Focus on Projects (continued from page 4)

MAMS TB trials finish recruitment

At the end of March 2014, the EDCTP-funded PanACEA MAMS TB-01 clinical trial project completed on schedule the recruitment of patients. The multi-arm multistage (MAMS) trial aims to identify treatment combination regimens to be included in a phase III trial to achieve shorter treatment of tuberculosis. The coordinators were pleased that the innovative trial design worked well and congratulated all sites with achieving their complex tasks and goals prior to the target date.

On 28 October 2011, the PanACEA consortium proposed to combine the remaining two trials under HIGHRIF (studies 3 and 4) and the remaining ones under SQ109 (studies 2 and 3) into a multi-arm, multistage study. This 'Multi-arm multistage trial to identify regimens to include in a phase III trial for shorter treatment of tuberculosis', is led by the three PanACEA investigators and sponsored by the Klinikum of the University of Munich, Department of Infectious Diseases and Tropical Medicine in Germany.

In a MAMS trial design several experimental interventions are tested simultaneously against a common control. A number of interim analyses are performed during the study to identify ineffective experimental interventions at an early stage. This trial methodology enables an efficient evaluation of multiple experimental treatment arms within one study in order to eliminate inefficient treatment arms at an early stage.

In this trial, the coordinators decided to combine and streamline their so far independent activities and test the initially proposed combinations using one adaptive MAMS design.

The **PanACEA consortium** originated in an EDCTP stakeholder meeting in Dublin, Ireland on 31 May 2007. The purpose was to discuss the challenges of simplifying TB treatment. The meeting delegates recommended that EDCTP should support a brokered programmatic strategy for conducting clinical trials for new drugs. This resulted in a call for expressions of interest released on 1 August 2007. Following this call, five applicants representing a collaboration of several institutions were invited to participate in a brokering meeting held in The Hague on 4 December 2007. This led to the formation of the PanACEA consortium, which developed a joint proposal to conduct regulatory standard phase IIa, IIb and phase III clinical trials for moxifloxacin, rifamycins and SQ109 using a shared governance, administration and capacity development strategy.

The treatment regimens are the following:

- Control: HRZE [isoniazid (H), rifampicin standard (R), pyrazinamide (Z), ethambutol (E)]
- Arm 1 (R_{35}): $HR_{35}ZE$ (isoniazid, rifampicin 35 mg/kg, pyrazinamide, ethambutol)
- Arm 2 (Q): HRZQ (isoniazid, rifampicin standard, pyrazinamide, SQ109 300 mg)
- Arm 3 ($R_{20}Q$): $HR_{20}ZQ$ (isoniazid, rifampicin 20 mg/kg, pyrazinamide, SQ109 300 mg)
- Arm 4 ($R_{20}M$): $HR_{20}ZM$ (isoniazid, rifampicin 20 mg/kg, pyrazinamide, moxifloxacin 400mg).

PROMISE-PEP and 2LADY at CROI 2014

Among the studies presented at the Conference on Retroviruses and Opportunistic Infections (CROI) in Boston, United States in early March 2014, were two EDCTP-cofunded clinical trials, PROMISE-PEP and 2LADY.

(photo credit: ANRS)

The PROMISE PEP team at the CROI in Boston, United States

The **PROMISE-PEP** study is coordinated by Prof. Philippe Van de Perre (University of Montpellier 1, France). It aimed to evaluate antiretroviral treatment in infants to prevent mother-to-child transmission of HIV. The study concluded follow-up of the infants in May 2013 and the final results were presented at CROI this year.

PROMISE-PEP clinical trial compared two prophylactic treatment regimens to prevent transmission of HIV from mother to child during 12 months of breastfeeding. Infant Lopinavir/Ritonavir (LPV/r) treatment was compared to Lamivudine (3TC) treatment from day 7 until 4 weeks after cessation of breastfeeding (maximum duration of prophylaxis: 50 weeks for a recommended maximum duration of breastfeeding of 49 weeks). These treatments were not evaluated before for such an extended period of 50 weeks.

The transmission rate of the disease from mother to child was reported as 1.4% at 12 months, the lowest rate ever reported during breastfeeding according to the PROMISE-PEP team. Moreover, the survival rate was 96.5 % among infants who remained uninfected for a period of 50 weeks, which is the highest rate ever reported, corroborating the health benefits of ART prophylactic treatment during breastfeeding. There was no significant difference in efficacy and tolerance of the two regimens between the two groups studied. The study supports the use of LPV/r as a good alternative to the 3TC treatment.

The **2LADY** project is coordinated by Prof. Eric Delaporte (University of Montpellier 1, France) and Prof. Sinata Koulla Shiro (University of Yaounde, Cameroon). The study aims to evaluate the two WHO-recommended second-line treatments for HIV infection. The phase III clinical trial was conducted in Burkina Faso, Senegal and Cameroon between November 2009 and October 2013. The project will finish in September 2014. Preliminary results were presented at CROI 2014.

Highly active antiretroviral therapy (ART) has dramatically altered the prognosis of individuals infected with HIV. In low-income countries with a high burden of HIV and AIDS, there has been a concerted

effort to increase access to ART. With this increasing exposure to ART, the risk of resistance and subsequent treatment failure has become a major consideration. Switching patients to alternative second-line regimens will be increasingly necessary. The study also illustrates the importance of early diagnosis of therapeutic failure in diminishing the emergence of resistant viral strains.

This clinical trial compares the efficacy and tolerance of three different second line treatment strategies: two recommended by WHO (Arm A: emtricitabine-tenofovir-lopinavir/ritonavir, Arm B: abacavir-didanosine-lopinavir/ritonavir) and a third combination strategy (Arm C: emtricitabine-tenofovir-darunavir/ritonavir) which had not been evaluated in sub-Saharan Africa.

The drug combinations in the Arms B and C were found to be non-inferior to the combination of antiretroviral drugs in Arm A. No differences between the three study arms as regards median CD4 cell count, severe adverse events and mortality were observed. The use of second-line antiretrovirals with a boosted protease inhibitor showed good efficacy results. The regimens recommended by WHO remain therefore valid options for countries with limited resources.

(Information based on ANRS press release of 7 March 2014.)

Meetings

Networking for EDCTP2

EDCTP participated in the **PDP Funders Group** meeting in Amsterdam on 21 February 2014. The PDP Funders Group is an informal initiative to exchange information on and ideas for collaboration and supporting PDPs. The meeting was attended by representatives of among others the Bill & Melinda Gates Foundation, USAID, Irish AID and the UK Department for International Development. EDCTP was represented by Ana Lucia Cardoso, North-North Networking Officer.

On 4 March, Dr Ole Olesen, EDCTP Director of North-North Cooperation, participated as a moderator in a workshop of the European Parliament (EP) on the role of **operational research** in low and middle income countries. The workshop was organised by the Science and Technology Options Assessment (STOA) unit of the EP. The meeting recognised the "huge gap between what we know from research and what we do with this knowledge" and that operational research could demonstrate how to introduce and scale-up new interventions which would have a major impact on global health. Participants also recognised that very limited funding is available for operational research within health programmes.

Moreover, Dr Olesen held **presentations about EDCTP2** at the World TB Day 2014 event 'Reach the 3 Million' in London, organised by the London School of Hygiene and Tropical Medicine, University College London on 24 March, as well as at the 2014 Global Health Product Development Forum in Seattle on 22-24 April.

ECSA-HC Ministers of Health meeting

The Ministers of Health of the East, Central and Southern African-Health Community (ECSA-HC) convened for a conference in Arusha, Tanzania on 27-28 February 2014. EDCTP was represented by Prof. Charles Mgone, Executive Director, and Dr Michael Makanga, Director of South-South Cooperation and Head of Africa Office. EDCTP was given the opportunity to present to the ministers its strategy for the second programme and efforts to strengthen African active participation in its programme.

WHO AFRO AARCHRD meeting

Dr Michael Makanga participated in the meeting of the African Advisory Committee on Health Research and Development (AACHRD) organised by the WHO Regional Office for Africa in Addis Ababa, Ethiopia on 21-22 March 2014. Dr Makanga presented to the meeting the structure of the second EDCTP programme as well as the opportunities it offers for African governments to commit to the programme and participate fully in its governance and funding.

EDCTP visit to Zambia

EDCTP country visits are focussed on countries where substantial financial investments have been made. This year the first visit was to Zambia from 17-21 March 2014. The EDCTP team consisted of Mr Abdoulie Barry, Director of Finance and Administration, Dr Pauline Beattie, Operations Manager, and Dr Thomas Nyirenda, South-South Networking manager. They focussed on research activities conducted at the Tropical Disease Research Centre Ndola (TDRC) and the University Teaching Hospital Lusaka (UTH). In addition to TDRC and UTH, there are a number of clinical sites for recruitement of study volunteers in Zambia which are part of EDCTP-funded clinical trials.

EDCTP-funded TB laboratory at the Clinical Research Centre of the University Teaching Hospital in Lusaka, Zambia

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The EDCTP Newsletter is available in English, French and Portuguese in electronic format on our website (www.edctp.org). To receive the electronic format, please subscribe online. The next Newsletters will be published in July and October 2014.

EDCTP
European & Developing Countries Clinical Trials Partnership

Vol 9, No 2 EDCTP Newsletter April 2014

Note from the EDCTP Executive Director

As part of the preparations for launching its second programme, EDCTP has changed its legal structure from a European Economic Interest Grouping (EEIG) to an international Association under Dutch law. This will enable Horizon 2020-associated countries as well as sub-Saharan countries to become full members.

This is a major step in cementing our genuine partnership as well as enhancing ownership and commitment of the participating countries from both Europe and Africa. To attain this, a landmark ceremony to incorporate the EDCTP-Association took place at The Hague on 10 April 2014.

At this ceremony, Mark Palmer representing the United Kingdom and Guillaume Fusai representing France signed the incorporation papers that gave birth to the EDCTP-Association as the dedicated implementation structure of the programme.

The other participating states including the African countries that have agreed to join EDCTP, will officially be invited to take their seats at the coming General Assembly of 5-6 May 2014. At the time of incorporation, the new countries that had joined the EDCTP Association as full members included Finland and the Republics of Cameroon, Congo, Ghana, Mozambique, Senegal, South Africa, Tanzania, Uganda and Zambia.

Mr Guillaume Fusai (France, on the left) and Dr Mark Palmer (United Kingdom, on the right) at the signing ceremony of the EDCTP Association in The Hague, the Netherlands

This is indeed a historic event. I, therefore, take this opportunity to welcome all new members to EDCTP.

Charles S. Mgone

Contents

EDCTP Forum

The Seventh EDCTP Forum will be held in Berlin, Germany from 30 June to 2 July 2014. The Forum will be held at the Maritim proArte Hotel and is expected to host approximately 350 participants. The theme of the Forum is 'The Partnership journey: New horizon for better health'. Participation in the Forum will be by invitation only.

The conference will welcome EDCTP stakeholders including representatives of scientific and health care communities, policy makers, regulators, product development partners, research and health funding organisations and foundations, private sector alliances, government representatives and non-governmental organisations. Keynote speakers include Prof. Gita Ramjee (HIV), Prof. Clara Menéndez (malaria), Dr Ann Ginsberg (tuberculosis), Prof. John Gyapong (Neglected Infectious Diseases). The Forum programme will mainly consist of oral presentations by researchers involved in EDCTP-funded projects, for which the abstracts were already peer reviewed. The focus is on advances in research, capacity development, research partnerships and collaborations as well as on agenda-setting for clinical research on HIV/AIDS, tuberculosis and malaria and the interactions of these three main poverty-related diseases with neglected infectious diseases. This Forum will not accommodate poster presentations.

More information on the Forum website: www.edctpforum.org

Towards EDCTP2

EDCTP2 workplan for 2014-2015

The development of effective, safe, accessible and affordable medical interventions for poverty-related and neglected infectious diseases is the primary objective of the EDCTP2 workplan, which is expected to be published in May 2014. The workplan is the operational document of the second EDCTP programme, and will include information about activities funded by EDCTP and its Participating States, including Calls for Proposals.

This first workplan will cover the initial two years of the second EDCTP programme (2014-2015), in order to align with the EC work programmes for Horizon 2020. In subsequent years the workplan will be published annually, covering one-year periods. It is anticipated that the Calls for Proposals for 2014-2015 will include broad topics in clinical research as well as various types of fellowships.

EDCTP activities will fall under three main categories:

- **Integrated Activities**, which will comprise clinical research and capacity development projects selected through open Calls for Proposals that are centrally managed by the EDCTP Secretariat
- **Participating States' Initiated Activities**, which are selected, implemented and funded by EDCTP Participating States, including national Calls for Proposals launched by these countries that fall within the scope of EDCTP, and therefore may be counted as Participating States' contributions to EDCTP2
- **Joint Actions** between one or more third parties, Participating States and EDCTP, including joint Calls for Proposals or funding of a specific joint activity.

European Parliament approves EDCTP2

On 15 April 2014, the European Parliament approved with overwhelming majority the participation of the European Union in the second programme of EDCTP. On 6 May, the Council will vote on the proposal. With a budget of € 683 million from the European Union to be matched by the participating Member States, the programme will support all stages of clinical trials on HIV/AIDS, tuberculosis, malaria and neglected infectious diseases.

Advocacy for wider European participation in EDCTP

EDCTP is actively reaching out to possible European partner countries. EDCTP offers important opportunities for researchers in the newer Member States of the European Union. The programme would enable them to participate in large clinical research consortia, engage with research teams across Europe and sub-Saharan Africa, and network with major pharmaceutical companies, as well as public and private funders.

On 26 March 2014, researchers in the Czech Republic attended an information day on the EDCTP programme in Prague. It was preceded by a meeting with the representatives from the Czech Ministry of Education, Youth and Sports, and the Horizon 2020 National Contact Point. Moreover, EDCTP will present the second EDCTP programme at the 11th Annual Conference of the Baltic Network Against Life-threatening Viral Infections in Vilnius, Lithuania from 24-27 April 2014.

EDCTP Governance

Strategic Advisory Committee

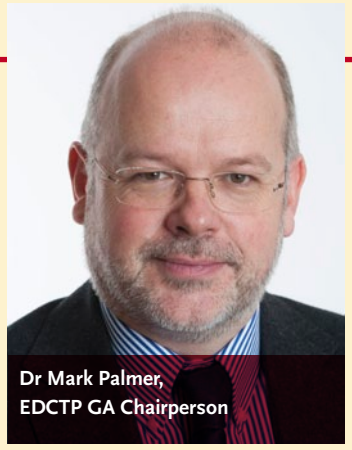
The Strategic Advisory Committee (SAC) met in The Hague from 3 to 4 April 2014. The participants discussed the workplan 2014-2015 in view of the anticipated start of the second EDCTP programme in the second half of 2014 as well as the programme of the Seventh EDCTP Forum. Prof. Tumani Corrah is the new chairperson of the SAC while Prof. Ali Zumla and Dr Eleni Aklilu will serve as vice-Chairs.

Back row, from left to right: Dr Michael Makanga, Prof. Simon Croft, Prof. Moses Bockarie, Dr Salim Abdulla, Prof. Ali Zumla, Prof. Tumani Corrah, Prof. Knut Fylkesnes, Mr Abdoulie Barry, Prof. Stefan Kaufmann, Prof. Philippe Sansonetti, Mr Jean Marie Talon and Dr Maryline Bonnet. Front row, from left to right: Prof. Marie-Louise Newell, Prof. Maria Fraga Oliveira Martins, Prof. Charles Mgone, Prof. Clara Menéndez Santos and Dr Eleni Aklillu

General Assembly

The General Assembly (GA) will convene for its regular meeting on 5-6 May 2014. The GA will discuss among other topics the Annual Report for 2013, the workplan for 2014-2015 and the commencement of the second programme. Most importantly, representatives of several African countries will join the meeting to finalise the procedure for full membership of these countries.

The Chairperson will be Dr Mark Palmer (Medical Research Council, United Kingdom). Dr Stefano Vella (Istituto Superiore di Sanità (ISS), Italy) and Dr Detlef Böcking (Projektträger im Deutschen Zentrum für Luft- und Raumfahrt, Germany) are the new vice-Chairs.



Dr Mark Palmer, EDCTP GA Chairperson

Dr Palmer joined the Research Management Group of the Medical Research Council (MRC) in 1999 and in 2002 became the programme manager responsible for global infections research, managing MRC's Units in the Gambia and Uganda. In 2006, he was appointed Director of International Strategy. He is responsible for MRC's international policy and coordination of global health

EDCTP Plus

Stakeholder Meeting on Capacity Development

A Stakeholder Meeting on Capacity Development will be held in Berlin, Germany on 3 July 2014. The objective of the meeting is to identify current and emerging capacity development gaps in order to inform the development of the strategy and operational plans of the second EDCTP programme. Participants will include researchers from academic and research institutions, representatives of product development partnerships and pharmaceutical industries, policy makers, funding agencies and other like-minded organisations.

Among the topics to be discussed are: EDCTP's integrated approach to capacity development in clinical trials projects; the regional Networks of Excellence; development of African scientific leadership through fellowship programmes; post-registration studies and pharmacovigilance; clinical trial sponsorship; grants management (including project and finance management); and the capacity for bio-banks.

The expected outcomes of the meeting are priority capacity development topics for future calls for proposals, recommendations for improvement of current EDCTP funding schemes, ideas for capacity building initiatives, and proposals for funding partnerships as part of joint activities under the second EDCTP programme.

Attendance is by invitation only, but an open online consultation for views and feedback from all interested members of the research community and other stakeholders has been set up on the EDCTP website (www.edctp.org).

A meeting report including recommendations will be published on the website.

EDCTP publications app available

As part of the advocacy and information efforts to enhance the visibility of the EDCTP programme, EDCTP produced an application (app) for tablets (Android and iOS systems). This app allows quick access to most EDCTP publications regarding its activities and the projects it funds. The app offers a mobile library of EDCTP's digital resources (PDFs): the complete EDCTP Project Portfolio (a technical compendium of all EDCTP funded projects with full search facilities); EDCTP Annual Reports and quarterly newsletters (available in English, French and Portuguese) as well as the reports of most conferences organised by EDCTP. Users receive automatic notification of new publications.

Download the app free of charge (Apple Store or Google Play)

strategy. Moreover, he is chairman of the Governing Council of the International Agency for Research in Cancer and will be the lead for health in Horizon 2020.

As of January 2014, he has taken over from Professor Hannah Akuffo (Swedish International Development Cooperation Agency (Sida), Sweden). Prof. Akuffo was Chairperson since 2010. At the meeting in November 2013, the General Assembly and the Executive Director expressed their gratitude for her dedication to EDCTP and her hard work during the years that the programme came to its full maturity, while EDCTP started preparing for the second programme as well.

Relocation of Europe Office

In preparation for the second programme with an extended Secretariat, EDCTP moved its Europe office to the Borneo building of the Netherlands Organisation for Scientific Research, next to its previous location. The new visiting address is Anna van Saksenlaan 51, 2593 HW Den Haag.
All other contact details remain unchanged.

New staff

Ms Jolanda Doorstam joined EDCTP staff in The Hague as a temporary Grants Financial Assistant. She has a background in business economics. She will handle financial activities regarding grants including budgets and financial reports.


Jolanda Doorstam

Calls and Grants

EDCTP–TDR partnership on fellowship programme

On 27 March 2014, WHO-TDR, the Special Programme for Research and Training in Tropical Diseases, and EDCTP signed an agreement that will harmonise and streamline their Fellowship programmes that offer pharmaceutical industry mentorship experience. TDR will offer around 7-8 positions per year and EDCTP up to 10 positions per year.

Professor John Reeder, Director, WHO – TDR Special Programme for Research and Training in Tropical Diseases, and Professor Charles Mgone, EDCTP Executive Director

EDCTP Executive Director Charles Mgone highlighted the value of this partnership. He said, "I am very happy we bring our resources together in partnership and offer African researchers easier access to these funding opportunities." TDR Director John Reeder said, "This is a win-win for all involved. Scientists get more opportunities and we're being more efficient with the funding provided by our donors."

The partnership should increase opportunities and efficiencies for scientists in a number of ways. Applications will be collected centrally and considered in a wider pool. The process and forms will be the same, and applicant backgrounds will be shared with more pharmaceutical companies. The partnership will conduct the review and selection process together, with the training programmes inter-related. The selection committee will be composed of experts identified by EDCTP and TDR. Administrative processes and budget management will remain separate under the management of each organisation. A joint call for applications will be published soon.

Each programme offers scientists and clinical staff hands-on experience with pharmaceutical companies and product development organisations in clinical product development processes. Participants learn how to improve standards of study design, project management, clinical and safety monitoring and data reporting.

The TDR Career Development Fellowships (CDF) programme, which was developed with the help of the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA), offers targeted training anywhere in the world to enhance competencies in clinical trials for drugs, vaccines and diagnostics on a broad range of infectious diseases of poverty.

EDCTP – with the support of the European Commission's Directorate-General for Research and Innovation – established an arrangement with the European Federation of Pharmaceutical Industries and Associations (EFPIA) to offer similar placements in European-based companies. EDCTP's focus is on clinical trials of new or improved drugs, vaccines, microbicides and diagnostics for HIV/AIDS, tuberculosis, malaria, and neglected infectious diseases.

For more information, contact Ana Lúcia Cardoso, EDCTP North-North Networking Officer (cardoso@edctp.org).

Focus on Projects

New milestone for PACTR: 300th trial registration

The EDCTP-funded Pan African Clinical Trials Registry (PACTR; www.pactr.org) is the first WHO-endorsed primary registry in Africa. PACTR aims to increase clinical trial registration in Africa, with the ultimate goal of contributing to the harmonisation of the regulation, registration and ethical oversight of clinical trials in Africa.

PACTR was initially developed in 2006 as the AIDS, Tuberculosis and Malaria (ATM) registry. It became PACTR in June 2009 with the aim to register all clinical trials conducted in Africa, regardless of the diseases involved. PACTR was recognised as a WHO primary registry in September 2009. Since then, the registry's database has grown exponentially. Of the total applications received, more than 50% were received in 2013-2014. In March 2014, the 300th clinical trial was registered.

Most registered trials (204) are single-centre; research centres/ sites are in 25 countries. The 90 multicentre trials have sites in 26 countries. Two of the multinational studies also have recruitment sites in India and France. A total of 317 principle investigators (PIs) are listed for the 300 trials, of which 9 trials list multiple PIs; 265 PIs are from African countries. Of the 300 trials registered 58 are funded by EDCTP. This makes EDCTP the largest funder of PACTR-registered trials.