EDCTP
European & Developing Countries Clinical Trials Partnership

Vol 10, No 3 EDCTP Newsletter July 2015

Note from the Executive Director

I take this opportunity to congratulate Dr Michael Makanga who after a rigorous search has been appointed the new EDCTP Executive Director.

Michael Makanga will assume his new role with effect from 1 January 2016 when I step down. Michael, who has been with EDCTP since 2004, knows the programme very well and has been associated with its growth and success, particularly in fostering African commitment and co-ownership. He is the right choice to take the programme to new heights.

In the current newsletter we continue to report on the results of the completed projects from the first programme, including those from the Primer Grants that were awarded in preparation for EDCTP2. These are already shedding new light on adolescent sexual and reproductive health as well as on the care of pregnant mothers.

There is also some information on calls for proposals including those that are still open and others that will be launched in the near future.

We also report on our new Board including newly elected members and promotions among our Secretariat members. Congratulations to all who have been elected and re-elected to the Board and to the promoted staff. I also thank the outgoing Board members for their excellent work.

Charles S. Mgone

Contents

Publications

Annual Report 2014 published

The EDCTP Annual Report 2014 "Starting EDCTP2" covers achievements of the programme over the years since its inception in 2003.

By the end of 2014, the programme had released 65 calls for proposals and awarded 254 grants involving researchers from 30 African countries and 16 European countries. The second EDCTP programme was launched on 2 December 2014. The EDCTP Annual Report 2014 is available in interactive format, as well as in PDF in English, French and Portuguese at **www.edctp.org**.

The EDCTP website now has updated information in new sections for Events, Publications, Videos and 'See how we work'.

EDCTP Governance

General Assembly

The General Assembly (GA) of EDCTP-EEIG and the EDCTP Association met on 4-5 June 2015 for its regular meeting. The members approved the financial statements and Annual Report 2014. Further, the GA discussed the work plans for 2015 and 2016, the Eighth EDCTP Forum (2016), and the appointment of a new Executive Director.

Additionally, the members have approved the admittance of the Republic of Gabon as an EDCTP Association Member. Currently, the EDCTP Association consists of 14 European countries and 14 African countries as Participating States.

The GA selected new members for the Board of the EDCTP Association: Dr Mark Palmer (United Kingdom, Chairperson), Dr Detlef Böcking (Germany), Dr Stefano Vella (Italy, vice-Chair), and Prof. Francine Ntoumi (Congo) were re-elected for a second two-year term. Dr Eusébio Macete (Mozambique, vice-Chair) was elected for his first two-year term as an EDCTP Association Board member.

The WHO Regional Office for Africa (WHO/AFRO) has appointed representatives as observers to the GA: Dr Joseph Cabore, Director for Programme Management is the observer representative; and

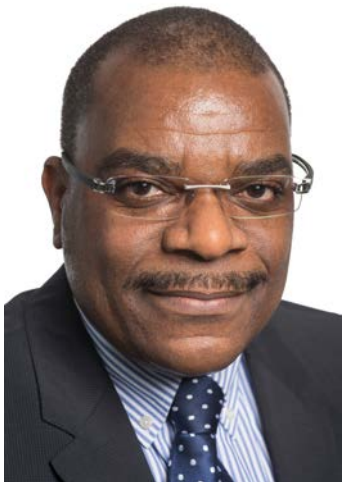
EDCTP Governance (continued)

Front row: Prof. Francine Ntoumi, Dr Mark Palmer and Prof. Charles Mgone.
Back row: Dr Eusébio Macete, Dr Stefano Vella and Dr Detlef Böcking

Dr Delanyo Dovlo, Director of Health Systems and Services, who was present at the GA meeting, as the deputy observer representative.

Dr Michael Makanga next EDCTP Executive Director

The General Assembly also designated Dr Michael Makanga to succeed Professor Charles Mgone as Executive Director. Prof. Mgone, who has been Executive Director for eight years, had decided to step down at the end of 2015 in order to pursue other interests. Dr Makanga will take up his role from 1 January 2016.



Dr Michael Makanga is a clinician-scientist born and raised in Uganda with (after medical qualification) 24 years of professional experience of working on health and poverty related diseases in sub-Saharan Africa. This includes 20 years of work experience on medical product development and clinical regulatory activities. He holds a Medical Degree from Makerere University, Uganda, and has been in various clinical and research positions before and after undertaking an MSc at the University of Liverpool, and then a PhD at the Liverpool School of Tropical Medicine, United Kingdom.

Dr Makanga joined EDCTP in 2004, where he held various management positions. In 2008, he was appointed as Director of South-South Cooperation and Head of EDCTP Africa Office in Cape Town, South Africa.

Carlos Moedas, European Commissioner for Research, Science and Innovation, commented: "EDCTP is a flagship initiative under Horizon 2020 whose ambitious goals require commitment and leadership. Michael Makanga's invaluable experience will help EDCTP deliver and succeed on its objectives".

Financial management

In the last two years, the EDCTP finance team has invested much effort implementing the Secretariat's Administrative and Operational Improvement Plan following an internal assessment in April 2013. This included putting in place the necessary systems and controls for the financial management of the EDCTP2 programme. This resulted in a very positive outcome of the ex-ante assessment, a pre-condition of the Delegation Agreement, carried out in August 2014 by Moore Stephens PLC on behalf of the European Commission. The EDCTP achieved satisfactory rating with no major findings in all the pillars assessed.

To address financial management challenges at the level of EDCTP beneficiaries, EDCTP is participating in the International Financial Governance Consortium (IFGC). This consortium aims to develop an integrated approach to address some of the financial management challenges faced by funders of research in sub-Saharan Africa. Partners in this initiative include the UK Medical Research Council and the Wellcome Trust. Various meetings to identify common ground were attended by EDCTP partners such as the Swedish International Development Agency (Sida), the Irish Department of Foreign Affairs and Trade (Irish Aid), the Danish Building Stronger Universities in Developing Countries (BSU), the Swiss Tropical and Public Health Institute (Swiss TPH), the Foundation Mérieux, and the Royal Society.

The meetings have resulted in initiatives by some of the partners comprising: exchange of inherent risk information, financial monitoring templates, policy documents, costing information and due diligence check lists; performance of joint internal audits; and joint financial management training. Discussions are currently in progress to develop a standardised Financial Management Assessment Tool (FMAT) for assessing the financial management capacity of beneficiaries. The ultimate

EDCTP Governance (continued)

objective is to develop an internationally recognised standard of what constitutes Good Financial Grant Practice (GFGP) that will be of mutual benefit to all partners involved.

EDCTP staff

Mr Christopher Dixon (ACCA accountant) who previously worked for the National Health Service in the United Kingdom, joined EDCTP as Financial Assistant in June.

Mr Christopher Dixon

Several EDCTP staff were appointed to new positions as of 1 July 2015: Dr Montserrat Blazquez-Domingo and Dr Monique Surette-Rijks to Senior Project Officer; Mrs Mary Jane Coloma Egelink to Grants Finance Officer Tuberculosis; Mrs Jing Zhao to Grants Finance Officer Malaria and Neglected Infectious Diseases (NIDs); Ms Daniela Pereira to Communications Officer; and Mrs Suzanne Hoogervorst to Travel & Events Officer.

From 8-11 June 2015, EDCTP organised staff training. The EDCTP staff attended workshops on Results-Based Management (RBM) and key performance indicators for EDCTP2; EDCTP systems such as 'EDCTPgrants', the platform to manage EDCTP-funded grants; and the Model Grant Agreement for grants funded under Horizon 2020 (a presentation from representatives of the European Commission). On Pampus island (Netherlands) staff attended a workshop on intercultural communication and cooperation and participated in team building activities.

Sitting: Dr Ole F. Olesen, Dr Gabrielle Breugelmans, Dr Michael Makanga, Dr Pauline Beattie and Chris Bruinings. Standing: Michele Nderu, Dr Monique Rijks-Surette, Daniela Pereira, Sayma Siddiqui, Lara Pandya, Christopher Dixon, Dr Montserrat Blázquez-Domingo, Dr Thomas Nyirenda, Nancy Kensmil, Mariska Louw, Hager Bassyouni, Suzanne Hoogervorst, Dr Perry Mohammed, Jennifer Stamatelos, Ana Lúcia Cardoso, Mary Jane Coloma-Egelink, Jean Marie Vianney Habarugira, Jing Zhao, Abdoulie Barry, Gert Onne van de Klashorst and Nuraan Fakier

Calls & Grants

Open calls for proposals

The following calls for proposals are open to applications. Their deadline was extended pending approval of the EDCTP 2015 Work plan by the European Commission. The name of the call for 'Strategic projects with major cofunding' changed to 'Strategic actions supporting large-scale clinical trials'.

- Strategic actions supporting large-scale clinical trials (two-stage procedure)
- Improved treatment and clinical management of poverty-related diseases (two-stage procedure)
- Research and capacity development in support of the EVD response (single-stage procedure); deadline for applications is 6 August 2015

Upcoming calls for proposals

Ethics and Regulatory capacities

Type of action: Coordination & Support Actions (CSAs)
Open for applications: 15 October 2015* (17:00 CET)
Closing date: 28 January 2016 (17:00 CET)
Expected number of grants: 5-10

The purpose of this Call for Proposals is to support sub-Saharan African countries to establish and develop robust national medicines regulatory systems and capacities for ethical review of clinical research and use of medicinal products and technologies for use in humans. This scheme targets both National Ethics Committees (NECs) and National Regulatory Authorities (NRAs).

EDCTP-TDR Clinical Research and Development Fellowships

Type of action: Training & Mobility Actions (TMAs)
Open for applications: 15 October 2015* (17:00 CET)
Closing date: 28 January 2016 (17:00 CET)

The purpose of this Joint Call for Proposals is to support researchers and key members of clinical trial research teams from Low and Middle Income Countries (LMICs) to acquire specific skills in clinical research and development through placements in pharmaceutical companies, product development partnerships (PDPs) and research institutions.

* Date pending the approval of the 2015 EDCTP2 Workplan by the European Commission.

For more information about calls for proposals, please visit www.edctp.org

Focus on Projects

Malaria in Pregnancy Consortium: research results

The Malaria in Pregnancy (MiP) consortium had its sixth and final annual meeting in Sitges, Spain on 24-26 June 2015. The objectives of the meeting were to share the latest MiP consortium's research results from the clinical trials and cross-cutting activities. Participants also reviewed the data from the projects that have been presented to the WHO Evidence Review Group in July 2015.

EDCTP funded three projects under the umbrella of the MiP consortium focusing on finding new drugs to treat and/or prevent malaria infection in pregnancy. These trials together recruited more than 15,000 African women. They were followed through pregnancy and the outcomes regarding the children that were born were studied. The trials have provided an extensive resource on malaria in pregnancy. The individual studies are summarised below.

1 – PREGACT
The PREGACT trial, led by Professor Umberto D'Alessandro (MRC The Gambia Unit), recruited 3,428 pregnant women with confirmed malaria infection in four countries (Burkina Faso, Ghana, Malawi and Zambia) in order to test the safety and efficacy of antiretroviral treatments (ACTs) (dihydroartemisinin-piperaquine, mefloquine-artesunate, amodiaquine-artesunate and artemether-lumefantrine) when administered to pregnant women with *P. falciparum* infection during the second and the third trimester.

Initial findings will be published in 2015. The results will feed directly into the WHO malaria treatment guidelines, in particular, regarding the performance of dihydroartemisinin-piperaquine, for which no recommendation was made earlier due to lack of data. Follow-up of the children born to the pregnant women in the trial is ongoing, as is the laboratory analysis of the data on pharmacokinetics and placental infection.

2 – Mefloquine for IPTp?
Given the rising resistance to sulphadoxine/pyrimethamine (SP), a consortium led by Professor Clara Menéndez (Hospital Clinic of Barcelona, Spain) conducted two trials to look at the potential for using mefloquine (MQ) as an alternative to SP.

The first trial compared the safety, tolerability and efficacy of MQ to SP as intermittent preventive treatment in pregnancy (IPTp) for mothers (HIV-uninfected women) and their infants. The trial recruited 4,749 pregnant women in Benin, Gabon, Mozambique, and Tanzania and compared two-dose MQ or SP for IPTp and MQ tolerability of two different regimens.


Training session in Lambaréné, Gabon (MiP project led by Prof. Clara Menéndez)

The results indicated that there was no difference in low birth weight prevalence (primary study outcome), as well as no differences in the prevalence of placental infection and adverse pregnancy outcomes between groups. Women receiving MQ had reduced risk of parasitaemia and anaemia at delivery and reduced incidence of clinical malaria. Despite these positive results, tolerability was poorer in the two MQ groups compared to SP. The most frequently reported related adverse events were dizziness and vomiting, with similar proportions in the full and split MQ arms. These findings do not support the use of MQ instead of SP for IPTp.

A second trial evaluated the safety and efficacy of MQ as IPTp for malaria in HIV-infected pregnant women receiving cotrimoxazole prophylaxis (CTXp) and long-lasting insecticide treated nets (LLITNs). A total of 1,071 HIV-infected women from Kenya, Mozambique, and Tanzania were randomised to receive either three doses of IPTp-MQ (15 mg/kg) or placebo given at least one month apart; all women received cotrimoxazole preventive therapy and a bed net. The IPTp-MQ arm was associated with reduced rates of maternal parasitaemia, placental malaria, and reduced incidence of non-obstetric hospital admissions. There were no differences in the prevalence of adverse pregnancy outcomes between groups.

Despite these positive findings, drug tolerability was poorer in the MQ group (dizziness and vomiting). Unexpectedly, HIV viral load at delivery was higher in the MQ group compared to the control group ($p = 0.048$) and the frequency of perinatal mother-to-child transmission of HIV was increased in women who received MQ. The trial results, which were published in 2014, confirmed that MQ was not well tolerated which limits its potential for IPTp.

A commentary on these results by the editor of PLOS Medicine *highlighted the need for increased attention on malaria in pregnant women and their children and called for a re-examination of strategies to prevent malaria in pregnancy, citing the potential utility of the intermittent screening and treatment approach which was the subject of two EDCTP-funded trials.*

3 - IPTp-SP and resistance
Current WHO policy recommends intermittent preventive treatment with sulphadoxine-pyrimethamine (IPTp-SP) in pregnancy. However, this policy is at risk due to increasing parasite resistance to SP. These problems prompted the IPT-SP study, coordinated by Professor Feiko ter Kuile (Liverpool School of Tropical Medicine, UK). The study investigates the declining IPTp effectiveness and studies alternative approaches to IPTp-SP.

The ISTp-A trial recruited 5,354 pregnant women across Burkina Faso, Ghana, Mali and The Gambia. Women were randomised to receive either IPTp-SP (which is the current policy) or scheduled intermittent screening and treatment in pregnancy (ISTp). The trial demonstrated that despite growing concerns about the impact of SP resistance in East and

Continues on page 5

Focus on Projects (continued)

Southern Africa, SP remains effective at clearing existing infections and improving haemoglobin concentration when provided as IPTp to asymptomatic pregnant women in Mali and Burkina-Faso. Results on impact on the birth parameters will soon be published.

The ISTp-B trial conducted in Malawi comparing ISTp with IPTp-SP showed that the effectiveness of IPTp is compromised in areas where the PfDHPS A581G mutation is present in the parasite populations. The results of this trial and the data on the relationship between SP resistance and SP-IPTp effectiveness were presented at the WHO Evidence Review Group on Malaria in Pregnancy.

Strategic Primer Grants: completed projects

The Strategic Primer Grants call for proposals was published on 12 December 2011. The purpose of the call was to provide funding to research groups in sub-Saharan Africa and Europe to conduct innovative studies that will generate results to inform future clinical trials. It also aimed to sustain and strengthen the capacity built under the first EDCTP programme as well as further the networking of research programmes in African and European countries. Fourteen projects received funding and three of these have recently been completed.

1 - Improving the reproductive health of adolescent girls in sub-Saharan Africa

Prevalence and incidence of HIV infection and other sexually transmitted infections (STI) are particularly high among adolescent girls in Southern and Eastern Africa. The mechanisms underlying this high vulnerability are poorly understood. However, there is some evidence suggesting that male-to-female transmission of HIV is more efficient in sub-Saharan Africa than in high-income countries. The project, led by Anne Buvé (Institute of Tropical Medicine, Belgium) aimed to assess the acceptability of studies on reproductive health in adolescent girls and to characterise their vaginal microbiome in Mwanza, Tanzania.

A total of 401 girls of 17-18 years old and attending school were recruited for a cross-sectional study; they were interviewed and tested for reproductive tract infections (RTIs). Self-administered vaginal swabs were used to test for RTIs and to assess the vaginal microbiome with qRT PCR. Of the enrolled girls, 43% reported that they had sex. HPV infection was the most common sexually transmitted infection (33%). The prevalence of bacterial vaginosis was 32% among sexually experienced girls and 19% among sexually naïve girls. Preliminary analyses showed large differences in the composition of the vaginal microbiome between sexually experienced and sexually naïve girls.

2 - Factors affecting HIV susceptibility in the adolescent genital mucosa

A project led by Dr Jo-Ann Passmore (University of Cape Town, South Africa) studied whether sexually transmitted infections (STIs) and microbiome fluctuations during puberty drive activation, inflammation and recruitment of HIV susceptible target cells to the genital tract. The project enrolled 297 adolescent females and 150 adolescent males (aged 16-22 year) from 3 clinical trial sites in South Africa to conduct mucosal sampling to investigate the influence of age on state of T cell activation and the type of inflammatory markers in the adolescent genital tracts.

The project showed that asymptomatic STIs and bacterial vaginosis are highly prevalent in young South African women and that there is an urgent need to complement the current national syndromic management guidelines. Levels of inflammation were higher in women from Cape Town than in women from Johannesburg, which was associated with significant shifts in the vaginal microbiome and HIV target cell activation.

In young males at the time of medical male circumcision (MMC), 16% had an asymptomatic STI at the time of surgery. The study found increased numbers of CD4+ T cells and Langerhans' Cells in foreskin tissue, both potential HIV target cells. It was concluded that MMC protects through removal of target cells that infiltrate this epithelial tissue. Asymptomatic STIs may increase HIV risk in uncircumcised men by increasing influx of HIV target cells. Significantly increased expression of the CCL27 gene in the outer foreskin in males with an asymptomatic STI was found, which has been associated with homing of memory T lymphocytes to the skin. This suggests that inflammatory conditions in the foreskin prior to MMC result in the migration of potential HIV target cells.

3 - Acceptability of vaginal rings for protection from HIV and unintended pregnancy

Vaginal rings are polymeric drug delivery devices designed to provide controlled release of drugs for intravaginal administration over extended periods of time. Compared to systemic dosing, the sustained local release of drug maximizes efficacy at lower doses, which reduces side effects. In recent years, vaginal rings have become popular for contraception and estrogen replacement therapy. However, contraceptive vaginal rings are not yet on the market in any African country, and acceptability of such rings has not yet been studied.

The project led by Tania Crucitti (Institute of Tropical Medicine, Belgium) aimed to study the acceptability of vaginal rings for women in Africa and to assess the effect of the ring on the vaginal microbiome. This open-label, single-centre, randomised, controlled clinical trial was conducted at Rinda Ubuzima (Kigali, Rwanda) among two groups of study participants. One group used a contraceptive vaginal ring (CVR) for three weeks followed by one week off. The other group used a CVR for three weeks and inserted a new CVR without break. Of the 174 women who were invited for enrolment, 126 attended the visit and 120 were enrolled on 27 December 2013. The last follow-up visit took place on 19 March 2014.

The study showed that women liked the ring because it had limited side effects and that it was used independently of the regimen. It increased appetite for food, lubrication, sexual desire and increased discussion about sex because men wanted to discuss the ring. There were no serious adverse events; a low incidence of self-reported or clinician-observed adverse events were reported. Characterisation of the vaginal flora and biofilm assessment is still ongoing.

Focus on Projects (continued)

Setting a TRAP for the malaria parasite

The Malaria Vectored Vaccines Consortium (MVVC) is a five-year project set up with the aim of integrating capacity-building and networking in the design and conduct of phase I and II clinical trials in East and West African adults, children, and infants. The overall objective of the project is to develop a safe, effective and affordable malaria vaccine for use by the malaria endemic populations of the world.

The participants at the final meeting of the MVVC consortium in Oxford, United Kingdom on 4-5 March 2015

One MVVC-funded study (published by Ogwang et al. in *Science Translational Medicine*) demonstrated that 67% protective efficacy against infection with *Plasmodium falciparum* can be achieved with a promising T cell-inducing vaccination strategy among adults living in a malaria-endemic area in Kenya.

The heterologous prime-boost immunisation regimen developed at the Jenner Institute, United Kingdom uses the recombinant chimpanzee adenovirus 63 (ChAd63) and the modified vaccinia Ankara (MVA), both encoding the malaria antigen ME-TRAP (multiple epitope string and thrombospondin-related adhesion protein). The vaccine stimulates the body's immune system to produce T cells to protect it from malaria.

The phase II clinical trial was conducted at the Kenya Medical Research Institute (KEMRI) field site located in Junju, Kilifi County, Kenya. Healthy adult male volunteers were randomly allocated to vaccination with either the T cell–inducing vaccine candidates or a control vaccine. Antimalarials were given to clear parasitaemia and frequent blood tests were done to identify new infections with the malaria parasite *P. falciparum*. Encouragingly, the authors found that the volunteers receiving the T cell-inducing vaccine had a 67% reduction in the risk of malaria infection during 8 weeks of follow-up.

MVVC is funded by EDCTP which granted funding to a total of €6,500,000. Further co-funding is provided by EDCTP member states (Austrian Federal Ministry of Science, Research and Economy; Irish Aid; Medical Research Council UK; and the Swedish International Development Cooperation Agency) as well as project partners. The total budget is €9,500,000.

Meetings

Dr Pauline Beattie and Jean Marie Habarugira with Dr Graeme Meintjes in Khayelitsha

BIO2015
EDCTP was represented at the BIO2015 international meeting in Philadelphia, United States of America from 16 to 18 June 2015. The EDCTP team consisted of Dr Michael Makanga (Director of South-South Cooperation and Head of Africa Office), Dr Gabrielle Breugelmans (North-North Networking Manager) and Gert Onne van de Klashorst (Communications Officer). The main objective was to network and inform potential partners from the biotech and pharmaceutical industry. The European Commission gracefully hosted EDCTP in its stand in the exhibition hall of the conference.

EDCTP country visit to South Africa
From 29 June to 3 July 2015 an EDCTP team visited EDCTP-funded projects at Stellenbosch University and University of Cape Town in South Africa. The team consisted of Mr Abdoulie Barry (Director of Finance and Administration), Dr Pauline Beattie (Operations Manager), Dr Thomas Nyirenda (South-South Networking and Capacity Development Manager) as well as Mr Jean Marie Vianney Habarugira and Ms Michelle Nderu (Project Officers).These country visits are a regular part of EDCTP's monitoring and evaluation of its projects in sub-Saharan Africa. The visits also serve our networking and advocacy strategies.

The EDCTP team conducted technical and financial assessments for selected projects at Stellenbosch University, Task Allied Sciences, Groote Schuur Hospital, the Institute of Infectious Diseases and Molecular Medicine and the Lung Institute. In addition the team visited the clinical trial site at the Khayelitsha Site B Township clinic established by researchers from University of Cape Town.

The selected projects included amongst others: the Network of excellence TESA; the PanACEA consortium for TB-treatment clinical trials; the TB-NEAT study which evaluates novel and emerging technologies for TB diagnosis; the XACT project, which studies the utility of intensified case finding combined with novel TB diagnostics performed at community-based clinics; and the TB-IRIS project, a phase 2b randomised double-blind placebo-controlled trial of prednisone for patients with HIV-associated TB starting early antiretroviral therapy.

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