, DOI: 10.1056/NEJMoa1407426

RIFAQUIN TB treatment trial results

Dr Amina Jindani presenting the results of the RIFAQUIN study at the Seventh EDCTP Forum in Berlin

The need for reduction of the TB treatment burden on patients also inspired the RIFAQUIN trial led by Dr Amina Jindani (INTERTB Consortium at St George's, University of London). The study was funded by EDCTP, Medical Research Council (United Kingdom), Sanofi-Aventis (France) and Wellcome Trust (United Kingdom). It assessed whether a combination treatment of six or four months duration that included rifapentine (a rifamycin) and moxifloxacin (a quinolone) could reduce the frequency of taking tablets by patients in a six-month treatment by introducing a weekly treatment, or reducing the length of treatment from six months to four months.

The trial involved seven research centres in Botswana, South Africa, Zambia, Zimbabwe and enrolled 827 patients. Study participants were assessed 12 months after finishing their treatment. It was shown that 95% of patients taking the six-month once-weekly drug combination were cured, which was similar to the standard regimen. Unfortunately, the four-month treatment proved less effective than the six-month treatment.

The new drug combination, therefore, could make treatment adherence easier. Dr Jindani said: "Fewer tablets means there is a higher chance of the patient completing their treatment. It also makes it easier for clinics to supervise treatment." According to the researchers, further consideration is needed regarding the effectiveness of the proposed regimen in HIV-positive patients and its general cost effectiveness.

New England Journal of Medicine, October 2014, DOI: 10.1056/NEJMoa1314210

Meetings

Forum Proceedings and video published

On 17 November, EDCTP published the Proceedings of the Seventh EDCTP Forum, held in Berlin, Germany from 30 June to 2 July 2014. The report gives a detailed overview of the research results presented and the discussions that took place. The report is in English and available for download on the website **www.edctp.org**.

The report was accompanied by a video report with highlights from a lively and successful conference where a new, young generation of African researchers made their mark.

Prof. Charles Mgone's opening address at the Seventh EDCTP Forum

House of Lords event on EDCTP

An event to celebrate UK support to EDCTP was held at the House of Lords in the UK Parliament in London, United Kingdom, on 21 October 2014. The panel event brought together experts and parliamentarians to showcase the role of innovative partnerships in R&D for poverty-related and neglected infectious diseases. It also discussed how the UK supports pioneering approaches to investment in global health R&D. The event provided an opportunity to discuss the benefits of effective partnership between European and sub-Saharan African countries based on EDCTP's achievements. Dr Mark Palmer, Chair of the EDCTP General Assembly, and Prof. Charles Mgone, EDCTP Executive Director, were among the speakers.

EAC Donors' Roundtable meeting in Tanzania

On 17 October 2014, the East African Community (EAC) Secretariat in collaboration with the Africa Union held a one-day Donors' Roundtable meeting at the East African Community Headquarters in Arusha, Tanzania. The meeting aimed at improving access to quality drugs for African citizens and exploring ways of financing the African Medicines Regulatory Harmonization (AMRH) Initiative at a time many countries are struggling to streamline medicine registration processes and systems.

EDCTP was represented at the Round Table Conference by its Executive Director, Prof. Charles Mgone. The meeting was also attended by representatives from the Bill & Melinda Gates Foundation, the UK Department for International Development, the World Bank, the World Health Organization, African Union Commission, the New Partnership for Africa's Development Agency, the Pan African Parliament, Southern African Development Community (SADC), the West African Health Organisation (WAHO) and the Economic Community Of West African States (ECOWAS).

EDCTP webinars with Fit for Health 2.0

In 2015, EDCTP will organise webinars and a workshop on project negotiation, management and implementation in collaboration with Fit for Health 2.0. The webinars aim to improve skills on grant writing and knowledge of Horizon 2020 requirements in general. The webinars will also provide detailed information on the application process for EDCTP's calls for proposals. To complement the webinars, a hands-on workshop will be offered to EDCTP grantees during the Eighth EDCTP Forum in 2016, date and location to be determined.

Fit for Health 2.0 is a European Union-funded project with the objective to promote and strengthen the participation of European industry in Horizon 2020. It offers support to small and medium enterprises and researchers, including EDCTP grantees, during all phases of research projects. For more information about Fit for Health 2.0, please visit **www.fitforhealth.eu**.

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