EDCTP

European & Developing Countries Clinical Trials Partnership

PROJECT PORTFOLIO

A COMPENDIUM OF CLINICAL TRIAL, CAPACITY BUILDING AND NETWORKING PROJECTS

LAST UPDATE: JUNE 2014

1 Introduction

The EDCTP Portfolio presents a synopsis of clinical trial, capacity building and networking projects funded by EDCTP since its inception in September 2003.

The Portfolio begins with a summary of projects according to disease (HIV/AIDS, tuberculosis and malaria). For each disease, a summary of funded projects is given, which includes an introduction and a summary table of funded clinical trials for that disease-area.

This is followed by EDCTP fellowships, MSc and PhD scholarships, Ethics, Regulatory, Networks of Excellence, other networking grants, Joint Programme Activities (Member States Initiated Projects and Joint Calls by Member States) and the Pan African Clinical Trial Registry.

Each entry includes a project synopsis which reports on the status, results, outputs and achievements.

The EDCTP Project Portfolio is a 'living' document which is updated regularly as new developments, facts and figures emerge from the projects.

2 HIV/AIDS

The EDCTP portfolio of funded projects on HIV/AIDS covers drugs, vaccines and microbicides as well as capacity building projects that do not involve testing of investigational products.

Table 2-1: HIV/AIDS clinical trials

Click on underlined text to link to project profiles and additional information contained in the clinical trial registry.

Grantee Grant Code Acronym	Disease area	Phase	Clinical Trial Registration Numbers	Product(s)	Manufacturer/ Developer	Study population	Status
BAKARI CT.2006.33111.007 TaMoVac- Phase I	HIV VACCINES	I	NCT01407497	Plasmid DNA (HIV-1 Env, Rev, Gag, Rtmut, Gag, Pol, Gp150, rpg 140) + MVA-CMDR + GLA-AF	Vecura at KI, Sweden (DNA); WRAIR of USA (MVA-CMDR)	ADULTS (HIV-, 18-25 years); N=25	Completed
BAKARI CT.2006.33111.007 TaMoVac -HIVIS 03	HIV VACCINES	I/II	PACTR2009040001075080 & ISRCTN90053831	Plasmid DNA (HIV-1 env subtype A, B and C, gag subtype A and B, RTmut and rev subtype B) + MVA-CMDR	Vecura	ADULTS (HIV-, 18-40 years); N= 60	Ongoing
BAKARI CT.2006.33111.007 TaMoVac-01	HIV VACCINES	I/II	PACTR2010050002122368	Plasmid DNA (HIV-1 Env, Rev, Gag, Rtmut, Gag, Pol, Gp150, rpg 140) + MVA-CMDR + GLA-AF	Vecura and Imperial College	ADULTS (HIV-, 18-40 years); N=40	Ongoing
CHINTU CT.2004.33011.001 CHAPAS-1	HIV TREATMENT	II	ISRCTN31084535	Pedimune (Triomune Baby/Junior) tablets: stavudine (d4T), lamivudine (3TC) and nevirapine (NVP) in paediatric co-formulated fixed-dose combinations	Cipla Pharmaceuticals	CHILDREN with HIV-1 (3 months - 14 years); N=211	Completed
CRUCITTI SP.2011.41304.043 The Ring Plus Project	HIV/AIDS MICROBICIDES	II	NCT01796613	Nuvaring®: etonogestrel/ethinylestradiol	N.V. Organon (Merck)	WOMEN (HIV-, 18 years - 35 years); N=120	Ongoing
DELAPORTE IP.2007.33011.004 2LADY	HIV TREATMENT	III	NCT00928187	Emtricitabine-tenofovir; lopinavir/ritonavir; Abacavir-didanosine-lopinavir/ritonavir; Emtricitabine-tenofovir-darunavir/ritonavir	Gilead Sciences, Janssen Pharmaceutica N.V., Matrix laboratory Ltd	ADULTS (≥18 years), HIV+ with virological failure; N=450	Ongoing

EGWAGA IP.2009.33011.003 REMSTART	HIV TREATMENT	III	PACTR201112000327297 & ISRCTN20410413	Early commencement of standard ART treatment available through National Programs	Standard treatment available through National Programs	ADULTS (≥18 years), HIV+ eligible for ART; N=2,300	Ongoing
EKOUEVI TA.2004.40200.003 TemAA	HIV TREATMENT	II	NCT00334256	Tenofovir (TDF), Emtricitabine (FTC)	Gilead Sciences	PREGNANT WOMEN (HIV+, ≥18 years, 28-38 weeks gestation); N=72	Completed
FILTEAU IP.2009.33011.004 NUSTART	HIV TREATMENT	III	PACTR201106000300631	Vitamin and mineral preparations and lipid-based nutrient supplement (LNS); Ready-to-Use Therapeutic Foods (RUTF)	Nutriset, France	ADULTS (HIV+, ≥18 years); N=2,300	Ongoing
FOMSGAARD MS.2009.10800.001 AFO-18	HIV VACCINES	I	NCT01141205 & PACTR201110000274327	AFO-18 (18 peptides representing CD8 and CD4 epitopes mainly on HIV-1 in an adjuvant (CAF01))		ADULTS (HIV-1+, 18-50 years); N=40	Completed
HANKE CT.2006.33111.002 PedVacc - PV001	HIV VACCINES	I	NCT00982579 & ATMR2008120000904116	MVA-HIVA (HIV-1 Clade A Gag + CD8+ T cell polyepitope)	IDT, Germany; University of Oxford, UK	INFANTS (HIV-, 20 weeks); Healthy infants born to HIV 1/2 uninfected mothers; N=48	Completed
HANKE CT.2006.33111.002 PedVacc – PV002	HIV VACCINES	I/II	NCT00981695 & PACTR20090100011152787	MVA-HIVA (HIV-1 Clade A Gag + CD8+ T cell polyepitope)	IDT, Germany; University of Oxford, UK	INFANTS (HIV-, 20 weeks); Healthy infants born to HIV-1-positive mothers; N= 72	Completed
HANKE SP.2011.41304.002 HIV-CORE004	HIV VACCINES	I/II	pending	pSG2.HIVconsv, MVA.HIVconsv, ChAdV63,HIVconsv	MRC UK	ADULTS (HIV 1/2-, 18-50 years); N=84	Not registered yet
HOELSCHER MS.2010.10800.001 FATI	HIV TREATMENT	II	PACTR201205000384379 & NCT01714414	Fozivudine (FZD), Lamivudine (3TC), Efavirenz (EFV), Zidovudine (AZT)		ADULTS, (≥18 years), HIV+ eligible for ART; N=120	Ongoing
JOSKA SP.2011.41304.065 Li in HAND	HIV TREATMENT	II	PACTR201310000635418 DOH-27-1013-4529	Camcolit®	Norgine	ADULTS (≥18 years), HIV+ individuals on ART with a suppressed viral load and neurocognitive impairment; N=108	Ongoing

KATZENSTEIN CT. 2006.33020.001 ComTru	HIV TREATMENT	III	NCT00346567	Combivir (ZDV & 3TC), Truvada (Emtricitabine &Tenofovir)	GlaxoSmithKline, Gilead	PREGNANT WOMEN (HIV+, 18-55 years) and INFANTS; N=566 recruits (288 mother-infant pairs evaluated)	Completed
KISANGA CT. 2006.33020.006 VITA-1	HIV TREATMENT	II	NCT00294892	Viramune® (NVP), Taver® (Carbamazepine), Epanutin (Phenytoin)	Boeringer Ingelheim, Medochemie, Pfizer	PREGNANT WOMEN (HIV+, ≥18 years) and INFANTS; N=144	Completed
KISANGA CT. 2006.33020.006 VITA-1	HIV TREATMENT	II	NCT01187719	Viramune® (NVP), Taver® (Carbamazepine), Epanutin (Phenytoin)	Boeringer Ingelheim, Medochemie, Pfizer	PREGNANT WOMEN (HIV+, ≥18 years) and INFANTS; N=67	Completed
KIWANUKA TA.2011.40200.035 STAR	HIV OTHER	III	PACTR201311000696101	Mobile phone versus physical contact tracing		ADULTS and ADOLESCENTS (15-49 years), HIV- high-risk individuals; N=662	Ongoing
LEROY IP.2007.33011.002 MONOD	HIV TREATMENT	III	NCT01127204	Azidothymidine-Zidovudine (AZT); Zidovudine (ZDV) syrup; Lamivudine (3TC) syrup; Nevirapine (NVP) syrup; Abacavir (ABC) syrup ; Efavirenz (EFV) syrup; Ritonavir boosted Lopinavir (LPV/r) ; Cotrimoxazole syrup	National programmes	CHILDREN (HIV+, 3 – 12 months); N=154	Ongoing
LYAMUYA IP.2007.33112.001 TaMoVac II	HIV VACCINES	II	NCT01697007 & PACTR201211000435126	DNA [Env +gp160 (subtype E, CM235), gag and pol (integrase-deleted and reverse transcriptase non-functional, subtype A, CM240] + MVA-CMDR	Vecura/WRAIR	ADULTS (HIV-, 18-40 years); N=198	Ongoing
MASIMIREMBWA TA.2011.40200.052 ClinPEZ	HIV TREATMENT	IV	pending	Efavirenz (EFV)-containing HAART		ADULTS, (≥18 years), HIV+ being initiated on HAART; N=250	Not registered yet
MCCORMACK CT.2005.33070.003 MRC CTU - MDP301/Pro2000	HIV/AIDS MICROBICIDES	III	NCT00262106 & ISRCTN64716212	PRO 2000 vaginal gel / HEC; Placebo gel	Indevus Pharmaceuticals (ENDO Pharma)/ CONRAD	ADULTS, HIV- women; N=9673	Completed
MCCORMACK CT.2005.33070.003 MRC CTU - TopUp Pilot study	HIV/AIDS MICROBICIDES	non-phase	PACTR2010060002133418	Hydroxyethyl cellulose (HEC)	CONRAD	ADULTS; Women and male partners who agree for interview; N=270	Completed

MERRY CT.2004.32011.003 APK.DDK	HIV TREATMENT	IV	PACTR201206000159453	Lopinavir/ritonavir, rifampicin		ADULTS (≥18 years), HIV+ individuals; N=24	Completed
MUGYENYI IP.2007.33011.003 EARNEST	HIV TREATMENT	III	NCT00988039	Aluvia(lopinavir/ritonavir co-formulated), Truvada(co-formulation of tenofovir and emtricitabine), Lamivudine, Emtricitabine, Didanosine, Abacavir, Tenofovir, Raltegravir	Abbott, Merck, Pfizer, GSK, Gilead	ADULTS and ADOLESCENTS (HIV+, ≥12 years); N=1,277	Ongoing
MULENGA IP.2007.33011.006 CHAPAS-3	HIV TREATMENT	II/III	ISRCTN69078957	Baby and Junior Triomune (d4T+3TC+NVP); Lamivir S (d4T+3TC); 3TC (lamivudine) +ABC (abacavir) baby and junior scored tablets; ZDV (zidovudine) +3TC (lamivudine) baby and junior scored tablets; ZDV (zidovudine) +3TC (lamivudine) +NVP (nevirapine) scored tablets.	Cipla Pharmaceuticals	CHILDREN (HIV+, 1 month – 13 years); N=420	Ongoing
NEWELL CT. 2006.33020.007 Kesho Bora	HIV TREATMENT	IV	ISRCTN71468401	Zidovudine (ZDV); Nevirapine (NVP); Lamivudine (3TC); Lopinavir/Ritonavir (LPV/r)	Cipla Pharm. Ltd, Abbot Lab.	PREGNANT WOMEN (HIV+, 32-36 weeks gestation) and INFANTS (birth – 1 year); N=845	Completed
ORRELL TA.2011.40200.015 TAP	HIV TREATMENT	IV	PACTR201311000641402	Wisepill® electronic adherence monitoring devise; Tenofovir (TDF); Lamivudine (3TC); Efavirenz (EFV); Nevirapine; Zidovudine (AZT)	Wisepill Technologies	ADULTS and ADOLESCENTS, HIV+ ART-naïve individuals (12-80 years); N=230	Ongoing
VAN DE PERRE CT. 2006.33020.004 PROMISE-PEP	HIV TREATMENT	III	NCT00640263	Lamivudine (3TC); Lopinavir/Ritonavir (LPV/r)	Generic/GlaxoSmith Kline Abbot Lab.	INFANTS (HIV-, 7 days old) breastfed by their HIV+ mothers; N=1,273 infants	Ongoing

Table 2-2: HIV/AIDS capacity building projects

Click on underlined text to link to project profiles and additional information.

Coordinator Grant code Grant abbreviation	Capacity Building Goal	Study population	Status
Van de Wijgert CT.2005.33070.001	Preparing for Phase III vaginal microbicide trials in Rwanda and Kenya: Preparedness studies, capacity building, and strengthening of medical referral systems	ADULTS, HIV- high-risk women N= 800	Completed
Hayes CT.2005.33070.002 TVMTU	To strengthen and expand the capacity for phase I, II and III clinical trials of candidate vaginal microbicides in Tanzania and Uganda, in order to facilitate the rapid evaluation of new products that, if shown to be effective, would provide a valuable tool for women to protect themselves against heterosexually-acquired HIV infection.	ADULTS, HIV- high-risk women N=1970	Completed
McCormack CT.2005.33070.003 MRC CTU	**MDP301:** To build additional infrastructure at the RHRU Orange Farm site, Johannesburg; training on ethics, GCP/GCLP training for collaboarators, personnel, etc.; database training; in order to conduct the clinical trial to evaluate the efficacy and safety of 0.5% and 2% PRO 2000/5 gels for the prevention of vaginally acquired HIV infection compared to placebo in preventing vaginally acquired HIV infection	ADULTS, HIV- women N=9673	Completed
McCormack CT.2005.33070.003 MRC CTU	**TopUp Pilot Study:** To determine the feasibility of conducting a microbicide trial of daily vaginal gel and to inform the way adherence should be assessed and to investigate the acceptability and adherence to daily intravaginal universal placebo gel over 12 weeks.	ADULTS Women and male partners who agree for interview N=270	Completed
McCormack CT.2005.33070.003 MRC CTU	**Mozambique Feasibility Study:** A Feasibility Study to evaluate the population and study site in the Healthcare centres of Mavalane and Manhiça in preparation for a phase III randomised controlled trial of a vaginal microbicide for the prevention of HIV (FS Microbicides)	ADULTS, women N=505	Completed
Mandaliya IP.2007.33070.001 Biomarkers	**HIV microbicide:** Establish baseline ranges of biomarkers related to the vaginal environment in groups of women targeted for microbicide trials in Kenya, Rwanda, and South Africa	ADULTS, HIV- high-risk women N=430	Completed
Buvé SP.2011.41304.066 RHASA	To inform future clinical trials of interventions to improve the reproductive health of adolescent girls in sub-Saharan Africa, including vaginal microbicides, vaccines and products that enhance the health of the vaginal environment such as probiotics.		Ongoing
Bekker CT.2006.33111.004 SASHA	**HPV study:** Preparing for adolescent HIV vaccine trials in South Africa: A multi-centre study to evaluate acceptability of the HPV vaccine in adolescents.	ADOLESCENTS (12-17 years) N = 834	Completed
Bekker CT.2006.33111.004 SASHA	**Community attitudes:** Prepare for adolescent involvement in HIV vaccine trials by exploring attitudes towards participation, informed consent, provision of adolescent prevention services and experiences of communication about HIV and sexual issues.	ADOLESCENTS (12-17 years), with parents/guardians and stakeholders. N=141	Completed

Kapiga CT.2006.33111.013 HIVTAB	Establish and strengthen research capacity and conduct specific research studies in preparation for clinical trials to assess the protective efficacy of HIV candidate vaccines.	ADULTS, High-risk women (18-44 years) N=950 HIV+ women working in bars, guest houses, hotels or other recreational facilities (Tanzania) as well as sex workers (Burkina Faso) N=220	Completed
Bakari CT.2006.33111.007 TaMoVac-01	Assess factors involved in the acceptability of a newborn/infant HIV vaccine trial, and evaluate knowledge and attitudes from mothers and families concerning HIV and vaccines.	ADULTS Mothers, fathers and grandmothers of infants N=200	Completed
Kaleebu CT.2006.33111.011 CHIVTUM	Assess the transmission dynamics and feasibility of conducting preventative trials on HIV and STI in fishing communities in Mangochi.	ADULTS and ADOLESCENTS (13-49 years); HIV- individuals working in fishing communities N = 1743	Completed
Passmore SP.2011.41304.038 FAHSAM/WISH	**"WISH" study (Women's Initiative in Sexual Health):** To identify whether age, bacterial microbiome species, and sexually transmitted infections influence the state of T-cell activation and the type of inflammatory markers in female adolescent genital tracts.	FEMALE ADOLESCENTS (16-22 years); Female adolescents and young adults aged 16–22 attending the Masipumelele Youth Center for health care N= 150	Ongoing
Weber CT.2006.33111.001 AfrEVacc	**Beira:** To estimate HIV incidence within a population at higher risk of HIV in Beira, Mozambique, in preparation for future HIV prevention interventions and intervention studies.	ADULTS, HIV- high-risk women N = 1000	Completed
Weber CT.2006.33111.001 AfrEVacc	**Manhica EVAS:** To contribute to capacity development and provide information needed for the conduction of HIV vaccine trials in Mozambique.	ADULTS N=70	Completed
Weber CT.2006.33111.001 AfrEVacc	**Manhica Epidemiology:** To develop capacity and provide epidemiological information needed for conducting HIV prevention trials including HIV vaccine trials in Mozambique.	ADULTS (18-50 years) N= 1735	Completed
Weber CT.2006.33111.001 AfrEVacc	**Africa Centre:** To complete an exploratory programme of research investigating key health issues for rural Zulu men and strategies for recruiting and retaining young men in community-based HIV prevention research; making these findings available to the AfrEVacc Network Partners and in so doing, defining a range of generalisable strategies for increasing men's involvement in bio-medical and behavioural HIV prevention research in southern African settings.	ADULTS, men (18-29 years) N= 200	Completed
Weber CT.2006.33111.001 AfrEVacc	**Joburg:** The overall purpose of this study is to determine the feasibility and acceptability of recruiting HIV sero-negative men into a future phase III HIV vaccine trial.	ADULTS, men N= 150	Completed

2.1 Integrated projects and clinical trials

2.1.1 CHAPAS-1

EDCTP Project Coordinator:	Chifumbe Chintu (University Teaching Hospital (UTH), Zambia)
EDCTP Call Title:	Trials assessing the effectiveness and safety of simplified anti-retroviral drug regimens and monitoring
EDCTP Project Title:	Children with HIV in Africa - Pharmacokinetics and Adherence of Simple Antiretroviral regimens
EDCTP Project Code:	CT.2004.33011.001
EDCTP Project Start Date:	3 November 2005
EDCTP Project End Date:	28 February 2009
Collaborators:	• Ganapati Bhat (University of Zambia (UNZA), Zambia) • David Marinus Burger (Radboud University Nijmegen, Netherlands) • Carlo Giaquinto (University of Padova, Italy) • Diana Mary Gibb (Medical Research Council, UK) • Veronica Mulenga (University Teaching Hospital, Zambia) • Andrew Nunn (Medical Research Council (MRC), UK) • Ann Sarah Walker (MRC, UK)
Study/Trial 1	**CHAPAS Trial 1**
Site Principal Investigator(s):	Chifumbe Chintu (Zambia)
Clinical Trial/Study Sponsor:	Medical Research Council (MRC), UK
Trial/Study title:	**C**hildren with **H**IV in **A**frica – **P**harmacokinetics and **A**dherence of **S**imple Antiretroviral Regimens (CHAPAS-1 Trial)
Goal:	To study the appropriate dosing of, and adherence to, a fixed-dose combination of stavudine (d4T), lamivudine (3TC) and nevirapine (NVP) in a new formulation specifically developed for children (Pedimune).
Primary Objective(s):	To describe toxicity (e.g. rash, hepatic toxicity) probably or possibly related to NVP when NVP is initiated at full dose versus half-dose in order to determine the necessity for dose escalation in African HIV-infected children using fixed dose combinations (FDCs)
Secondary Objective(s):	1. To determine the pharmacokinetics (PK) of NVP, d4T and 3TC in two daily paediatric doses co-formulated fixed-dose crushable/dispersible tablet combinations (Pedimune) in African HIV-infected children, with and without malnutrition and in different age groups, from a subset of children enrolled in the CHAPAS-1 trial 2. To determine possible PK interactions between NVP and common concomitant medications, such as rifampicin and fluconazole in children and adolescents enrolled in the CHAPAS-1 trial 3. To evaluate a visual analogue scale for assessing 28-day adherence to antiretroviral therapy (ART), by comparing with 3-day recall, pill and bottle counts (including unannounced checks at home and measures from Medication Event Monitoring System caps [MEMs caps], which records when the pill bottle has been opened). Unannounced pill counts and MEMs caps will be performed on a subset of children enrolled in the CHAPAS-1 trial 4. To describe mortality, disease progression, hospital admission rates and laboratory markers (CD4 percent, haemoglobin, viral load as measured by plasma HIV RNA)

	after starting effective ART 5. To estimate the budget impact and cost-effectiveness of effective ART in human immunodeficiency virus (HIV) infected children in Zambia.
Clinical Trial/Study site(s):	UTH (Zambia)
Collaborating site(s):	• MRC (UK) • Radboud University Medical Centre Nijmegen (Netherlands) • San Fransisco General Hospital (USA) • St James' Hospital (Ireland)
Study design and population:	Phase I/II open-label randomised controlled trial on 211 HIV-1 infected children, aged 3 months to 14 years. Children randomised in a 1:1 ratio to start with Pedimune either at full dose in a twice daily schedule or in a dose escalation schedule of once-daily administration for 14 days, which is then increased to full dose. This latter schedule thus has 50% of the normal daily dose of NVP for the first 14 days; an additional 3TC/d4T tablet (Lamivir-S) will be provided during this period to allow full dosing of 3TC and D4T.
Product(s):	Pedimune (Triomune Baby/Junior) tablets: stavudine (d4T), l amivudine (3TC) and nevirapine (NVP) in paediatric co-formulated fixed-dose combinations
Manufacturer/Developer:	Cipla Pharmaceuticals Ltd
Cofunders:	• Cipla Pharmaceuticals Ltd (India) • UTH (Zambia) • Irish Aid (Ireland)
Trial Registration number(s):	ISRCTN 31084535
Sub-studies:	**The CHAP 2 Cohort** Objective: To provide information on children before, during and after the introduction of ART in a resource limited setting; document the natural history of HIV infected children in Zambia by monitoring mortality and morbidity prior to the introduction of ART; monitor the introduction of ART, and its effects on mortality and morbidity; and provide data on the health service needs of HIV-infected children for economic analyses
	CHAPAS RIFNVP Objective: To study the pharmacokinetics of nevirapine (NVP) in HIV-infected children younger than three years who are being treated with nevirapine-containing ART and rifampin (RIF) for HIV/TB co-infection
	Adherence sub-study Objective: To investigate the best adherence measure for the clinic setting - MEMS data will be used as gold standard and compared with child/carer adherence questionnaire answers, clinic pill counts and unannounced pill counts with the aim of validating one or more simple questions that could be used widely; and to predictors of adherence - to gain an insight into routes for a possible intervention, which could be used widely
Status:	Completed
Results and Outcomes:	The main study "Children with HIV in Africa: Pharmacokinetics and Adherence of Simple Antiretroviral Regimens (CHAPAS Trials)" was successfully completed in February 2009. The findings of this study were published in major journals. The results contributed to the approval of Triomune Baby/Junior for use in HIV infected children by the FDA in August 2007. The results from the study were used by the WHO Formulation and

	Pharmacology Group to define the optimal weight bands for antiretrovirals in children worldwide.
Publications:	1. Rafaella F. A. L'homme, Tim Dijkema, Adilia Warris, Andre J. A. M. van der Ven, Diana M. Gibb and David M. Burger. Pharmacokinetics of two generic fixed-dose combinations for HIV-infected children (Pedimune Baby & Pedimune Junior) are similar to the branded products in healthy adults. *Journal of Antimicrobial Chemotherapy*, 2007;59:92-96 2. Rafaella F. A. L'homme, Tim Dijkema, Adilia Warris, Andre J. A. M. van der Ven, Diana M. Gibb and David M. Burger. Pharmacokinetics of two generic fixed-dose combinations for HIV-infected children (Pedimune Baby & Pedimune Junior) are similar to the branded products in healthy adults. *Journal of Antimicrobial Chemotherapy*, 2007;59:92-96 3. Rafaella F.A. L'homme, Desire Kabamba, Fiona M. Ewings, Veronica Mulenga, Chipepo Kankasa, Margaret J. Thomason, A. Sarah Walker, Chifumbe Chintu, David M. Burger and Diana M. Gibb. Nevirapine, stavudine and lamivudine pharmacokinetics in African children on paediatric fixed-dose combination tablets. *AIDS* 2008;22:557-65 4. Mairin Ryan, Susan Griffin, Bona Chitah, A. Sarah Walker, Veronica Mulenga, Donald Kalolo, Neil Hawkins, Concepta Merry, Michael G. Barry, Chifumbe Chintu, Mark J. Sculpher and Diana M. Gibb. The cost-effectiveness of cotrimoxazole prophylaxis in HIV-infected children in Zambia. *AIDS* 2008;22:749-57 5. Mairin Ryan, Susan Griffin, Bona Chitah, A. Sarah Walker, Veronica Mulenga, Donald Kalolo, Neil Hawkins, Concepta Merry, Michael G. Barry, Chifumbe Chintu, Mark J. Sculpher and Diana M. Gibb. The cost-effectiveness of cotrimoxazole prophylaxis in HIV-infected children in Zambia. *AIDS* 2008;22:749-57 6. Rafaella F.A. L'homme, Desire Kabamba, Fiona M. Ewings, Veronica Mulenga, Chipepo Kankasa, Margaret J. Thomason, A. Sarah Walker, Chifumbe Chintu, David M. Burger and Diana M. Gibb. Nevirapine, stavudine and lamivudine pharmacokinetics in African children on paediatric fixed-dose combination tablets. *AIDS* 2008;22:557-65 7. David Burger, Fiona Ewings, Desire Kabamba, Rafaella L'homme, Veronica Mulenga, Chipepo Kankasa, Margaret J. Thomason, Diana M. Gibb, Chifumbe Chintu and A. Sarah Walker. 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* 2010;32:369–372. 8. David Burger, Fiona Ewings, Desire Kabamba, Rafaella L'homme, Veronica Mulenga, Chipepo Kankasa, Margaret J. Thomason, Diana M. Gibb, Chifumbe Chintu and A. Sarah Walker. 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* 2010;32:369–372. 9. 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.Strategies for Nevirapine Initiation in HIV-Infected Children Taking Pediatric Fixed-Dose Combination ""Baby Pills"" in Zambia: A Randomized Controlled Trial. *Clinical Infectious Diseases* 2010; 51 (9):1081-1089 10. Haberer, JE; Cook, A; Walker, AS; Ngambi, M; Ferrier, A; Mulenga, V; Kityo, C; Thomason, M; Kabamba, D; Chintu, C; Gibb, DM; Bangsberg, DR. Excellent Adherence to Antiretrovirals in HIV plus Zambian Children Is Compromised by Disrupted Routine, HIV Nondisclosure, and Paradoxical Income Effects. *PLOS ONE* 2011; 6(4) 11. Fillekes, Q; Mulenga, V; Kabamba, D; Kankasa, C; Thomason, MJ; Cook, A; Ferrier, A; Chintu, C; Walker, AS; Gibb, DM; Burger, DM. Pharmacokinetics of nevirapine in HIV-infected infants weighing 3 kg to less than 6 kg taking paediatric fixed dose combination tablets. *AIDS* 2012; 26(14): 1795-1800

2.1.2 CHAPAS-3

EDCTP Project Coordinator:	Veronica Mulenga (University Teaching Hospital (UTH), Zambia)
EDCTP Call Title:	Call to support the establishment of regional networks of excellence for conducting clinical trials and provide mentorship programmes in sub-Saharan Africa
EDCTP Project Title:	Expanding the Availability of Fixed Dose Combination Antiretroviral Formulations for First-line Treatment of HIV-infected Children - the Children with HIV in Africa Pharmacokinetics and Acceptability/Adherence of Simple Antiretroviral Regimens (CHAPAS-3 trial)
EDCTP Project Code:	IP.2007.33011.006
EDCTP Project Start Date:	9 December 2009
EDCTP Project End Date:	31 July 2013
Collaborators:	• Alice Asiimwe Rwego (Baylor College of Medicine Children's Foundation, Uganda) • David Marinus Burger (Radboud University, Nijmegen, Netherlands) • Chifumbe Chintu (University Teaching Hospital, Zambia) • Carlo Giaquinto (University of Padova, Italy) • Diana Mary Gibb (Medical Research Council (MRC), UK) • Chipepo Kankasa (University Teaching Hospital, Zambia) • Adeodata Kekitiinwa (Baylor College of Medicine Children's Foundation, Uganda) • Cissy Mutuluuza Kityo (Joint Clinical Research Center, Uganda) • Nigel Klein (University College London (UCL), UK) • Gary Maartens (University of Cape Town (UCT), South Africa) • Helen McIlleron (UCT, South Africa) • Concepta Merry (Makerere University, Uganda) • Victor Musiime (Joint Clinical Research Center, Uganda) • Jose Ramos (Hospital Universitario de Getafe, Spain) • Mairin Ryan (Trinity College, Ireland) • Chafye Siuluta (University of Zambia) • Margaret Thomason (MRC, UK) • Ann Sarah Walker (MRC, UK)
Site Principal Investigator(s):	• Diana Gibb (UK) • Addy Kekiitinwa (Uganda) • Cissy Kityo (Uganda) • Veronica Mulenga (Zambia)
Clinical Trial/Study Sponsor:	Medical Research Council (MRC), UK
Trial/Study title:	Children with human immunodeficiency virus (HIV) in Africa - pharmacokinetics and acceptability/adherence of simple antiretroviral regimens (CHAPAS-3 trial)
Goal:	The CHAPAS-3 project aims to conduct a paediatric clinical trial and several sub studies (addressing in particular pharmacokinetics (PK) and antiretroviral toxicity) using four new simplified paediatric antiretroviral (ARV) solid-based formulations administered according to WHO dosing tables. Alongside the trial, over four years the project aims to build all aspects of capacity for implementing paediatric clinical trials in the African region. This includes enhancing capacity at African institutions with some research experience and establishing research capacity alongside newly developing paediatric HIV services in a Ugandan satellite site. The infrastructure and expertise from this project will create a network with internationally accepted standards for performing clinical trials and PK studies and valuable regional collaboration.
Primary Objective(s):	1. To compare toxicity (grade 3 or 4 laboratory or clinical

	adverse events) of stavudine (d4T) versus abacavir (ABC) or zidovudine (ZDV) in combination with lamivudine (3TC) as fixed dose combination (FDC) backbone dual nucleoside reverse transcriptase inhibitor (NRTI) in ART-naïve HIV-infected children initiating non-nucleoside reverse transcriptase inhibitor (NNRTI) based first-line and in those who have already received d4T+3TC+NNRTI (most frequently, adult/junior/baby triomune FDC) for a minimum of two years and currently have undetectable HIV viral load 2. To determine via nested PK sub studies: – The plasma PK of ZDV, 3TC and ABC taken as twice daily new paediatric-formulated fixed-dose crushable tablet combinations of ZDV+3TC+nevirapine (NVP), ZDV+3TC and ABC+3TC in African HIV-infected children with and without malnutrition and across different ages according to weight-based dosing tables – The plasma PK of new efavirenz (EFV) 200mg scored tablets administered once daily according to weight-based dosing tables – The plasma PK of 3TC and ABC paediatric-formulated fixed-dose crushable-tablet combinations taken with EFV once versus twice daily (using a crossover design) in African HIV-infected children with and without malnutrition and across different ages according to WHO weight-based dosing tables.
Secondary Objective(s):	1. To compare skinfold thickness as a measure of lipodystophy/lipoatrophy between randomised trial arms 2. To compare acceptability and adherence between randomised trial arms, and also between once and twice daily abacavir, using questionnaires, pill counts and a visual analogue scale (all being used and compared with electronic monitoring devices (MEMscaps) in the CHAPAS-1 trial) 3. In view of recent data on possible cardiovascular toxicity of abacavir4, to compare measures of cardiac and vascular function and markers of immune activation across the three randomised trial arms. This is done using measures of structural and functional vasculature (using newly developed, simple and validated portable techniques to measure intimal thickness and pulse wave velocity). In addition plasma samples will be stored for a later measurement of biomarkers of vascular injury (e.g. D-dimer, interleukin 6, hsCRP and endothelial microparticles) which have been reported to be related to the risk of cardiovascular events in adults and could be involved in the pathogenesis of toxicity 4. To validate methods to quantify NRTI and NNRTI concentrations in whole blood (50µL samples dried onto filter paper which can be stored at room temperature) 5. Population PK modelling will be done using whole blood and plasma PK data generated within the study, and in addition to other data from African children (e.g. from the CHAPAS-1 trial). The models will be used: – To optimise sparse PK sampling strategies (e.g. one or two samples only being taken at an outpatient visit) for future studies evaluating dosing approaches for ARVs in children – To evaluate the association between PK and adverse drug effects as well as immunological and virological responses – To provide reference population PK models which can be used for individual patient management

	– To simulate dosing approaches in different categories of children based on age, weight, gender and other parameters. Study is expected to gain consent for storage of human DNA and test for associations between three known single nucleotide polymorphisms (CYP2B6*6, CYP2B6*18, CYP2B6*26) and PK measurements 6. To compare changes in growth, disease progression, mortality and HIV laboratory markers (CD4 cell count and percent; HIV RNA viral load measured retrospectively on stored plasma samples) between randomised arms 7. To undertake an economic analysis comparing the cost-effectiveness of the three randomised regimens, and to model the cost-effectives of switching from initial d4T to ZDV or ABC-containing regimens in HIV-infected African children. This approach builds on the economic analyses undertaken in the CHAP cotrimoxazole trial (before use of ARVs became available, funded by IrishAID) and the CHAPAS-1 trial (funded by EDCTP, Health Research Board of Ireland and IrishAID).
Clinical Trial/Study site(s):	• University Teaching Hospital (UTH), Lusaka , Zambia • Baylor College of Medicine Bristol Myers Squibb Children's Clinical Centre of Excellence formerly Paediatric Infectious Diseases Centre (PIDC) Mulago Hospital, Kampala, Uganda • Joint Clinical Research Centre (JCRC), Kampala, Uganda • Joint Clinical Research Centre satellite site at Gulu Hospital, Uganda
Collaborating site(s):	• MRC Clinical Trials Unit, UK • Radboud University of Nijmegen Medical Centre, Netherlands • University of Cape Town, South Africa
Product(s):	• ARV products in the urgent or high priority list as recommended by WHO • Baby and Junior Triomune (d4T+3TC+NVP); Lamivir S (d4T+3TC) • 3TC (lamivudine) +ABC (abacavir) baby and junior scored tablets • ZDV (zidovudine) +3TC (lamivudine) baby and junior scored tablets • ZDV (zidovudine) +3TC (lamivudine)+NVP (nevirapine) scored tablets.
Manufacturer/Developer:	Cipla Pharmaceuticals Ltd
Study design and population:	Phase II/III open-label randomised controlled trial with three arms. Stavudine arm: d4T/3TC/NVP or d4T/3TC + EFV Abacavir arm: 2 arm ABC: ABC/3TC/NVP or ABC/3TC +EFV Zidovudine arm: ZDV/3TC/NVP or ZDV/3TC +EFV 450 HIV-infected children, aged one month to 13 years will be enrolled over 18 months and followed for a minimum of 96 weeks (total trial length 3.5 years) in three clinical centres in Zambia (UTH, Lusaka) and Uganda (PIDC and JCRC, Kampala).
Cofunders:	• Cipla Pharmaceuticals Ltd (India) • MRC UK (UK) • Instituto de Salud Carlos III (Spain) • Health Research Board Ireland (Ireland) • Instituto Superiore de Sanita (Italy)
Trial Registration number(s):	ISRCTN69078957 PACTR201006000222401
Sub-studies:	**Population/sparse PK study** Purpose: To optimise dosing of ART in young children in Africa

	Primary objective: to evaluate the impact of pharmacokinetics (PK) on toxicity and efficacy in all randomised children Secondary objective: to describe variability of ARV PK across the study population and over time and identify factors affecting PK including pharmacogenetic variants. **The Cardiovascular sub-study** Title: The Impact of HIV and Antiretroviral Therapy on the Cardiovascular System of HIV-infected children. Purpose: To ascertain whether HIV-infected children have evidence of early cardiovascular damage and the impact that different formulations of ART have on any changes seen. Objectives: 1. To determine the influence of HIV infection on vascular phenotype by comparing HIV-infected Antiretroviral Therapy (ART) naïve children with HIV-uninfected African controls 2. To determine the effects of ART on vascular phenotype by comparing children stable on ART to drug naïve about to start treatment and monitor changes in vascular function over time 3. To gain insight into the potential mechanisms operating to mediate vascular dysfunction looking specifically at: – Structural and functional arterial changes – Evidence of ongoing inflammation and immune activation – Vascular and endothelial injury. **The Lipodystrophy sub-study** Title: Lipodystrophy among HIV-infected children in Uganda and Zambia Purpose: To ascertain the optimal use of antiretroviral therapy that minimises the development of lipodystrophy among HIV-infected children Primary objective: To determine the pattern and relative rates of lipodystrophy as well as the associated factors among study participants Secondary objectives: 1. To determine the clinical and biochemical markers of lipodystrophy among the children 2. To relate any changes in lipid distribution or content with direct and indirect measures of cardiac and vascular function and measures of immune activation 3. To compare findings in HIV-infected children with those in HIV-uninfected controls.
Status:	Ongoing
Results and Outcomes:	Recruitment to the main trial was completed on 28 December 2011, with a total of 480 children enrolled, 450 children are actively being followed up, and according to the protocol, and the last recruited child will reach 96 weeks of follow up in November 2013. In addition, 249 uninfected controls were enrolled. Preliminary analysis on the specimens from the full PK sub-study has been done and the findings were presented at the 2012 IAS conference in Washington.

	Preliminary findings from the CHAPAS-3 sub-studies: • Evidence of increased araterial stiffness in HIV-infected children compared to controls • In HIV-infected children, no significant effects on Intimal media thickness (IMT) or Pulse Wave Velocity PWV of age of prior ART exposure • Efavirenz pharmacokinetic parameters of African children weighing 10-<20 Kg, on dialy efavirenz using current 2010 WHO weight-bands and new generic tablets were lower ana highly variable compared to adult data, but similar to previously reported paediatric values • The CHAPAS-3 sub-study demonstrated the challenges of fixed-dosing when therapeutic range is narrow.
PhD studies:	Title: The management of Paediatric HIV – infection: strategies to improve treatment outcomes in resource limited settings Candidate: Victor Musiime (Joint Clinical Research Centre, Uganda University of Antwerp, Belgium) Dates: 2010-March 2013
MSc studies:	Title: Masters in Clinical Trials (by distance based learning from London School of Hygiene and Tropical Medicine) Candidate: Chishala Chabala (University Teaching Hospital, Zambia) Dates: September 2012-July 2015
Publications:	

2.1.3 MONOD

EDCTP Project Coordinator:	Valeriane Leroy (Victor Segalen Bordeaux 2 University, France)
EDCTP Call Title:	Call for the support of clinical trials, capacity building and networking for HIV/AIDS treatment
EDCTP Project Title:	International phase 2b-3 randomized clinical trial to assess a once-daily simplified antiretroviral triple therapy among HIV-infected children treated early by a 12-month twice daily triple therapy between 6 weeks and 24 months of age and in virological success in Africa: The MONOD Project
EDCTP Project Code:	IP.2007.33011.002
EDCTP Project Start Date:	16 November 2009
EDCTP Project End Date:	30 September 2014
Collaborators:	• Vic Arendt (Public Research Centre for Health, Luxembourg) • Stéphane Blanche (University of Paris V - René Descartes, France) • Michael Kramer (Ministry of Health, Rwanda) • Philippe Lepage (Hôpital Universitaire des Enfants Reine Fabiola, Belgium) • Nicolas Meda (University of Ouagadougou, Burkina Faso) • Philippe Van de Perre (Montpellier University Hospital Centre (CHU), France) • Christine Rouzioux (University of Paris V - René Descartes, France) • Roger Salamon (Victor Segalen Bordeaux 2 University, France) • Marguerite Timite-Konan (Centre Hospitalier Universitaire de Yopougon, Cote d'Ivoire)
Site Principal Investigator(s):	• Marguerite Timite-Konan (Cote d'Ivoire) • Nicolas Meda (Burkina Faso)
Clinical Trial/Study Sponsor:	French National Agency for Research on AIDS and Viral Hepatitis (ANRS)
Trial/Study title:	Evaluation of Simplified Antiretroviral Treatment Strategies in HIV Infected Children Treated by Antiretroviral (ARV) Before One Year of Age
Goal:	This trial aims at identifying simplified antiretroviral treatments strategies to be given once daily in children infected with HIV from the age of 15 months (from 6 kg) in real field conditions of use in Africa. It will improve the antiretroviral roll-out in children, with a specific focus on long-term strategies adapted to resource-limited settings. The overall project is aimed at study the feasibility of early HIV diagnosis and antiretroviral access of HIV-infected infants in field conditions of low-income countries to improve their longterm survival.
Primary Objective(s):	To study the proportion of treatment success (alive, under follow-up and without virologic failure) of a once daily simplified triple therapy ABC-3TC-EFV in a phase IIb-III randomised controlled-trial among HIV-infected children above the age of 15 months old and in virologic success after a 12-month initial phase with a twice daily triple therapy using AZT-3TC-LPV/r in Burkina Faso and Côte d'Ivoire.
Secondary Objective(s):	1. To study the tolerance, the pharmacokinetic properties, treatment observation, the profiles of viro-immunological responses and the cost/efficiency aspects during the randomised phase 2. To study the survival without virological failure, the kinetics of virological success, the tolerance, the

	pharmacokinetic properties, the clinical response and the co-morbidities, the adherence of children treated initially with a twice-daily triple therapy 3. To study the compliance over time in children treated initially twice-daily, then once-daily 4. To study the clinical evolution of the children treated initially twice-daily, then once-daily 5. To describe the resistance profiles in children who would develop virological failure 6. To study the cost/efficiency aspects of these combinations 7. To study the social acceptance of these early antiretrovirals regimens.
Clinical Trial/Study site(s):	• Abidjan: within the PACCI programmes, FSU Abobo-Avocatier, CEPREF-Yopougon, Yopougon and Cocody Teaching hospitals, Ivory Coast • Ouagadougou: Yalgado Ouédraogo Teaching Hospital and Charles de Gaulle Teaching Hospital, Burkina Faso
Collaborating site(s):	• Inserm U897, Institut de Santé Publique, Epidémiologie et Développement (ISPED), Université Victor Segalen Bordeaux 2, France • Centre Hospitalier de Luxembourg (CHU), Luxembourg • Hôpital Universitaire des Enfants Reine Fabiola, Belgium • EA 3620, Faculté de Médecine Necker Enfants Malades and Université Paris-Descartes, France • University Montpellier 1, Research Team "EA 4205: Transmission, pathogenesis and prevention of HIV and associated infections", France
Product(s):	• Azidothymidine-Zidovudine (AZT) • Zidovudine (ZDV) syrup • Lamivudine (3TC) syrup • Nevirapine (NVP) syrup • Abacavir (ABC) syrup • Efavirenz (EFV) syrup • Ritonavir boosted Lopinavir (LPV/r) • Cotrimoxazole syrup
Manufacturer/Developer:	National Programs, Local Pharmacies, IDA foundation
Study design:	Open phase IIb-III randomised, international, multicentre clinical trial of non-inferiority, conducted in two consecutive steps: **Initial therapeutic cohort of 12 months**: Prospective treatment cohort of a 154 HIV-infected children (confirmed with PCR) from six weeks to 24 months of life under triple therapy starting at 10-12 weeks with 2 nucleoside reverse transcriptase inhibitors (NRTIs) ([AZT, ABC, or 3TC] + LPV/r) twice-daily together with prophylaxis against opportunistic infections with Cotrimoxazole and education regarding treatment. All these children will also receive an anti-pneumococcal vaccine (3 doses of Prevenar13) on the top of the existing child national immunisation programme schedule. **Simplified randomised phase from 13 to 25 months:** Those children (N=146) with virological success at the end of phase 1 (on two consecutive samples at three month intervals) will be randomised in two arms: • Combination with a treatment class change sparing the protease inhibitors (PIs) in one daily dose (ABC-3TC-EFV) • A control arm: Continuation of the twice-daily regimen of the initial phase (AZT, ABC, or 3TC-LPV/r).

Cofunders:	• ANRS (France) • INSERM (France) • HUDERF (Belgium) • CRP Luxembourg • Cooperation Luxembourg, • CHU Abidjan • CHU Ouagadougou
Trial Registration number(s):	NCT01127204
Status:	Ongoing
Results and Outcomes:	**Burkina Faso** Actual start and end of recruitment: 16/05/2012 to 21/01/2013 Number of patients enrolled:69 **Ivory coast** Actual start and end of recruitment: 24/08/2011 to 31/01/2013 Number of patients enrolled:114 **Expected results:** Identify an early, simplified antiretroviral strategy that can be used on a long-term basis for HIV-1 infected children, to reduce problems of treatment adherence, to spare a therapeutic class (i.e. PIs), and usable in various contexts in Africa.
PhD study:	Title: Challenges of comprehensive and early antiretroviral care of HIV-infected children in Africa: access, tolerance, adherence, clinical and immunovirological response to long-term antiretroviral treatment Candidate: Malik Coulibaly (University of Ouagadougou, Burkina Faso, Bordeaux Segalen University, France) Dates: 2011-2014
MSc studies:	Title: Early infant diagnosis and access to pediatric HIV care before inclusion in the MONOD trial: barriers and challenges in Abidjan, Côte d'Ivoire in 2011-2012 Candidate: Nizie Pelagie Edith Divine Avit Edi (Centre Hospitalier Universitaire de Cote d'Ivoire, Cote d'Ívoire) Dates: October 2012-October 2013
	Title: Clinical presentation of children in an early ARV treatment program in three African countries with specific interest to scoring systems: diagnosis of HIV, diagnosis of TB, IRIS, efficacy and tolerance of treatment Candidate: Clarisse Amani-Bosse (Centre Hospitalier Universitaire de Cote d'Ivoire, Cote d'Ivoire) Dates: September 2013-September 2014
	Title: Description of HIV infected infants included in the ANRS 12206 MONOD trial Candidate: Désiré Dahourou (University of Ouagadougou , Burkina Faso) Dates: October 2012-October 2014
Publications:	

2.1.4 EARNEST

EDCTP Project Coordinator:	Peter Mugyenyi (Joint Clinical Research Center, Uganda)
EDCTP Call Title:	Call for the support of clinical trials, capacity building and networking for HIV/AIDS treatment
EDCTP Project Title:	The Europe - Africa Research Network for Evaluation of Second Line Therapy: The EARNEST Trial
EDCTP Project Code:	IP.2007.33011.003
EDCTP Project Start Date:	15 September 2009
EDCTP Project End Date:	31 March 2014
Collaborators:	• Jose Arribas (La Paz Hospital, Spain) • Abdel Babiker (Medical Research Council (MRC), UK) • Robert Colebunders (Prince Leopold Institute of Tropical Medicine, Belgium) • Graham Stephen Cooke (Imperial College, London, UK) • Marisa De Rosa (CINECA - Interuniversity Consortium, Italy) • Philippa Easterbrook (Makerere University, Uganda) • Charles Gilks (World Health Organisation, Switzerland) • Marina Giuliano (Istituto Superiore di Sanità (ISS), Italy) • James Gita Hakim (University of Zimbabwe) • William Hall (University of Dublin, Ireland) • Andrew Kambugu (Makerere University, Uganda) • Cissy Mutuluuza Kityo (Joint Clinical Research Center, Uganda) • Francis Kiweewa (Joint Clinical Research Center, Uganda) • Joseph Marie Albert Lange (ICRH-International Centre of Reproductive Health, The Netherlands) • Patrick William Mallon (University of Dublin, Ireland) • Christine Nabiryo (Makerere University, Uganda) • Marie Louise Newell (Africa Centre for Health and Population Studies, South Africa) • Pius Okong (San Raphael of St. Francis Hospital Nsambya, Uganda) • Joep van Oosterhout (University of Malawi) • Nick Paton (Medical Research Council, UK) • William Powderly (University of Dublin, Ireland) • Andrew Reid (University of Zimbabwe) • Ann Sarah Walker (Medical Research Council, UK) • Patrick Paul Walsh (University of Dublin, Ireland)
Site Principal Investigator(s):	Nick Paton (UK)
Clinical Trial/Study Sponsor:	Medical Research Council (MRC, UK)
Trial/Study title:	EARNEST – A randomised controlled Phase III trial to evaluate options for second-line therapy in patients failing first-line 2NRTI + NNRTI regimen in Africa
Goal:	The EARNEST trial aims to determine the best treatment regimen for patients failing first-line therapy in resource limited settings. The EARNEST trial also aims to strengthen capacity at the selected sites for conducting clinical trials through establishing a network with complementary expertise in different aspects of the study.
Primary Objective(s):	The overall objective of this trial is to find out what, if anything, needs to be combined with a boosted protease inhibitor (PI) in second-line therapy, in order to maximise the chance of a good long-term clinical and immunological outcome following late immunological/clinical failure on a first-line nucleoside reverse transcriptase inhibitor (NRTI) and non-nucleoside reverse transcriptase inhibitor (NNRTI)-containing regimen.

	More specifically the EARNEST trial aims to determine whether, in patients failing a first-line NRTI and NNRTI-containing regimen • The use of bPI plus raltegravir (an integrase inhibitor) is superior to standard of care (bPI plus 2 new NRTIs) in achieving good HIV disease control at 96 weeks after randomisation • The use of bPI monotherapy is non-inferior to standard of care in achieving good HIV disease control at 96 weeks after randomisation.
Secondary Objective(s):	1. To answer the two aforementioned questions in a way that is relevant to large scale ART rollout programs now and that will remain relevant for many years to come (i.e. that applies to patients who fail relatively late on first- line therapy after low CD4 and/or new WHO stage 4 events and likely with multiple resistance mutations, that can be generalized to situations where viral load (VL) monitoring is performed infrequently or not at all and where resistance testing is generally not performed, and that uses standardised treatment regimens with drugs that can be made available at an affordable cost to roll-out programs 2. To ensure that the evidence obtained through the trial is widely disseminated, and leads promptly to change in public health policy (if appropriate) 3. To expand capacity for conducting clinical trials to new sites and also build new cadres of young researchers to lead future clinical trials 4. To build a well-functioning group of research sites and institutes that will become internationally-recognised as a network of excellence for addressing second-line therapy 5. To extend the network beyond established collaborations to new institutions and sites.
Clinical Trial/Study site(s):	• Academic Model for the Prevention and Treatment of HIV/Aids (AMPATH) Centre, Eldoret (Kenya) • Infectious Disease Institute (IDI), Kampala (Uganda) • JCRC Fort Portal Regional Centre of Excellence, Fort Portal (Uganda) • JCRC Gulu (Uganda) • JCRC Kabale (Uganda) • JCRC Kakira (Uganda) • JCRC Mbale (Uganda) • JCRC Mbarara Regional Centre of Excellence, Mbarara (Uganda) • Joint Clinical Research Centre (JCRC), Kampala (Uganda) • Mzuzu Central Hospital, Mzuzu (Malawi) • St Francis Nsambya Hospital, Kampala (Uganda) • University of Malawi, Queen Elizabeth Hospital, Blantyre • University of Zimbabwe Clinical Research Centre (UZCRC), Harare (Zimbabwe) • University Teaching Hospital (UTH), Lusaka (Zambia)
Collaborating site(s):	• MRC Clinical Trials Unit (UK) • University College Dublin (Ireland) • Istituto Superiore di Sanita (Italy) • CINECA (Italy) • Institute of Tropical Medicine (Belgium) • Hospital La Paz (Spain)
Study design:	Phase III open-label randomised controlled trial with three arms. Patients will be randomised in a ratio of 1:1:1 to one of the following three treatment arms.

	Arm A: bPI + 2 NRTIs chosen by clinician according to local standard of care and availability Arm B: bPI + raltegravir 400 mg twice daily Arm C: bPI alone (after an initial 12-week induction phase with raltegravir) The bPI will be standardised to Aluvia (lopinavir/ritonavir 400 mg/100 mg b.d.). Follow up will be for a minimum of 96 weeks. The primary outcome parameter for the trial is "good HIV disease control" defined as a composite endpoint consisting of all of: No new WHO Stage 4 events between randomisation and week 96 AND CD4 count > 250 cells/mm3 at week 96 AND VL < 10,000 copies/ml or > 10,000 copies/ml with no PI resistance mutations at week 96
Product(s):	• Aluvia (lopinavir/ritonavir co-formulated) • Truvada (co-formulation of tenofovir 300mg and emtricitabine 200mg) • Lamivudine • Raltegravir • Abacavir • Tenofovir
Manufacturer/Developer:	• Merck • Abbott • GSK • Gilead
Cofunders:	• MRC (UK) • Istituto Superiore di Sanità (Italy) • Instituto de Salud Carlos III (Spain)
Trial Registration number(s):	ISRCTN37737787 NCT00988039
Sub-studies:	• EARNEST Virology Substudy • EARNEST Resistance Substudy • EARNEST Immunophenotyping Substudy • EARNEST Quantiferon Substudy • EARNEST Bone Mineral Density Substudy • EARNEST Socioeconomic Substudy • EARNEST PK Rifabutin Substudy • EARNEST Genital Secretions Substudy
Status:	Ongoing
Results and Outcomes:	Recruitment target reached in 4 August 2011. The 1277 enrolled participants are being followed up.
Total number of subjects (clinical trials only):	1277 HIV-infected adults failing first-line therapy
PhD studies:	Title: Bone Mineral Density Substudy Candidate: Bonnie Wandera (IDI, Uganda) Dates: September 2012-September 2012
	Title: Socioeconomic Substudy Candidate: Jupiter Simbeye (University of Malawi, Malawi) Dates: September 2012-September 2012
	Title: Public Health Candidate: Willard Tinago (University of Zimbabwe, Zimbabwe) Dates:September 2010- September 2014
	Title: Health Economics Candidate: Gibson Mandozana (University of Zimbabwe) Dates: September 2010-September 2014
MSc studies:	Title: MSc in clinical trials at the London School of Hygiene and Tropical Medicine (LSHTM)

	Candidate: Ennie Chidziva (UZCRC, Zimbabwe) Dates:2010-2014
	Title: MSc in clinical trials at the London School of Hygiene and Tropical Medicine (LSHTM) Candidate: Michael Katwere (IDI, Uganda) Dates:2011-2014
	Title: MSc in clinical trials at the London School of Hygiene and Tropical Medicine (LSHTM) Candidate: Abbas Lugemwa (Uganda) Dates: 2011-2014
Publications:	

2.1.5 2LADY

EDCTP Project Coordinator:	Eric Delaporte (University of Montpellier 1, France)
EDCTP Call Title:	Call for support of integrated projects on clinical trials, capacity building and networking
EDCTP Project Title:	A multicentre phase III trial of second-line antiretroviral treatment in African adults
EDCTP Project Code:	IP.2007.33011.004
EDCTP Project Start Date:	13 July 2009
EDCTP Project End Date:	30 September 2014
Collaborators:	• Alexandra Calmy (Médecins Sans Frontières (MSF), Switzerland) • Robert Colebunders (Prince Leopold Institute of Tropical Medicine, Belgium) • Josef Eberle (Ludwig-Maximilians Universitat Munchen, Germany) • Pierre-Marie Girard (University Hospital Sain-Antoine, France) • Michael Hoelscher (Ludwig-Maximilians Universitat Munchen, Germany) • Sinata Koulla-Shiro (National Agency for AIDS Research (ANRS), France) • Arne Kroidl (Mbeya Medical Research Programme, Tanzania) • Vincent Lemoing (University of Montpellier 1, Fance) • Benjamin Longo-Mbenza (University of Limpopo, South Africa) • Leonard Maboko (Mbeya Medical Research Programme, Tanzania) • Zinhle Makatini (University of Limpopo, South Africa) • Nchabeleng Maphoshane (University of Limpopo, South Africa) • Olga Mogiyana Mzileni (University of Limpopo, South Africa) • Papa Salif Sow (University Cheikh Anta DIOP de Dakar (UCAD), Senegal) • Kyaw Thanda (University of Limpopo, South Africa)
Site Principal Investigator(s):	• Sinata Koulla Shiro (Cameroon) • Papa Salif Sow (Senegal) • Adrien Sawadogo (Burkina Faso)
Clinical Trial/Study Sponsor:	French National Agency for Research on AIDS and Viral Hepatitis (ANRS)
Trial/Study title:	A multicentre phase III trial of second-line antiretroviral treatment in African adults
Goal:	This trial aims at evaluating the efficacy and tolerance of 3 different second line treatment strategies: two recommended by WHO combine two non-nucleoside reverse transcriptase inhibitor associated with a ritonavir boosted protease inhibitor (emtricitabine-tenofovir-lopinavir/ritonavir and abacavir-didanosine-lopinavir/ritonavir); the third strategy combines emtricitabine-tenofovir-darunavir/ritonavir and is not yet evaluated in Sub-Saharan Africa. Darunavir has a potentially superior antiviral efficacy, a better tolerance and its single daily administration may facilitate treatment adherence.
Primary Objective(s):	To compare, in an African setting, in patients with virological failure after first-line antiretroviral treatment including a non-nucleoside reverse transcriptase inhibitor, the virological response (plasma HIV RNA < 50 copies/ml) at 48 weeks, in three groups of patients receiving three different antiretroviral combinations: the combination of emtricitabine-tenofovir-

	lopinavir/ritonavir in arm A, the combination of abacavir-didanosine-lopinavir/ritonavir in arm B, and the combination of emtricitabine-tenofovir-darunavir/ritonavir in a single daily dose in arm C.
Secondary Objective(s):	Patients will be followed up for secondary endpoints during the all duration of the trial. To compare the following parameters of response to antiretroviral treatment across the three arms: • Clinical outcome (AIDS events, non-AIDS events, death, adverse events) • Virological response (plasma HIV RNA < 200 and 50 copies/ml) at 24 weeks and after 48 weeks until the end of the trial • Virological response (plasma HIV RNA < 200 copies/ml) at 48 weeks • Immune response: variation in CD4 lymphocytes • Treatment discontinuation • Tolerance, particularly the occurrence of, hypersensitivity syndromes, renal impairment, gastrointestinal disorders and changes in lipids profile • Changes in anthropometric measures • Adherence (measured by pill count and questionnaire).
Clinical Trial/Study site(s):	• The Central Hospital of Yaounde (YCH, Cameroon) • The military hospital in Yaounde (Cameroon) • The University Hospital of Fann (Senegal)
Collaborating site(s):	• Institute of Tropical Medicine, Antwerp (Belgium) • MSF Access Campaign and University of Geneva, (Switzerland) • University of Munich, Munich (Germany) • University of Montpellier/IRD (France)
Study design:	Allocation: Randomized Endpoint Classification: Efficacy Study Intervention Model: Parallel Assignment Masking: Open Label Primary Purpose: Treatment A multicentre, non-inferiority, randomised, open label phase III trial comparing the virological efficacy and tolerance of three antiretroviral treatment regimens: the combination of emtricitabine-tenofovir-lopinavir/ritonavir in arm A, the combination of abacavir-didanosine-lopinavir/ritonavir in arm B, and the combination of emtricitabine-tenofovir-darunavir/ritonavir in arm C for 48 weeks in HIV-1-infected patients with treatment failure after first-line antiretroviral treatment in Cameroon, Senegal, and Burkina Faso.
Product(s):	• Emtricitabine-tenofovir and lopinavir/ritonavir • Abacavir-didanosine- lopinavir/ritonavir • Emtricitabine-tenofovir-darunavir/ritonavir
Manufacturer/Developer:	• Gilead Sciences • Janssen Pharmaceutica N.V.
Cofunders:	• Swiss National Science Foundation (Switzerland) • Hôpitaux Universitaire de Genève (Switzerland) • Deutsches Zentrum fuer Luft und Raumfahrt DLR (Germany) • l'Institut de Recherche pour le Dévelopment-IRD (France) • French National Agency for Research on AIDS and Viral Hepatitis (ANRS, France) • Prins Leopold Instituut voor Tropische Geneeskunde (Belgium)
Trial Registration	NCT00928187

number(s):	
Sub-studies:	**The Metabody sub-study** The Metabody sub-study in conducted in Senegal, Cameroun and Burkina Faso with the primary objective of describing morphological changes and metabolic disorders (metabolic syndrome, cardiovascular and fracture risks) in HIV positive patients failing first line antiretroviral treatment and beginning second line ART. **The OSTEOVIH sub-study** This is a complementary study to the Metabody study. This is a cross sectional study conducted in Senegal with the purpose of estimating the prevalence of osteoporosis and osteopenia in aging population living with HIV, receiving antiretroviral treatment.
Status:	Ongoing
Results and Outcomes:	**Recruitment and follow up:** 2LADY trial recruitment was completed at the end of 2012. Follow up is continuing for each patient for 48 weeks, and the last visit for the last patient is expected by end of October 2013. **Expected results:** First results of the trial are expected in the fourth quarter of 2013. A simplified strategy by using boosted protease inhibitor for patients who will have suppressed their viral load is planned for the future. **Training:** GCP, protocol and study specific procedures trainings in Cameroon and Senegal in 2009 and 2010 Associative members involved in research: workshop for staff in Yaoundé facilitated by the GTIA (association network on research)- 3, 10 and 17th of February 2010 in Cameroon Exchange programmes and mentorship for 1 Lab technologist from Senegal to Cameroon (Viral load assay by Biocentric technique) – March-April 2011.
Total number of subjects (clinical trials only):	N=450
PhD studies:	Title: Prevalence of Hepatitis B viremia in HIV/HBV co-infected patients on lamivudine containing antiretroviral first line therapy and virological outcome after 48 weeks of Tenofovir containing second line therapy from the ALISA and 2Lady Trials Candidate: Lucas Maganga (Mbeya Medical Research Programme, Tanzania) Dates: 2011-2014
	Title: to be determined Candidate: Bahati Kaluwa (Mbeya Medical Research Programme, Tanzania) Dates: 2012-2015
	Title: HIV and other retrovirus genetic diversity in Cameroon Candidate: Julius Chia (Cameroun) Dates: 2011-2014
Other/Sub-studies:	ALISA Cohort: Following termination of the ALISA trial, the consortium proposed to establish a second line cohort that will serve as a mock trial to increase the knowledge on adherence, failure and tolerability of standard 2nd line treatment in Mbeya and prepare for future trials that will evaluate novel strategies to keep patients on sustained ARV treatment.
Publications:	

2.1.6 NUSTART

EDCTP Project Coordinator:	Suzanne Filteau (London School of Hygiene and Tropical Medicine, UK)
EDCTP Call Title:	Call for the support of clinical trials, capacity building and networking on treatment of HIV/AIDS
EDCTP Project Title:	Nutritional support for African adults starting antiretroviral therapy (NUSTART)
EDCTP Project Code:	IP.2009.33011.004
EDCTP Project Start Date:	15 November 2010
EDCTP Project End Date:	31 October 2014
Collaborators:	• Aase Bengaard Andersen (Copenhagen University Hospital, Denmark) • Kathy Baisley (London School of Hygiene and Tropical Medicine (LSHTM), UK) • Muhammad Bakari (Muhimbili University College of Health Sciences, Tanzania) • Sekelani S. Banda (University of Zambia) • John Changalucha (National Institute for Medical Research, Tanzania) • Molly Chisenga (University Teaching Hospital, Zambia) • Yolanda Fernandez (LSHTM, UK) • Henrik Friis (Copenhagen University Hospital, Denmark) • Tsinuel Girma (Jimma University, Ethiopia) • Douglas Heimburger (Vanderbilt University, USA) • Samuel Kalluvya (Bugando Medical Centre, Tanzania) • Saidi Kapiga (LSHTM, UK) • Lackson Kasonka (University Teaching Hospital, Zambia) • Paul Kelly (Barts and The London School of Medicine and Dentistry, UK) • John Robert Koethe (Vanderbilt University, USA) • Natasha Larke (LSHTM, UK) • Hildah Banda Mabuda (University Teaching Hospital, Zambia) • Clemens Masesa (National Institute for Medical Research, Mwanza Centre, Tanzania) • Nick Paton (Medical Research Council, UK) • George Praygod (National Institute for Medical Research, Tanzania) • Joshua Siame (University Teaching Hospital, Zambia) • David Thurnham (University of Ulster, UK) • Andrew Tomkins (University College London, UK) • G Wandore (National Institute for Medical Research, Tanzania) • Suzanna Woodd (London School of Hygiene and Tropical Medicine, UK) • Daniel Yilma (Jimma University, Ethiopia)
Site Principal Investigator(s):	• Suzanne Filteau (UK) • Lackson Kasonka (Zambia) • John Changalucha (Tanzania)
Clinical Trial/Study Sponsor:	LSHTM (UK)
Trial/Study title:	Nutritional support for African adults starting antiretroviral therapy (NUSTART)
Goal:	The overall goal of the project is to improve health and survival of HIV-infected Africans by improving African clinicians' ability to research and manage nutritional problems. It will help African clinicians and government health managers integrate nutritional

	support into management of patients with HIV and improve understanding of: • How nutritional metabolism and status interact with HIV and associated infectious diseases • How to interpret research findings and bring them into policy and practice.
Primary Objective(s):	To decrease mortality between referral for ART and 12 weeks after starting ART by using a two-stage intervention to stabilize nutritional metabolism and initiate the return of appetite and weight recovery during the preparatory phase before starting ART and during the first 6 weeks of ART
Secondary Objective(s):	• By stabilising nutritional metabolism during the preparatory phase before starting ART and during the first 6 weeks of ART to: – decrease admission to hospital during the study period – increase BMI and lean body mass by 12 weeks – increase functional lean body mass as measured by grip strength – cause appetite to return more rapidly, enabling nutritional recovery – increase adherence to ART • To compare serum electrolyte shifts early in ART in patients given the vitamin-mineral supplements compared to those given placebo • To compare markers of iron status at 12 weeks in patients given the vitamin-mineral supplements compared to those given placebo.
Clinical Trial/Study site(s):	• University Teaching Hospital (Zambia) • National Institute for Medical Research (Tanzania)
Collaborating site(s):	• Barts & The London School of Medicine, London (UK) • Jimma University Specialised Hospital, Jimma (Ethiopia) • Mwanza Medical Research Centre, Mwanza City (Tanzania) • Odense University Hospital, Odense (Denmark) • University of Copenhagen, Copenhagen (Denmark) • University Teaching Hospital, Lusaka (Zambia) • Vanderbilt University, Nashville (USA)
Study design:	Phase III randomised controlled trial comparing in a two-stage protocol of vitamin and mineral supplements with placebo given from referral to ART until 6 weeks after starting ART. In the first stage the vitamins and minerals will be given with minimal calories, only as the lipid-based carrier, from referral to 2 weeks of ART and then the same nutrients or placebo will be given in a calorie-rich supplement, ready-to-use therapeutic lipid-based food (RUTF), from 2-6 weeks of ART. Although control paste and RUTF will be used, it may be hard to completely blind the taste of the micronutrients in the active preparations; however, our use of the hard primary endpoint of mortality limits potential bias.
Product(s):	Vitamin and mineral fortified lipid nutritional supplements (LNS) developed and produced by Nutriset, France
Manufacturer/Developer:	Nutriset, France
Cofunders:	• MRC (UK) • Nutriset (France) • London School of Hygiene and Tropical Medicine (LSHTM, UK) • Danish International Development Assistance (Danida, Denmark) • University Teaching Hospital (Zambia) • Vanderbuilt School of Medicine (USA)

	• Queen Mary & Westfield College, University of London (UK) • University of Copenhagen (Denmark)
Trial Registration number(s):	PACTR201106000300631
Status:	Ongoing
Results and Outcomes:	Recruitment and follow up are completed. Database closed January 2014
Total number of subjects (clinical trials only):	1814
PhD studies:	Title: Pharmacokinetic studies of first line anti-tuberculosis drugs, treatment outcome and associated factors among sputum smear Candidate: Jeremiah Kidola, University of Copenhagen, Tanzanian Dates: 1 January 2012-1 December 2013
	Title: Severe acute malnutrition in children: body composition and linear growth during rehabilitation Candidate:Tsinuel Girma, University of Copenhagen, Ethiopian Date: 1 July 2009-1 June 2013
	Title: Serum phosphate, vitamin D and renal function in HIV-infected patients initiating ART in Southwest Ethiopia Candidate: Daniel Yilma, University of Copenhagen, Ethiopian Date: 1 January 2012-1 January 2015
	Title: The Onset, Course and Outcome of Common Mental Disorder Symptoms in Adults Living with HIV/AIDS in Southwest Ethiopia: a hospital based cohort study Candidate: Markos Tesfaye, University of Copenhagen, Ethiopian Date: 1 January 2012-1 January 2015
	Title: Improving efficacy and safety of HIV treatment by nutritional supplementation: pharmacokinetical and virological aspects Candidate: Alemseged Lencho, University of Copenhagen, Ethiopian Date: 1 December 2010-1 December 2013
	Title: The effect of malnutrition on renal excretion of micronutrients and antiretroviral drugs among Zambian HIV/AIDs Patients Candidate: Derick Munkombwe, University Teaching Hospital, Zambian Date: 1 September 2012-1 August 2015
	Title: T cell subsets during nutritional supplementation of Zambian patients starting ART Candidate: Caroline Chisenga, University Teaching Hospital, Zambian Date: 1 May 2012-1 April 2015
MSc studies:	Title: MSc in Public Health Informatics Candidate: Aswile Jonas, Staffordshire University, Tanzanian Date: 1 October 2011-1 September 2014
	Title: MSc in Infectious Diseases Candidate: Joshua Siame, LSHTM, Zambian Date: 1 October 2011-1 September 2013
	Title: MSc in Public Health / Health Services Research Candidate: Lackson Kasonka, LSHTM, Zambian Date: 1 October 2012-1 September 2014

	Title: MSc in Infectious Diseases Candidate: Mutinta Muchimba, LSHTM, Zambian Date: 1 October 2012-1 September 2014
Postdoctoral fellow:	Title: Body composition following nutritional supplementation of malnourished patients starting ART. Candidate: George Proygood, LSHTM, Tanzanian Date: 1 November 2010-1 August 2012
Publications:	1. M Hebie, S Jungjohann, G Praygod, S Filteau. Acceptability of different lipid-based nutrient supplements for adults with HIV. Afr J Food Agriculture Nutr Devel; vol 13, Jan 2013

2.1.7 PROMPT

EDCTP Project Coordinator:	Joep Lange (University of Amsterdam, Netherlands)
EDCTP Call Title:	Call for the support of clinical trials, capacity building and networking on treatment of HIV/AIDS
EDCTP Project Title:	Prevention of early mortality by presumptive tuberculosis treatment in HIV-infected patients initiating antiretroviral therapy
EDCTP Project Code:	IP.2009.33011.007
EDCTP Project Start Date:	17 September 2010
EDCTP Project End Date:	1 July 2013
Collaborators:	• Jantje C. Bos (University of Amsterdam, Netherlands) • Frank Cobelens (University of Amsterdam, Netherlands) • Robert Colebunders (Prince Leopold Institute of Tropical Medicine, Belgium) • Josefo Joao Ferro (Catholic University of Mozambique) • Matthias Frank (University of Tübingen, Germany) • Martin Peter Grobusch (University of Amsterdam, Netherlands) • Moses Lutaakome Joloba (Ministry of Health, Uganda) • Ulrich Davy Kombila (Albert Schweitzer Hospital, Gabon) • Frank van Leth (KNCV Tuberculosis Foundation, The Netherlands) • Yukari C Manabe (Makerere University, Uganda) • Harriet Mayanja-Kizza (Makerere University, Uganda) • Roy Mugerwa (Makerere University, Uganda) • Olga Mogiyana Mzileni (University of Limpopo, South Africa) • Nadine Pakker (IATEC, Netherlands) • Jan Marinus Prins (University of Amsterdam, Netherlands) • Afsatou Ndama Traoré (Albert Schweitzer Hospital, Gabon) • William Ofuti Worodria (Makerere University, Uganda)
Site Principal Investigator(s):	• Yuka Manabe (Uganda) • William Ofuti Worodria (Uganda) • Josefo J. Ferro (Mozambique) • Mahomed Riaz Mobaracaly (Mozambique) • Afsatou Traore (Gabon) • Zinhle Makatini (South Africa)
Clinical Trial/Study Sponsor:	Academic Medical Center (AMC), University of Amsterdam (Netherlands)
Trial/Study title:	Prevention of early mortality by presumptive tuberculosis treatment in HIV infected patients initiating antiretroviral therapy
Goal:	The overall goal of the project is to evaluate a strategy for reducing early mortality during antiretroviral treatment in settings with high incidence of TB and limited facilities for diagnosing TB in symptomatic, severely immunosuppressed HIV-infected patients. The project also aims to identify the patients who would most benefit from this intervention.
Primary Objective(s):	1. To determine in a randomised-controlled trial whether TB treatment in HIV-infected patients with CD4<50 cells/µl and BMI<18 who do not have verifiable or suspected pulmonary TB at the time of ART initiation prevents early mortality, by comparing the death rate during the first 6 months among patients started on ART only with that among patients started on anti-TB treatment followed after 1-2 weeks by ART 2. To determine, by sputum culture, the prevalence of pulmonary TB disease at the time of ART initiation among HIV infected patients with CD4<50 cells/µl and BMI<18

	and cough, and to assess sensitivity and specificity of clinical predictors (symptoms, signs, laboratory parameters) for prevalent TB in this patient population 3. To assess the incidence of unmasking TB in the first 6 months of ART among HIV-infected patients with CD4<50 cells/µl and BMI<18 who do not have verifiable or suspected smear-negative TB at the time of ART initiation 4. To determine the sensitivity and specificity of clinical predictors (symptoms, signs, laboratory parameters) for incident unmasking TB, and the association in this patient population between unmasking TB and prevalent TB at the time of ART initiation 5. To assess, by post-mortem investigations, the causes of death among HIV-infected patients with CD4<50 cells/µl and BMI<18 who do not have verifiable or suspected smear-negative TB at the time of ART initiation in the two groups in the first 6 months after ART 6. To build or strengthen capacity in 4 sites in sub-Saharan Africa for clinical trials of therapeutic interventions of HIV and/or TB disease by infrastructural adjustments, training and supervised engagement in trial procedures with focus on ICH-GCP, data monitoring and management, and good (clinical) laboratory practice.
Secondary Objective(s):	1. CD4 T cell absolute increase 2. Causes of death 3. Safety and tolerability of anti-tuberculous medications 4. HIV viral suppression 5. TB incidence rates after ART initiation
Clinical Trial/Study site(s):	• Infectious Diseases Institute, Makerere University (Uganda) • Mulago National Referral Hospital, Kampala (Uganda) • Tshepang clinic Pretoria, Limpopo (South Africa) • George Mukhari Hospital, Pretoria, Limpopo (South Africa) • Catholic University of Mozambique • Research Center for Infectious Diseases (Mozambique) • Medical Research Unit, Albert Schweitzer Hospital (MRU-HAS, Gabon) • Satellite site - Lambarene General Hospital – HG (Gabon)
Collaborating site(s):	• Academic Medical Center, University of Amsterdam (Netherlands) • Amsterdam Institute for Global Health and Development, (Netherlands) • Catholic University of Mozambique • Infectious Diseases Institute, University Makarere (Uganda) Universitätsklinikum Institut für Tropenmedizin (Germany) • Institute of Tropical Medicine (Belgium) • Medical Research Unit, Albert Schweitzer Hospital (Gabon) • Ministry of Health (Mozambique) • University of Limpopo (South Africa)
Study design:	Phase III open-label randomised controlled trial. Consenting HIV-infected patients with CD4 T cell counts<50 cells/µl and with a body mass index (BMI)<18 will be randomised to: 1. Initiation of 4 drug TB treatment followed by ART (efavirenz-based) within 2 weeks (completion of 6 month full-course TB treatment) 2. ART (efavirenz-based) only (+ pyridoxine 50mg) given within 2 weeks after enrolment
Product(s):	• Antiretroviral treatment: Stavudine (d4T) or zidovudine (AZT)/lamivudine (3TC)/efavirenz (EFV) generic fixed dose

	combination will be administered according to country specific local guidelines. • Anti-tuberculosis treatment: Isoniazid (INH) 5 mg/kg, rifampin (RIF) 10 mg/kg, pyrazinamide (PZA) 10 mg/kg, and ethambutol (ETH) orally for 8 weeks (intensive phase) followed by INH and RIF (plus pyridoxine 50 mg) for an additional 4 months (continuation phase). Sites are given fixed drug combinations if they are available at the site. Although directly observed therapy would be optimal, other measures of drug adherence are used.
Manufacturer/Developer:	No specific manufacturer information is provided, but all drugs utilised in the study are available through national programmes.
Cofunders:	• Health Foundation (Netherlands) • Prins Leopold Instituut voor Tropische Geneeskunde (Belgium) • German Aerospace Center (PT-DLR, Germany) • German Ministry of Education (BMBF, Germany) • Academic Medical Center at the University of Amsterdam (Netherlands) • University of Antwerp (Belgium)
Trial Registration number(s):	NCT01417988
Status:	Terminated
Results and Outcomes:	Trial terminated – final close out report due Oct 2013
Total number of subjects (clinical trials only):	334 patients
PhD study:	Title: Prophylaxis and treatment of patients with Cryptococcal antigenemia and a CD4 count <100 cells/µL Candidate: Ndivhuho Makhado, University of Limpopo, South Africa Dates: 1 Jan 2011 – 30 Jun 2013
MSc study:	Masters in Public Health, Orientation Disease Control Candidate: Ndagire Gloria Kisake, Institute of Tropical medicine, Ugandan) Dates: 1 January 2011-30 June 2013
Publications:	1. Manabe Y, Worodria W, Cobelens F. Empirical tuberculosis treatment or improved diagnostics? Int J Tuberc Lung Dis 2012;16:280.

2.1.8 RAFA

EDCTP Project Coordinator:	Corinne Merle (London School of Hygiene and Tropical Medicine, UK)
EDCTP Call Title:	Call for the support of clinical trials, capacity building and networking on treatment of HIV/AIDS
EDCTP Project Title:	A randomised controlled trial of 3 strategies for the treatment of ARV naive HIV infected patients with tuberculosis – RAFA project
EDCTP Project Code:	IP.2009.33011.009
EDCTP Project Start Date:	21 January 2011
EDCTP Project End Date:	30 October 2014
Collaborators:	• Dissou Affolabi (Centre National Hospitalier de Pneumo-Phtisiologie, Benin) • Evelyne Akinocho (Programme National de Lutte contre le SIDA, Benin) • Severin Anagonou (Centre National Hospitalier de Pneumo-Phtisiologie, Benin) • Boubacar Bah (Hôpital National Ignace Deen, Guinea) • Bouke de Jong (Institute of Tropical Medicine, Belgium) • Mouctar Dialo (Hôpital National Ignace Deen, Guinea) • Awa Helene Diop (National Tuberculosis Control Program, Senegal) • Sian Floyd (London School of Hygiene and Tropical Medicine (LSHTM), UK) • Andre Furco (University College London, UK) • Katerina Tatiana Galperine (Tenon University Hospital, France) • Judith Glynn (LSHTM, UK) • Martin Gninafon (Centre National Hospitalier de Pneumo-Phtisiologie, Benin) • Anandi Martin (Institute of Tropical Medicine, Belgium) • Helen McIlleron (University of Cape Town, South Africa) • Alimatou N'Diaye (National Tuberculosis Control Program, Senegal) • N'Dira Sanoussi (Centre National Hospitalier de Pneumo-Phtisiologie, Benin) • Marie Sarr (National Tuberculosis Control Program, Senegal) • Oumou Younoussa Sow (Hôpital National Ignace Deen, Guinea) • Abdoulaye Sidibe Wade (Ministere de la sante et de la prevention medicale, Senegal)
Site Principal Investigator(s):	• Marie Saar (Senegal) • Oumou Bah-Sow (Guinea) • Martin Gninafon (Benin)
Clinical Trial/Study Sponsor:	LSHTM (UK)
Trial/Study title:	A randomised controlled trial of 3 strategies for the treatment of ARV naive HIV infected patients with tuberculosis – RAFA project
Goal:	To assess, using a three-arm approach, whether aggressive management of TB in HIV-infected patients during the 2 first months of TB treatment with a high dose of rifampicin might result in a decrease in the early HIV/TB mortality, without the negative effects of the early severe complications that can arise from the use of early ARV treatment.
Primary Objective(s):	1. To conduct a phase III randomised controlled trial to assess in ARV-naïve TB/HIV patients with CD4 counts more than 50 cells/mm3 and less than 350 cells/mm3 the efficacy in terms of morbidly and mortality of 3 treatment strategies:

	– Early ARV initiation (week 2) with a standard TB treatment – Delayed ARV treatment (week 8) with a standard TB treatment – Delayed ARV treatment (week 8) with high dose rifampicin during the intensive phase of TB treatment (15mg/Kg instead of 10 mg/Kg) and standard TB treatment in the continuation phase 2. To characterise anti-tuberculosis drug pharmacokinetics among HIV-TB co-infected patients, to assess treatment strategy-related sources of pharmacokinetic variation, and to evaluate differences in pharmacokinetics between patients with different treatment outcomes 3. To strengthen the research capacities of 3 well-established Tuberculosis Control Programmes to conduct clinical trials, through providing appropriate technology transfer and training (including 1 PhD program and 3 MSc programs), and guidance and mentoring from experienced researchers, in order to create sustainable research capacities 4. To reinforce the structures and to develop a West African clinical trial TB and TB/HIV network based around sites of excellence for field research in order that in the near future these sites are in a position to initiate, as well as to participate in, further international multicentre trials of new drugs or vaccines.
Clinical Trial/Study site(s):	• TB centres of MBAO and FAN hospital, Dakar (Senegal) • Pulmonary department of Igance Deen hospital and TB centre of Mattam, Conakry (Guinea) • National TB centre of Cotonou and the TB centre of Porto Novo (Benin)
Collaborating site(s):	• LSHTM, London (UK) • UCL, London (UK) • UCT, Rondebosch (South Africa) • Centre Hôspitalier de Pneumo-Phtisiologie, Cotonou (Benin) • CHU Ignace Deen, Service de Pneumo Phtisiologie, Conakry (Guinea) • National TB control Program (NTCP), Dakar (Senegal) • Hôpital Tenon, Paris (France) • Prince Leopold Tropical Institute of Medicine of Antwerp (Belgium)
Study design:	Phase III open-label multicentre randomised controlled trial with three arms. This trial includes as well a nested pharmacokinetic (PK) study in a sub-sample of patients. Subjects will be randomised to receive either arm A, B or C treatment regimen. The treatment schedule is as follows: • Early ARV initiation (after week 2 of TB treatment) combined with standard TB treatment • Delayed ARV treatment (after 8 weeks of TB treatment) combined with standard TB treatment • Delayed ARV treatment (after 8 weeks of TB treatment) combined with a high dose of rifampicin during the intensive phase of TB treatment (15mg/Kg instead of 10 mg/Kg) and standard TB treatment in the continuation phase 375 adult male or female patients in each arm will be recruited (1125 patients in total). Among these, 300 patients will be selected to contribute to the population PK study.
Product(s):	**Early ARV:**

	TB: Isoniazid, Rifampicin (10 mg/kg), Pyrazinamide and Ethambutol during 2 months / followed by Rifampicin (10 mg/kg) andIsoniazid treatment in the continuation treatment phase HIV: 2 nucleoside Reverse Transcriptase Inhibitor (NRTI) + Efavirenz (600mg) initiated 2 weeks after initiating TB treatment **Delayed ARV:** TB: Isoniazid, Rifampicin (10 mg/kg), Pyrazinamide and Ethambutol during 2 months / followed by Rifampicin (10 mg/kg) and Isoniazid treatment in the continuation treatment phase HIV: 2 NRTI + Efavirenz (b) (600 mg) initiated 2 months after initiating TB treatment **High dose Rifampicin:** TB: Isoniazid, Rifampicin (15 mg/kg), Pyrazinamide and Ethambutol during 2 months / followed by Rifampicin (10 mg/kg) and Isoniazid treatment in the continuation treatment phase HIV: 2 NRTI + Efavirenz (b) (600 mg) initiated 2 months after initiating TB treatment
Manufacturer/Developer:	All drugs utilised in the study are available through national programmes.
Cofunders:	• Prince Leopold Institute of Tropical Medicine (Belgium) • MRC (UK) • Centre Hôspitalier de Pneumo-Phtisiologie (Benin) • National TB Control Program (Senegal)
Trial Registration number(s):	PACTR201105000291300
Status:	Ongoing
Results and Outcomes:	The trial is recruiting.
Total number of subjects (clinical trials only):	780 patients
PhD study:	Title: Assessing the impact on the patient's outcome, acceptability, costand cost effectiveness of the intervention for reduction of early mortality among HIV infected individuals on ART in Tanzania and Zambia (LSHTM) Candidate: University of Cape Town, South Africa Dates: September 2012-December 2013
MSc studies:	Title: MSc Clinical Trial by Distance learning Candidate:N'Dira Sanoussi, LSHTM, Benin Dates: Sepember 2011-October 2013
	Title: MSc Clinical Trial by Distance learning Candidate: Moubacar Bah, LSHTM, Senegalese Dates: September 2011-Octtober 2013
	Title: MSc Clinical Trial by Distance learning Candidate: Alimatou Ndiaye, LSHTM, Senegalese Dates: September 2011-October 2013
Publications:	

2.1.9 REMSTART

EDCTP Project Coordinator:	Saidi Egwaga (Tanzanian Ministry of Health and Social Welfare, Tanzania)
EDCTP Call Title:	Call for the support of clinical trials, capacity building and networking on treatment of HIV/AIDS
EDCTP Project Title:	Reduction of early mortality among HIV-infected subjects starting antiretroviral therapy: a randomised trial (The REMSTART trial)
EDCTP Project Code:	IP.2009.33011.003
EDCTP Project Start Date:	7 March 2011
EDCTP Project End Date:	30 November 2014
Collaborators:	• Shabir Banoo (Management Sciences for Health, South Africa) • Christian Bottomley (London School of Hygiene and Tropical Medicine (LSHTM), UK) • Jeremiah Chakaya (Kenya Medical Research Institute, Kenya) • Lorna Guinness (LSHTM, UK) • Thomas Harrison (St. George's University of London, UK) • Jaffar, Shabbar (LSHTM, UK) • Moses Joloba Lutaakome (Ministry of Health, Uganda) • Lars Lindqvist (Karolinska Institute, Sweden) • Sayoki Mfinanga (National Institute for Medical Research, Tanzania) • Peter Mwaba (University of Zambia) • Philip C. Onyebujoh (WHO, Switzerland) • Alex Pym (Medical Research Council, South Africa) • Giorgio Roscigno (Foundation for Innovative New Diagnostics (FIND), Switzerland) • Mahnaz Vahedi (WHO, Switzerland) • Alimuddin Zumla (University College London, UK)
Site Principal Investigator(s):	• Peter Mwaba (Zambia) • Sayoki G Mfinanga (Tanzania)
Clinical Trial/Study Sponsor:	LSHTM (UK)
Trial/Study title:	Reduction of early mortality among HIV-infected subjects starting antiretroviral therapy: a randomised trial (The REMSTART trial)
Goal:	To evaluate a health service strategy for reducing the high early mortality associated with antiretroviral therapy in Africa. The strategy involves: accelerated initiation of ART when patients with very advanced disease present to clinic; increased involvement of lay-workers in adherence; increased frequency of diagnostic testing for cryptococcal meningitis and tuberculosis. A simple and large trial – "lean and mean" will be conducted.
Primary Objective(s):	The primary objective of the trial are to determine the effects of the intervention, accelerated initiation of ART and enhanced monitoring, support and diagnostics just before and during the first 4-6 weeks of therapy, as compared with standard care. The primary endpoint will be all-cause mortality up to 12 months after enrolment into the study. Other objectives are: 1. To develop capacity in population-based research, with a special focus on training PhD students in epidemiology and health economics. The overall goal is to train population-based research leaders of the future 2. To strengthen the capacity of the health hospital centres

	in clinical care and diagnostics through the conduct of research 3. To increase linkages between the different partners such that this consortium can bid for funding in clinical and health services research.
Secondary Objective(s):	1. To determine the costs incurred by the health service with this intervention strategy (in relation to standard care) and to relate these to the survival. To determine also the costs associated with accessing care for patients in the two arms of the trial 2. To determine the effects of the intervention on patient retention, hospital admissions, outpatient attendance as compared to standard care 3. To determine the uptake of voluntary counselling and testing services and simple tuberculosis screening among family members of patients on antiretroviral therapy.
Clinical Trial/Study site(s):	• Temeke, Amana and Mwanayamala sites, Dar es Salaam (Tanzania) • Kayama, Matero, Chipata, George, Chelstone sites, Lusaka (Zambia)
Collaborating site(s):	• Karolinska University Hospital, Huddinge (Sweden) • LSHTM (UK) • Ministry of Health (Zambia) • Ministry of Health and Social Welfare (Tanzania) • Special Programme for Research and Training in Tropical Disease (TDR, Switzerland) • St Georges Medical School (UK) • Unit for Tuberculosis Research, South African Medical Research Council (South Africa) • University of Zambia
Study design:	Phase III open-label randomised controlled trial. An estimated 2500 HIV-infected adults with CD4 count<100 cells per microlitre will be randomised to the intervention or the standard of care and followed up for 12 months.
Product(s):	Standard treatments for HIV, TB, cryptococcal meningitis will be used in this study. These are approved by WHO and are available through national programmes.
Manufacturer/Developer:	All drugs used in the study are available through national programmes as essential drugs.
Cofunders:	• Karolinska University Hospital (Sweden) • LSHTM (UK) • Ministry of Health (Zambia) • Ministry of Health and Social Welfare (Tanzania) • MRC (UK) • WHO Tropical Diseases Research (Switzerland)
Trial Registration number(s):	ISRCTN20410413 PACTR201112000327297
Status:	Ongoing
Results and Outcomes:	
Total number of subjects (clinical trials only):	2300 patients
PhD study	Title: The Outcomes of pre-ART individual and Cost and cost-effectiveness of involvement of lay workers, improved screening of opportunistic infections, and accelerated initiation of ARV among ARV naïve individuals in Tanzania Candidate: Godfather Kimaro, LSHTM, Tanzian
Publications:	

2.1.10 Kesho Bora study

EDCTP Project Coordinator:	Marie Louise Newell (Africa Centre for Health and Population Studies, South Africa)
EDCTP Call Title:	Support of studies for the Prevention of Mother to Child Transmission of HIV, including prevention of transmission during breast feeding
EDCTP Project Title:	Impact of HAART during Pregnancy and Breastfeeding on MTCT and Mother's Health: The Kesho Bora Study
EDCTP Project Code:	CT.2006.33020.007
EDCTP Project Start Date:	12 June 2007
EDCTP Project End Date:	30 November 2010
Collaborators:	• Siva Danaviah (University of KwaZulu-Natal, South Africa) • Stanley Luchters (University of Ghent, Belgium) • Stephen Mepham (Africa Centre for Health and Population Studies, South Africa) • Kevi Naidu (University of KwaZulu-Natal, South Africa) • Marcel Reyners (ICRH-International Centre of Reproductive Health, Netherlands) • Nigel Campbell Rollins (Africa Centre for Health and Population Studies, South Africa)
Site Principal Investigator(s):	• Marie Louise Newell (South Africa) • Nigel Rollins (South Africa) • Stanley Luchters (Kenya) • Marcel Reyners (Kenya) • Ruth Nduati (Kenya) • Nicolas Meda (Burkina Faso)
Clinical Trial/Study Sponsor:	World Health Organization (WHO, Switzerland)
Trial/Study title:	Impact of Highly Active Anti-Retroviral Therapy (HAART) during Pregnancy and Breastfeeding on Mother-To-Child-Transmission of HIV and Mother's Health: The Kesho Bora Study
Goal:	The overall goal of the study was to optimise the use of Anti-Retroviral (ARV) drugs during the antepartum, intrapartum and postpartum periods to prevent Mother-To-Child Transmission (MTCT) of Human Immunodeficiency Virus (HIV) type-1 and preserve the health of the mother in settings where the majority of HIV-positive women breastfeed.
Primary Objective(s):	The primary objectives of the prospective cohort study are to describe the rates and correlates of acquired immune deficiency syndrome (AIDS)-free maternal survival and HIV-free child survival among HIV-positive pregnant women and their children receiving care at participating clinical centres, and to assess the acceptability and safety of ARVs offered to these women and children according to World Health Organization (WHO) guidelines. The primary objectives of the randomised controlled trial among women with CD4+ cell counts in the range 200-500 cells/mm3 are to compare the efficacy and safety of the triple-ARV MTCT-prophylaxis regimen with that of the short-course MTCT-prophylaxis regimen with regard to: • HIV-free infant survival at 6 weeks (in utero/intrapartum/early postpartum) and 12 months among all infants, irrespective of mode of infant feeding (intent-to-treat analysis) • AIDS-free survival of mothers at 12 months following delivery • HIV-free infant survival at 12 months among infants who received any breast milk • Incidence of serious adverse events in mothers.

Secondary Objective(s):	1. Assess HIV-free survival at birth, 2 weeks, 6 weeks, 6 months, 9 months (a point when all breast feeding is likely to have ceased) and 12 months of age among all enrolled children 2. Estimate the rates of early and late postpartum transmission in ever breastfed infants, according to maternal HIV status and treatment received 3. Describe the correlates of infant HIV-free survival including stage of maternal HIV disease (clinical, immunological and virological factors), ARV prophylaxis and/or therapy given to the mother, and mode of infant feeding 4. Describe the correlates of mother's HIV disease progression and survival including socio-demographic characteristics, disease and nutritional status at enrolment, ARV prophylaxis and/or therapy given to the mother, and mode of infant feeding 5. Identify immunological and virological determinants of residual HIV-1 transmission during breastfeeding 6. Describe and compare the feasibility, acceptability, safety, tolerability of and adherence to the maternal ARV prophylaxis 7. Describe the feasibility and acceptability of current UNAIDS/UNICEF/WHO recommendations on HIV and infant feeding 8. Assess the feasibility and safety of rapid weaning over a two week period with complete cessation of breastfeeding by 6 months of age, and assess nutritional status and growth of children up to two years of age 9. Describe changes in viral load and emergence of viral resistance in blood and breast milk according to the maternal ARV prophylaxis and therapy regimens and immunological and virological status at enrolment 10. Describe the extent of partner involvement, family planning practices, condom use and sexual activity of couples 11. Describe and analyse the social and cultural factors that may increase or reduce HIV rates of transmission through breastfeeding 12. Describe family HIV-care needs and accessibility of HIV-care services 13. Assess the cost-effectiveness of the ARV prophylaxis and therapy regimens in preventing MTC.
Clinical Trial/Study site(s):	• KwaZulu-Natal University Health (Pty) Ltd (South Africa) • Durban and University of KwaZulu-Natal Mtubatuba (South Africa), University of Nairobi, Nairobi (Kenya) • International Centre for Reproductive Health (ICRH), Mombasa (Kenya) • Centre MURAZ, Bobo Dioulasso (Burkina Faso)
Collaborating site(s):	• Africa Centre for Health and Population Studies, University of KwaZulu-Natal, Mtubatuba (South Africa) • KwaDabeka site, University of KwaZulu-Natal University Health (Pty) Ltd., Durban (South Africa) • International Centre for Reproductive Health, ICRH, Mombasa (Kenya) • University of Nairobi, Nairobi (Kenya), Centre MURAZ, Bobo Dioulasso (Burkina Faso) • Centre de Recherche Cultures, Santé, Sociétés, Aix-en-Provence (France), CHR Montpellier (France) • Institut de Recherche pour le Développement (IRD)

	Montpellier (France) • International Centre for Reproductive Health, Ghent (Belgium)
Study design:	Phase IV randomised controlled trial. Eligible women with CD4+ cell count between 200 and 500 cells/mm3 with no contraindication and willing to be randomised will receive one of two different regimens for MTCT prevention: • A triple-ARV regimen (ZDV, 3TC and LPV/r) beginning at 34-36 weeks gestation, through delivery, until six months postpartum; or • A short-course regimen consisting of ZDV beginning at 34-36 weeks gestation until the onset of labour, plus one dose of ZDV and one dose of NVP at the onset of labour All infants born to women enrolled in either part of the study will receive one dose of NVP within 72 hours of birth. All enrolled women and their HIV-infected children whose HIV disease progresses to the point of meeting WHO criteria for treatment will be offered HAART provided they do not have any contraindications to initiating HAART.
Product(s):	• Zidovudine (ZDV) • Lamivudine (3TC) • Lopinavir/ritonavir (LPV/r) • Nevirapine (NVP)
Manufacturer/Developer:	• Cipla Pharmaceuticals Ltd • Abbot Laboratories
Cofunders:	• Belgium Cooperation (Belgium) • Centre for Disease Control (CDC, USA) • Department for International Development [DFID] (UK) • French National Agency for Research on AIDS and Viral Hepatitis [ANRS] (France) • GlaxoSmithKline Foundation • National Institutes of Health (NIH, USA) • Thrasher Research Foundation (USA) • World Health Organization [WHO] (Switzerland)
Trial Registration number(s):	ISRCTN 71468401
Status:	Completed
Results and Outcomes:	The findings of this study, known as the Kesho Bora Study, showed that triple ART during pregnancy and breastfeeding is safe and reduces the risk of HIV transmission to infants. These results led to the revision of the WHO guidelines on prevention of HIV infection in pregnant women, mothers and their infants. WHO now recommends ART for all pregnant women infected with HIV who have CD4 counts of 350 cells per µL or less, and antiretroviral prophylaxis during breastfeeding either to the women not on ART or to the infant.
Total number of subjects (clinical trials only):	845
PhD study	Title: Primary HIV in Pregnancy and its impact on mother-to-child transmission Candidate: Stephen Mepham (Africa Center, South Africa and Aberdeen University, UK) Dates: 2 January 2008 – 30 September 2011
Other/Sub-studies:	Primary HIV in pregnancy and its impact on mother-to-child transmission
Publications:	1. Arrivé E, Kyabayinze DJ, Marquis B, Tumwesigye N, Kieffer MP, Azondekon A, Wemin L, Fassinou P, Newell ML, Leroy V, Abrams EJ, Cotton M, Boulle A, Mbori-Ngacha D and Dabis F; KIDS-ART-LINC Collaboration. Cohort profile: the

paediatric antiretroviral treatment programmes in lower-income countries (KIDS-ART-LINC) collaboration. *Int J Epidemiol.* 2008; 37(3):474-480
2. Rouet F, Foulongne V, Viljoenc J, Steegen K, Becquart P, Valéa D, Danaviah S, Segondy M, Verhofstede C, Van de Perre P, and the WHO/ANRS 1289 Kesho Bora Study Group. Comparison of the Generic HIV Viral Load® assay with the Amplicor™ HIV-1Monitor v1.5™ and Nuclisens HIV-1 EasyQ® v1.2 techniques for plasma HIV-1 RNA quantitation of non-B subtypes: The Kesho Bora preparatory study. *J. Virol. Methods* 2010; 163(2):253-7
3. Mepham SO, Bland RM and Newell ML. Prevention of mother-to-child transmission of HIV in resource-rich and -poor settings. *International Journal of Obstetrics and Gynaecology* 2010; 118(2): 201-218
4. Kesho Bora Study Group (Newell ML). Eighteen-Month Follow-Up of HIV-1–Infected Mothers and Their Children Enrolled in the Kesho Bora Study Observational Cohorts. *J Acquir. Immune Defic. Syndr*. 2010; 54(5): 533-541
5. The Kesho Bora Study Group (authors include Mepham S, Naidu K and Newell ML). 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* 2011; 11(3): 171-180
6. The Kesho Bora Study Group (authors include Mepham S, Naidu K and Newell ML). Safety and effectiveness of antiretroviral drugs during pregnancy, delivery and breastfeeding for prevention of mother-to-child transmission of HIV-1: The Kesho Bora Multicentre Collaborative Study rationale, design, and implementation challenges.*). Contemporary Clinical Trials* 2011; 32: 74–85
7. Mepham S, Zondia Z, Mbuyazia A, Mkhwanazi N and Newell ML. Challenges in PMTCT antiretroviral adherence in northern KwaZulu-Natal, South Africa. *AIDS Care* 2011; 23(6): 741-747
8. Irungu E, Chersich MF, Sanon C, Chege R, Gaillard P, Temmerman M, Read JS, Luchters S. Changes in sexual behaviour among HIV-infected women in west and east Africa in the first 24 months after delivery. *AIDS* 2012; 26(8): 997-1007
9. Fao P, Fao P, Ky-Zerbo O, Gouem C, Somda P, Hien H, Ouedraogo PE, Kania D, Sanou A, Kossiwavi IA, Sanogo B, Ouedraogo M, Siribie I, Valea D, Ouedraogo S, Some R, Rouet F, Rollins N, McFetridge L, Naidu K, Luchters S, Reyners M, Irung for the Kesho Bora Study Group. Maternal HIV-1 Disease Progression 18-24 Months Postdelivery According to Antiretroviral Prophylaxis Regimen (Triple-Antiretroviral Prophylaxis During Pregnancy and Breastfeeding vs Zidovudine/Single-Dose Nevirapine Prophylaxis): The Kesho Bora Randomised. *Clinical Infectious Diseases* 2012; 55: 449-460
10. 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. Infant Feeding Modes and Determinants Among HIV-1–Infected African Women in the Kesho Bora Study. *J Acquir. Immune Defic. Syndr.* 2013; 62(1): 109–118

2.1.11 ComTru Study

EDCTP Project Coordinator:	Terese Lea Katzenstein (University Hospital Copenhagen, Denmark)
EDCTP Call Title:	Support of studies for the Prevention of Mother to Child Transmission of HIV, including prevention of transmission during breast feeding
EDCTP Project Title:	Backup with Combivir (AZT/3TC) or single dose Truvada (FTC/TDF) in order to avoid Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI) resistance after single dose Nevirapine for the prevention of mother-to-child transmission (MTCT)
EDCTP Project Code:	CT.2006.33020.001
EDCTP Project Start Date:	29 October 2007
EDCTP Project End Date:	31 January 2012
Collaborators:	• Mercy Chiduo (National Institute for Medical Research (NIMR), Tanzania) • Leo Flamholc (University Hospital of Malmoe, Sweden) • Jan Gerstoft (University Hospital Copenhagen, Denmark) • Martha Lemnge (National Institute for Medical Research (NIMR), Tanzania) • Godfrey Mgaya (Makorora Health Centre, Tanzania) • Margareth Mhando (Bombo Regional Hospital, Tanzania) • Alice Mliga (Ngamiani Health Centre, Tanzania) • Frederick Mtatifikolo (Bombo Regional Hospital, Tanzania) • Tine Strand (University Hospital Copenhagen, Denmark) • Zahra Theilgaard (Copenhagen University Hospital, Denmark)
Site Principal Investigator(s):	• Terese Lea Katzenstein (Denmark) • Tine Strand/Zahra Theilgaard (Denmark) • Celine Mandara (Tanzania) • Mercy G Chiduo (Tanzania) • Martha Lemnge (Tanzania)
Clinical Trial/Study Sponsor:	Rigshospitalet (Denmark)
Trial/Study title:	Backup with Combivir (AZT/3TC) or single dose Truvada (FTC/TDF) in order to avoid Non Nucleoside Reverse Transcriptase Inhibitor (NNRTI) resistance after single dose Nevirapine for the prevention of mother-to-child transmission (MTCT)
Goal:	The aim of the study is to find short course alternatives to single dose (sd) nevirapine for the prevention of mother-to-child HIV-transmission with the same or better degree of transmission protection than single dose nevirapine but with less NNRTI resistance development.
Primary Objective(s):	1. To assess the efficacy of zidovudine (ZDV) from week 28 with single dose Nevirapine plus 7 days Combivir and Zidovudine from week 28 with single dose Nevirapine plus single dose Truvada for the prevention of vertical transmission of HIV-1 from pregnant women to neonates in Tanzania 2. To assess Truvada to the same extent as Combivir reduces the risk of NNRTI resistance after single dose Nevirapine given during delivery compared to historical controls. Main study end points will be differences between the study groups in: • HIV-1 infection of neonates at age 6-8 weeks measured by HIV-RNA • NNRTI-associated resistance mutations K103N and Y181C in mothers and children at 6-8 weeks postpartum detected by

	sensitive assays.
Secondary Objective(s):	1. Monitor acceptance of VCT and participation among pregnant women in Tanga, Tanzania 2. Monitor ZDV adherence from initiation at 28 weeks or as soon as possible thereafter, until delivery, through measurement of MCV, self-reported adherence questioning and comparison with pharmacy records 3. Evaluate heat dissociation-boosted (HDB) p24-antigen ultra sensitive assay for diagnosis of HIV-1 infection and quantification of viral load for infants by birth, week six-eight and month nine and for women at enrolment, delivery, day seven, week six-eight and month nine, using HIV-RNA as reference 4. Determine side effects of the medications 5. Assessment of compliance between the two treatment groups 6. Determine HIV-1 subtypes and correlation to risk of MTCT and NNRTI resistance at birth, week six-eight and month nine for each of the subtypes A, C and D, which are expected to account for one third each 7. Determine blood and breast milk drug levels of Nevirapine in the woman at day one, day seven and week 6-8 and relations to development of NVP resistance among the subtypes A, C and D 8. Measure breast milk HIV-RNA day seven, week six-eight and month nine and correlated to postpartum MTCT at week six-eight and month nine 9. Compare HIV-1 RNA levels in vaginal secretion and the risk of HIV-1 MTCT at birth among subtypes A, C and D 10. Investigate successful referral and retention rates at CTC through close collaboration with the staff at CTC examination of the patient database at CTC.
Clinical Trial/Study site(s):	• Ngamiani and Makorora Health Centres (Tanzania) • Bombo Regional Hospital (Tanzania) • National Institute of Medical Research (Tanzania)
Collaborating site(s):	• University of Copenhagen (Denmark) • University Hospital of Malmoe (Sweden) • National Institute of Medical Research (Tanzania) • Bombo Hospital (Tanzania) • Kilimanjaro Christian Medical College [KCMC] (Tanzania)
Study design:	Phase III open-label randomised controlled trial with two arms. Women are 1:1 randomly assigned to National guideline pre/intra/postpartum including sd-Nevirapine and Combivir or to National guideline prepartum followed by sd-Nevirapine and Truvada. Thus all women will receive Zidovudine from week 28 of pregnancy or as soon as possible thereafter. **Arm 1: National guideline pre/intra/postpartum:** AZT 300 mg BD from 28 weeks. Intrapartum: sdNVP 200 mg at the onset of labour. AZT 300mg and 3TC 150 mg at the onset of labour. Continue AZT every 3 hours and 3TC every 12 hours until delivery. During the postpartum period: Combivir (AZT 300 mg and 3TC 150 mg) BD for 7 days. **Arm 2: National guidelines prepartum:** AZT 300 mg BD from 28 weeks. Intrapartum: sdNVP 200 mg and sdTruvada (300 mg Tenofovir and 200 mg Emtricitabine).

	Children will receive sd NVP syrup (2 mg/kg) and AZT syrup (4 mg/kg BD) according to the national guidelines.
Product(s):	• Zidovudine and Lamivudine (Combivir) • Emtricitabine and Tenofovir (Truvada)
Manufacturer/Developer:	• GlaxoSmithKline • Gilead
Cofunders:	• University Hospital Copenhagen (Denmark) • Statens Serum Institute and Novo Nordisk (Denmark) • University Hospital Malmo and Swedish Orphan (Sweden) • Bjorn Astrups Foundation (Denmark) • Jens Christensen and Wife Korna Christensen Foundation (Denmark)
Trial Registration number(s):	NCT 00346567
Status:	Completed
Results and Outcomes:	A summary of the major findings are given below: • Mother-to-child transmission rates at 6-8 weeks: Combivir arm = 5.8%, Truvada arm = 5.6% (RR =1.0 95%CI = 0.4 – 2.4.) • Mother-to-child transmission rates at 9 months: Combivir arm= 9.5%, Truvada arm = 11.7% (RR = 1.2, 95% CI = 0.6 – 2.6) • NNRTI resistance data are being finalized. We expect these analyses to be completed by August 2012 • P24 antigen for early infant diagnosis compared to HIV RNA PCR: the sensitivity of the p24 antigen analysis was found to be 33% at birth, 80% at week SEW and 100% at month nine (Table 3). The specificity was found to be 94%, 99% and 97% at birth, SEW weeks and nine months respectively (Table 3). The overall sensitivity and specificity was found to be 79% and 97%, respectively • STIsHIV-infected women had significantly higher prevalence of trichomoniasis (18.8% versus 5.0%; P, 0.003) and candidiasis (16.5% versus 2.0%; P, 0.001) while the higher rate of gonorrhoea (3.5% versus 0%; P ¼ 0.095) was not statistically significant when compared with HIV-uninfected women. There were no statistically significant differences in prevalence of chlamydial infection (0% versus 3.0%; P ¼ 0.156) or syphilis (2.4% versus 3.0%; P ¼ 1) between HIV-infected and uninfected women. Other STIs were common in both HIV-infected and uninfected pregnant women • Stigma is highly prevalent in Tanga, and a major contributing factor to attrition from ART for women.
Total number of subjects (clinical trials only):	Mother-infant pairs 450 planned, 566 recruits, 288 mother-infant pairs evaluated
PhD studies:	Title: Antiretroviral Therapy for Women in a resource-limited setting – success, efficacy and challenges Candidate: Zahra Theilgaard (University of Copenhagen, Denmark) Date: 1 January 2009-28 February 2013
	Title: Levels of Zidovudine in Cervico-vaginal secretions and Sexual Transmitted Infections in relation to Mother-to-child transmission of HIV among pregnant women in Tanga north-eastern Tanzania Candidate: Mercy Chiduo (University of Copenhagen, Denmark and NIMR, Tanzania) Dates: 1 January 2009-February 2014
MSc study:	Title: Exploring how community leaders perceive the effects of antiretroviral treatment: A grounded theory study in Tanga,

	Tanzania Candidate: Christiane Pahl (MSc in Public Health at the Lund University, Sweden) Dates: 1 January 2008-1 December 2010
Publications:	1. Arreskov A, Minja E, Theilgaard Z, Mandara C, Gerstoft J, Lemnge M, Katzenstein TL. Referral success among HIV-infected women and HIV-exposed children referred for monitoring and treatment in Tanga, Tanzania. *International Health* 2010; 2(1): 36-41 2. Salado-Rasmussen K, Theilgaard ZP, Chiduo M, Pedersen C, Gerstoft J, Katzenstein TL. Good performance of an immunoassay based method for nevirapine measurements in human breast milk. *Clin Chem Lab Med* 2011; 49(7): 1171-5. 3. Chiduo M, Theilgaard ZP, Bakari V, Mtatifikolo F, Bygbjerg I, Flanholc L, Gerstoft J, Christiansen CB, Lemnge M, Katzenstein TL. Prevalence of Sexually Transmitted Infections among women attending antenatal clinics in Tanga, north eastern Tanzania. *International Journal of STD & AIDS* 2012; 23: 325-329

2.1.12 VITA Studies

EDCTP Project Coordinator:	Elton R. Kisanga (Kilimanjaro Christian Medical Centre (KCMC), Tanzania)
EDCTP Call Title:	Support of studies for the Prevention of Mother to Child Transmission of HIV, including prevention of transmission during breast feeding
EDCTP Project Title:	The effect of single dose carbamazepine on the pharmacokinetics of single dose nevirapine (VIramune®, NVP) and development of NVP resistance for the prevention of mother-to-child transmission in TAnzania & Zambia (VITA studies)
EDCTP Project Code:	CT.2006.33020.006
EDCTP Project Start Date:	15 October 2007
EDCTP Project End Date:	30 September 2012
Collaborators:	• David Marinus Burger (Radboud University Nijmegen, Netherlands) • Catherine Chunda (University Teaching Hospital, Zambia) • Quirine Fillekes (Radboud University Nijmegen, Netherlands) • Diana Mary Gibb (Medical Research Council, UK) • Chipepo Kankasa (University Teaching Hospital, Zambia) • Eva P Muro (Kilimanjaro Christian Medical Centre (KCMC), Tanzania) • Werner Schimana (Kilimanjaro Christian Medical Centre (KCMC), Tanzania) • Margaret Thomason (Medical Research Council, UK) • Andreas van der Ven (Radboud University Nijmegen, Netherlands) • Ann Sarah Walker (Medical Research Council, UK) • Leszek Wojnowski (The Johannes Gutenberg University Mainz, Germany)
Study/Trial 1	**VITA 1 study**
Site Principal Investigator(s):	• Elton R. Kisanga (Tanzania) • David Burger (Netherlands) • Chipepo Kankasa (Zambia) • Diana Gibb (UK)
Clinical Trial/Study Sponsor:	Radboud University Nijmegen Medical Centre (RUNMC, Netherlands)
Trial/Study title:	The effect of single dose carbamazepine on the pharmacokinetics of single dose nevirapine (VIramune®, NVP) and development of NVP resistance, PMTCT program of Moshi, TAnzania (VITA1)
Goal:	Test the hypothesis that single dose carbamazepine decreases development of resistance to nevirapine (NVP) in HIV-positive pregnant Tanzanian women by decreasing NVP half-life.
Primary Objective(s):	1. To determine the pharmacokinetics of single dose nevirapine in HIV seroconverted pregnant women and their newborns 2. To determine the effect of single dose carbamazepine on the pharmacokinetics of single dose nevirapine in HIV seroconverted pregnant women and their newborns 3. To determine resistance against nevirapine in women before and after a single dose of nevirapine or a single dose of nevirapine/carbamazepine 4. Follow-up of newborns with focus on the HIV status, resistance and toxicity 5. To examine the possible relation between nevirapine levels in cord blood and plasma (of both mother and child) just after delivery and the HIV status of the newborn.
Secondary Objective(s):	1. To determine the safety of single dose nevirapine and single

	dose nevirapine/carbamazepine.
Clinical Trial/Study site(s):	Majengo Antenatal Clinic and Kilimanjaro Christian Medical Centre (Tanzania)
Collaborating site(s):	• Kilimanjaro Christian Medical Centre (Tanzania) • University Teaching Hospital (Zambia) • Radboud University Nijmegen Medical Centre (Netherlands) • Medical Research Council (UK)
Study design:	Phase IIa open-label randomised pharmacokinetic trial with two arms. **Arm 1 (Active Comparator):** An oral dose of 400 mg carbamazepine is added to the 200 mg oral dose nevirapine intake prior delivery. **Arm 2 (Placebo Comparator):** Standard therapy of 200 mg nevirapine oral prior to delivery.
Product(s):	• Taver® (Carbamazepine) • Viramune ® (Nevirapine, NVP) tablets & oral suspension
Manufacturer/Developer:	• Medochemie Ltd. • Boeringer Ingelheim
Cofunders:	• NACCAP (Netherlands) • Medical Research Council (MRC, UK)
Trial Registration number(s):	NCT 00294892
Total number of subjects (clinical trials only):	144 mother-infant pairs
Status:	Completed
Results and Outcomes:	The results of the VITA1 shows that addition of single-dose carbamazepine to single-dose nevirapine at labour onset in HIV-infected, pregnant women did not affect nevirapine plasma concentration at delivery, but significantly reduced it one week postpartum, with a trend towards fewer nevirapine resistance mutations, although missing samples reduced power to reach statistical significance.
Study/Trial 2	**VITA 2 study**
Site Principal Investigator(s):	• Elton R. Kisanga (Tanzania) • Werner Schimana (Tanzania) • David Burger (Netherlands) • Andreas J. van der Ven (Netherlands)
Clinical Trial/Study Sponsor:	Radboud University Nijmegen Medical Centre (Netherlands)
Trial/Study title:	The effect of phenytoin on the pharmacokinetics of nevirapine and the development of nevirapine resistance after a single dose nevirapine (VIramune®), which is part of ARV prophylaxis for PMTCT in Moshi, TAnzania, and in Lusaka, Zambia (VITA2 Trial)
Goal:	To test the hypothesis that phenytoin reduces the elimination half-life of SD NVP and thereby decreases development of resistance to NVP in HIV positive pregnant Tanzanian and Zambian women
Primary Objective(s):	1. To determine the elimination half-life of NVP in HIV positive pregnant women receiving it as a single dose in labour in addition to the ZDV and 3TC with or without seven days phenytoin (pilot PK phase) 2. To determine NVP resistance in HIV positive pregnant women receiving it as a single dose in labour in addition to ZDV and 3TC with or without seven days phenytoin (main trial phase).
Secondary Objective(s):	1. To determine the safety of single dose nevirapine with seven days phenytoin as a part of ARV prophylaxis for

	PMTCT vs. single dose of nevirapine without phenytoin as a part of ARV prophylaxis for PMTCT 2. To determine the HIV status of the infant 3. To determine the safety of the ARV prophylaxis for PMTCT with seven days of phenytoin on the newborn.
Clinical Trial/Study site(s):	Majengo Antenatal Clinic, Mawenzi ANC, Pasua ANC and Kilimanjaro Christian Medical Centre (Tanzania)
Collaborating site(s):	• Kilimanjaro Christian Medical Centre (Tanzania) • University Teaching Hospital (Zambia) • Radboud University Nijmegen Medical Centre (Netherlands) • Medical Research Council (UK)
Study design:	Phase IIa/IIb open-label multi-centre randomised pharmacokinetic trial. ARV prophylaxis for PMTCT follows national guidelines (which differ slightly): **Mother:** • Antepartum: start zidovudine 300 mg BID from 28 weeks of gestation or as soon as feasible thereafter, at least four weeks before delivery. • Intrapartum (Tanzania): single dose NVP 200 mg at onset of labour, continue zidovudine 300 mg at onset of labour every three hours until delivery and start lamivudine 150 mg every 12 hours at onset of labour. • Intrapartum (Zambia): single dose NVP 200 mg at onset of labour, start zidovudine 600 mg and lamivudine 300 mg at onset of labour every 12 hours until delivery. • Postpartum: continue zidovudine 300 mg BID and lamivudine 150 mg BID for seven days. • If randomised to phenytoin intrapartum: start phenytoin 184 mg (2 tablets of 92mg) OD at onset of labour and continue for seven days. **Child:** • Postpartum (within 24-72 hours): Single dose nevirapine 2mg/kg and zidovudine 4 mg/kg BID for seven days.
Product(s):	• Taver® (Carbamazepine) • Viramune ® (Nevirapine) tablets & oral suspension • Epanutin® (Phenytoin)
Manufacturer/Developer:	• Medochemie Ltd • Boeringer Ingelheim • Pfizer
Cofunders:	• NACCAP (Netherlands) • Medical Research Council (MRC, UK)
Trial Registration number(s):	NCT 01187719
Status:	Completed
Results and Outcomes:	**VITA 1 study**: the results shows that addition of single-dose carbamazepine to single-dose NVP at labour onset in HIV-infected, pregnant women did not affect NVP plasma concentration at delivery, but significantly reduced it one week postpartum, with a trend towards fewer NVP resistance mutations, although missing samples reduced power to reach statistical significance. These results were published by Muro EP, et al. in J. Acquir. Immune Defic. Syndr. (2012), 1;59(3):266-73. (PMID:22134145). Enzyme inducers, such as carbamazepine, may show new possibilities for pMTCT programs to reduce the development of NVP resistance in settings where other ART regimens are limited. **VITA 2 pilot study**: recruited 67 participants instead of 50 as

	per the protocol. This was discussed with the external monitors and DSMB members. The aim was to get 40 complete datasets (analysable) to have enough power to address the primary objectives of the pilot trial, i.e. pharmacokinetics studies. The investigators have submitted the findings to the Clinical Infectious Diseases Journal and presented the data at CROI, March 2013. In brief, it is observed that addition of an enzyme inducer (i.e. phenytoin) for 7 days to sdNVP for the prevention of MTCT reduced the presence of sub-therapeutic NVP levels by shortening the NVP elimination half-life; no NVP resistance was observed. As prolonged sub-therapeutic NVP exposure is known to lead to resistance emergence, in the absence of a larger phase III trial, sdNVP could be used with phenytoin if other ARV drugs are unavailable, since it is safely and widely used in pregnancy. VITA 2 main study: was not conducted as it was considered unethical to begin the study which could not be completed for various reasons, i.e. slow recruitment, expected high loss to follow-up (as per experienced in VITA 1 and VITA 2 pilot studies), unrealistic timelines, etc. Other accomplishments: 1. Capacity building & infrastructure upgrade: significant short training coursed in GCP/GCLP and ethics were accomplished during the grant. In addition, it took place the construction of the two upper floors of Kilimanjaro Clinical Research Institute (KCRI) with NACCAP funding. 2. Dissemination: One scientific article published in March 2012 (VITA 1 results). VITA 2 pilot study results submitted to Clinical Infectious Diseases Journal. Possibly, a manuscript in preparation from the MSc dissertation of Lutengano George. 3. Training: 2 PhD students and 2 MSc students have been trained. An additional PhD student was included after establishing the collaboration with the University of Mainz, Germany) (Mrs Dorothea Baranyai). The 2 MSc students graduated but the PhDs defences are still ongoing.
Total number of subjects (clinical trials only):	VITA 2 pilot study: planned 50, recruits 67 (HIV-positive, ARV naive, African, pregnant women and their newborns) VITA 2 main study: planned 150 (HIV-positive, ARV naive, African, pregnant women and their newborns) – **main study cancelled**
PhD studies:	Title: Joining forces in the fitght against HIV/AIDS in Africa (Clinical Pharmacology of ARV agents in resource limited settings) Candidate: Quirine Fillekes (Radboud University, Netherlands) Dates: October 2007-27 August 2013
	Title: Clinical Pharmacology of pMTCT Candidate: Eva Muro (Radboud University, Nijmegen, Netherlands) Dates: October 2007-February 2014
	Title: The importance of inter-individual differences in Phase I-III proteins for the response to drugs and hormone homeostasis Candidate: Dorothea Baranyai (University of Mainz, Germany) Dates: September 2010-September 2013
MSc studies:	Title: Age standardization in relative survival Candidate: Humphrey Mkali (MSc in Biostatistics at the Leicester University, United Kingdom) Date: October 2007-September 2011
	Title: MSc in Clinical research Candidate: Lutengano George (KCM College, Tanzania)

	Completion date: October 2007-September 2012
Publications:	1. Muro EP, Fillekes Q, Kisanga ER, L'homme R, Aitken SC, Mariki G, Van der Ven, AJAM, Dolmans W, Schuurman R, Walker AS, Gibb DM, Burger DM. Intrapartum single-dose carbamazepine shortens nevirapine elimination half-life and may reduce resistance after a single dose of nevirapine for perinatal HIV prevention. *J. Acquir. Immune. Defic. Syndr.* 2012; 59(3): 266-273 2. Fillekes Q, Muro EP, Chunda C, Aitken S, Kisanga ER, Kankasa C, Thomason MJ, Gibb DM, Walker AS, Burger DM. Effect of 7 days of phenytoin on the pharmacokinetics of and the development of resistance to single-dose nevirapine for perinatal HIV prevention: a randomized pilot trial. *J. Antimicrob. Chemother*. 2013; 68(11): 2609-2615.

2.1.13 PROMISE-PEP Studies

EDCTP Project Coordinator:	Philippe Van de Perre (Montpellier University Hospital Centre (CHU), France)
EDCTP Call Title:	Support of studies for the Prevention of Mother to Child Transmission of HIV, including prevention of transmission during breast feeding
EDCTP Project Title:	A randomised controlled trial comparing the efficacy of infant peri-exposure prophylaxis with Lopinavir/Ritonavir (LPV/r) versus Lamivudine to prevent HIV-1 transmission by breastfeeding
EDCTP Project Code:	CT.2006.33020.004
EDCTP Project Start Date:	21 March 2008
EDCTP Project End Date:	30 April 2014
Collaborators:	• Stéphane Blanche (University of Paris V - René Descartes, France) • Tanya Doherty (Medical Research Council South Africa (MRC), South Africa) • Pierre Dujols (University of Montpellier 1, France) • Eva-Charlotte Ekström (Uppsala University, Sweden) • Vincent Foulongne (University of Montpellier 1, France) • Knut Fylkesnes (University of Bergen, Norway) • Harry Hausler (University of the Western Cape, South Africa) • Debra Jackson (University of the Western Cape, South Africa) • Chipepo Kankasa (University of Zambia (UNZA), Zambia) • Nicolas Meda (Centre Muraz, Burkina Faso) • Philippa Musoke (Makerere University, Uganda) • Nicolas Nagot (University of Montpellier 1, France) • Dorine Neveu (University of Montpellier 1, France) • Vernice Cheryl Nikodem (University of the Western Cape, South Africa) • Marie-Christine Picot (University of Montpellier 1, France) • Francois Rouet (Centre Muraz, Burkina Faso) • David Sanders (University of the Western Cape, South Africa) • Michel Segondy (University of Montpellier 1, France) • Seter Siziya (University of Zambia) • Halvor Sommerfelt (University of Bergen, Norway) • Jean-Marc Tréluyer (University of Paris V - René Descartes, France) • James K Tumwine (Makerere University, Uganda) • Thorkild Tylleskar (University of Bergen, Norway)
Site Principal Investigator(s):	• Thorkild Tylleskar (Norway) • Nicolas Meda (Burkina Faso) • James K Tumwine (Uganda) • Chipepo Kankasa (Zambia) • Justus Hofmeyr (South Africa) • Eva-Charlotte Ekström (Sweden) • Stephane Blanche (France)
Clinical Trial/Study Sponsor:	France National Agency for Research on AIDS & Hepatitis (ANRS)
Trial/Study title:	A randomised controlled trial comparing the efficacy of infant peri-exposure prophylaxis (PEP) with Lopinavir/Ritonavir (LPV/r) versus Lamivudine to prevent HIV-1 transmission by breastfeeding (ANRS 12174 trial)
Goal:	To assess, in a multi-centre randomised clinical trial, the efficacy and safety of prolonged peri-exposure prophylaxis (PEP) on

	postnatal transmission of HIV-1 from infected breastfeeding (BF) mothers not eligible for HAART to their infants, after perinatal antiretroviral prophylaxis.
Primary Objective(s):	1. To compare the efficacy of infant Lopinavir/Ritonavir (LPV/r, 80/20mg twice a day) vs lamivudine (3TC, 12 mg twice daily if <6 kg, 24 mg per day if 6.0 to 9.0 kg, and 36 mg per day if ≥ 9.0 kg) from day 7 until one week after cessation of BF (maximum duration of prophylaxis: 50 weeks for a maximum duration of breastfeeding of 49 weeks) to prevent postnatal HIV-1 acquisition between 7 days and 50 weeks of age.
Secondary Objective(s):	1. To assess the safety of long-term infant prophylaxis with LPV/r versus lamivudine (including resistance, adverse events and growth) at 50 weeks 2. To assess HIV-1-free survival until 50 weeks 3. To build clinical trials capacity at the four study sites.
Clinical Trial/Study site(s):	• University of Ouagadougou (Burkina Faso) • University of the Western Cape (South Africa) • Makerere University (Uganda) • University Teaching Hospital (Zambia)
Collaborating site(s):	• University of Montpellier and University of Paris V (France) • University of Bergen (Norway) • University of Uppsala (Sweden) • South African Medical Research Council (South Africa)
Study design:	Phase III double-blinded randomised controlled trial with two arms. **Arm 1 (Experimental):** infant peri-exposure prophylaxis with lopinavir/ritonavir (LPV/r) Oral liquid formulation lopinavir/ritonavir(80 mg lopinavir + 20 mg ritonavir/mL). Dosing: 40/10mg twice daily if infant weight is between 2 to 4 kg and 80/20mg twice daily if infant weight is above 4kg. The lopinavir/ritonavir will be given to the baby from Day 7 postnatal until one week after the cessation of breastfeeding. **Arm 2 (Active Comparator):** infant peri-exposure prophylaxis with lamivudine (3TC) Oral liquid solution lamivudine (10 mg/mL). Dosing: 7.5 mg twice daily if infant weight is between 2 to 4 kg; 25 mg twice daily if infant weight is between 4 to 8 kg; 50 mg twice daily if infant weight is above 8kg. The lamivudine will be given to the baby from Day 7 postnatal until 4 weeks after the cessation of breastfeeding.
Product(s):	• Lopinavir/ritonavir (LPV/r) • Lamivudine (3TC)
Manufacturer/Developer:	• GlaxoSmithKline/Generic supplier (for lamivudine) • Abbott (for lopinavir/ritonavir)
Cofunders:	• French National Agency for Research on AIDS and Viral Hepatitis (ANRS, France) • The Research Council of Norway (Norway) • Swedish International Development Cooperation Agency (SIDA, Sweden)
Trial Registration number(s):	NCT 00640263
Status:	Ongoing
Results & Outcomes:	The participant recruitment took place from November 2009 to October 2010 (in Burkina Faso, Zambia, Uganda, and South Africa and was considered completed in May 2012. The trial has

	enrolled 1,273 infants (84.8% of the original sample size, i.e. above the set power of 80% as per the study protocol) and follow-up of the last participant is expected to be in May 2013. The team had to extended the enrolment period until May 2012 because the recruitment rate was lower than expected, mainly due to lower than anticipated HIV prevalence in pregnant women in Burkina Faso (1.5% vs. 4%) and in Uganda (5% vs. 8%). In South Africa, the regulatory approval process delayed the recruitment initiation, and the recruitment was much impacted by both a history of formula feeding for HIV-infected mothers, and the implementation of a national policy to administer nevirapine to infants during the breastfeeding period. Furthermore, the increase threshold for HAART initiation to 350 cell/µL in all countries also influenced substantially on the recruitment potential of each site. In contrast, the Zambian study site recruits more infants than expected, which partly compensates for the low number in the other study sites. Preliminary results show that the transmission rate of the disease from mother to child is of 1.1% at 12 months, the lowest rate ever reported during breastfeeding. Moreover, the survival rate was 96% 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. Data analyses for the comparative efficacy and tolerance of the two regimens are expected to be available in September 2013. The final report will be submitted by end of 2013. The major infrastructure upgrades took placed in: • Burkina Faso, two empty rooms split and upgraded for recruitment and follow-up; new house rented for other staff; upgrade of some antenatal clinics as needed. • Zambia, the study site moved to a new 'Paediatric Centre of HIV Excellence' at the University Teaching Hospital in Lusaka in November 2011. • Uganda, a building has been rehabilitated within the local hospital to host the study team. • South Africa, four research rooms rehabilitated for the study within the Cecilia Makewane Hospital. Networking activities: • This project has led to the consolidation of the PROMISE EBF/PEP Research Consortium Group • Several Poster Presentations were made at the 6th EDCTP Forum in Addis Ababa.
Total number of subjects (clinical trials only):	1,500
PhD studies:	Title: Male involvement in the PMTCT programme in Uganda Candidate: Robert Byamugisha (University of Bergen, Norway) Completion date: December 2007-September 2013
	Title: The social context of prevention of mother-to child transmission of HIV in Mbale District Eastern Uganda Candidate: Joseph Rujumba (University of Bergen, Norway) Completion date: April 2008-27 November 2012
	Title: Anthropometry in the PROMSE-PEP study Candidate: Amwe Sunday Aku (University of Bergen, Norway) Completion date: January 2013-June 2015
MSc study:	Title: Assessment of the PMTCT programme in Ouagadougou

	and impact of the implementation of PROMISE-PEP on this programme Candidate: Hugues Traore (University of Nancy, France) Completion date: September 2011-21 September 2012
Other/Sub-studies:	Sub-studies are planned based on the biological sample storage, but no protocol has been discussed and approved by the trial scientific committee yet.
Publications:	1. Tylleskar T. Making it happen, level 2. *Glob Health Action* 2010; 1:3. doi: 10.3402/gha.v3i0.5370 2. Byamugisha R, Tumwine JK, Semiyaga N, Tylleskar T. Determinants of male involvement in the prevention of mother-to-child transmission of HIV programme in Eastern Uganda: a cross-sectional survey. *Reprod Health* 2010; 7: 12 3. Byamugisha R, Tumwine JK, Ndeezi G, Karamagi CA, Tylleskar T. Attitudes to routine HIV counselling and testing, and knowledge about prevention of mother to child transmission of HIV in eastern Uganda: a cross-sectional survey among antenatal attendees. *J Int AIDS Soc*. 2010; 13: 52 4. Engebretsen IM, Tylleskar T. HIV, breast feeding and antiretroviral agents. *Norwegian Tidsskr Nor Laegeforen*. 2010; 130(5); 520-2 5. Byamugisha R, Tylleskar T, Kagawa MN, Onyango S, Karamagi CA, Tumwine JK. Dramatic and sustained increase in HIV-testing rates among antenatal attendees in Eastern Uganda after a policy change from voluntary counselling and testing to routine counselling and testing for HIV: a retrospective analysis of hospital records, 2002-2009. *BMC Health Serv Res*. 2010; 10: 290 6. Rubbo, PA; Tuaillon, E; Nagot, N; Chentoufi, AA; Bollore, K; Reynes, J; Vendrell, JP; Benmohamed, L; Van de Perre, P. HIV-1 Infection Impairs HSV-Specific CD4(+) and CD8(+) T-Cell Response by Reducing Th1 Cytokines and CCR5 Ligand Secretion. *Journal Acquired Immune Deficiency Syndromes* 2011; 58(1): 9-17 7. Nagot N, Kankasa C, Meda N, Hofmeyr J, Nikodem C, Tumwine JK, Karamagi C, Sommerfelt H, Neveu D, Tylleskar T, Van de Perre P for the PROMISE-PEP group. Lopinavir/Ritonavir (LPV/r) versus Lamivudine peri-exposure prophylaxis to prevent HIV-1 transmission by breastfeeding: the PROMISE-PEP trial Protocol - ANRS 12174. *BMC Infectious Diseases* 2012; 12; 246 8. Van de Perre P, Rubbo PA, Viljoen J, Nagot N,Tylleskar T, Lepage P, Vendrell JP, Tuaillon E. HIV-1 Reservoirs in Breast Milk and Challenges to Elimination of Breast-Feeding Transmission of HIV-1. *Science Translational Medicine*, 2012; 4(143): 143sr3

2.1.14 Li in HAND

EDCTP Project Coordinator:	John Joska (Groote Schuur Hospital, South Africa)
EDCTP Call Title:	EDCTP Strategic Primer Grants
EDCTP Project Title:	A randomized controlled trial of lithium carbonate in individuals with HIV clade C-associated neurocognitive impairment: a proof of principle study.
EDCTP Project Code:	SP.2011.41304.065
EDCTP Project Start Date:	1 December 2012
EDCTP Project End Date:	30 November 2014
Collaborator(s)	• Eric Decloedt (University of Cape Town, South Africa) • Carla Freeman (University of Cape Town, South Africa) • Kleni Koutsilieri (University of Wuerzburg (Würzburg), Germany) • Simon Lovestone (King's College London, UK) • Gary Maartens (University of Cape Town, South Africa)
Study/Trial 1	
Site Principal Investigator(s):	John Joska (South Africa)
Clinical Trial/Study Sponsor:	University of Cape Town (South Africa)
Trial/Study title:	A randomised controlled trial of lithium carbonate in individuals with HIV clade C-associated neurocognitive impairment: a phase IIb proof of principle study. (Li in HAND RCT)
Goal:	To determine the efficacy, safety and tolerability of lithium in the treatment of neurocognitive impairment in HIV-infected patients who are stable on ART.
Primary Objective(s):	To measure the change in neuropsychological function as determined by the Global Deficit Score (GDS) from baseline to week 24.
Secondary Objective(s):	1. To measure changes in magnetic resonance spectroscopy (MRS)-based (glutamate and glutamine) Glx in the frontal grey matter and measures of tensor diffusivity (including fractional anisotropy, and radial, axial and mean diffusivity) in white matter from baseline to week 24 2. To assess the severity and frequency of adverse events 3. To measure changes in Human immunodeficiency virus (HIV) viral load in the plasma and cerebrospinal fluid (CSF) 4. To measure changes in CSF:serum albumin ratio 5. To measure changes in CSF:serum viral load ratio 6. To measure changes in glycogen synthase kinase-3-beta (GSK-3-ß) in human peripheral blood mononuclear cells (PBMC) 7. To study the effect of lithium on CSF dopamine and peripheral lymphocytes expressing dopamine receptors 8. To study the effect of lithium brain-derived neurotrophic factor (BDNF) in serum and CSF 9. To explore outcome measure potential associations with putative biomarkers, inflammatory markers or genes that might be identified during the course of the study.
Clinical Trial/Study site(s):	Division of Neuropsychiatry, Groote Schuur Hospital, University of Cape Town
Collaborating site(s):	University of Cape Town (South Africa) University of Wuerzburg (Würzburg) (Germany) King's College London (UK)
Study design:	Phase IIb - Double-blind randomised placebo-controlled trial. Participants will be randomized to either lithium or placebo for 24 weeks.
Number of subjects:	HIV-infected patients established on ART for at least 6 months with a suppressed viral load and neurocognitive impairment. 108 participants
Product(s):	Camcolit®,
Manufacturer/Developer:	Norgine

Cofunders:	• Medical Research Council, (United Kingdom) • Federal Ministry of Education and Research (BMBF), (Germany) • Department of Science and Technology (DST), (South Africa) • University of Cape Town, (South Africa) • University of Wuerzburg (Würzburg), (Germany) • King's College London, (United Kingdom)
Trial registration number(s):	Not yet registered – Awaiting approval from South African Medicines Control Council
Status:	Ongoing
Results and Outcomes:	
Publications:	

2.1.15 PedVacc

EDCTP Project Coordinator:	Tomáš Hanke (University of Oxford, UK)
EDCTP Call Title:	Capacity building in preparation for the conduct of preventive HIV vaccine trials (EDCTP/Gates Foundation/MS joint call)
EDCTP Project Title:	Building capacity of Infant HIV-1 Vaccine Clinical Trial Centres in Nairobi, Kenya and Fajara, The Gambia
EDCTP Project Code:	CT.2006.33111.002
EDCTP Project Start Date:	7 April 2008
EDCTP Project End Date:	30 April 2012
Collaborators:	• Katie Flanagan (formerly at MRC Gambia now at Launceston General Hospital, Australia) • Walter Jaoko (University of Nairobi, Kenya) • Grace John-Stewart (University of Washington, US) • Joan Joseph (Hospital Clinic of Barcelona) • Andrew McMichael (University of Oxford, UK) • Marie Reilly (Karolinska Institute, Sweden) • Sarah Rowland-Jones (MRC The Gambia)
Study/Trial 1	**PV001 Gambian trial**
Site Principal Investigator(s):	Katie Flanagan (The Gambia)
Clinical Trial/Study Sponsor:	Medical Research Council (UK)
Trial/Study title:	An open randomised phase I study evaluating safety and immunogenicity of a candidate HIV-1 vaccine, MVA.HIVA, administered to healthy infants born to HIV-1 and HIV-2-uninfected mothers
Goal:	To establish infant phase I HIV-1 vaccine safety and immunogenicity
Primary Objective(s):	1. To evaluate the safety and immunogenicity of MVA.HIVA vaccine in 20-week old healthy Gambian infants born to HIV-1/2-uninfected mothers
Secondary Objective(s):	1. To determine the gross impact of MVA.HIVA on the immunogenicity of expanded programme on immunisation (EPI) vaccines (DTwPHib, HepB, PCV-7 and OPV) when administered at 20 weeks (4 weeks after the last EPI vaccines) to infants who have had Bacillus Calmette-Guérin (BCG) anti-TB vaccine within the first 4 weeks of life 2. To build capacity for infant HIV-1 vaccine clinical trials centre in Fajara, The Gambia.
Clinical Trial/Study site(s):	Sukuta Health Centre (The Gambia)
Collaborating site(s):	• University of Oxford (UK) • MRC Laboratories (The Gambia) • Karolinska Institute (Sweden)
Study design:	Phase I open-label randomised controlled trial (immunology lab blinded)
Number of subjects:	Group 1: EPI+MVA.HIVA administered at 20 weeks of age (N=24) Group 2: EPI and no MVA.HIVA (control group, N=24)
Product(s):	MVA.HIVA (recombinant non-replicating modified vaccinia virus Ankara expressing HIV-1-derived immunogen HIVA) focusing on induction of anti-HIV-1 T cell immunity
Manufacturer/ Developer:	Impfstoffwerk Dessau-Tornau Biologika GmbH, Germany/University of Oxford, UK
Cofunders:	• Bill & Melinda Gates Foundation (USA) • SIDA and Karolinska Institut (Sweden) • Institute of Health Carlos III (ISCIII, Spain)

	• MRC (UK)
Trial Registration number(s):	NCT00982579 ATMR2008120000904116
Status:	Completed
Results and Outcomes:	Two infant vaccine clinical trials PV001 (HIV-1-negative mothers) and PV002 (HIV-1-positive mothers) were successfully completed. A total of 121 infant-mother pairs were randomised, of whom half received the Investigational Medicinal Product. These trials showed that the vaccine MVA.HIVA was well tolerated in 20-week old infants with no reported serious adverse reactions, neither study detected MVA.HIVA interference with antibodies induced by other childhood vaccines (the Expanded Programme on Immunization) and preliminary analysis of the vaccine immunogenicity in PV001 suggests induction of weak, but definite T cell responses specific for HIV-1 elicited in small number of vaccinated infants. These responses are expected to increase by a priming vaccination and when a standard rather than low (safety) boosting dose of rMVA is used. The trials have been conducted to the highest scientific and ethical standards in compliance with the protocol, ICH/GCP and applicable regulatory requirements. GLP BCG.HIVA preparation BCG.HIVACAT antibiotic selection-free master seed and working vaccine seed stocks have been prepared in compliance with Good Laboratory Practice and its immunogenicity confirmed in preclinical models.
Study/Trial 2	**PV002 Kenyan trial**
Site Principal Investigator(s):	• Walter Jaoko (Kenya) • Grace John-Stewart (Kenya)
Clinical Trial/Study Sponsor:	Medical Research Council (UK)
Trial/Study title:	An open randomised phase I/II study evaluating safety and immunogenicity of a candidate HIV-1 vaccine, MVA.HIVA, administered to healthy infants born to HIV-1-infected mothers
Goal:	To establish safety and immunogenicity of candidate HIV-1 vaccine MVA.HIVA
Primary Objective(s):	1. To evaluate the safety and immunogenicity of MVA.HIVA vaccine in 20 week old healthy Kenyan infants born to HIV-1-infected mothers
Secondary Objective(s):	1. Comparison of HIV-1-specific T cell responses between MVA.HIVA-vaccinated and age-matched unvaccinated infants 2. Comparison of responses to certain Kenyan Extended Programme on Immunization (KEPI) vaccines (OPV, DTP, HBV, and HiB) between MVA.HIVA-vaccinated and age-matched unvaccinated infants 3. Comparison of immune activation and phenotypic profile of lymphocytes between MVA.HIVA-vaccinated and age-matched unvaccinated infants 4. Build capacity for Infant HIV-1 Vaccine Clinical Trials Centre in Nairobi, Kenya.
Clinical Trial/Study site(s):	Kenyatta National Hospital (Kenya)
Collaborating site(s):	• University of Oxford (UK) • MRC (UK) • University of Nairobi (Kenya) • Kenya AIDS Vaccine Initiative (Kenya) • University of Washington (USA) • Karolinska Institute (Sweden)
Study design:	Open, randomised, controlled phase I/II trial (immunology

	laboratory blinded)
Number of subjects:	Group 1: KEPI+MVA.HIVA administered at 20 weeks of age (N=36) Group 2: KEPI and no MVA.HIVA (control group, N=36)
Product(s):	MVA.HIVA (recombinant non-replicating modified vaccinia virus Ankara expressing HIV-1-derived immunogen HIVA) focusing on induction of anti-HIV-1 T cell immunity
Manufacturer/ Developer:	Impfstoffwerk Dessau-Tornau Biologika GmbH, Germany/University of Oxford, UK
Cofunders:	• Bill & Melinda Gates Foundation (USA) • Swedish International Developmental Cooperation Agency (SIDA) Karolinska Institut (Sweden) • Institute of Health Carlos III (ISCIII, Spain) • MRC (UK)
Trial Registration number(s):	NCT00981695 PACTR2009010001152787
Status:	Completed
Results and Outcomes:	Two infant vaccine clinical trials PV001 (HIV-1-negative mothers) and PV002 (HIV-1-positive mothers) were successfully completed. A total of 121 infant-mother pairs were randomised, of whom half received the Investigational Medicinal Product. These trials showed that the vaccine MVA.HIVA was well tolerated in 20-week old infants with no reported serious adverse reactions, neither study detected MVA.HIVA interference with antibodies induced by other childhood vaccines (the Expanded Programme on Immunization) and preliminary analysis of the vaccine immunogenicity in PV001 suggests induction of weak, but definite T cell responses specific for HIV-1 elicited in small number of vaccinated infants. These responses are expected to increase by a priming vaccination and when a standard rather than low (safety) boosting dose of rMVA is used. The trials have been conducted to the highest scientific and ethical standards in compliance with the protocol, ICH/GCP and applicable regulatory requirements. GLP BCG.HIVA preparation BCG.HIVACAT antibiotic selection-free master seed and working vaccine seed stocks have been prepared in compliance with Good Laboratory Practice and its immunogenicity confirmed in preclinical models.
PhD study:	Title: Regulatory T cells and vaccines: correlation or coincidence? Candidate: Jorjoh Ndure (MRC The Gambia) Dates: January 2011-December 2013
MSc studies:	Topic: Epidemiology Candidate: Christine Gichuhi (LSHTM, UK (distance learning)) Dates: September 2009-June 2013
	Title: The BCG transcriptome signature and relationship with host immune responses Candidate: Fatoumatta Darboe (MRC The Gambia) Dates: December 2011-March 2013
	Title: Anxiety and depression in HIV positive mothers whose infants are completing HIV vaccine studies Candidate: Dorcas Murei (University of Nairobi, Kenya) Dates: October 2009-August 2012
	Title: A software system for advanced flow cytometry data analysis Candidate: Amos Thairu (KAVI, Kenya/KI, Sweden) Dates: February 2011-April 2012
	Title: Immune Responses in HIV/Schistosoma mansoni

	Coinfection and Associations to Disease Progression Candidate: Moses Muriuki Mundia (KAVI/University of Hertfordshire, UK) Dates: January 2012-January 2015
Postdoc studies:	Yaowaluck Roshorm (University of Oxford, UK) Dates: April 2008-May 2012
	Raquel Fernandez Lloris (University of Barcelona, Spain) Dates: April 2008-May 2012
Other/Sub-studies:	Preparation of GLP grade BCG.HIVA222 vaccine for GMP production
Publications:	1. Saubi, N, Mbewe-Mvula, A, Gea, E, Rosario, M, Gatell, JM, Hanke, T, Joseph, J. (2012) Pre-clinical development of BCG.HIVA^{CAT}, an antibiotic-free selection strain, for HIV-TB pediatric vaccine vectored by lysine auxotroph of BCG. *PLoS ONE*, 7: 10.1371/journal.pone.0042559. 2. Njuguna, I, Reilly, M, Jaoko, W, Gichuhi, C, Ambler, G, Maleche-Obimbo, Lohman-Payne B, Hanke, T, John-Stewart, G (2013) Infant Neutropenia Associated with Breatfeeding During Maternal Antiretroviral Treatment for Prevention of Mother-to-Child Transmission of HIV. Retrovirology: Research and Treatment, 2014:6
Press releases:	EDCTP press release MRC press release

2.1.16 TaMoVac-01

EDCTP Project Coordinator:	Muhammad Bakari (Muhimbili University College of Health Sciences, Tanzania)
EDCTP Call Title:	Capacity building in preparation for the conduct of preventive HIV vaccine trials (EDCTP/Gates Foundation/MS joint call)
EDCTP Project Title:	HIV vaccine trial capacity building in Tanzania and Mozambique by continued exploration of optimal DNA priming and MVA boosting strategies
EDCTP Project Code:	CT.2006.33111.007
EDCTP Project Start Date:	4 March 2008
EDCTP Project End Date:	31 December 2012
Collaborators:	• Sören Andersson (Örebro University Hospital, Sweden) • Gunnel Biberfeld (Karolinska Institute, Sweden) • Pontus Blomberg (Karolinska Institute, Sweden) • Frances Gotch (Imperial College, UK) • Bo Hejdeman (Karolinksa Institute, Sweden) • Michael Hoelscher (LMU, Germany) • Nesrina Imami (Imperial College, UK) • Ilesh Jani (Instituto Nacional de Saúde (INS), Mozambique) • Andrew Kitua (WHO/Special Programme for Research and Training in Tropical Diseases, Switzerland) • Leonard Maboko (MMRP, Tanzania) • Sayoki Mfinanga (NIMR, Tanzania) • Fred Mhalu (University of Dar es Salaam, Tanzania) • Charlotta Nilsson (Karolinska Institute, Sweden) • Nafissa Osman (Instituto Nacional de Saúde (INS), Mozambique) • Eric Sandstrom (Karolinska Institute, Sweden) • Willy Urassa (MUHAS, Tanzania) • Paula Vaz (Instituto Nacional de Saúde (INS), Mozambique) • Jonathan Weber (Imperial College, UK)
Study/Trial 1	**HIVIS 03 continuation**
Site Principal Investigator(s):	Fred Mhalu (Tanzania)
Clinical Trial/Study Sponsor:	Muhimbili University College of Health & Allied Sciences/Swedish Institute of Infectious diseases
Trial/Study title:	A Phase I/II trial to assess the safety and immunogenicity of a plasmid DNA-MVA prime boost HIV-1 vaccine candidate among volunteers in Dar es Salaam, Tanzania
Goal:	Assess the safety and immunogenicity of a plasmid DNA-MVA prime boost HIV-1 vaccine candidate. HIVIS 03 is a follow-up phase I/II HIV vaccine study in Tanzania of HIV plasmid DNA prime MVA boost that was successfully completed in Sweden
Primary Objective(s):	To determine safety and immunogenicity of HIVIS-DNA candidate vaccine
Secondary Objective(s):	To build expertise and capability in evaluating HIV-1 vaccine candidates in Dar es Salaam, Tanzania
Clinical Trial/Study site(s):	Muhimbili University College of Health & Allied Sciences, Dar es Salaam (Tanzania)
Collaborating site(s):	• Swedish Institute for Infectious Disease Control (Sweden)
Study design:	Phase I/II double-blinded randomised controlled trial
Number of subjects:	Healthy adults (police officers), N= 60
Product(s):	Priming – env (HIV-1 subtype A, B, C), rev (HIV-1 subtype B), gag (HIV-1 subtype A, B) and RTmut (HIV-1, subtype B) Boosting – MVA-CMDR expressing HIV-1 genes – gp160 (subtype E, CM235) and gag and pol (subtype A, CM240)

Manufacturer/Developer:	Vecura Company (Sweden) (DNA) WRAIR (USA) (MVA-CMDR)
Cofunders:	• Bill & Melinda Gates Foundation (US) • Walter Reed Army Institute of Research (WRAIR, US) • BMBF (Germany) • LMU München (Germany) • NACCAP (Netherlands) • EU • SIDA (Sweden) • Embassy of Sweden (Sweden) • MRC (UK) • Imperial College (UK)
Trial Registration number(s):	ISRCTN90053831 ATMR2009040001075080
Status:	Completed
Results and Outcomes	First patient in: February 2009 Last patient out: July 2010 42 volunteers out of 60 received the second MVA boost. The vaccine was deemed safe, and a total of 11 SAE unrelated to vaccination have been observed. Study closure visit was done on 24 June 2010. Preliminary results of the immunological analyses show a broad and potent immune response in volunteers.
Study/Trial 2	**Phase I/II Tanzania combined project with Weber's AfrEVacc (CT.2006.33111.001)**
Site Principal Investigator(s):	Muhammad Bakari (Tanzania) Leonard Maboko (Tanzania)
Clinical Trial/Study Sponsor:	Swedish Institute for Communicable Disease Control (Sweden) MUHAS (Tanzania)
Trial/Study title:	A phase I/II trial to assess safety and immunogenicity of i.d. DNA priming, i.m. MVA and i.m. rgp140/GLA-AF boosting in healthy volunteers in Tanzania and to develop further HIV vaccine trial capacity building in Tanzania.
Goal:	Exploration of the optimal delivery method of HIV-1 DNA vaccine
Primary Objective(s):	1. Determine safety of HIVIS-DNA at a dose of 600 µg or 1000 µg delivered ID in combination with MVA-CMDR boost IM 2. Determine immunogenicity of HIVIS-DNA at a dose of 600 µg or 1000 µg delivered ID in combination with MVA-CMDR boost IM
Secondary Objective(s):	1. Compare immunogenicity of HIVIS-DNA at a dose of 600 µg given as combined plasmid pools or separate plasmid pools ID in combination with MVA-CMDR boost IM 2. Explore the safety and immunogenicity of boosting with two doses of rgp140 in the adjuvant GLA-AF, administered IM 3. To build expertise and capability in evaluating HIV-1 vaccine candidates in Tanzania
Clinical Trial/Study site(s):	MUHAS, Dar es Salaam (Tanzania) NIMR-MMRP, Mbeya (Tanzania)
Collaborating site(s):	• NIMR (Tanzania) • Swedish Institute for Infectious Disease Control (Sweden) • WRAIR (USA) • University of München (Germany) • Imperial College (UK)
Study design:	Phase I/II double-blinded randomised controlled trial
Number of subjects:	Healthy adults (Police Officers, no less than 30 females), N = 120

Product(s):	**Priming** Pool 1: env (HIV-1 subtype A, B, C) and rev (HIV-1 subtype B) Pool 2: gag (HIV-1 subtype A, B) and RTmut (HIV-1, subtype B) **Boosting:** Modified Vaccinia Ankara vaccine (MVA-CMDR) expressing HIV-1 genes – gp150 (subtype E, CM235) and gag and pol (subtype A, CM240) **Further boosting (amended protocol):** Recombinant C clade trimeric envelope protein (rgp140) derived from the Chinese isolate CN54 mixed with glucopyranosyl lipid A (GLA)
Manufacturer/Developer:	DNA: Vecura (Sweden) MVA-CMDR: WRAIR (USA) rgp140/GLA: Imperial College (London, UK)
Cofunders:	• Bill & Melinda Gates Foundation (USA) • WRAIR (USA); • BMBF (Germany) • LMU München (Germany); • NACCAP (Netherlands); • SIDA and Embassy of Sweden (Sweden); • MRC UK and Imperial College (UK); • AfrEVacc project, Imperial College (UK); • Wellcome Trust UK HIV Vaccine Consortium (UK)
Trial Registration number(s):	PACTR2010050002122368
Status:	Completed
Results and Outcomes	A total of 509 individuals were screened of whom 129 received the 1st DNA/placebo vaccine in MUHAS and MMRP. 116 received the 2nd MVA placebo, and a further 40 of the above received rgp140/GLA. The vaccines were safe. Preliminary analysis has shown that there is no difference in giving DNA as Env and Gag plasmids either in separate or combined pools. DNA priming with 2 i.d. injections, each containing 300mg (total 600mg) is almost as equivalent to 5 i.d. injections each with 200mg (total 1000mg). Additionally, giving DNA as 0.2 mL i.d. was well tolerated and feasible with a Zetajet. Follow-up of volunteers has been completed. Data cleaning and analysis is being finalised so as to write the respective manuscripts. Additional testing of HIV specific antibody responses induced by the rgp140/GLA boosting vaccinations will be performed.
Study/Trial 3	**Phase I HIV Vaccine Trial in youths**
Site Principal Investigator(s):	Ilesh Vinodrai Jani (Mozambique) Nafissa Bique Osman (Mozambique)
Clinical Trial/Study Sponsor:	Swedish Institute for Communicable Disease Control (SMI, Sweden)
Trial/Study title:	A phase I trial to assess safety and immunogenicity of i.d. DNA priming and i.m. MVA boosting in healthy volunteers in Mozambique and to develop further HIV vaccine trial capacity building in Mozambique.
Goal:	Assess the safety and immunogenicity of a plasmid DNA-MVA prime boost HIV-1 vaccine candidate.
Primary Objective(s):	1. Determine safety of the DNA vaccine at a dose of 600 µg and 1200 µg delivered i.d in combination with MVA-CMDR

	boost i.m. 2. Determine immunogenicity of HIVIS-DNA at a dose of 600 µg and 1200 µg delivered i.d in combination with MVA-CMDR boost i.m.
Secondary Objective(s):	1. To build expertise and capability in evaluating HIV-1 vaccine candidates in Mozambique.
Clinical Trial/Study site(s):	Instituto Nacional de Saúde – Centro de Investigação e Treino em Saúde da Polana Caniço (CISPOC, Mozambique)
Collaborating site(s):	• Instituto Nacional de Saúde (INS, Mozambique) • The Swedish Institute for Communicable Disease Control (Sweden) • U.S. Military HIV Research Program-Walter Reed Army Institute of Research (MHRP-WRAIR, USA) • Imperial College (UK)
Study design:	Phase I double-blinded randomised placebo-controlled vaccine trial
Number of subjects:	A Phase I/II HIV Vaccine Trial will be performed on 24 consenting youths (18-26 years)
Product(s):	**Priming:** Pool 1: env (HIV-1 subtype A, B, C) and rev (HIV-1 subtype B) Pool 2: gag (HIV-1 subtype A, B) and Rtmut (HIV-1, subtype B) **Boosting:** Modified Vaccinia Ankara vaccine (MVA-CMDR) expressing HIV-1 genes – gp150 (subtype E, CM235) and gag and pol (subtype A, CM240)
Manufacturer/Developer:	DNA: Vecura (Sweden) MVA-CMDR: WRAIR (USA)
Cofunders:	Swedish International Development Cooperation Agency (SIDA)
Trial Registration number(s):	NCT01407497 PACTR201106000304583
Status:	Completed
Results and Outcomes:	All vaccinations have been completed. Follow upwas completed in March 2013. Some immunological assays will continue to be performed throughout the year 2013.
Total number of subjects (clinical trials only):	204
PhD studies:	Title: Evaluation of HIV testing strategies and monitoring of immune responses in HIV vaccinated individuals in Tanzania Candidate: Said Aboud (Karolinska Institute, Sweden) Dates: December 2004-October 2011
	Title: Tuberculosis and HIV infections: Magnitude of HIV in the Police cohort and its suitability for HIV Vaccine trials, suitability of rapid tests for diagnosis of HIV associated TB Candidate: Patricia Munseri (Karolinska Institute, Sweden) Dates: May 2007-May 2013
	Title: What motivates participation in HIV vaccine trials: A study among Police Officers in Dar es Salaam, Tanzania Candidate: Edith Tarimo (Karolinska Institute, Swden) Dates: April 2007-June 2011
	Title: Studies of immune responses induced by immunization with HIV-1 DNA followed by HIV-1 MVA in healthy individuals in Dar es Salaam, Tanzania Agricola Joachim (Karolinska Institute, Sweden) Dates: December 2011-December 2015
Other/Sub-studies:	In Maputo, Mozambique: Sub-study of HBV (Hepatitis B) frequency: HBV and HPV testing will be performed for both HIV negative and positive volunteers

	Sub-study of Immune response patterns against HIV antigens and control antigens: Determined the frequencies and types of cells that are responding to antigenic stimulus, the quantity and specificity of neutralizing antibodies, and the molecular characterization of HIV isolates. The establishment of reference values: The establishment of reference values for haematological, biochemistry, and immunological parameters Strengthening of group for education on prevention: This component aims to improve the functioning and train the existing group in education for prevention.
Publications:	1. Bakari, M, Aboud, S, Nilsson, C, Francis, J, Buma, D, Moshiro, C, Aris, EA, Lyamuya, EF, Janabi, M, Godoy-Ramirez, K, Joachim, A, Polonis, VR, Bråve, A, Earl, P, Robb, M, Marovich, M, Wahren, B, Pallangyo, K, Biberfeld, G, Mhalu, F, Sandström, E. (2011) Broad and potent immune responses to a low dose intradermal HIV-1 DNA boosted with HIV-1 recombinant MVA among healthy adults in Tanzania. *Vaccine*, 29(46): 8417-8428. 2. Bakari, M, Munseri, P, Francis, J, Aris, E, Moshiro, C, Siyame, D, Janabi, M, Ngatoluwa, M, Aboud, S, Lyamuya, E, Sandström, E, Mhalu, F (2013) Experiences on recruitment and retention of volunteers in the first HIV vaccine trial in Dar es Salam, Tanzania - the phase I/II HIVIS 03 trial. *BMJ Public Health,* 13: 1149 3. Mbunda, T, Bakari, M, Tarimo, EAM, Sandstrom, E, Kulane, A (2014) Factors that influence the willingness of young adults in Dar es Salaam, Tanzania, to participate in phase I/II HIV vaccine trials. *Global Health Action* 7: 22853 - http://dx.doi.org/10.3402/gha.v7.22853

2.1.17 TaMoVac II

EDCTP Project Coordinator:	Eligius Lyamuya (Muhimbili University College of Health Sciences, Tanzania)
EDCTP Call Title:	Call for the support of clinical trials, capacity building and networking in HIV/AIDS vaccines development
EDCTP Project Title:	HIV vaccine trial capacity building in Tanzania and Mozambique by continued exploration of optimal DNA and MVA boosting strategies: TaMoVac II
EDCTP Project Code:	IP.2007.33112.001
EDCTP Project Start Date:	1 July 2009
EDCTP Project End Date:	30 November 2014
Collaborators:	• Said Aboud (Muhimbili University College of Health Sciences, Tanzania) • Sören Andersson (Karolinska Institute, Sweden) • Gunnel Biberfeld (Karolinska Institute, Sweden) • Pontus Blomberg (Karolinska Institute, Sweden) • Sumeilman Chum ((Muhimbili University College of Health Sciences, Tanzania) • Frances Gotch (Imperial College London, UK) • Bo Hejdeman (Karolinska Institute, Sweden) • Michael Hoelscher (Ludwig-Maximilians Universitat Munchen, Germany) • Nesrina Imami (Imperial College London, UK) • Mohamed Yakub Janabi (Muhimbili University College of Health Sciences, Tanzania) • Ilesh Jani (Instituto Nacional de Saúde (INS), Mozambique) • Arne Kriodl (Ludwig-Maximilians Universitat Munchen, Germany) • Leonard Maboko (Mbeya Medical Research Programme, Tanzania) • Eulália Macovala Clara Américo (Karolinska Institute, Sweden) • Theodora Mbunda (Muhimbili University College of Health Sciences, Tanzania) • Sheena McCormack (Medical Research Council, UK) • Sayoki Mfinanga (National Institute for Medical Research (NIMR), Tanzania) • Fred S Mhalu (University of Dar es Salaam, Tanzania) • Marco Missanga (Mbeya Medical Research Programme, Tanzania) • Candida Moshiro (Muhimbili University College of Health Sciences, Tanzania) • Patricia Jane Munseri (Muhimbili University College of Health Sciences, Tanzania) • Charlotta Nilsson (Karolinska Institute, Sweden) • Nafissa Osman (Instituto Nacional de Saúde (INS), Mozambique) • Kisali Pallangyo (Muhimbili University College of Health Sciences, Tanzania) • Eric Sandstrom (Karolinska Institute, Sweden) • Erica Sanga (Mbeya Medical Research Programme, Tanzania) • Willy Urassa (Muhimbili University College of Health Sciences, Tanzania) • Paula Vaz (Instituto Nacional de Saúde (INS), Mozambique) • Britta Wahren (Karolinska Institute, Sweden)
Site Principal	• Leonard Maboko (NIMR, Tanzania)

Investigator(s):	• Muhammad Bakari (MUHAS, Tanzania) • Ileshi Jani (INS, Mozambique)
Clinical Trial/Study Sponsor:	• Muhimbili University College of Health & Allied Sciences (MUHAS, Tanzania) • Swedish Institute of Infectious Disease Control (SMI, Sweden)
Trial/Study title:	A Phase II trial to assess the safety and immunogenicity of HIV-DNA priming administered by the ID Zetajet® with or without ID Derma Vax™ electroporation followed by IM HIV-MVA boosting with or without CN54 rgp140/GLA-AF in healthy volunteers in Tanzania and Mozambique; TaMoVacII Clinical trial
Goal:	To assess if electroporation will increase the efficiency of HIV-DNA priming in terms of immune responses and will lead to a dose sparing vaccine regimen. Furthermore, to assess if increased HIV DNA concentration will reduce the number of shots necessary to deliver the full dose and induce comparable immune responses to a lower DNA vaccine concentrations.
Primary Objective(s):	1. To compare the safety and immunogenicity of 600mg HIVIS-DNA (3mg/ml) administered ID via Zetajet® with or without ID Derma Vax™ Electroporation followed by HIV-MVA-CMDR given IM with or without CN54 rgp140/GLA-AF to healthy low risk HIV-uninfected adult participants. 2. To compare the safety and immunogenicity of 600µg HIVIS-DNA administered ID via Zetajet® in 2 injections of a concentration of 3mg/ml versus one injection of a concentration of 6mg/ml followed by ID Derma Vax™ Electroporation subsequently boosted by IM MVA-CMDR with or without IM 100µg CN54 rgp140 adjuvanted with 5µg GLA-AF in healthy HIV-uninfected adult participants.
Secondary Objective(s):	1. To build expertise and capacity for the evaluation of HIV-1 vaccine candidates in Tanzania and Mozambique 2. To evaluate the perception, attitude and knowledge towards the TaMoVac vaccine trials by study participants and their social environment
Clinical Trial/Study site(s):	• NIMR-MMRP Mbeya (Tanzania) • MUHAS (Tanzania) • Instituto Nacional de Saúde (INS) Maputo (Mozambique)
Collaborating site(s):	• National Institute for Medical Research (NIMR) Muhimbili station (Tanzania) • Central Hospital Maputo (Mozambique) • Karolinska Institute (Sweden) • Vecura (Sweden) • University of Munich (Germany) • Imperial College (UK) • MRC-CTU (UK) • Venhälsan, Södersjukhuset (Sweden) • SMI (Sweden)
Study design:	Phase I/II double blinded randomised controlled trial
Number of subjects:	ADULTS (≥18 years) HIV uninfected volunteers N=198
Product(s):	Priming: DNA plasmids derived from puC8 with a kanamycin resistance gene, hCMV promotor, HPV 16 poly A and origin of replication for E. coli. Env HIV-1 genes of subtypes A, B, C : pKCMVgp160A, KCMVgp160B, pKCMVgp160C, pKCMVrev, pKCMVp37A(ba), pKCMVp37B, and pKCMVpRTB. Boosting: MVA CMDR expressing HIV-1 genes: gp160 (subtype

	E, CM235), gag and pol (integrase-deleted and reverse transcriptase non-functional, Subtype A, CM240).
Manufacturer/Developer:	DNA plasmids from Vecura (Sweden) MVA CMDR from Walter Reed Army Institute of Research (WRAIR) (USA)
Cofunders:	• Sida (Sweden) • DfID (UK) • MRC (UK) • Klinikum University of München (Germany) • Federal Ministry of Education and Research (Germany)
Trial Registration number(s):	NCT01697007 PACTR201211000435126
Sub-studies:	Baseline Epidemiological Study: Epidemiological and Social-Behavioural Studies Among High-Risk Young Women in Dar es Salaam, Tanzania; Preparation for HIV Vaccine Studies. The objectives are: to determine the prevalence of HIV, Syphilis and Hepatitis B. (Other STIs will be investigated under a different grant); to study the acceptability of vaccines against STIs such as HIV and HBV on an individual and societal level; to determine factors associated with risky sexual behaviors among young women at high risk for HIV aged 18-25 years; and, to find out barriers and incentives to participate in HIV vaccine trials in a cohort of young women at high risk for HIV aged 18-25 years. Completed – results pending data analysis
Status:	Ongoing
Results and Outcomes:	Recruitment of participants has been completed for MUHAS and NIMR-MMRC sites and is ongoing at the Maputo site.
PhD studies:	Title: Studies of immune responses induced by immunization with HIV-1 DNA followed by HIV-1 MVA with or without gp 140 in healthy individuals in Dar es Salaam, Tanzania Candidate: Agricola Joachim (MUHAS, Tanzania) Dates: December 2011-end 2015
	Title: Recruitment, retention and participation in HIV vaccine trials targeting youth in Tanzania Candidate: Theodora Mbunda (MUHAS, Tanzania) Dates:30 September 2011-June 2015
	Title: Virus infections in Obstetrics in Mozambique Candidate: Eulalia Macovela (INS, Mozambique) Dates: 2011-2016
MSc studies:	Title: International Health Master Programme Candidate: Doreen Pamba (NIMR-MMRC, Tanzania) Dates: 5 April 2012-5 April 2015

2.1.18 The Ring Plus Project

EDCTP Project Coordinator:	Tania Crucitti (Institute of Tropical Medicine, Belgium)
EDCTP Call Title:	Strategic Primer Grants
EDCTP Project Title:	Preparing for clinical trials with vaginal rings that protect women from HIV and unintended pregnancy
EDCTP Project Code:	SP.2011.41304.043
EDCTP Project Start Date:	15 December 2012
EDCTP Project End Date:	31 November 2014
Collaborators:	• Tania Crucitti (Institute of Tropical Medicine (ITM), Belgium) • Vicky Jespers (ITM, Belgium) • Therese Delvaux (ITM, Belgium) • Joris Menten (ITM, Belgium) • Stephen Agaba (Projet Rinda Ubuzima, Rwanda) • Evelyne Kestelyn (Projet Rinda Ubuzima, Rwanda) • Janneke van de Wijgert (Liverpool School of Tropical Medicine, UK)
Study/Trial	**The Ring Plus Project**
Site Principal Investigator(s):	• Stephen Agaba (Rwanda)
Clinical Trial/Study Sponsor:	The Institute of Tropical Medicine, Antwerp
Trial/Study title:	Preparing for clinical trials with vaginal rings that protect women from HIV and unintended pregnancy. The Ring Plus Project.
Project Acronym:	The Ring Plus Project
Primary Objective(s):	1. To assess the impact on the vaginal microbiome of the use of a vaginal ring intermittently or continuously. 2. To assess the level of acceptability and reported adherence to intermittent and continuous CVR use in women in Rwanda.
Secondary Objective(s):	3. To assess the general safety of the CVR. 4. To assess vaginal biofilm formation and to detect the presence or absence of a biofilm on the CVRs after intermittent or continuous use. 5. To determine the impact of intermittent or continuous use of the CVR on markers of inflammation and immune activation in the vagina. 6. To identify and describe the context specific attitudes and beliefs regarding family, family planning, sexuality, and gendered norms. Exploratory Objectives: To explore how women and men in Rwanda perceive and experience risk related to unwanted pregnancy and HIV and their attitudes and expectations toward multi-purpose rings (e.g. HIV and family planning).
Clinical Trial/Study site(s):	• Rinda Ubuzima Kigali (Rwanda)
Study design:	The study is a clinical trial with in addition a behavioural research component. The first component is an open label, single centre, randomized controlled trial. The second component is a qualitative study using in-depth interview (IDI) and focus group discussion (FGD) methodology.
Study population:	WOMEN (≥18 years); HIV-negative healthy women from the general population N= 120
Product(s):	• NuvaRing®: etonogestrel/ethinylestradiol
Manufacturer:	• N.V. Organon (a subsidiary of Merck & Co., Inc.,) (the Netherlands)
Cofunders:	
Trial Registration number(s):	NCT01796613

Status:	Ongoing
Results and Outcomes:	Enrolment completed as at 27 December 2013.
Publications:	

2.1.19 HIV-CORE004

EDCTP Project Coordinator:	Tomas Hanke (University of Oxford, UK)
EDCTP Call Title:	EDCTP Strategic Primer Grants
EDCTP Project Title:	A phase I/IIa clinical trial of universal HIV-1 vaccines pSG2.HIVconsv, MVA.HIVconsvand ChAdV63.HIVconsv in combined regimens in healthy HIV-1/2-negative adults in Nairobi. (HIV-CORE004)
EDCTP Project Code:	SP.2011.41304.002
EDCTP Project Start Date:	1 December 2012
EDCTP Project End Date:	30 November 2012
Collaborator(s):	• Tomas Hanke (University of Oxford, UK) • Marie Reilly (Karolinska Institute, Sweden) • Walter Godfrey Jaoko (University of Nairobi, Kenya) • Patricia Fast (International AIDS Vaccine Initiative (IAVI), USA)
Study/Trial 1	HIV-CORE004
Site Principal Investigator(s):	Walter Godfrey Jaoko (University of Nairobi, Kenya)
Clinical Trial/Study Sponsor:	University of Oxford (UK)
Trial/Study title:	A phase I/IIa clinical trial of universal HIV-1 vaccines pSG2.HIVconsv DNA, MVA.HIVconsv and ChAdV63.HIVconsv in combined regimens in healthy HIV-1/2-negative adults in Nairobi.(HIV-CORE004)
Goal:	• The study is part of a long-term aim to develop an effective HIV-1 vaccine and will evaluate safety and immunogenicity of HIVconsv vaccines in two heterologous regimens in African adults.
Primary Objective(s):	• To evaluate the safety and tolerability of candidate HIV-1 vaccines pSG2.HIVconsv DNA (D), ChAdV63.HIVconsv (C) and MVA.HIVconsv (M) administered intramuscularly in heterologous prime-boost regimens.
Secondary Objective(s):	• To evaluate the magnitude, specificity and breadth of HIV-1-specific T cell responses elicited by HIVconsv vaccines and their potential to inhibit HIV-1-replication *in vitro*.
Clinical Trial/Study site(s):	KAVI-Kangemi site, Nairobi (Kenya)
Collaborating site(s):	• KAVI-KNH Laboratory, Dept Medical Microbiology, University of • Nairobi (Kenya) • Jenner Institute, University of Oxford (UK) • Karolinska Institute (Sweden)
Study design:	A phase I/IIa double-blind, randomised, placebo controlled study in healthy, low risk, HIV-1-negative adults in Nairobi.
Number of subjects:	84 Subjects
Product(s):	candidate HIV-1 vaccines pSG2.HIVconsv DNA (D), ChAdV63.HIVconsv (C) and MVA.HIVconsv (M)
Manufacturer/Developer:	Bristol Institute of Transfusion Sciences, Clinical Biotechnology Centre, University of Bristol
Cofunders:	• Swedish International Development Cooperation Agency (Sida, Sweden) • Medical Research Council (MRC, UK) • Karolinska Institute (Sweden) • National Institute of Health (NIH, USA) • University of Oxford (United Kingdom) • IAVI (USA)
Status:	Ongoing
Results and Outcomes:	Project not yet recruiting patients
Publications:	

2.1.20 Van de Wijgert

EDCTP Project Coordinator:	Janneke van de Wijgert (University of Amsterdam, Netherlands)
EDCTP Call Title:	Capacity building for the conduct of phase I/II and Phase III trials of vaginal microbicides against sexual transmission of HIV
EDCTP Project Title:	Preparing for Phase III vaginal microbicide trials in Rwanda and Kenya: Preparedness studies, capacity building, and strengthening of medical referral systems
EDCTP Project Code:	CT.2005.33070.001
EDCTP Project Start Date:	10 April 2007
EDCTP Project End Date:	9 April 2011
Collaborators:	• Anne Buvé (Prince Leopold Institute of Tropical Medicine, Belgium) • Patricia Claeys (University of Ghent, Belgium) • Tania Crucitti (Prince Leopold Institute of Tropical Medicine, Belgium) • Eveline Geubbels (Projet Ubuzima, Rwanda) • Peter Gichangi (International Centre for Reproductive Health (ICRH), Kenya) • Vicky Jespers (Prince Leopold Institute of Tropical Medicine, Belgium) • Kishor Mandaliya (International Centre for Reproductive Health (ICRH), Kenya) • Justin Ntirushwa (Projet Ubuzima, Rwanda) • Marcel Reyners (International Centre for Reproductive Health (ICRH), Kenya) • Barbara Suligoi (Istituto Superiore di Sanità (ISS), Italy) • Marleen Temmerman (University of Ghent, Belgium) • Joseph Vyankandondera (Projet Ubuzima, Rwanda)
Study/Trial 1	
Site Principal Investigator(s):	• Janneke van de Wijgert (Netherlands) • Anne Buve (Belgium) • Marleen Temmerman (Belgium) • Kishor Mandalayi (Kenya) • Joseph Vyankandondera (Rwanda)
Trial/Study titles:	• Kigali HIV Incidence Study • Mombasa HIV Incidence Study • Reproductive Health Study • SEARCH study
Goal:	Preparing for phase III vaginal microbicide trials in Rwanda and Kenya. Preparedness studies, strengthening of medical referral systems, and capacity building
Primary Objective(s):	1. Conduct cross-sectional HIV surveys in Kigali and Mombasa using BED capture enzyme immunoassay (BED-CEIA) measures and Avidity Index (AI) testing, to estimate HIV prevalence in potential microbicide trial target populations, and to validate BED/AI testing in African settings 2. Establish cohorts of high-risk women in Kigali and Mombasa, after expanding community outreach into high-risk populations, to measure incidence of HIV, reproductive tract infections (RTIs) and pregnancy, and to evaluate recruitment and retention strategies 3. Improve microbicide trial capacity in Kigali and Mombasa by strengthening the clinical, laboratory, and data management infrastructure, local ethics committees, and reproductive health referral systems and by staff development at the sites as well as the wider research

	communities.
Clinical Trial/Study site(s):	• Projet Ubuzima (PU, Rwanda) • ICRHK (Kenya)
Collaborating site(s):	• AMC-CPCD (Netherlands) • ITM (Belgium) • Gent University (Belgium)
Study design:	Cross-sectional studies; and establishment of cohort of high-risk women
Cofunders:	• AMC-CPCD (Netherlands) • ITM (Belgium) • Gent University (Belgium) • ICRH (Kenya) • Projet Ubuzima (Rwanda) • NACCAP (Netherlands)
Status:	Completed
Results and Outcomes:	Both the HIV prevalence and incidencestudies in Kigali and Mombasa have been completed successfully. Additionally, PU has conducted two IPM-sponsored microbicide safety studies and was selected as trial site for the upcoming Phase III microbicide trial of IPM. The PU team has generated seventeen papers thus far using data from the Kigali HIV Incidence Study (KHIS) and the Reproductive Health Study (RHS); nine papers have been published (see publications list) and the others are in various stages of the submission and review process. The ICRH-Kenya team has published two papers. The Rwanda government is currently planning interventions for sex workers, and is leaning heavily on PU's experience. The Rwanda government is furthermore implementing an integrated HPV screening and vaccination program and the KHIS, RHS and SEARCH HPV results will be valuable in monitoring HVP type-specific distribution post-vaccination. The reproductive health clinic established at the Kigali Teaching Hospital is still up and running, increasing treatment options for cervical cancer and infertility. The successful Rwanda-Kenya-Belgium-Netherlands collaboration that was established in this project will continue in the next few years under the EDCTP funded Biomarkers project led by Dr Kishor Mandaliya entitled "Characterisation of novel microbicide safety biomarkers in East and South Africa".
Total number of subjects (cohort/epidemiological/ other studies):	Kigali: • Cross-sectional survey VCT clients: 1,250 • Cross-sectional survey high-risk women: 800 • Prospective cohort study HIV-negative high-risk women: 400 • Reproductive Health Study: 312 infertile women – 254 infertile male partners / 312 fertile women – 189 fertile male partners • SEARCH study: 300 HIV positive women + 100 HIV positive men. Mombasa: • Cross-sectional survey female sex workers: 800 • Cross-sectional survey post-partum women: 800 • Prospective cohort study HIV-negative female sex workers: 400
PhD studies:	Title: The Epidemiological Utility of antibody-based assays for estimating HIV incidence in Kigali, Rwanda Candidate: Sarah Braunstein (Columbia University, USA) Dates: 2005 - September 2009

	Title: The epidemiology of HIV and HPV among high-risk women and steady couples in Kigali, Rwanda Candidate: Nienke Veldhuijzen (University of Amsterdam, the Netherlands) Dates: 2006-9 June 2011
	Title: Clinical, epidemiological and socio-cultural aspects of infertility in resource-poor settings. Evidence from Rwanda Candidate: Nathalie Dhont (Ghent University, Belgium) Dates: 2007-15 April 2011
MSc studies:	Title: Both health and life matter becoming a sex worker: the experiences of women living in Kigali, Rwanda Candiate: Chantal Ingabire (University of Amsterdam, Netherlands) Dates: September 2009-17 August 2010
	Title: MSc Public Health Candidate: Sanbola Fulgencio (ITM, Belgium [Kenya]) Dates: 2007-2008
	Title: MSc Public Health Candidate: Jean Paul Balinda (National University of Rwanda, Rwanda) Dates: January 2011-December 2011
	Title: MSc Public Health Candidate: Aline Umutoni (National University of Rwanda, Rwanda) Dates: January 2011-December 2012
BSc studies:	Title: BSc Administration Candidate: Clair Bukuru (Free University Kigali, Rwanda) Dates: January 2011-December 2013
Other/Sub-studies:	The "Reproductive Health Study" (RHS): an observational study on infertility, and the links between HIV, sexually transmitted infections (STIs), and infertility, in the new CHUK clinic, as part of Dr Dhont's PhD fellowship. RHS is a case-control study in which the cases are infertile and the controls fertile Rwandan women. Their male partners are also invited to participate. All female study participants are interviewed, counselled, physically examined (including a pelvic examination), and tested for HIV, pregnancy, and a variety of reproductive tract infections (RTI) at study visits. They are screened for cervical precancerous lesions and treated if necessary. Infertile women also receive hysterosalpingography. The SEARCH Kigali: this study aims to evaluate reproductive health outcomes in HIV-positive women who are or are not yet taking HAART treatment. The study is being conducted in the TracPlus HIV clinic in Kigali. Most of the study is funded by the INTERACT program in Kigali (which is funded by the Dutch Government via the NACCAP mechanism and by EuropeAID).
Publications:	1. Veldhuijzen NJ, Braunstein SL, Vyankandondera J, Ingabire C, Ntirushwa J, Kestelyn E, Tuijn C, Wit FW, Umutoni A, Uwineza M, Crucitti T, van de Wijgert JH. The epidemiology of human papillomavirus infection in HIV-positive and HIV-negative high-risk women in Kigali, Rwanda. *BMC Infect Dis.* 2011 Dec 2;11:333. doi: 10.1186/1471-2334-11-333 2. Veldhuijzen NJ, Dhont N, Vyankandondera J, Gasarabwe A, Busasa R, Crucitti T, van de Wijgert JH. Prevalence and concordance of HPV, HIV, and HSV-2 in heterosexual couples in Kigali, Rwanda. *Sex Transm Dis*. 2012 Feb;39(2):128-35. doi: 10.1097/OLQ.0b013e3182367c4c. 3. Rusine J, Ondoa P, Asiimwe-Kateera B, Boer KR, Uwimana

	JM, et al. (2013) High Seroprevalence of HBV and HCV Infection in HIV-Infected Adults in Kigali, Rwanda. PLoS ONE 8(5): e63303. doi:10.1371/journal.pone.0063303

2.1.21 TVMTU

EDCTP Project Coordinator:	Richard Hayes (London School of Hygiene and Tropical Medicine (LSHTM), UK)
EDCTP Call Title:	Capacity building for the conduct of phase I/II and phase III trials of vaginal microbicides against sexual transmission of HIV
EDCTP Project Title:	Site preparation and capacity strengthening for trials of vaginal microbicides in Tanzania and Uganda
EDCTP Project Code:	CT.2005.33070.002
EDCTP Project Start Date:	5 May 2007
EDCTP Project End Date:	27 February 2011
Collaborators:	• John Changalucha (National Institute for Medical Research (NIMR), Tanzania) • Anatoli Kamali (Medical Research Council Programme on AIDS - Uganda Virus Research Institute (MRC/UVRI), Uganda) • Sheena McCormack (Medical Research Council, UK) • Janneke van de Wijgert (ICRH-International Centre of Reproductive Health, Netherlands)
Study/Trial 1	
Site Principal Investigator(s):	• Richard Hayes (UK) • Saidi Kapiga • Judith Vandepitte • Janneke van de Wijgert (Netherlands) • Sheena McCormack (UK)
Trial/Study title:	1. A feasibility study to assess potential cohort suitability for future microbicide trials in North West Tanzania 2. Studies on the epidemiology and prevention of HIV and other sexually transmitted infections in a cohort of women involved in high risk sexual behaviour in Kampala
Goal:	To strengthen and expand the capacity for phase I, II and III clinical trials of candidate vaginal microbicides in Tanzania and Uganda, in order to facilitate the rapid evaluation of new products that, if shown to be effective, would provide a valuable tool for women to protect themselves against heterosexually-acquired HIV infection.
Primary Objective(s):	1. To strengthen clinical trial resources at research units in Mwanza and Entebbe to provide additional capacity to carry out future microbicide trials to ICH/GCP standards. This will include strengthening of laboratory and clinical resources to support safety studies in phase I, II and III trials, strengthening of ethical review, work to ensure access of trial participants to appropriate HIV care, and staff development and training for Tanzanian and Ugandan scientists in the skills required to carry out clinical trials and to develop future scientific leaders 2. To establish new study cohorts in towns and roadside settlements near Mwanza (Tanzania) and in Kampala (Uganda). In each site, women at high-risk of HIV infection will be recruited to a feasibility study and followed up for 12 months to record retention rates and the prevalence and incidence of HIV, STIs and pregnancy, to develop and test study procedures and to establish effective community liaison.
Secondary Objective(s):	1. Capacity strengthening activities in both study sites to make an optimal contribution to current and future microbicide research in cooperating with the multi-centre collaboration coordinated by the Microbicide Development

	Programme (MDP).
Clinical Trial/Study site(s):	• Mwanza: Geita, Shinyanga, and Kahama (Tanzania) • Entebbe: Kibuye (Uganda)
Collaborating site(s):	• Mwanza Intervention Trials Unit (MITU, Tanzania) • National Institute for Medical Research (NIMR, Tanzania) • Medical Research Council/Uganda Virus Research Institute (MRC/UVRI, Uganda) • Academic Medical Center - Center for Proverty-related Communicable Diseases (AMC-CPCD, Netherlands) • Medical Research Council Clinical Trials Unit (MRC CTU, UK) • London School of Hygiene & Tropical Medicine (LSHTM, UK)
Study design:	Mwanza: prospective cohort study The study will recruit 1,000 women who work in recreational facilities in the northwest region of Tanzania. This is a cohort study with objectives including determining prevalence and incidence of HIV and other sexually transmitted infections; determining retention and pregnancy rates identifying key factors associated with retention; and establishing capacity to conduct a clinical trial. Kampala: A similar protocol was developed to recruit a cohort of 1,000 women involved in high risk sexual behaviour in Kampala, of which 500 HIV-negative women contributed to this study.
Status:	Completed
Results and Outcomes:	**Mwanza:** Enrolled 970 women (Geita 377, Shinyanga 286, Kahama 307). In 2010 follow-up activities continued until August 2010 with mop-up activities continuing until September 2010. During this time the baseline dataset for analysis was being worked on and from September to December 2010 the follow-up dataset was finalised. Preliminary results indicate that among 1,775 women who attended screening at all sites, 21.8% were already HIV positive (prevalence). The HIV incidence rate over 12 month period was 4.1/100 person-years. The pregnancy incidence rate was 30.3/100 person-years. Also observed high prevalence and incidence of other sexually transmitted infections, low condom usage, and substantial self report of risky sexual behaviours. Overall retention rate at 12 months was 84.0%, with some variation among the three sites (80.9% Geita, 87.7% Shinyanga, 84.4% Kahama). The capacity building activities involved establishing systems and routines in order to conduct a clinical trial following ICH/GCP standards. Three dedicated, functioning research clinics which can be used for future research were set up. Numerous staff trainings were conducted in main areas of clinical trial: laboratory, clinical management, data management, ethical review and research ethics, as well as financial and management training and system improvement. Further, project colleagues were supported in pursuing post-graduate learning within the Unit. In terms of overall achievements, the project successfully developed the research infrastructure required for future research activities to test new interventions, including microbicide trials. Project staffs were trained to conduct research according to the highest ethical and scientific standards

	and a system to recruit and follow-up women working in these settings and retain them in active follow-up for a period of up to one year was developed. A strong community liaison system was established to ensure effective communication between researchers, the participants, and other local stakeholders. **Uganda:** Outcomes show it is feasible to enrol and keep a cohort of female sex workers (high attendance rates achieved). Offering general care for them and their children under five is a major asset to motivate them to join and stay in the project. Results indicate: High HIV prevalence (37%) and incidence (16 HIV seroconverters over 374 person years, HIV incidence rate = 4.28 per 100 person years (95% CI 2.62-6.99)) • HIV seroconversion is not associated with any of the investigated behavioural factors in this high risk population, but is strongly associated with STIs (NG, HSV2, high titre active syphilis) • High prevalence of other STIs at baseline (NG 8%, CT 9%, high titer active syphilis 2%, TV 11% and BV48%); only CT and TV infection rates significantly decreased over the one year follow up period • High pregnancy rate: 59 new pregnancies; Pregnancy incidence rate = 16.78 per 100 person year (95% CI 13.00-21.66) • Relatively low uptake of hormonal contraceptives (oral pill 13%, injectable 31%), which did not significantly improve over one year of follow up despite continued promotion of family planning. Overall, the first female high risk cohort has been set up in Uganda providing important information for policy makers and scientists. Further, the project succeeded to build up a well performing new study site that has the capacity to carry out future microbicide trials to ICH/GCP standards. The site has all the facilities to run the research activities and to provide general care and includes office space for social science and administrative staff. The dedicated research team is well trained. An appropriate referral system for HIV care is established. Senior staff have improved their skills required to carry out clinical trials. The project has demonstrated that the study populations of women in both Tanzania and Uganda at high risk of HIV are suitable for the implementation of future trials of microbicides or other HIV prevention tools, with high HIV incidence and high retention rates. The high pregnancy rate and low use of effective contraceptive methods in the study point to the need for more intensive measures in any future trial to promote contraceptive use and reduce the rate of pregnancy. As a result of the studies, the MRC funded a project titled "Intravaginal practices in Tanzania and Uganda: Relationships with the vaginal microenvironment, HIV and other STIs" which was carried out in close collaboration with the EDCTP project. This research was to better understand potential risk factors for HIV infection among women. Intravaginal practices (IVP) are

	common in Africa and have been shown to be associated with HIV in some cross-sectional studies. The only two prospective studies investigating these behaviours in Africa have shown conflicting results. More prospective studies are needed to investigate the effects of IVP on HIV incidence. In addition, the MRC also funded a Population Health Sciences fellowship based on secondary analyses of data from three observational cohorts and the testing and analysis of stored specimens to do in-depth analyses of the correlates of BV and recurrence, description and correlates of BV-specific bacteria, and description of immune responses associated with BV or BV-specific bacteria.
Cofunders:	• UK MRC (UK) • AMC-CPCD/NACCAP (Netherlands) • MITU NIMR (Tanzania) • MRC UVRI (Uganda) • MRC CTU (UK) • LSHTM (UK)
Total number of subjects (cohort/epidemiological/ other studies):	1,970
MSc stuies:	Title: Distance Learning MSc programme at LSHTM Candidate: Joseph Masanja (MRC NIMR, Tanzania) Dates: 2009-2011
	Title: Distance Learning MSc programme at LSHTM Candidate: Erick Mgina (MRC NIMR, Tanzania) Dates: 2009-2011
Other/Sub-studies:	MITU/NIMR: Investigation of intravaginal practices among the study cohort by way of two sub studies – social science diary sub study and the inflammation sub-study.
Publications:	1. Vandepitte J, Bukenya J. Weiss H et al. HIV and Other Sexually Transmitted Infections in a Cohort of Women Involved in High-Risk Sexual Behavior in Kampala, Uganda. *Sexually Transmitted Diseases* 2011 - Volume 38 - Issue 4 - pp 316-323 2. Kamali a, Byomire H, Muwonge C, Bakobaki J, Rutterford C, Okong P, Profy A, Byaruhanga R, Namukwaya S, McComarck S, Grosskurth H, Nunn AJ, Lacey CJ. A randomised placebo-controllled safety and acceptability trial of PRO 2000 vaginal microbicide gel in sexually active women in Uganda. *Sex. Transm. Infcet* 2010;86(3):222 3. Nunn A, McComarck S, Crook AM, Pool R, Rutteford C, Hayes R. Microbicides Development Programme: design of a phase III trial to measure the efficacy of the vaginal microbicide PRO 2000/5 for HIV prevention. *Trials*. 2009;10:99 4. Vandepitte J, Bukenya J, Hughes P, Muller E, Buvé A, Hayes R, Weiss HA, Grosskurth H. Clinical characteristics associated with Mycoplasma genitalium infection among women at high risk of HIV and other STI in Uganda. *Sex Transm Dis.* 2012 Jun;39(6):487-91. doi: 10.1097/OLQ.0b013e31824b1cf3 5. Vandepitte J, Muller E, Bukenya J, Nakubulwa S, Kyakuwa N, Buvé A, Weiss H, Hayes R, Grosskurth H Prevalence and correlates of Mycoplasma genitalium infection among female sex workers in Kampala, Uganda. *J Infect Dis*. 2012 Jan 15;205(2):289-96. doi: 10.1093/infdis/jir733. Epub 2011 Nov 18 6. Vandepitte J, Weiss HA, Bukenya J, Nakubulwa S, Mayanja Y, Matovu G, Kyakuwa N, Hughes P, Hayes R, Grosskurth

	H. Alcohol use, mycoplasma genitalium, and other STIs associated With HIV incidence among women at high risk in Kampala, Uganda. *J Acquir Immune Defic Syndr*. 2013 Jan 1;62(1):119-26. doi: 10.1097/QAI.0b013e3182777167.

2.1.22 MRC CTU/MDP 301

EDCTP Project Coordinator:	Sheena McCormack (Medical Research Council, UK)
EDCTP Call Title:	Capacity building for the conduct of phase I/II and phase III trials of vaginal microbicides against sexual transmission of HIV
EDCTP Project Title:	Establishing HIV microbicide clinical trial capacity in Mozambique and expanding an existing site in South Africa
EDCTP Project Code:	CT.2005.33070.003
EDCTP Project Start Date:	3 May 2007
EDCTP Project End Date:	31 December 2010
Collaborators:	• Pedro Alonso (University of Barcelona, Spain) • Sibone Mocumbi (Instituto Nacional de Saúde (INS), Mozambique) • Paula Monjane (Community Develoment Foundation (FDC), Mozambique) • Helen Rees (University of the Witwatersrand, South Africa) • Jonathan Weber (Imperial College London, UK)
Study/Trial 1	**MDP 301**
Site Principal Investigator(s):	Gita Ramjee (RHRU)
Clinical Trial/Study Sponsor:	Medical Research Council (MRC, UK)
Trial/Study title:	An international multi-centre, randomised, double-blind, placebo-controlled trial to evaluate the efficacy and safety of 0.5% and 2% PRO 2000/5 gels for the prevention of vaginally acquired HIV infection Microbicides Development Programme (MDP) 301 (version 2.1)
Goal:	To evaluate the efficacy and safety of 0.5% and 2% PRO 2000/5 gels for the prevention of vaginally acquired HIV infection
Primary Objective(s):	To determine the efficacy and safety of 0.5% and 2% PRO 2000/5 Gel (P) compared to placebo in preventing vaginally acquired HIV infection
Secondary Objective(s):	To collect qualitative data via multi-method data collection strategy, involving triangulation of sexual behaviour data from case record forms (which will be collected in all participants), in-depth interviews and coital diaries
Clinical Trial/Study site(s):	• Reproductive Health & HIV Research Unit [RHRU] Orange Farm (South Africa) • NIMR Mwanza (Tanzania) • UVRI MRC (Uganda) • UTH Mazabuka (Zambia) • HPRU Durban (South Africa) • Africa Centre for Health and Population Studies Kwazulu Natal (South Africa)
Collaborating site(s):	• University of Barcelona (Spain) • RHRU (South Africa) • Imperial College of Science • Technology and Medicine (UK) • LSHTM (UK) • University Teaching Hospital Lusaka (Zambia) • UVRI MRC (Uganda) • NIMR Mwanza (Tanzania) • Africa Centre for Health and Population Studies Kwazulu Natal (South Africa) • South Africa African Medical and Research Foundation (AMREF, South Africa) • St George's Hospital Medical School (UK)
Study design:	Phase III multi-centre double-blinded randomised placebo-

	controlled trial
Product(s):	• PRO 2000 vaginal gel • HEC Placebo gel
Manufacturer/Developer:	• Indevus Pharmaceuticals (ENDO Pharma) • CONRAD (USA)
Cofunders:	• MRC (UK) • University of Barcelona (Spain) • RHRU (South Africa) • Imperial College of Science • Technology and Medicine (UK) • DfID (UK) • IPM (USA) • Indevus Pharmaceuticals (USA)
Trial Registration number(s):	ISRCTN 64716212
Status:	Completed
Results and Outcomes:	The study screened 15,818 of which 9,385 were enrolled into three arms; 2% PRO 2000 (n=2734), 0.5% PRO 2000 (N=3326) and the Placebo (n=3325). The RHRU centre successfully enrolled 2508 women, which was the largest contribution to the overall accrual of 9385, although lower than the original target agreed for this centre of 2800. The following HIV and STIs rates were found at enrolment: • HIV positive at screening: 26% • Chlamydia trachomatis: 8% • Neisseria gonorrhoea: 3% • Herpes (serology): 60% • Syphilis: 4% • Trichomonas vaginalis: 10% This study provided negative results which revealed that PRO 2000 (0.5 % concentration) was safe as tested but did not provide protection against HIV as compared to a placebo. Albeit negative, MDP301 did demonstrate that microbicides are highly acceptable to women and their partners, and that adherence was high at 92%. The key messages of the trial were: • Women and their partners liked the gel and used it • The study teams made supreme efforts to remind women about their appointments and the women came • Therefore the participants and staff gave PRO 2000 the best chance, and it is disappointing that the gel did not add benefit to the HIV prevention package • The study benefited women: regular exams, STI testing and treatment, risk reduction and supportive counselling Capacity for microbicide trials has been built in Mozambique as demonstrated by the successful completion of the Top Up study in two clinics, Manhica and Maputo. Further, the Mozambique team became a partner in the MDP network, and subsequently MDP has completed the Top Up study in 5 sub-Saharan African countries, and is actively engaged in raising funds (grant applications, advocacy) for the MDP302 trial to assess a single pre-sex dose of tenofovir 1% vaginal gel. Two Mozambican clinical research centres (Manhica and Maputo 1 de Junho) now have capacity for HIV prevention trials using unlicensed products. Because staff also have

	experience of the service sector, including ARV provision for therapy, they are well positioned to inform and support implementation of tenofovir gel should it become licensed in future. Laboratory capacity has been boosted for HIV, HSV-2 and syphilis testing **Challenges and setbacks** With the original funding of this EDCTP application, it was intended for Wits Health Consortium (Pty) Ltd) (the legal entity for Reproductive Health and HIV Research Unit (RHRU), Johannesburg Orange Farm site to expand so that 1,500 MDP301 participants could be enrolled. The RHRU was unable to purchase the plot for expansion within the timeframe of enrolment to the clinical trial. This did not impact on the overall power of the trial as the estimate for HIV incidence (4/100 person years) used in the sample size calculation was conservative and a smaller number than the target 9673 was needed to achieve 90% power. The original plan for Mozambique to become the seventh MDP301 recruiting trial site was ambitious and could only have been achieved with an earlier start to the award. A rogue blogger in Zambia caused reputational damage to MDP, which proved difficult to contain and ultimately led to a halt in microbicide research being approved in Zambia, notably VOICE which NIH had to withdraw. In February 2010 a meeting was organised by Dr Chisembele with MoH and Zambian researchers to set the record straight, and finally after several months approval for the Top Up study was obtained and the successful implementation of this in Zambia demonstrated that microbicide research was still viable. This was an important achievement for the MDP network with their partner CONRAD.
PhD study:	Title: PhD Social Anthropology Candidate: Jonathan Stadler (University of Pretoria, South Africa) Dates:2007-2011
MSc studies:	Title: MSc Epidemiology & Biostatistics Candidate: Jocelyn Moyes (University of the Witwatersrand (Wits), South Africa) Dates: 2009 – 2010
	Title: MSc Epidemiology & Biostatistics Candidate: Ananta Nanoo (University of the Witwatersrand (Wits), South Africa) Dates: 2009- 2010
	Title: MSc Epidemiology & Biostatistics Candidate: Sibongile Walaza (University of the Witwatersrand (Wits), South Africa) Dates: 2009-2010
	Title: Masters in Public Health Candidate: Mdu Mntambo Dates: 2008-2010
Study/Trial 2	**TopUp pilot study**
Site Principal Investigator(s):	• Robert Pool (Spain) • Khátia Munguambe (Mozambique)
Clinical Trial/Study Sponsor:	MRC UK
Trial/Study title:	A study to determine the feasibility of conducting a microbicide trial of daily vaginal gel and to inform the way adherence

	should be assessed: Top-Up Study
Goal:	To determine the feasibility of conducting a microbicide trial of daily vaginal gel and to inform the way adherence should be assessed
Primary Objective(s):	To investigate the acceptability and adherence to daily intravaginal universal placebo gel over 12 weeks.
Secondary Objective(s):	1. To inform the way adherence is assessed in a future clinical trial by comparing the following outcomes across three methods for monitoring adherence: – Adherence to daily use of gel – Consistency of the adherence measure – Retention of participants.
Clinical Trial/Study site(s):	Manhica and Maputo (CISM, Mozambique)
Collaborating site(s):	• CRESIB (Spain) • LSHTM (UK) • MRC CTU (UK) • MDP Programme Muzabuka (Zambia) • CISM (Mozambique) • HPRU MRC, Durban (South Africa) • NIMR (Tanzania) • UVRI MRC (Uganda)
Study design:	A multi-centre open-label randomised study, in which participants are randomised to one of three methods for monitoring adherence.
Product(s):	Hydroxyethyl cellulose (HEC) [placebo vaginal gel]
Manufacturer/Developer:	CONRAD (USA)
Cofunders:	• MRC (UK) • CRESIB (Spain)
Trial Registration number(s):	PACTR 201006000213418
Status:	Completed
Results and Outcomes:	The trial started June 2010 and finished follow up November 2010. There were 75 (40 in Manhica, 35 in Maputo) women screened of which 63 (31 in Manhica, 32 in Maputo) were enrolled. With respect to the daily placebo gel, women also found this acceptable, and reported adherence was higher than expected at 79% overall, albeit lower than reported in MDP301 when women were instructed to use a single dose of gel prior to sex. The TopUp study provided the first experience of microbicides in Mozambique and an opportunity to widely disseminate the CAPRISA 004 results raising hope for the future.
Publications:	1. Montgomery CM, Lees S, Stadler J, Morar NS, Ssali A, Mwanza B, Mntambo M, Phillip J, Watts C and Pool R. The role of partnership dynamics in determining the acceptability of condoms and microbicides. *AIDS Care*. 2008 Jul;20(6):733-40. 2. Sayles JN, Macphail CL, Newman PA and Cunningham WE. Future HIV Vaccine Acceptability Among Young Adults in South Africa. *Health Educ Behav*. 2009 Jun 9.
Study/Trial 3	**Mozambique feasibility study**
Site Principal Investigator(s):	Sibone Mocumbi (Mozambique)
Clinical Trial/Study Sponsor:	MRC (UK)
Trial/Study title:	A Feasibility Study to evaluate the population and study site in the Healthcare centres of Mavalane and Manhiça in preparation for a phase III randomised controlled trial of a vaginal microbicide for the prevention of HIV (FS Microbicides)
Goal:	A Feasibility Study to evaluate the population and study site in

	the Healthcare centres of Mavalane and Manhiça in preparation for a phase III randomised controlled trial of a vaginal microbicide for the prevention of HIV (FS Microbicides)
Primary Objective(s):	The primary objectives are to measure the prevalence and incidence of HIV and HSV2 infections, the prevalence of NG and CT; the maximal achievable rate of recruitment and retention in follow-up at 40 weeks, the frequency of vaginal intercourse and other sexual practices and the impact of safe sex counselling on the rate of condom use.
Secondary Objective(s):	1. Assess the level of HIV/AIDS awareness in the general community and within the target population 2. Assess the willingness of women to participate in a microbicide trial
Clinical Trial/Study site(s):	Manhiça Health Research Centre (Mozambique)
Collaborating site(s):	• MRC (UK) • Foundation for the Development of the Community (FDC) • Mavalane General Hospital (HGM, Mozambique) • Manhiça Health Research Centre (CISM, Mozambique) • Centre for International Health Hospital Clinic Barcelona (Spain)
Study design:	Prospective cohort study
Cofunders:	• MRC (UK) • University of Barcelona (Spain) • Reproductive Health and Research Unit • University of the Witswatersrand (South Africa)
Status:	Completed
Results and Outcoms:	Incidence in the Feasibility confirmed that women enrolled through these two clinics were a suitable target population, and indeed was higher than expected at 5/100 person years (95% CI 3.1-8.0). Recruitment was slow in Mozambique at both centres, but particularly in Manhica where there was no reimbursement according to the centre policy. In contrast to participation in the Demographic survey, women have to give up considerable time to take part in the Feasibility and Top Up studies. However, through a variety of community mobilisation exercises, this challenge was overcome, and the target number of 500 was exceeded. There were also challenges due to the language differences in the provision of training to the larger body of staff, and for data entry staff, for who English was not familiar. The database was programmed to enable staff to 'flip' between English and Portuguese screens to overcome this, and CRFs were developed with both languages on the same page. The skills gained in recruiting the 505 women, achieving 71% (361) retention according to the combined database increasing to 79% if the 35 pregnancies and 13 seroconvertors are subtracted from the denominator, and regular genital examinations and laboratory testing of adults have been a valuable addition to the existing capacity in Manhica which was predominantly demographic surveillance and vaccine trials in infants. Moreover, the Feasibility Study provided the first incidence data in Mozambique, complementing the national ante-natal data and raising awareness amongst government and policy makers that HIV is a major threat to health in Mozambique.

Publications:	1. McCormack S et al. PRO2000 vaginal gel for prevention of HIV-1 infection (Microbicides Development Programme 301): a phase 3, randomised, double blind, parallel-group trial. The Lancet.2010;376(9749):1329-37 2. Kamali a, Byomire H, Muwonge C, Bakobaki J, Rutterford C, Okong P, Profy A, Byaruhanga R, Namukwaya S, McCormack S, Grosskurth H, Nunn AJ, Lacey CJ. A randomised placebo-controllled safety and acceptability trial of PRO 2000 vaginal microbicide gel in sexually active women in Uganda. Sex. Transm. Infcet 2010;86(3):222-6 3. Nunn A, McCormack S, Crook AM, Pool R, Rutteford C, Hayes R. Microbicides Development Programme: design of a phase III trial to measure the efficacy of the vaginal microbicide PRO 2000/5 for HIV prevention. Trials.2009;10:99

2.1.22 Mandaliya – Biomarkers HIV Mic

EDCTP Project Coordinator:	Kishor Mandaliya (International Centre for Reproductive Health (ICRH), Kenya)
EDCTP Call Title:	Call for the support of clinical studies, capacity building and networking for HIV/AIDS microbicides
EDCTP Project Title:	Characterisation of novel microbicide safety biomarkers in East and South Africa
EDCTP Project Code:	IP.2007.33070.001
EDCTP Project Start Date:	6 April 2009
EDCTP Project End Date:	4 January 2013
Collaborators:	• Saade Ahmed Abdallah (International Centre for Reproductive Health (ICRH), Kenya) • Bazil Baltazar (National Institute for Medical Research, Mwanza Centre, Tanzania) • Anne Buvé (Prince Leopold Institute of Tropical Medicine, Belgium) • John Changalucha (National Institute for Medical Research (NIMR), Tanzania) • Joseph Chilongani (National Institute for Medical Research (NIMR), Tanzania) • Tania Crucitti (Prince Leopold Institute of Tropical Medicine, Belgium) • Gustavo Doncel (CONRAD, USA) Eechoutte, Mario Van (University of Ghent, Belgium) • Suzanna Francis (London School of Hygiene and Tropical Medicine (LSHTM), UK) • Richard Hayes (London School of Hygiene and Tropical Medicine (LSHTM), UK) • Betsy Herold (Albert Einstein College of Medicine, USA) • Rene Hol (Pantarhei Devices/Pantarhei Biosciences, Netherlands)
Site Principal Investigator(s):	• Mary Mwaura (Kenya) • Sinead Delany-Moretlwe (South Africa) • Gilles Ndayisaba (Rwanda)
Clinical Trial/Study Sponsor:	International Centre for Reproductive Health Kenya (ICRHK)
Trial/Study title:	Characterisation of novel microbicide safety biomarkers in East and South Africa
Goal:	Establish baseline ranges of biomarkers related to the vaginal environment in groups of women targeted for microbicide trials in Kenya, Rwanda, and South Africa
Primary Objective(s):	1. Characterise the vaginal environment with respect to: the vaginal microbial flora; biomarkers of epithelial integrity; and soluble and cellular biomarkers of immune activation, including target cells for HIV, in HIV-negative adult women in good health at low risk for HIV 2. Determine the presence of laboratory-confirmed genital infections, clinical signs of epithelial disruption and inflammation, and any other clinical observations and self-reported symptoms in these women 3. Compare the vaginal environment as described in primary objective 1 in HIV-negative adult women in good health at low risk for HIV with and without bacterial vaginosis.
Secondary Objective(s):	1. Assess the primary parameters (primary objective 1 and 2 in: HIV-negative adolescents; HIV-negative adult women using traditional vaginal practices; HIV-negative adult women at high-risk for HIV; and asymptomatic HIV-positive adult women

	2. Describe the association between presence/quantity of biomarkers of immune activation/epithelial integrity, visible signs of inflammation/epithelial integrity during pelvic exam/colposcopy, and self-reported symptoms indicative of genital irritation/inflammation
Tertiary Objective(s):	1. Compare cervicovaginal lavage (CVL) by self-sampling with the Pantarhei® screener with CVL clinician sampling and determine the feasibility of these methods 2. Compare the results of this study in African populations with results available in the literature (mostly from non-African populations), with future results of a similar vaginal characterization study by the CONRAD in the US population (study protocol A04-097), and results of similar study in a European population (EMPRO)
Clinical Trial/Study site(s):	• ICRHK (Kenya) • Reproductive Health Research Unit (South Africa) • Project Ubuzima (Rwanda)
Collaborating site(s):	• MITU/NIMR (Tanzania) • AMC-CPCD (Netherlands) • ITM (Belgium) • LSHTM • MRC CTU (UK)
Study design:	Multi-country prospective cohort study in 430 HIV- high-risk women
Product(s):	Pantarhei® screener
Manufacturer/Developer:	Pantarhei Devices
Cofunders:	• Medical Research Council (MRC, UK) • ITM (Belgium) • Ghent University (Belgium) • Pantarhei Devices (Netherlands)
Trial Registration:	DOH-27-0910-3223
Status:	Completed
Results and Outcomes:	In Kenya, Rwanda and South Africa, the study characterised the vaginal environment in 430 women at seven time points over eight months, and in Tanzania, the study characterised the vaginal environment in 100 women at 12 time points over 28 days. The vaginal microbiome was assessed by Amsel and Nugent criteria; quantitative PCR (qPCR) of 6 Lactobacillus species known to be related to vaginal health and five bacterial vaginosis associated species; a phylogenetic DNA micro-array containing probes for 251 vaginal bacteria; and Lactobacillus culture. Principal component analysis (PCA) of the qPCR data showed that a score based on levels of L. crispatus, L. jensenii, L. vaginalis, A. vaginae and G. vaginalis can be used as an indicator of a healthy or unhealthy vaginal microbiome. The L jensenii and L. crispatus species will be used in in vitro models to test new molecules for safety in the future. Preliminary micro-array data indicate the presence of 4 to 6 vaginal microbiome clusters dominated by either individual Lactobacillus species or by different levels and combinations of anaerobic bacteria. Both the PCA scores and the clusters correlated well with bacterial vaginosis status by Nugent score but not with bacterial vaginosis status by Amsel criteria (which are currently used for diagnosis in clinical settings). Furthermore, soluble biomarkers of inflammation and immune responses, such as cytokines, chemokines and antimicrobial peptides, were measured. The study identified several biomarkers that correlated with a healthy or unhealthy vaginal

	microbiome.
MSc studies:	Title: MSc in Public Health and Developing Countries Candidate: Bazil Baltazar (MITU-NIMR, Tanzania) Dates: 10 January 2011-1 November 2011
	Title: Master in Public Health Candidate: Marie Michelle Umulisa (PU) Dates: August 2011-November 2013
	Title: Master in Business Administration Candidate: Irene Kibara (ICRHK) Dates: 8 May 2010-29 June 2013
	Title: Master in Nutrition Candidate: Faith Musyoka (ICRHK) Dates:11 October 2009-9 September 2011
	Title: Master in Health Informatics Candidate: Masesa Clemens (MITU/NIMR) Dates: 2011-2012
PhD studies:	Title: Defining the immune vaginal environment and factors affecting HIV transmission Candidate: Jordan Kyongo (Kenya) Dates:July 2010-July 2013
	Title: Epidemiology and medical statistics & Advanced course in epidemiology analysis Candidate: Mary Mwaura (Kenya) (site PI) Dates: 21 June-9 July 2010/5-16 September 2011
BSc studies:	Title: BSc in Biomedical Laboratory Sciences Candidate: Lambert Mwambarangwe (PU) Dates: January 2012- June 2014
	Title: BSc Information Systems Candidate: Mary Thiongo (ICRHK) Dates: January 2011-June 2014
Other/Sub-studies:	The 'inflammation Sub-study' in Tanzania was an intensive longitudinal sub-study of 100 women carried out to look at rapid changes in the vaginal environment over one menstrual cycle. This study was also designed to capture changes in the vaginal environment due to previously documented highly prevalent vaginal practices. Participants in the Inflammation Sub-study were followed up every two to three days for 28 days (12 visits) with retention of 97%. Experiences gained from the in the Inflammation Sub-study were shared to allow for optimisation of study procedures, laboratory testing and analysis for the Biomarker Study in Rwanda, Kenya, and South Africa. The data from the Inflammation Sub-study will be analysed in conjunction with the Biomarkers study data.
Publications:	Ndayisaba G, Verwijs M, van Eeckhoudt S, Gasarabwe A, Hardy L, Borgdorff H, Kestelyn E, Jespers V, van de Wijgert J. Feasibility and Acceptability of a Novel Cervicovaginal Lavage Self-Sampling Device among Women in Kigali, Rwanda. Sexually Transmitted Diseases.2013;40:7

2.1.23 RHASA

EDCTP Project Coordinator:	Anne Buvé (Prince Leopold Institute of Tropical Medicine (ITM), Belgium)
EDCTP Call Title:	Strategic Primer Grants
EDCTP Project Title:	Preparing for clinical trials of interventions to improve the reproductive health of adolescent girls in sub-Saharan Africa
EDCTP Project Code:	SP.2011.41304.066
EDCTP Project Start Date:	1 December 2012
EDCTP Project End Date:	31 October 2014
Collaborators:	• Aura Georgina Aguirre-Andreasen (London School of Hygiene and Tropical Medicine, UK) • Kathy Baisley (London School of Hygiene and Tropical Medicine, UK) • John Changalucha (National Institute for Medical Research, Tanzania) • Tania Crucitti (Prince Leopold Institute of Tropical Medicine, Belgium) • Suzanna Francis (London School of Hygiene and Tropical Medicine, UK) • Soori Nnko (National Institute for Medical Research, Mwanza Centre, Tanzania) • Koen Peeters (Prince Leopold Institute of Tropical Medicine, Belgium) • Deborah Watson-Jones, (London School of Hygiene and Tropical Medicine, UK)
Trial/Study title:	Preparing for clinical trials of interventions to improve the reproductive health of adolescent girls in sub-Saharan Africa
Goal:	The overall aim is to inform future clinical trials of interventions to improve the reproductive health of adolescent girls in sub-Saharan Africa, including vaginal microbicides, vaccines and products that enhance the health of the vaginal environment such as probiotics.
Primary Objective(s):	1. To assess the acceptability of procedures for research on reproductive health among adolescent girls – To assess the acceptability, at the level of the community and among parents, of studies on reproductive health of young adolescents – To assess the impact on parent-child relationships of participation in a reproductive health study among adolescents under the age of legal consent – To assess the acceptability among the girls themselves 2. To characterise the vaginal microbiome in adolescent girls in Tanzania – To characterise and compare the vaginal microbiome of girls who have not yet initiated sexual activity and girls who have initiated sexual activity, using quantitative real time PCR (q RT PCR) – To compare the composition of the vaginal microbiome in adolescent girls in Mwanza (Tanzania) and adolescent girls in Antwerp (Belgium) – To explore vaginal practices and other risk factors for disturbances of the vaginal microbiome in adolescent girls in Mwanza – To explore whether bacterial vaginosis is associated with biofilm formation – To assess the inter-laboratory variability of real time PCR for the quantification of the major constituents of the vaginal microbiome.

Clinical Trial/Study site(s):	National Institute for Medical Research (NIMR, Tanzania)
Collaborating site(s):	• Prince Leopold Institute of Tropical Medicine (ITM, Belgium) • London School of Hygiene and Tropical Medicine (LSHTM, UK) • National Institute for Medical Research (NIMR, Tanzania)
Study design and population:	Observational (for objective 1) Cross sectional (for objective 2)
Number of subjects:	400 adolescents girls
Cofunders:	• Medical Research Council (MRC, UK) • ITM (Belgium) • LSHTM (UK)
Status:	Ongoing
Results and Outcomes:	
Publications:	

2.1.24 SASHA

EDCTP Project Coordinator:	Linda-Gail Bekker (University of Cape Town, South Africa)
EDCTP Call Title:	Capacity building in preparation for the conduct of preventive HIV vaccine trials (EDCTP/Gates Foundation/MS joint call)
EDCTP Project Title:	Feasibility of and Capacity Building for Adolescent HIV Vaccine Trials in South Africa
EDCTP Project Code:	CT.2006.33111.004
EDCTP Project Start Date:	21 January 2008
EDCTP Project End Date:	29 July 2011
Collaborators:	• Thola Bennie (Centre for the AIDS Programme of Research in South Africa (CAPRISA), South Africa) • Jimmy Chandia (Walter Sisulu University, South Africa) • Gavin Churchyward (Aurum Institute for Health Research, South Africa) • François Dabis (Victor Segalen Bordeaux 2 University, France) • Matthias Egger (University of Bern, Switzerland) • Glenda Gray (Perinatal HIV Research Unit (PHRU), South Africa) • Mary Latka (Klerksdorp Research Site (KOSH), South Africa) • Surita Roux (Desmond Tutu HIV Centre (DTHF), South Africa) • Maphoshane Nchabeleng (University of Limpopo, South Africa) • Catherine Slack (HIV AIDS Vaccines Ethics Group (HAVEG), South Africa) • Leslie Swartz (Stellenbosch University, South Africa) • Eftyhia Vardas (University of the Witwatersrand, South Africa)
Study/Trial 1	**HPV study**
Site Principal Investigator(s):	• Surita Roux (South Africa) • Glenda Gray (South Africa) • Mary Latka (South Africa) • Thola Bennie (South Africa) • Maphoshane Nchabeleng (South Africa) • Jimmy Chandia (South Africa)
Clinical Trial/Study Sponsor:	Merck Sharp & Dohme (Pty) Ltd
Trial/study title	Preparing for adolescent HIV vaccine trials in South Africa: A multi-centre study to evaluate acceptability of the HPV vaccine in adolescents
Goal:	Identify potential challenges to the inclusion of adolescents in HIV prevention trials by the use of the HPV vaccine as a proxy.
Primary Objective(s):	1. To assess recruitment and retention of adolescents in a vaccine trial for STDs and identify characteristics associated with recruitment, vaccine update and retention.
Secondary Objective(s):	1. Document prevalence and incidence of HIV, other STDs, pregnancies and circumcisions in adolescents 2. Compare methods of assessing understanding of vaccine assent 3. Determine the impact of vaccine receipt on sexual risk behaviour 4. Explore adolescent perceptions of risk and sexual behaviour 5. Investigate adolescent and parental attitudes towards informed consent norms 6. Assess social harms and benefits associated with adolescent participation in an HIV-related study

	7. Document adolescent health service needs.
Clinical Trial/Study site(s):	South African AIDS Vaccine Initiative (SAAVI) sites: • Desmond Tutu HIV Centre (DTHC, South Africa) • Perinatal HIV Research Unit (PHRU, South Africa) • Klerksdorp Research Site (KOSH, South Africa) • Centre for the AIDS Programme of Research in South Africa (CAPRISA), (South Africa) • Medunsa Clinical Research Unit (MeCRU, South Africa) • Walter Sisulu University (South Africa)
Collaborating site(s):	• University of KwaZulu Natal & HIV AIDS Vaccines Ethics Group (HAVEG, South Africa) • Institute of Public Health, Epidemiology & Development (France)
Study design and population:	Prospective cohort study with self-selecting intervention and control groups of 834 adolescents (aged 12-17 years)
Product(s):	GARDASIL
Manufacturer/ Developer:	Merck Sharp & Dohme (Pty) Ltd
Cofunders:	• Bill & Melinda Gates Foundation (USA) • ANRS (France) • Irish Aid (Ireland) • NACCAP (Netherlands) • SIDA (Sweden) • SNSF (Switzerland) • MRC (UK), Merck Sharp & Dohme (Pty) Ltd (South Africa)
Status:	Completed
Results and Outcomes:	In all, 834 adolescents were enrolled in the HPV vaccine study and 816 of these chose to be vaccinated. Overall, 85% of those screened were enrolled. Out of the total number of recruits, 502 were female and 698 were under 16 years. The SASHA group speculated that it is possible that the requirements for adolescents over 16 years to be sexually active and have their parents' consent to participation may have acted as a barrier to this age group. They concluded that further analysis is needed to establish this. SASHA collected incidence data for South African adolescents in HIV, pregnancy, STI and circumcision. In addition, the study gathered key social science data such as sexual risk behaviour, family communication, substance use, social support, and attitudes. By simulating a vaccine trial with a STI related licensed vaccine, the consortium got a handle on the ethical and legal aspects and the interaction with ethics committees. Consequently, the study developed ethical-legal guidelines and resources for the conduct of adolescent clinical trials in South Africa, which are currently open source and are rapidly becoming a nationally- and internationally-used reference.
Study/Trial 2	**Community attitudes study**
Site Principal Investigator(s):	• Surita Roux (South Africa) • Glenda Gray (South Africa) • Mary Latka (South Africa) • Thola Bennie (South Africa) • Maphoshane Nchabeleng (South Africa) • Jimmy Chandia (South Africa)
Trial/study title	Community Attitudes towards Adolescent Involvement in HIV Vaccine Trials: a Multi-Centre South African Study
Goal:	Prepare for adolescent involvement in HIV vaccine trials by exploring attitudes towards participation, informed consent, provision of adolescent prevention services and experiences of

	communication about HIV and sexual issues.
Primary Objective(s):	1. Assess adolescent attitudes towards participation in HIV vaccine trials 2. Explore adolescent attitudes towards disclosure of sexual activity to parent/guardian 3. Assess adolescent attitudes towards appropriate age of informed consent and disclosure of trial information to parent/guardian 4. Assess adolescent, parent/guardian and stakeholder views on the potential impact of HIV vaccine trial participation on sexual disinhibition 5. Examine adolescent, parent/guardian and stakeholder views on requirements for adolescent health services 6. Examine adolescent, parent/guardian and stakeholder attitudes toward male circumcision as a risk reduction method 7. Explore adolescent, parent/guardian and stakeholder perceptions of sexual risk behaviour in adolescents 8. Explore adolescent and parent/guardian attitudes toward and experiences of communicating about HIV and sexual issues.
Clinical Trial/Study site(s):	South African AIDS Vaccine Initiative (SAAVI) sites: Desmond Tutu HIV Centre (DTHC), Nyanga district, Cape Town (South Africa) Perinatal HIV Research Unit (PHRU), Johannesburg (South Africa) Klerksdorp Research Site (KOSH), Matlosana district (South Africa) Centre for the AIDS Programme of Research in South Africa (CAPRISA), Durban (South Africa) Medunsa Clinical Research Unit (MeCRU), Limpopo (South Africa) Walter Sisulu University, Mthantha (South Africa)
Collaborating site(s):	• University of KwaZulu Natal & HIV AIDS Vaccines Ethics Group (HAVEG, South Africa) • Institute of Public Health, Epidemiology & Development (France)
Study design:	Cross-sectional qualitative focus group study, with separate focus groups with parents/guardians, adolescents and stakeholders. Three focus groups will be conducted with adolescents, two with parent/guardians and two stakeholders. Adolescents (aged 12-17 years) from Nyanga Cape Town and their parents/guardians will be recruited. For the focus group, approximately 7-9 focus groups will be conducted at each site, with approximately 8 participants in each group (N= ca. 72 per site).
Cofunders:	• Bill & Melinda Gates Foundation (USA) • ANRS (France) • Irish Aid (Ireland) • NACCAP (Netherlands) • SIDA (Sweden) • SNSF (Switzerland) • MRC (UK)
Status:	Completed
Results and Outcomes:	In all, 141 Adolescents, 104 Parents, and 117 Stakeholders took part in the focus group. Preliminary data has shown that communication about sex is

	difficult between parents and adolescents;there are many misunderstandings and miscommunications between the two; and 3) third parties such as relatives seem to facilitate communication between parents and adolescents.
MPH study:	Title: Predictors of sexual risk behaviour in adolescents Candidate: Agnes Rowan (University of Cape Town, South Africa) Supervisor: Landon Myer (University of Cape Town, South Africa/Columbia University Mailman School of Public Health, USA) Dates: November 2009-June 2012
Publications:	1. Ellen, J., Wallace, M., Sawe, F.K. and Fisher, K. (2010). Community Engagement and Investment in Biomedical HIV Prevention Research for Youth: Rationale, Challenges and Approaches. *JAIDS*, 54 Suppl 1, S7-S11 2. Selected ethical-legal norms in child and adolescent HIV prevention research in south africa: consent, confidentiality and mandatory reporting

2.1.25 HIVTAB

EDCTP Project Coordinator:	Saidi Kapiga (London School of Hygiene and Tropical Medicine (LSHTM), UK)
EDCTP Call Title:	Capacity building in preparation for the conduct of preventive HIV vaccine trials (EDCTP/Bill & Melinda Gates Foundation/MS joint call)
EDCTP Project Title:	Capacity development and strengthening in preparation for HIV vaccine trials in Tanzania and Burkina Faso
EDCTP Project Code:	CT.2006.33111.013
EDCTP Project Start Date:	12 March 2008
EDCTP Project End Date:	11 September 2011
Collaborators:	• Dorothy Bray (ImmunoClin Ltd, UK) • John Changalucha (National Institute for Medical Research, Tanzania) • Mario Clerici (University of Milano–Bicocca, Italy) • Richard Hayes (London School of Hygiene and Tropical Medicine (LSHTM), UK) • Philipe Mayaud (LSHTM, UK) • Nicolas Meda (UFR-SDS University of Ouagadougou & Centre Muraz/site ANRS, Burkina Faso) • Nicolas Nagot (University of Montpellier 1, France) • Balthazar Nyombi (Kilimanjaro Christian Medical Centre (KCMC), Tanzania) • Philippe Van de Perre (Montpellier University Hospital Centre (CHU), France) • John Shao (KCMC, Tanzania) • Deborah Watson-Jones (LSHTM, UK) • Basia Zaba (LSHTM, UK)
Study/Trial 1	**Capacity development and strengthening in preparation for HIV vaccine trials in Tanzania and Burkina Faso**
Site Principal Investigator(s):	• Saidi Kapiga (Tanzania) • John Changalucha (Tanzania) • Balthazar Nyombi (Tanzania) • Nicolas Meda (Burkina Faso)
Trial/Study title:	Capacity development and strengthening in preparation for HIV vaccine trials in Tanzania and Burkina Faso
Goal:	Establish and strengthen research capacity and conduct specific research studies in preparation for clinical trials to assess the protective efficacy of HIV candidate vaccines
Primary Objective(s):	1. To develop and maintain study cohorts among high-risk populations and characterise potential study populations for future phase II/III HIV vaccine trials in Burkina Faso and Tanzania 2. To characterise HIV-1 viral isolates and assess factors associated with viral genotypes among identified target populations 3. To determine immunological and genetic factors that could confer resistance to HIV infections and/or slow down disease progression 4. To establish and strengthen research capacity in the study sites in Burkina Faso and Tanzania and promote South-South and North-South collaboration.
Clinical Trial/Study site(s):	• Mwanza Intervention Trials Unit (Tanzania) • Kilimanjaro Christian Medical Centre and National Institute for Medical Research (Tanzania) • UFR-SDS University of Ouagadougou & Centre Muraz/Site ANRS du Burkina Faso (Burkina Faso)

Collaborating site(s):	• London School of Hygiene & Tropical Medicine and ImmunoClin (UK) • University of Montpellier (France) • Milano University Medical School (Italy)
Study design:	Prospective cohort study **Tanzania:** • Develop and maintain study cohorts with adult women (18-44 years) working in bars, guest houses, hotels or other food and recreational facilities for future phase II/III vaccine trials: – Dataset from well-characterised high-risk populations from previous studies in Mwanza and Moshi will be analysed; – Additional data collected from ongoing cohort study to assess feasibility of future microbicides trials in Geita town, Mwanza region and Kahama and Shinyanga towns in Shinyanga region; – Establish new cohort from Moshi town and surrounding areas. • To characterise HIV-1 viral isolates and assess factors associated with viral genotypes among identified target populations (adult women, 18-44 years, HIV-sero-positive): – From ongoing microbicide feasibility study in Geita, Kahama and Shinyanga; – From serological surveillance system established in Kisesa to assess the feasibility of a future phase III intervention trial, including trials of new microbicide candidates; – From new cohort of high-risk women working in Moshi Town. • To determine immunological and genetic factors that could confer resistance to HIV infection and/or slow down disease progression: – Mainly adult men and women from the Kisesa serological surveillance system in Mwanza. Looking for: – Long-term non-progessors (LTNP); – Exposed sero-negative (repeated exposure, remain HIV-uninfected, ESN); – HIV-sero-positives infected after short exposure; – HIV-sero-positives who are rapid progressors. **Burkina Faso** • Develop and maintain study cohorts with adult women (18-44 years) sex workers and characterise potential study populations for phase II/III vaccine trials: – Datasets from well-characterised Yerelon Cohort population from previous studies in Bobo-Dioulasso will be analysed – Additional datasets to be collected from: – Ongoing Yerelon Cohort assessing the effectiveness of HIV prevention and care interventions among high-risk professional and part-time female sex workers – New cohort of HIV-sero-negative high-risk women (18-25 years) working as professional or part-time sex workers to be established in Ouagadougou. • To characterise HIV-1 viral isolates and assess factors associated with viral genotypes among identified target populations (adult women, 18-44 years, HIV-sero-positive): – HIV-sero-positive women from Yerelon cohort; – Newly diagnosed HIV-sero-positive women (18-25 years)

	from Ouagadougou. • To determine immunological and genetic factors that could confer resistance to HIV infection and/or slow down disease progression: – From Yerelon study, will classify subjects as: HIV-sero-postitive before HAART; HIV-sero-postitive taking HAART with undetectable plasma load; LTNP; ESN.
Number of subjects:	Moshi and Mwanza: 150 prevalent HIV+ve and 70 incident HIV+ve; Burkina Faso: 150 prevalent HIV+ve and 30 incident HIV+ve
Cofunders:	• Bill & Melinda Gates Foundation (USA) • ANRS & IRD (France) • Irish Aid (Ireland) • Milano University Medical School (Italy) • MRC (UK) • LSHTM & ImmunoClin (UK)
Status:	Completed
Results and Outcomes	Apart from maintaining existing cohorts in Tanzania (Moshi and Mwanza) and Burkina Faso (Yerelon), two new cohorts of high-risk women were established in Moshi, Tanzania (n = 650) and Ouagadougou, Burkina Faso (n = 300). In Tanzania, the prevalence of HIV in the general population decreased from 7.1% (95% CI 6.7-7.7%) in 2001 to 5.6% in 2009 (USAID, 2010). Although the incidence of HIV among women in the general population is unknown, it is likely to be much less than what was observed in the Moshi cohort [14.7% prevalence, with an incidence of 3.7/100 person-years (PYs) (95% CI: 2.2-6.2)]. This suggests that the Moshi cohort is suitable for future HIV vaccine trials. The prevalence (8%) as well as the incidence (0%) of HIV infection in the Ouagadougou cohort was not significantly different from that in the general population. This low incidence of HIV among these high-risk women may be related to the declining HIV prevalence in the general population in Burkina Faso and the positive impact of the risk reduction intervention delivered to the cohort by the study team. Therefore, this cohort is not suitable for future trials to test the efficacy of HIV candidate vaccines. HIV viral isolates in the two Tanzanian sites were characterised. Preliminary results show that there are multiple HIV subtypes in Moshi and Mwanza, with a substantial proportion of recombinant viruses. The study team suggest that Tanzania may be ideal place to study characteristics of different viruses and also in testing new vaccines against a range of viruses. When looking at the immunological and genetic factors that could confer resistance to HIV infection, the study team reported preliminary results that pointed to the importance of genes located in chromosome 22 in the resistance and control of HIV infection. However, they suggest that there might be differences between Caucasians and Africans. Collaborators in Montpellier developed an ELISpot assay which, combined with PCR techniques, examined factors associated with HIV-1 replication and immune responses. Using these techniques, samples from 52 HIV-1 infected women (33 of these

	were on HAART) from Burkina Faso were investigated. Results suggest that HIV-1 sexual transmission may occur independently of the HIV-1-infected cells located in the genital secretions but mostly involve HIV-1 secreted by cells from genital lymph nodes. This work reinforced the hypothesis that the genital compartment is separated from the vascular system in terms of HIV-1 reservoir and viral replication. In terms of capacity building, the following was achieved in this grant: • Strengthened the Mwanza Intervention Trials Unit (MITU) with administrative and technical support from LSHTM • Developed laboratory capacity to separate plasma and process PBMC, HIV viral genotyping (a genetic sequencer was purchased with the help of this grant and staff received related training), monitoring safety of future trial participants • Developed a GCP-compliant data management system in Tanzanian and Burkina Faso sites. This capacity will be helpful for future vaccine trials • Provided a range of training courses (short courses, ethics training, GCP, GCLP, data management, ethics review) within the consortium and beyond.
MSc study:	Title: Impact of Co-infection of herpes simplex virus (HSV-1) with human immunodeficiency virus (HIV-1) on HIV-1 Progression and HAART efficacy among High Risk women in Burkina Faso Candidate: Isodore Traore (University of Montpellier, France) Dates: September 2010-September 2011
Publications:	Kapiga, SH, Ewings, FE, Ao, T, Chilongani, J, Mongi, A, Baisley, K, Francis, S, Andreasen, A, Hashim, R, Watson-Jones, D, Changalucha, J, Hayes, R (2013). The Epidemiology of HIV and HSV-2 Infections among Women Participating in Microbicide and Vaccine Feasibility Studies in Northern Tanzania. PLoS ONE 8(7), doi:10.1371/journal.pone.0068825

2.1.26 TaMoVac-01

EDCTP Project Coordinator:	Muhammad Bakari (Muhimbili University College of Health Sciences, Tanzania)
EDCTP Call Title:	Capacity building in preparation for the conduct of preventive HIV vaccine trials (EDCTP/Gates Foundation/MS joint call)
EDCTP Project Title:	HIV vaccine trial capacity building in Tanzania and Mozambique by continued exploration of optimal DNA priming and MVA boosting strategies
EDCTP Project Code:	CT.2006.33111.007
EDCTP Project Start Date:	4 March 2008
EDCTP Project End Date:	31 December 2012
Collaborators:	• Sören Andersson (Örebro University Hospital, Sweden) • Gunnel Biberfeld (Karolinska Institute, Sweden) • Pontus Blomberg (Karolinska Institute, Sweden) • Frances Gotch (Imperial College, UK) • Bo Hejdeman (Karolinksa Institute, Sweden) • Michael Hoelscher (LMU, Germany) • Nesrina Imami (Imperial College, UK) • Ilesh Jani (Instituto Nacional de Saúde (INS), Mozambique) • Andrew Kitua (WHO/Special Programme for Research and Training in Tropical Diseases, Switzerland) • Leonard Maboko (MMRP, Tanzania) • Sayoki Mfinanga (NIMR, Tanzania) • Fred Mhalu (University of Dar es Salaam, Tanzania) • Charlotta Nilsson (Karolinska Institute, Sweden) • Nafissa Osman (Instituto Nacional de Saúde (INS), Mozambique) • Eric Sandstrom (Karolinska Institute, Sweden) • Willy Urassa (MUHAS, Tanzania) • Paula Vaz (Instituto Nacional de Saúde (INS), Mozambique) • Jonathan Weber (Imperial College, UK)
Study/Trial	**Feasibility of Neonatal Vaccination in Maputo**
Site Principal Investigator(s):	Paula Vaz (Mozambique)
Trial/Study title:	Feasibility study for HIV Vaccination Among Children in Maputo City, Mozambique
Goal:	Assess factors involved in the acceptability of a newborn/infant HIV vaccine trial
Primary Objective(s):	Evaluate knowledge and attitudes from mothers and families concerning HIV and vaccines
Clinical Trial/Study site(s):	Maputo Central Hospital, Maputo, Mozambique Polana Caniço Health Centre, Maputo, Mozambique
Study design and population:	A pilot study, including qualitative and quantitative methods, on 200 mothers, fathers and grandmothers of infants to assess factors involved in the acceptability of a newborn/infant HIV vaccine trial.
Status:	Completed
Results and Outcomes:	A pilot acceptability study has been undertaken in November 2011 aimed at preparing IEC interventions for an eventual HIV vaccine trial in neonates. The study took place in Maputo Central Hospital (MCH) and Polana Caniço Health Center (PCHC) whereby 36 respondents filled in questionnaires and underwent interviews. These were women and men sitting in waiting rooms at the maternity and pediatric services, as well as husbands and mothers-in-law. After analysis of the data, it has been learnt that husbands and mothers-in-law must be reached by direct invitation to facilitate neonatal vaccination. The conditions have

	therefore been set to actually implement the study.
Publications:	

2.1.27 CHIVTUM

EDCTP Project Coordinator:	Pontiano Kaleebu (Medical Research Council Programme on AIDS - Uganda Virus Research Institute (MRC/UVRI), Uganda)
EDCTP Call Title:	Capacity building in preparation for the conduct of preventive HIV vaccine trials (EDCTP/Gates Foundation/MS joint call)
EDCTP Project Title:	Strengthening of long-term clinical and laboratory research capacity, cohort development, and collection of epidemiological and social science baseline data in Uganda and Malawi to prepare for future HIV vaccine trials
EDCTP Project Code:	CT.2006.33111.011
EDCTP Project Start Date:	20 November 2007
EDCTP Project End Date:	31 December 2011
Collaborators:	• Frans van den Boom (International AIDS Vaccine Initiative (IAVI), Netherlands) • Jill Gilmour (IAVI, Netherlands) • Simon Heck (The WorldFish Center, Malawi) • Robert Heyderman (Malawi-Liverpool-Wellcome Trust Research Programme, Malawi) • David Lalloo (University of Liverpool, UK) • Victor Mwapasa (Malawi-Liverpool-Wellcome Trust Research Programme, Malawi)
Study/Trial 1	**Malawi epidemiological and social science study**
Site Principal Investigator(s):	Victor Mwapasa (Malawi)
Trial/Study title:	HIV and STI in fishing communities in Mangochi: assessing the transmission dynamics and feasibility of conducting future preventative trials
Goal:	Assess the transmission dynamics and feasibility of conducting preventative trials on HIV and STI in fishing communities in Mangochi
Primary Objective(s):	1. Determine and understand the transmission dynamics of STIs, including HIV in fishing communities 2. Determine factors promoting or preventing the participation of these communities in research studies and/or health interventions.
Secondary Objective(s):	1. Explore how different constituents comprising fishing communities shape vulnerability/resilience to STIs including HIV 2. Assess the acceptability of the fishing communities to participate in preventative health research and health interventions, including HIV testing and counselling, anti-retroviral treatment and vaccine trials 3. Determine the prevalence, incidence and type of HIV and STIs in the fishing communities in Mangochi 4. Determine the retention rates of clients from a fishing community participating in a prospective cohort study and explore factors promoting and preventing study participation.
Clinical Trial/Study site(s):	Fishing communities of Namaso, Nkope, Malembo, Msaka, Mvunguti and Chirombo villages. Sample processing and short-term sample storage was done at Mangochi District Hospital. Lab analyses were conducted at the Mangochi District Hospital and Malawi-Liverpool-Wellcome Trust Clinical Research Programme in Blantyre.
Collaborating site(s):	• Division of Community Health and Research on Equity and Access to Community Health (REACH) Trust (Malawi) • Liverpool School of Tropical Medicine (UK) • World Fish Centre (Malawi)

Study design and population:	**Participatory and qualitative studies:** The participatory methods will provide contextual information from the perspective of the participants on the characteristics of the fishing community: livelihoods, mobility, health service provision and access to health services and views on health research. Whereas the quantitative research (interviews, focus groups and participant observation) will collect information on: how social norms and behaviours can affect vulnerability/resilience to HIV and other STIs, levels of mobility and sexual interactions amongst different groups, health seeking behaviour, level of utilisation of HIV and AIDS services and views and experiences of health research. Study population: Adult men and women (over 20yrs) and young women (under 20) from fishing communities of Namaso, Nkope, Malembo, Msaka, Mvunguti and Chirombo villages. N= 382 **Prospective cohort study:** Participants will be screened for HIV and those that are HIV-negative will be followed up at 3 month intervals to obtain data on the incidence of HIV, STIs and pregnancy. Study population: Men and women (15-49yrs) as well as young people classified as "mature minors" (13-15yrs) who are married or have children residing in the fishing communities of Namaso, Nkope, Malembo, Msaka, Mvunguti and Chirombo villages for at least 3 months prior to recruitment and who plan to stay for the following two years, either continuously or intermittently. N=1000
Cofunders:	• Bill & Melinda Gates Foundation (USA) • IAVI (Netherlands) • Irish Aid (Ireland) • Malawi-Liverpool-Wellcome Trust Clinical Research Programme and WorldFish Center (Malawi) • SIDA (Sweden) • UVRI (Uganda) • MRC (UK) • WHO African AIDS Vaccine Programme (Switzerland) • Canadian HIV Trials Network (Canada) • Foundation for the National Institutes of Health (USA)
Status:	Completed
Results and Outcomes	The rates of HIV in the Malawi study population were found to be similar to the general population. This was suspected to be because a significant proportion of study participants (around 44%) knew of their HIV negative status prior to enrolment. Consequently, there was evidence of changes in sexual networking, whereby study participants who tested negative preferred to engage in sexual relations amongst each other. However, high-risk behaviours were identified during the course of the study such as unprotected sex or coerced sex. In addition, high rates of herpes simplex, a surrogate marker of high-risk behaviour, were found, suggesting that this population is still at higher risk for HIV infection than the general population.

Study/Trial 2	**Uganda epidemiological, social science and virology study**
Site Principal Investigator(s):	Pontiano Kaleebu (Uganda)
Trial/Study title:	Prospective cohort study to determine HIV incidence, risk factors for HIV infection, describe the molecular epidemiology and the social and behavioural characteristics in fishing populations of three lakeshore districts in Uganda in preparation for future HIV prevention research
Goal:	Determine HIV incidence, risk factors for HIV infection, describe social and behavioural characteristics and the molecular epidemiology in fishing populations in three lakeshore districts in Uganda in preparation for future HIV prevention research
Primary Objective(s):	Main cohort study: 1. Identify HIV-negative high-risk populations within fishing communities in which preliminary prevalence data indicate that new high incidence cohorts could be established 2. Recruit, counsel and test for HIV infection, determine retention rates and factors that impact loss to follow-up 3. Assess risk factors and understand social and behavioural characteristics for HIV infection in these populations.
Secondary Objective(s):	Virology sub-study: 1. Characterise the circulating HIV-1 subtypes in order to better understand the molecular epidemiology in these populations. Social and behavioural context sub-study: 1. Describe the broader social and behavioural characteristics of the general population in the fishing communities 2. Assess the acceptability to people living in fishing communities of preventative health research and health interventions, including HIV testing and counselling, anti-retroviral therapy and vaccine trials.
Clinical Trial/Study site(s):	Fishing villages in the Wakiso, Masaka and Mukono districts (Uganda)
Collaborating site(s):	• MRC/UVRI Uganda Research Unit on AIDS and UVRI-IAVI HIV Vaccine Program (Uganda)
Study design and population:	The **main cohort study** is a prospective cohort study, through which a demographic, medical history questionnaire will be administered and volunteers requested to provide blood samples at each visit. Study population: Male and female volunteers (13-49yrs), N=1000 The **virology sub-study** will have blood collected to be used to describe the molecular epidemiology of circulating virues. Study population: Sub sample (N= 300) of HIV+ volunteers who screen out due to HIV sero-positivity at enrolment from the main cohort and those who enrol and seroconvert during follow-up. The **social and behavioural context sub-study** will utilise qualitative and quantitative methods, including mapping, semi-structured and in-depth interviews. N= 50
Cofunders:	• Bill & Melinda Gates Foundation (USA) • IAVI (Netherlands) • Irish Aid (Ireland) • Malawi-Liverpool-Wellcome Trust Clinical Research Programme (Malawi)

	• WorldFish Center (Malawi) • SIDA (Sweden) • UVRI (Uganda) • MRC (UK) • WHO African AIDS Vaccine Programme (Switzerland) • Canadian HIV Trials Network (Canada) • Foundation for the National Institutes of Health (USA)
Status:	Completed
Results and Outcomes	A new high-risk population has been identified in Uganda which has great potential for inclusion in future HIV prevention research. This is particularly important given recent findings related to ARV-based prevention, which may eventually make it difficult to work with cohorts that are comprised solely of discordant couples. Findings from the cohort include an HIV and active syphilis prevalence of about 28.8% and 4.3% respectively while HIV incidence has been reported as 4.9%. High-risk behaviours have been reported in this population as well. When the study team identified HIV-1 sub-types from study participants, the major subtypes identified were subtypes A and D but with a high percentage (21%) of unique recombinant viruses. Results also pointed to a high degree of sexual mixing in this population. Significant capacity has been developed both in Uganda and Malawi: • Increased capacity for immunological research at the UVRI with expanded laboratory space, new equipment enabling new assays to be conducted, training and experience in new techniques such as microarray assay • Increased data management capacity at the UVRI • Clinical teams have built upon their capacity to develop new protocols and studies • Integration of social science into the development of new protocols and studies • Increased capacity in Malawi for the conduct of population based studies, community mobilization and social science • Developed guidelines and training manuals for Community Advisory Groups which have are being used in other research sites • Development of a new south-south network which has been mutually beneficial and which has led to new projects and collaborations • Increased capacity at UVRI for south–south training in laboratory techniques and in GCP and GCLP • Increased the ability of the MLW laboratory to progress towards GCLP compliance • Increased capacity at UVRI and MLW in managing large international grants and in managing activities within a consortium.
Other/Sub-studies (including cohorts/ epidemiology studies):	Yellow Fever DNA Microarray Assay study A study to compare DNA microarray immune response profiles in healthy Ugandan adults against DNA microarray immune response profiles in South and North American populations using the Yellow Fever vaccine. This study will investigate a novel method of tracking the immune response to vaccines, the microarray assay, which tracks the expression of genes involved in the innate and adaptive immune responses.

	Schistosomiasis sub study (among those from main cohort) – pending approval of protocol To determine the odds of worm infections diagnosed using stool samples obtained on three consecutive days for intestinal Schistosoma mansoni infection in stool (Kato Katz method) and using blood samples for Mansonella perstans (Knott's method) in 50 incident cases of HIV infection compared to 150 HIV-negative controls from the fisher folk main cohort. To compare prevalence of S. mansoni infection status from stored blood samples at enrolment and at 18 months among 50 HIV incident cases and 150 HIV-negative controls from the fisher folk cohort. To investigate innate and adaptive immune responses among HIV incident cases with worm infections.
PhD study:	Title: Immunological interactions between helminths and HIV infection Candidate: Andrew Obuku Akii (Makerere University, Uganda) Dates: December 2010-March 2015
MSc studies:	Title: Monoclonal B-cell lymphocytosis in a rural Ugandan population Candidate: Aloysious Ssemaganda (Makerere University, Uganda) Dates: August 2010-January 2013
	Title: Hepatitis C Virus Genotypes and Confirmation of Antibody Reactive Serum Samples from East Africa using Reverse Transcriptase and Real Time PCR Candidate: Paul Kato Kitandwe (Makerere University, Uganda) Dates: November 2007-December 2011
Publications:	1. Asiki, G, Mpendo, J, Abaasa, A, Agaba, C, Nanvubya, A, Nielsen, L, Seeley, J, Kaleebu, P, Grosskurth, H, Kamali, A. (2011) HIV and syphilis prevalence and associated risk factors among fishing communities of Lake Victoria, Uganda. *Sex Transm Infect*. Oct;87 (6):511-5, doi: 10.1136/sti.2010.046805 2. Seeley, J, Nakiyingi-Miiro, J, Kamali, A, Mpendo, J, Asiki, G, Abaasa, A, De Bont, J, Nielsen, L, Kaleebu, P; CHIVTUM Study Team. (2012) High HIV incidence and socio-behavioural risk patterns in fishing communities on the shores of Lake Victoria, Uganda. *Sex Transm Dis*., Jun;39(6):433-9. doi: 10.1097/OLQ.0b013e318251555d 3. Nazziwa, J, Njai, HF, Ndembi, N, Birungi, J, Lyagoba, F, Gershim, A, Nakiyingi-Miiro, J, Nielsen, L, Mpendo, J, Nanvubya, A, Debont, J, Grosskurth, H, Kamali, A, Seeley, J, Kaleebu, P, The Chivtum Study Team. (2013) Transmission clusters and evidence of HIV-1 transmitted drug resistance among recently infected antiretroviral naïve individuals from Ugandan fishing communities of Lake Victoria. *AIDS Res Human Retroviruses*, May;29(5):788-95, doi: 10.1089/AID.2012.0123 4. MacPherson, EE, Sadalaki, J, Njoloma, M, Nyongopa, V, Nkhwazi, L, Mwapasa, V, Lalloo, DG, Desmond, N, Seeley, J, Theobald, S. (2012) Transactional sex and HIV: understanding the gendered structural drivers of HIV in fishing communities in southern Malawi. *J Int AIDS Soc*. 15 Suppl 1:1-9, doi: 10.7448/IAS.15.2.17364.

2.1.28 FAHSAM/WISH

EDCTP Project Coordinator:	Jo-Ann Passmore (University of Cape Town, South Africa)
EDCTP Call Title:	Strategic Primer Grants
EDCTP Project Title:	Factors affecting HIV susceptibility in the adolescent genital mucosa (FAHSAM)
EDCTP Project Code:	SP.2011.41304.038
EDCTP Project Start Date:	15 December 2012
EDCTP Project End Date:	31 November 2014
Collaborators:	• Clive Gray (University of Cape Town (UCT), South Africa) • Heather Jaspan (UCT, South Africa) • Linda-Gail Bekker (UCT, South Africa) • Anna Lisa Williamson (UCT, South Africa) • Carolyn Williamson (UCT, South Africa) • Nicola Mulder (UCT, South Africa) • David Lewis (National Institute for Communicable Diseases, South Africa) • Glenda Gray (Perinatal HIV Research Unit (PHRU) Soweto, South Africa) • Douglas Wilson (Edendale Hospital KwaZulu-Natal Health Department, South Africa) • Lynn Morris (National Institute for Communicable Diseases, South Africa) • Fransesca Chiodi (Karolinska Institutet, Sweden) • Robin Shattock (Imperial College, UK) • Thomas Hope (Northwestern University, USA)
Study/Trial	**FAHSAM/WISH**
Site Principal Investigator(s):	• Jo-Ann Passmore (South Africa)
Clinical Trial/Study Sponsor:	UCT, South Africa
Trial/Study title:	Factors affecting HIV susceptibility in the adolescent female genital tract: "WISH" study (Women's Initiative in Sexual Health)
Project Acronym:	FAHSAM/WISH
Primary Objective(s):	1. To identify whether age, bacterial microbiome species, and sexually transmitted infections influence the state of T-cell activation and the type of inflammatory markers in female adolescent genital tracts.
Clinical Trial/Study site(s):	• Masiphumelele Adolescent Centre Cape Town (South Africa) • PHRU Soweto (South Africa)
Study design:	A longitudinal, observational cohort study
Study population:	FEMALE ADOLESCENTS (16-22 years); Female adolescents and young adults aged 16–22 attending the Masipumelele Youth Center for health care N= 150
Cofunders:	Department Of Science And Technology (South Africa)
Status:	Ongoing
Results and Outcomes:	
Publications:	

2.1.29 AfrEVacc

EDCTP Project Coordinator:	Jonathan Weber (Imperial College London, UK)
EDCTP Call Title:	Capacity building in preparation for the conduct of preventive HIV vaccine trials (EDCTP/Gates Foundation/MS joint call)
EDCTP Project Title:	African-European HIV Vaccine Development Network (AfrEVacc)
EDCTP Project Code:	CT.2006.33111.001

EDCTP Project Start Date:	28 March 2008
EDCTP Project End Date:	27 May 2012
Collaborators:	• Sinead Delany-Moretlwe (University of the Witwatersrand, South Africa) • Josefo Joao Ferro (Faculty of Medicine of Universidade Católica de Moçambique, Mozambique) • Michael Hoelscher (Ludwig-Maximilians Universitat Munchen, Germany) • John Imrie (Africa Centre for Health and Population Studies, South Africa) • Joep Lange (Academic Medical Center, University of Amsterdam, Netherlands) • Leonard Maboko (Mbeya Medical Research Programme, Tanzania) • Sheena McCormack (MRC, UK) • Khátia Munguambe (Manhiça Health Research Center (Mozambique) • Denise Naniche (Hospital Clinic of Barcelona, Spain) • Marie Louise Newell (Africa Centre for Health and Population Studies, South Africa) • Giuseppe Pantaleo (Centre Hospitalier Universitaire Vaudois-CHUV/EuroVacc Foundation, Switzerland) • Robert Pool (Manhiça Health Research Center, Mozambique) • Gita Ramjee (MRC, South Africa) • Helen Rees (University of the Witwatersrand, South Africa) • Wendy Stevens (University of the Witwatersrand, South Africa) • James Tartaglia (Sanofi-Aventis, France) • Kylie Glasgow (Imperial Colege, UK) • Roger Tatoud (Imperial College, UK) • Hans Wolf (University of Regensburg, Germany) • Arlinda Zango (Faculty of Medicine of Universidade Católica de Moçambique (UCM), Mozambique)
Study/Trial 1	**Beira Study**
Site Principal Investigator(s):	Josefo João Ferro and Arlinda Zango (Mozambique)
Trial/Study title:	Combined cross-sectional and prospective cohort study for measurement of HIV incidence in Beira, Mozambique
Goal:	To estimate HIV incidence within a population at higher risk of HIV in Beira, Mozambique, in preparation for future HIV prevention interventions and intervention studies.
Primary Objective(s):	1. To estimate HIV incidence in women at higher risk in Beira using a cross-sectional methodology, and to compare the results with HIV incidence measured prospectively within a subgroup of initially HIV-negative women from the cross-sectional phase 2. To determine the percentage of known HIV infected individuals (12+ months) that are identified by BED assay as having a recent infection 3. To assess UCM's ability to recruit and retain a cohort of approximately 400 women at higher risk for one year.
Secondary Objective(s):	1. To validate the BED assay for use in HIV incidence estimation in the Beira context 2. To estimate HIV incidence in sub-groups, for example according to HIV risk behaviours/groups and age, and to describe demographic characteristics and HIV risk behaviours of participants 3. To determine prevalence and incidence of pregnancy and herpes simplex virus type 2 (HSV-2) in the prospective

	cohort study.
Clinical Trial/Study site(s):	Universidade Católica de Moçambique, Beira (Mozambique)
Collaborating site(s):	• FHI, Research Triangle Park (USA) • Amsterdam Medical Center (The Netherlands)
Study design and population:	• **Cross-sectional survey:** Approximately 1000 women at risk of sexual acquisition of HIV with unknown HIV status and will be tested for recent HIV infection using the Calypte HIV-1 BED Incidence EIA (BED), which estimates the rate of new HIV infections in populations by determining what population of HIV-positive individuals were infected within six months of sample collection. • **Prospective cohort study:** HIV-negative individuals in the cross-sectional survey will be invited to join a prospective cohort study for 12 months. At each monthly visit, cohort participants will be tested for HIV antibodies. Those who seroconvert during the 12 month follow-up period will have previous samples tested by HIV-1 RNA PCR to pinpoint the time of seroconversion; study conducted on approximately 400 women who tested HIV-negative in cross-sectional survey and who volunteer for follow-up. • **BED false recent calibration:** HIV-positive individuals who have been infected for 12+ months and who have not used antiretroviral treatment will be eligible for the BED False Recent phase. The BED assay will be used to determine the percentage of established HIV infections that are falsely labelled as 'recent'. This will be done by Western blot and HIV-1 RNA PCR. Study will be completed on approximately 400 HIV-positive adults known to be HIV-infected for 12+ months from study start and who have not used ART.
Cofunders:	• Bill & Melinda Gates Foundation (USA) • US Agency for International Development (USAID)
Status	Completed
Results and Outcomes	The team successfully established a new clinical research centre at the UCM in Beira – the CIDI. During the course of the study, very high incidence rates of HIV were found in this region. CIDI enrolled 1,020 women with unknown HIV status (18-35 years of age) in a cross-sectional HIV seroprevalence survey, of whom 406 HIV-negative women were subsequently followed in a prospective cohort study for 12 months. In addition, CIDI enrolled 408 women and men with chronic HIV infection (also 18-35 years of age) in the BED false recent survey. This was to determine the local false recent rate to be used for HIV incidence estimation using the BED assay. Interim analysis results are as follows: The HIV prevalence in the cross-sectional survey was 33% (95% CI 30.1-35.9). The prospective HIV incidence rate was 8.4 per 100 women-years (95% CI: 5.2–12.8), with 21 seroconversions over 251.2 women-years (WY) of follow-up. Prospective HIV incidence was higher among the 18–24 age group (9.1 per 100 WY; 95% CI: 5.4–14.3) than the 25–35 age group (5.7 per 100 WY; 95% CI: 1.2–16.7). The estimated cross-sectional incidence using the BED assay results was 9.6% (95% CI: 6.5–12.6) using the Hargrove correction formula and the locally derived false recent rate of 1.8%.
Study/Trial 2	**Manhica Feasibility Studies (EVAS) (capacity building)**

Site Principal Investigator(s):	• Khátia Munguambe (Mozambique) • Denise Naniche (Spain)
Trial/Study title:	A feasibility and acceptability study in preparation for phase I/II clinical trials of an HIV vaccine candidate in Manhiça, Mozambique (EVAS)
Goal:	To contribute to capacity development and provide information needed for the conduction of HIV vaccine trials in Mozambique
Primary Objective(s):	1. To assess the feasibility and acceptability of future HIV vaccine trials in Manhiça by determining: – The recruitment: screening: enrolment ratio by assessing the proportion of individuals contacted that enrol in the cohort study – The proportion of those enrolled, who complete the follow-up period – Acceptability of study procedures (including blood draws) – Willingness to participate in future HIV vaccine trials – Potential barriers and motivators to participation of adults in vaccine interventions. 2. To develop the Manhiça site in specific procedures related to future HIV vaccine trials by assessing: – The ability to retrieve viable peripheral blood lymphocytes after separation and freezing measured by cell viability – The suitability of different data collection tools to retrieve information regarding risk behaviour – The ability to engage and liaise with the community through the introduction of locally acceptable community advisory boards.
Clinical Trial/Study site(s):	Centro de Investigaçao em Saúde da Manhiça (CISM), Manhiça district (Mozambique)
Collaborating site(s):	National Health Laboratory Services, Johannesburg (South Africa)
Study design and population:	The feasibility study will adopt the design of a follow-up study, in which a cohort will be clinically followed-up for a period of 16 weeks after enrolment. The study population (70 participants, 50 men and 20 women) comprises mostly of subsistence farmers and employees of the sugar estates from Maragra and Xinavane. Manhiça is a source of migrant labour to South Africa, which contributes to a highly mobile population. A significant number of people, mainly women, are engaged in vending activities in markets and on the streets.
Cofunders:	• Bill & Melinda Gates Foundation (USA) • Fondo de Investigaciones Sanitarias (FIS) – Instituto de Salud Carlos III, (Spain)
Status:	Completed
Results and Outcomes:	A total of 77 potential participants were screened, of which 71 (20 women and 51 men) were enrolled. Nine participants (7 men and 2 women) withdrew from the study and a 12 week follow up was completed for 62 participants. During clinical follow-up, participants underwent two rounds of in-depth interviews (IDI) to assess their level of acceptability and barriers/ enabling factors to enrol and remain under follow-up. Preliminary results suggest that participants had a good understanding of the purpose of the study. Vaccination in adults

	was mostly welcome as it would help prevent and/or decrease the spread of HIV and other diseases such as malaria. Adults would be willing to participate in HIV vaccine trials as it would provide them with guaranteed treatment and clinical care. The barriers to trial participation included fear of injections, blood draws and being the first recipient of an investigational vaccine.
Study/Trial 3	**Manhiça Epidemiology Study (capacity building)**
Site Principal Investigator(s):	• Khátia Munguambe (Mozambique) • Denise Naniche (Spain)
Trial/Study title:	Establishment of community prevalence of human immunodeficiency virus infection and sexual transmitted infections in Manhiça district, southern Mozambique
Goal:	To develop capacity and provide epidemiological information needed for conducting HIV prevention trials including HIV vaccine trials in Mozambique.
Primary Objective(s):	1. To establish age-specific community HIV prevalence in adults aged 18-27, 28-37 and 38-47 years old 2. To estimate the incidence of HIV in the community in adults aged 18-47 3. To determine community prevalence of STI relevant to HIV transmission.
Clinical Trial/Study site(s):	Centro de Investigaçao em Saúde da Manhiça (CISM), Manhiça district (Mozambique)
Study design:	Two cross sectional studies with an interval of two years between both studies. The HIV incidence will be estimated by randomly recruiting subjects the demographic surveillance (DSS) in Manhica. The prevalence of selected STI will be determined by a single cross sectional study. The first cross-sectional study will determine age-specific HIV prevalence in the Manhiça region. The second cross sectional study will determine age-specific HIV incidence and prevalence of selected STIs in Manhiça community.
Study population:	First cross sectional study: Adults (men and women), 18-47 years, part of the Manhiça DSS area, 232 subjects per age group (18-27 years, 28-37 years and 38-47 years), N= 696. Second cross sectional study: Adults (men and women), 18-47 years, part of the Manhiça DSS area, 232 subjects per age group (18-27 years; 28-37 years and 38-47 years), N= 696.
Cofunders:	• Fondo de Investigaciones Sanitarias (FIS) – Instituto de Salud Carlos III (Spain)
Status:	Completed
Results and Outcomes:	HIV community prevalence in the Manhiça Demographic surveillance district was established in two cross sectional surveys conducted in 2010 and 2012. In the first cross sectional study, a total of 839 individuals (ages 18-47 years) were invited to participate in the study, of which 722 were recruited. HIV community prevalence was 39.9% [95% CI 35.9–43.8%]. HIV prevalence increased with increasing age group and was higher among women than men in all age groups. In the second cross sectional study, a total of 896 individuals (aged 18 -50 years) were invited to participate, of which 792 were recruited. Preliminary results indicate an overall HIV prevalence 37.4%. Prevalence was found to be higher in women in all three age groups. It was also found that HIV prevalence

	increases with age, in both men and women, with incidence estimated to peak in the 20-24 age group. The team found two limiting factors in the study: participant absence during home visits and the exclusion of teenagers from the study. The high HIV prevalence in this region suggests that the epidemic is in a mature stable phase. Incidence rates estimation combining data from the 2010 and 2012 prevalence studies is on-going. It is noteworthy that a smartphone-based method of data collection was introduced for this epidemiological study.
Study/Trial 4	**Africa Centre Impilo Yamadoda - Men's Health Study (capacity building)**
Site Principal Investigator(s):	John Imrie (South Africa)
Trial/Study title:	An exploratory study of issues in men's health and mechanisms to increase participation and retention of male participants in community-based HIV prevention research
Goal:	To complete an exploratory programme of research investigating key health issues for rural Zulu men and strategies for recruiting and retaining young men in community-based HIV prevention research; making these findings available to the AfrEVacc Network Partners and in so doing, defining a range of generalisable strategies for increasing men's involvement in bio-medical and behavioural HIV prevention research in southern African settings.
Primary Objective(s):	1. Explore and map the main general health and HIV concerns of rural Zulu men with specific attention to issues of understanding of the role and relevance of research and particularly, HIV prevention research 2. Describe, define and test different community engagement strategies to establish a cohort of young Zulu men from the local area surrounding of the Africa Centre (i.e. Hlabisa Health Sub-district) and test mechanisms to increase participants ongoing engagement with the Africa Centre and its programme of behavioural and biomedical HIV prevention research 3. Test the feasibility and efficacy of different follow-up/retention strategies, including monetary and non-monetary incentive packages for use with men recruited to an individually randomised study involving multiple observations and collection of bio-specimens 4. Develop guidance and recommendations for other AfrEVacc Network Partners regarding recruitment and retention for community samples of young adult men for biomedical, vaccine and behavioural HIV prevention trials from rural and peri-urban settings in South Africa.
Clinical Trial/Study site(s):	Africa Centre for Health and Population Studies, Hlabisa Health sub-district of the Umkhanyakude District in northern KwaZulu-Natal (South Africa)
Study design:	Adult men (N=200, 18-29 years) from the community settings in the Hlabisa Health sub-district will be recruited. Baseline and follow-up procedures will involve collection of behavioural, attitudinal and knowledge measures as well as a blood specimen for unnamed HIV testing. Collection of baseline data will occur at the time the participant completes the study's informed consent procedures. All men who agree to participate and complete enrolment will be invited to attend the intervention which will

	involve a half-day men's health fair. The men's health fairs will follow a format similar to the Africa Centre's regular road shows. They will consist of a programme of information and interactive sessions relating to key health issues identified by men in the earlier phases of the study and HIV prevention. On completing the intervention men will be randomised in equal numbers to one of two follow-up methods (face-to-face interview vs self-report using cellular telephone interviews) and then randomised a second time to provision of a follow-up blood specimen at the end of the study either at a clinic (venepuncture) or in the community (dried blood spots). Two follow-ups are planned, one at 3-months post enrolment (for behavioural measures only), and a second at 6-months post-enrolment (for behavioural measures and bio-specimens). Biological specimens will be tested for HIV to estimate prevalence in the cohort at baseline and after 6 months follow-up. Participants will not be informed of their results but rapid named HIV testing will be available either on-site (clinics) or via on-call VCT counsellor from the Africa Centre, as per routine service.
Cofunders:	• Bill & Melinda Gates Foundation (USA)
Status:	Completed
Results and Outcomes:	Community-based organisations (including social, sports, religious and employers) are efficient mechanisms to locate and engage men, and if properly supported, can become genuine research partners with study investigators. Men are enthusiastic about participating in research that they feel takes account of their needs as men and that targets them specifically. Some of men's enthusiasm can be explained by social capital and cultural beliefs about the importance of contributing to community well-being and supporting activities that are perceived to bring wider benefits to their communities. The team reported that of the 223 male study participants, 7 (3.1%) reported sex with a male partner at least once in the survey rounds, which lasted 3 months. When looking at the study participants' responses, the team emphasised why detailed research into the sexual attitudes, lifestyles and experiences of young men - those that identify themselves as men who have sex with men (MSM) and men who do not, but report same-sex behaviour - is needed to ensure an appropriate sexual health, HIV prevention and treatment and care response. It is the team's hypothesis that MSM is underreported in these communities and propose making MSM a research priority in South Africa. The team also examined whether follow-up modality, biospeciment collection method or the form of participant reimbursement made a difference in improving male participant retention. They found that modality of follow-up interview and method of biospecimen collection method had no impact on follow-up completions. However, microcapillary collection facilitated men being followed-up in their communities, which was operationally easier, reduced staff-costs and the time between questionnaire completion and specimen delivery. Where possible, the team recommends that investigators

	consider varying, or allowing participants to choose the type of reimbursement they receive.
Study/Trial 5	**Johannesburg study (capacity building)**
Site Principal Investigator(s):	Sinead Delaney-Moretlwe (South Africa)
Trial/Study title:	Acceptability and Feasibility of Recruiting Men into a future Phase III HIV Vaccine Trial: Experiences of Surrogate Vaccination Use (AfrEVacc 001)
Goal:	The overall purpose of this study is to determine the feasibility and acceptability of recruiting HIV sero-negative men into a future phase III HIV vaccine trial.
Primary Objective(s):	1. To assess the feasibility of recruiting a cohort of HIV negative men and following them up at regular intervals for a period of 12 months
Secondary Objective(s):	1. To assess whether men's social, and/or economic background and cultural context influences their participation in the study 2. To assess the acceptability of study procedures 3. To determine prevalence of HIV, STIs and non-specific symptoms such as fever, headache and cough and to estimate HIV incidence in this population 4. To evaluate and identify the most appropriate methods of methods of data collection in this population of men.
Clinical Trial/Study site(s):	RHRU Research & Training Centre in Hillbrow, Johannesburg (South Africa)
Study design and population:	Randomised controlled trial: A surrogate vaccine (hepatitis B vaccine ENGERIX-B or equivalent generic) will compared to no vaccination among healthy HIV sero-negative male (N=15 , over 18 years) volunteers to assess the feasibility and acceptability of enrolling HIV seronegative men into a future phase III HIV vaccine trial.
Product(s):	Heberbiovac HB
Manufacturer/Developer:	GSK Biologicals (UK)
Status:	Completed
Results and Outcomes:	The group implemented a randomised controlled trial to assess the feasibility and acceptability of enrolling HIV seronegative men into a future Phase III HIV vaccine trial in inner city Johannesburg. Hepatitis B vaccine was used as a surrogate for a future HIV vaccine, and randomised men received either immediate vaccination or vaccination deferred until the end of the 12-month follow up period. In all, 287 men were screened for the study and 150 were enrolled. In total, 93% of participants completed follow up. The study found that it is feasible and acceptable to recruit and retain a cohort of high-risk HIV negative men. Follow-up was equal by randomization arm, suggesting that men were motivated to join the trial irrespective of the randomization arm, and benefited from access to quality services and information about sexual and reproductive health. Fifteen focus group discussions, 64 in-depth interviews and 8 home visits were conducted. Preliminary results show that the majority of men (mean age of 30yrs) were South African-born (67%), single (81%), employed (54%) and perceived themselves to be in good health (87%). 40% reported >10 lifetime sexual partners, 32% had never used a condom in the last 3 months, and 36% were circumcised. 8% reported genital symptoms at screening, and 12% were found to have chlamydia while <3% had gonorrhoea or trichomoniasis respectively. HIV,

	HSV-2 and HepB prevalences were 9%, 33% and 34%. HepB was found to be associated with number of lifetime sexual partner and a history of STIs.
PhD studies:	Title: "Engaging young men in biomedical HIV prevention research: Lessons from a community-based study in rural KwaZulu-Natal" Candidate: Sebastian Fuller (University College London Centre for Sexual Health & HIV Research, UK) Dates: March 2008-Ocotber 2011
	Title: "What is it 'to do' in the context of change? Toward and operational model of the act for school-community-based HIV prevention." Candidate: Graeme Hoddinott (University of KwaZulu-Natal, South Africa) Dates: September 2011-September 2014
MSc studies:	Title: MSc Data Networks & Security Candidate: Gerald Feldmann (Birmingham City University, UK) Dates: January 2009-November 2010
	Title: MSc in public health Candidate: Helena Boene (London School of Hygiene & Tropical Medicine, UK) Dates: September 2011-October 2013
	Title: HIV testing patterns in 2 population probability samples from South Africa and the UK Candidate: Kyle Jones (London School of Hygiene & Tropical Medicine, UK) Dates: September 2011-September 2012
	Title: Popping the bubble: Do bubble plot presentations distort interpretation of circle size and data values Candidate: Stephen Oliver (University of KwaZulu-Natal, South Africa) Dates: September 2010-September 2012
	Title: Development Studies: Community engagement/involvement in biomedical HIV prevention trials Candidate: Ntombikayise Mncwango (University of South Africa) Dates: September 2011-December 2014
	Title: MSc in epidemiology with AfrEVacc data Candidate: Ivete Meque (University of Queensland, Australia) Dates: January 2012-January 2014
	Title: MSc in public health Candidate: Arlinda Zango (Eduardo Mondlane University, Mozambique) Dates: February 2012-pending
	Title: Masters in Epidemiology Candidate: Chacha Mangu (University of London (online course)) Dates: November 2011-September 2014
	Title: A Review of AfrEVacc 001 and Informed Consent Practices Candidate: Robin Jakob (University of Edinburgh, UK) Dates: September 2011-July 2012
Publications:	1. Serna-Bolea C., de Deus, N., Acácio S., Muñoz J., Nhalungo D., Letang E., Alonso P., Naniche D. (2012) Recent HIV-1 infection: Identification of individuals with high viral load setpoint in a vobekkerluntary counselling and testing centre in rural Mozambique. *Plos One* 7(2):e31859. Feb 21. 2. González R, Munguambe K, Aponte J, Bavo C, Nhalungo D, Macete E, Alonso P, Menéndez C, Naniche D. (2012) High HIV prevalence in a southern semi-rural area of

	Mozambique: a community-based survey. *HIV Medicine*. Nov 13(10), 581-588. 3. Meque, I, Dubé, K, Feldblum, PJ, Clements, ACA, Zango, A, Cumbe, F, Chen, PL, Ferro, JJ, van de Wijgert, JH (2014) Prevalence, Incidence and Determinants of Herpes Simplex Virus Type 2 Infection among HIV-Seronegative Women at High-Risk of HIV Infection: A Prospective Study in Beira, Mozambique. *PloS ONE*, 9(2): e89705. doi:10.1371/ journal.pone.0089705

3 Tuberculosis

Table 3-1: Tuberculosis clinical trials

Click on underlined text to link to project profiles and additional information contained in the clinical trial registry.

Grantee Grant Code Acronym	Disease area	Phase	Clinical Trial Registration Numbers	Product(s)	Manufacturer/ Developer	Study population	Status
ADETIFA TA.2005.40203.001	TUBERCULOSIS DIAGNOSTICS	evaluation	n/a	Ex-vivo ELISPOT, QuantiFERON-TB Gold In-Tube test		ADULTS (≥18 years); Patients with newly diagnosed smear positive TB and their household contacts; N=274	Completed
ANDERSEN IP.2007.32080.001 THYB-04	TUBERCULOSIS VACCINES	II	SATVI SANCTR: DOH-27-0612-3947	Ag85B-ESAT-6 + adjuvant (500 nmol KLK and 20 nmol ODN1a	SSI	ADOLESCENTS (12-18 years); TST positive healthy individuals; N= 240	Ongoing
ANDERSEN IP.2007.32080.001 THYB-04 -IRIPT	TUBERCULOSIS TREATMENT	III	PACTR20110100027 3931	Isoniazid, Rifampicin		CHILDREN (0-15 years); TST positive healthy individuals exposed to TB at home; N=749	Ongoing
ASEFFA CT.2005.32080.003 THYB-03	TUBERCULOSIS VACCINES	I	NCT01049282	Ag85B-ESAT-6 +I C31	SSI		Completed
BERTILSSON CT.2005.32030.001 HIV-TB Pharmagene	HIV/TB TREATMENT	IV	PACTR20090400012 61177	Efavirenz, Rifampicin, 3TC, D4T	GlaxoSmith Kline	ADULTS (≥18 years); HIV+ and HIV+/TB infected; N=400	Completed
BOEREE IP.2007.32011.012 PanACEA-High Rif 2	TUBERCULOSIS TREATMENT	II	NCT00760149 & PACTR20090600014 93909	Rifampicin, Isoniazid, Pyrazinamide, Ethambutol	Svizera, Sanofi-Aventis	ADULTS (18-65 years); Newly diagnosed, previously untreated, smear-positive pulmonary TB ; N=150	Ongoing
BOEREE IP.2007.32011.012 PanACEA-High Rif 1	TUBERCULOSIS TREATMENT	II	PACTR20110400028 1203	Rifampicin, Isoniazid, Pyrazinamide, Ethambutol	Svizera, Sanofi-Aventis	ADULTS (16-65 years); Newly diagnosed, previously untreated, smear-positive	Ongoing

						pulmonary TB; N=68	
BOEREE/HOELSCHER /GILLESPIE IP.2007.32011.011 / IP.2007.32011.012 / IP.2007.32011.013 PanACEA-High Rif/ PanACEA-SQ-109	TUBERCULOSIS TREATMENT	II	NCT01785186	Rifampicin, Moxifloxacin, Isoniazid, Pyrazinamide, Ethambutol	Svizera, Sanofi-Aventis	ADULTS (≥18 years); Newly diagnosed, previously untreated, smear-positive pulmonary TB; N=372	Ongoing
CHURCHYARD IP.2009.32080.002 Aurum 102/THYB-05	TUBERCULOSIS VACCINES	II	PACTR201105000289276	Ag85B-ESAT-6 (50 Pg) (SSI H1)+ adjuvant (500 nmol KLK and 20 nmol ODN1a)	SSI	ADULTS (≥18 years); HIV+, BCG-vaccinated individuals with CD4+ counts >350 Cells/mm^3; N=48	Ongoing
CUEVAS SP.2011.41304.021 NEAT-MDRTB	TUBERCULOSIS DIAGNOSTICS	evaluation	n/a	TBDx, GeneDrive		ADULTS (≥18 years); Suspected TB; N = 1650	Ongoing
DHEDA IP.2009.32040.009 TB NEAT - LAM prospective cohort	TUBERCULOSIS DIAGNOSTICS	evaluation	n/a	Urine LAM lateral flow strip test (Determine TB®)	Inverness Medical Professional Diagnostics	ADULTS (≥18 years); HIV+ individuals with suspected TB; N=400	Completed
DHEDA IP.2009.32040.009 TB NEAT - LAM RCT	TUBERCULOSIS DIAGNOSTICS	demonstration	NCT01770730	Urine LAM lateral flow strip test (Determine TB®)	Inverness Medical Professional Diagnostics	ADULTS (≥18 years); HIV+ individuals with suspected TB; N=2400	Ongoing
DHEDA MS.2011.10800.003 LAM-XACT	TUBERCULOSIS DIAGNOSTICS	demonstration	NCT01990274	Urine LAM lateral flow strip test (Determine TB®)	Inverness Medical Professional Diagnostics	ADULTS (≥18 years); HIV-infected or uninfected individuals; N=1200	Ongoing
DHEDA IP.2009.32040.009 TB-NEAT -Paediatric study	TUBERCULOSIS DIAGNOSTICS	evaluation	n/a	GeneXpert MTB/RIF	Cepheid Inc.	CHILDREN (≤15 years), with and without HIV clinically suspected of having pulmonary TB or extrapulmonary TB; N=1100	Completed
DHEDA IP.2009.32040.009 TB NEAT-Xpert/RIF	TUBERCULOSIS DIAGNOSTICS	demonstration	NCT01554384	GeneXpert MTB/RIF	Cepheid Inc.	ADULTS (≥18 years); Individuals with suspected TB; N= 1472	Completed

DIACON SP.2011.41304.076	TUBERCULOSIS TREATMENT	IIa	NHREC no 3609	faropenem, meropenem/CA, isoniazid, rifampicin, pyrazinamide, ethambutol		ADULTS (18– 65 years); Individuals with newly diagnosed pulmonary TB; N=53	Ongoing
GILLESPIE CT.2004.32011.001/ IP.2007.32011.011 PanACEA - REMox	TUBERCULOSIS TREATMENT	III	NCT00864383 & PACTR201110000124315	Moxifloxacin, Rifampicin, Isoniazid, Pyrazinamide, Ethambutol	Aptuit, GATB, Bayer, Sanofi-Aventis, Svizera, Tubingen	ADULTS (≥18 years); Newly diagnosed, previously untreated, smear-positive pulmonary TB; N=1931	Ongoing
HATHERILL IP.2007.32080.003 Aeras 402/Crucell Ad35	TUBERCULOSIS VACCINES	II	NCT01198366 & PACTR20120300030 6280	AERAS-402	Aeras	INFANTS (16-26 weeks); BCG vaccinated, HIV- infants with no evidence of TB; N=487	Ongoing
HOELSCHER IP.2007.32011.013 PanACEA - SQ-109	TUBERCULOSIS TREATMENT	II	NCT01218217 & PACTR20100900025 2144	SQ109 (novel TB drug)	Sequella Inc.	ADULTS (≥18 years); Newly diagnosed, smear-positive pulmonary TB; N=90	Completed
JINDANI CT.2004.32011.002 Rifaquin	TUBERCULOSIS TREATMENT	III	PACTR20080600008 61040	Ethambutol, Isoniazid, Moxifloxacin, Pyrazinamide, Rifampicin, Rifapentine	INTERTB	ADULTS (≥18 years); Newly diagnosed, previously untreated pulmonary TB; N=827	Completed
KOUANDA TA.2011.40200.026	HIV/TB TREATMENT	II	pending	Rifabutin, Opinavir, Ritonavir		ADULTS (≥18 years); HIV+ individuals; N=30	Not registered yet
LAMORDE TA.2011.40200.047 ARTEM-TB	TUBERCULOSIS TREATMENT	I/II	PACTR20130200048 3287	Rifampicin, Dihydoartemisinin-piperaquine, Artesunate-amodiaquine, Intravenous artesunate		ADULTS (18-65 years); Individuals receiving TB-therapy containing rifampicin for at least 2 weeks; N=36	Not recruiting yet
LANGE IP.2009.33011.007	HIV/TB TREATMENT	III	NCT01417988	Rifampicin, Isoniazid, Pyrazinamide, Ethambutol, ART (efavirenz-based)		ADULTS (≥18 years); HIV+ individuals with CD4 T cell count <50 cells/ul; N=44	Terminated prematurely
LWILLA IP.2009.32040.007 TB CHILD	TUBERCULOSIS DIAGNOSTICS	feasibility, development, evaluation	n/a	Mtb DNA extraction from stool, Serum microRNAs, LHSD Rapid Test (LAM detection), Lab-on-chip based new platform (In-checkTM), Pari eFlowrapid nebulizer, IP10 and other biomarkers, T cell activation markers on	Lionex STMicroelectronics Biotech Pari Pharma Cepheid Inc.	STUDY A: ADULTS (≥18 years); 180 TB cases (90 smear positive TB cases and 90 smear negative but Xpert MTB positive /culture positive TB cases), 120 healthy cases STUDY B: CHILDREN (6	Ongoing

				Mycobacterium tuberculosis (MTB) specific T cells (TAM-IGRA), Ustar TB IAD Kit, GeneXpert MTB/RIF		weeks - 14 years); N=600	
MCSHANE (OTA) IP.2007.32080.002 TB-021: Aeras485 MVA85A	TUBERCULOSIS VACCINES	II	NCT01151189	MVA85A	Aeras/ OETC	ADULTS (≥18 years); Healthy, HIV+ individuals; N=650	Ongoing
MEINTJES SP.2011.41304.074 Pred-ART	HIV/TB TREATMENT	II	PACTR201304000511413	Prednisone, Placebo	Gulf Drug Company	ADULTS (18– 65 years); Individuals with newly diagnosed pulmonary TB; N=53	Recruiting
MERLE IP.2009.33011.009 RAFA	HIV/TB TREATMENT	III	PACTR201105000291300	ARV treatment, standard TB treatment, rifampicin		ADULTS (≥18 years); HIV+ individuals (CD4 count 50-350) with confirmed TB; N=1125	Ongoing
MERRY CT.2004.32011.003 APK.LCM	HIV/TB TREATMENT	IV	n/a	Efavirenz, Nevirapine, Lopinavir, Ritonavir, Rifampicin, Isoniazid, Pyrazinamide, Ethambutol		ADULTS (≥18 years); HIV+ individuals with TB; N=50	Completed
MERRY CT.2004.32011.003 PPK.EFV	HIV/TB TREATMENT	IV	n/a	Efavirenz, Nevirapine, Lopinavir, Ritonavir, Rifampicin, Isoniazid, Pyrazinamide, Ethambutol		CHILDREN (3- 15 years); HIV+ individuals with tuberculosis; N= 96	Completed
MERRY CT.2004.32011.003 PPK.DDK	HIV/TB TREATMENT	II	PACTR200806000085276 7	Efavirenz, Nevirapine, Lopinavir, Ritonavir, Rifampicin, Isoniazid, Pyrazinamide, Ethambutol	DuPont Pharmaceuticals, Tübingen, Boehringer Ingelheim	CHILDREN (6 - 15 years); Individuals with HIV/TB co-infection; N=186	Terminated early on advice of DSMB.
NACHEGA TA.2008.40200.021	HIV/TB TREATMENT	II	NCT02060006	NSAIDs, Placebo		ADULTS (≥18 years); Men and non-pregnant women with TB/HIV co-infection; N=266	Recruiting
NICOL TA.2007.40200.009	TUBERCULOSIS DIAGNOSTICS	evaluation	PACTR201010000255244	GeneXpert MTB/RIF	Cepheid Inc.	ADULTS (≥18 years); Individuals with suspected TB; N=1700	Completed
PADAYATCHI TA.2011.40200.044	TUBERCULOSIS TREATMENT	II	NCT02114684	Isoniazid, rifampin, pyrazinamide, moxifloxacin, ethambutol		N=362	Recruiting

SCHON JP.2009.10800.006	TUBERCULOSIS TREATMENT	IV	NCT00857116	Albendazole, Placebo		ADULTS (≥18 years); Individuals with newly diagnosed pulmonary TB and positive stool sample for helminths (excluding Schistosoma spp.); N=140	Completed
VAN DE PERRE SP.2011.41304.070 PROMISE-TB	TUBERCULOSIS DIAGNOSTICS	evaluation	n/a	Diagnostic accuracy test (ELISA)		CHILDREN (1-15 years); Confirmed TB patients and healthy controls; N = 150	Ongoing
WALZL IP.2009.32040.011 AE TBC	TUBERCULOSIS DIAGNOSTICS	feasibility	n/a	Biomarkers to predict antimicrobial success	n/a	ADULTS (≥18 years);HIV-infected or uninfected individuals with suspected TB; N=1200 (HIV- 800, HIV+ 400)	Ongoing

3.1 Integrated projects and clinical trials

3.1.1 TB SurMark

EDCTP Project Coordinator:	Paul van Helden (Stellenbosch University, South Africa)
EDCTP Call Title:	Trials of studies of surrogate markers of drug efficacy. These should emphasise non-clinical predictors of sterilizing activity and relapse following anti-TB therapy.
EDCTP Project Title:	Surrogate markers to predict the outcome of antituberculosis therapy
EDCTP Project Code:	CT.2004.32040.001 (2004.01.T.d1)
EDCTP Project Start Date:	19 September 2005
EDCTP Project End Date:	30 June 2009
Collaborators:	• Nulda Beyers (Stellenbosch University, South Africa) • Gillian Black (Stellenbosch University, South Africa) • Jacqueline Cliff (London School of Hygiene and Tropical Medicine (LSHTM), UK) • Hazel Dockrell (London School of Hygiene and Tropical Medicine (LSHTM), UK) • Ken Duncan (GlaxoSmithKline, UK) • Nsovo Mathebula (University of Pretoria, South Africa) • Jen Page (Aeras Global Tuberculosis Foundation, USA) • Simon Thanyani (University of Pretoria, South Africa) • Jan Verschoor (University of Pretoria, South Africa) • Gerhard Walzl (Stellenbosch University, South Africa)
Study 1	
Site Principal Investigator(s):	Paul van Helden (South Africa)
Clinical Trial/Study Sponsor:	Stellenbosch University
Trial/Study title:	Surrogate markers to predict the outcome of antituberculosis therapy
Goal:	To analyse stored samples and identify biomarkers that correlate with clinical outcome and to validate them in a multi-centre prospective study recruiting new TB patients
Primary Objective(s):	1. To complete the follow-up of the patient cohort (funded by GSK) 2. To analyse stored samples from TB patients, particularly those samples collected before initiation of therapy and during the early phases of treatment from recurrent/relapse patients, using microbiological, serum, blood parameters, immunological and genetic markers 3. To develop a test (algorithm) based on the findings that these parameters can be used to discriminate between disease states, enabling selection of specific patient type for PoC study and detection of 'cured' patients early during treatment and detection of relapse patients much sooner than the standard two-year follow up.
Clinical Trial/Study site(s):	Stellenbosch University
Collaborating site(s):	• Stellenbosch University (South Africa) • London School of Hygiene and Tropical Medicine (LSHTM, UK) GlaxoSmithKline (UK) • University of Pretoria (South Africa)
Study design:	Prospective study to validate biomarkers
Number of subjects:	313
Cofunders:	• Medical Research Council South Africa (MRC, South Africa)

	• Stellenbosch University (South Africa) • NRF Centre of Excellence for Biomedical TB Research (South Africa)
Status:	Completed
Results and Outcomes:	Patients who subsequently relapse or who remain healthy following drug cure can be readily discriminated during their first episode of TB based on their gene expression profile in the peripheral blood. While this pattern was seen in ex vivo blood, it was much more striking and statistically significant when TB-specific responses were measured in diluted whole blood cultures. From these data, the patients who were to suffer relapse after initial apparent cure had exaggerated cytotoxic and proliferative responses, which were evident at diagnosis and in the first four weeks of treatment, when compared to patients who would remain disease-free. There was a consistent pattern of differential expression of around 2000 genes between relapse and cured patients.
PhD studies:	Title: Differential expression of IL-4 and IL-4δ2, but not TGF-β, TGF-βRII, FOXP3, IFN-γ, T-bet or GATA-3 mRNA in Fast and Slow Responders to Anti-tuberculosis Treatment Candidate: JF Djoba Siawaya (Stellenbosch University, South Africa) Dates: December 2008 (complete)
	Title: Vitamin D receptor gene polymorphisms and sputum conversion time in pulmonary tuberculosis patients Candidate: C Babb (Stellenbosch University, South Africa) Dates: December 2007 (completed)
	Title: Potential of novel Mycobacterium tuberculosis infection phase-dependent antigens in the diagnosis of TB disease in a high burden setting Candidate: N Chegou (Stellenbosch University, South Africa) Dates: July 2009 (completed)
	Title: Downstream validation of results obtained from the microarray gene expression profiling including the collection of fresh TB patient samples Gulab Devi hospital, Lahore, Pakistan and qRT-PCR validation of identified biomarkers Candidate: Syeda Saleha (LSHTM, UK) Dates: December 2011 (completed)
	Title: An assessment of two evanescent field biosensors in the development of an immunoassay for tuberculosis Candidate: Simon T Thanyani (University of Pretoria, South Africa) Dates: April 2009 (completed)
Publications:	1. Djoba Siawaya JF, Chegou NN, van den Heuvel MM, Diacon AH, Beyers N, Helden PV, Walzl G. Differential cytokine/chemokines and KL-6 profiles in patients with different forms of tuberculosis. *Cytokine*. 2009; 47(2):132-136. (PMID: 19570688) 2. Hesseling AC, Walzl G, Enarson DA, Carroll NM, Duncan K, Lukey PT, Lombard C, Donald PR, Lawrence KA, Gie RP, van Helden PD, Beyers N. Baseline sputum time to detection predicts month two culture conversion and relapse in non-HIV-infected patients. *Int J Tuberc Lung Dis*. 2010 May;14(5):560-70 3. S. Brahmbhatt, G. F. Black, N. M. Carroll, N. Beyers, F. Salker, M. Kidd, P. T. Lukey, K. Duncan, P. van Helden and G. Walzl. Immune markers measured before treatment predict outcome of intensive phase tuberculosis therapy.

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3.1.2 HIV-TB Pharmagene

EDCTP Project Coordinator:	Leif Bertilsson (Karolinska Institute, Sweden)
EDCTP Call Title:	Identification of safe and efficacious ARV in combination with tuberculosis drugs in tuberculosis patients with HIV infection
EDCTP Project Title:	Optimisation of tuberculosis and HIV co-treatment in Africa: Pharmacokinetic and pharmacogenetic aspects on drug-drug interactions between rifampicin (rif) and efavirenz (efv).
EDCTP Project Code:	CT.2005.32030.001
EDCTP Project Start Date:	9 January 2007
EDCTP Project End Date:	9 April 2012
Collaborators:	• Eleni Aklillu (Karolinska Institute, Sweden) • Wondwossen Amogne Degu (University of Addis Ababa, Ethiopia) • Ahmed Bedru (Armauer Hansen Research Institute (AHRI), Ethiopia) • Jurgen Burhenne (University of Heidelberg, Germany) • Miles Davies (Karolinska Institute, Sweden) • Getachew Aderaye Desta (University of Addis Ababa, Ethiopia) • Ulf Diczfalusy (Karolinska Institute, Sweden) • Eliford Engamisi (Karolinska Institute, Sweden) • Lars Gustafsson (Karolinska Institute, Sweden) • Abiy Habtewolde (Karolinska Institute, Sweden) • Walter Emil Haefeli (University of Heidelberg, Germany) • Mohamed Yakub Janabi (Muhimbili University College of Health Sciences, Tanzania) • Gideon Kwesigabo (Muhimbili University College of Health Sciences, Tanzania) • Lars Lindqvist (Karolinska Institute, Sweden) • Eyasu Makonnen, (University of Addis Ababa, Ethiopia) • Collen Masimirembwa (African Institute of Biomedical Science & Technology (AIBST), Zimbabwe) • Omari Minzi (Muhimbili University College of Health Sciences, Tanzania) • Ferdinand Mugusi (Muhimbili University College of Health Sciences, Tanzania) • Sabina Mugusi (Karolinska Institute, Sweden) • Eric Sandstrom (Karolinska Institute, Sweden) • Jane Sayi (Muhimbili University College of Health Sciences, Tanzania) • Anders Sonnerborg (Karolinska Institute, Sweden)
Trial 1	
Site Principal Investigator(s):	• Getachew Aderaye (Ethiopia) • Ferdinand Mugusi (Tanzania) • Eleni Aklillu (Sweden)
Clinical Trial/Study Sponsor:	Karolinska Institute (Sweden)
Trial/Study title:	Population pharmacokinetics, pharmacogenetics, safety/efficacy of efavirenz (EFV) based HAART, defined as stavudine (d4T) + lamivudine (3TC) + efavirenz, with and without RIF in Ethiopians and Tanzanians
Goal:	To investigate the magnitude and variation of 16 h EFV plasma and intracellular drug concentration and metabolic ratios at steady state, safety/efficacy of EFV based HAART in patients with and without TB treatment; influence of genetic polymorphisms in drug metabolizing enzymes and transporters on plasma/intracellular levels of EFV, metabolic ratio and on

	drug interaction between RIF and EFV. Thirty patients TB/HIV patients from Trial 1 to be treated for HIV and TB will be requested randomly to participate into a three-phase intensive PK study during RIF based TB
Primary Objective(s):	To identify the optimal dose of EFV to be used with RIF in African patients receiving TB treatment. Specific objectives are: 1. To identify the optimal dose of EFV to be used with RIF 2. To evaluate plasma and intracellular pharmacokinetics of EFV depending on genetic polymorphisms, co-administration of RIF, and drug transporter expression 3. To evaluate the extent of RIF interaction on detailed EFV pharmacokinetics and treatment outcome 4. To investigate the pharmacogenetics of CYP3A and CYP2B6 and their influence on EFV pharmacokinetics and induction by RIF using EFV metabolic ratio and the endogenous CYP3A4/5 marker, 4 β-OH cholesterol plasma level.
Secondary Objective(s):	1. To train African clinicians and researchers at PhD and Masters level in clinical trial research and capacity building 2. To develop research capacities to conduct clinical trials in developing countries and provide the necessary infrastructure through appropriate training and technology transfer with the aim of developing a network of clinical trial centres for HIV/TB research.
Clinical Trial/Study site(s):	Black Lion Medical University Hospital Addis Ababa, Ethiopia St. Peter's TB Specialized Hospital, Addis Ababa, Ethiopia. Muhimbili National Hospital, Dar es Salaam, Tanzania
Collaborating site(s):	• Armauer Hansen Research Institute (AHRI, Ethiopia) • Muhimbili University College of Health Sciences (Tanzania) • African Institute of Biomedical Science & Technology (AIBST, Zimbabwe) • Karolinska Institute (Sweden) • University of Heidelberg (Germany)
Study design and population:	Non-randomised, open label, active control, parallel assignment, PK and safety/efficacy, pharmacogenetic study. **Control group Arm-1:** A cohort of 200 HIV-infected adults without TB co-infection receiving EFV 600 mg based HAART **Case group Arm-2:** A cohort of 200 newly diagnosed treatment naive HIV+TB co-infected adults on concomitant RIF based anti-TB and EFV based HAART) participated in the study.
Number of subjects:	400 subjects. At end of enrolment 486 patients ultimately enrolled.
Product(s):	Efavirenz, Rifampicin (RIF)
Manufacturer/Developer:	• GlaxoSmithKline (lamivudine) • Bristol Myers Squibb (stavudine) • DuPont Pharmaceuticals (efavirenz) • Tubingen (rifampicin)
Cofunders:	• University of Heidelberg (Germany) • Karolinska Institute (Sweden) • Stockholm County Council (Sweden)
Trial Registration Number(s):	PACTR200904000126177
Status:	Completed
Results and Outcomes:	Efavirenz is the preferred non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI) to be used with rifampicin in TB-HIV coinfected patients. When used together, rifampicin reduces plasma efavirenz concentration by about 25%. Hence some treatment guidelines (The British HIV association (BHIVA) and

	Center for Diseases Control and Prevention (CDC) revised the HIV/TB co-treatment guideline) suggested increasing the dose of efavirenz from 600 mg/day to 800mg/day during concomitant TB-HIV co-treatment. However the use of a higher dose of efavirenz manifested increased Central Nervous System (CNS) side effects mainly in black HIV patients. Thus the main objective of the project was to determine whether there is a need for efavirenz dosage adjustment when it is co-administered with rifampicin. This was done by comparing efavirenz pharmacokinetics, safety and efficacy between HIV patients receiving efavirenz based HAART alone versus those receiving with rifampicin. The study was conducted in two countries (Ethiopia and Tanzania). Study results: Rifampicin co-administration had no significant effect on efavirenz pharmacokinetics or on the efficacy of 600mg/day efavirenz based HAART in Ethiopian and Tanzanian HIV patients. Mortality and DILI was relatively higher in Arm-2 (TB/HIV coinfection) patients mainly due to TB coinfection and concomitant TB treatment. Thus increasing efavirenz dose in Arm-2 patients may aggravate the relatively higher adverse events. The conclusion is that there is no need to increase efavirenz dosage during concomitant therapy when given with rifampicin based anti-tuberculosis therapy in TB-HIV coinfected patients.
PhD studies:	Title: Optimization of HIV/TB co treatment in Ethiopian Patients: Pharmacokinetic and pharmacogenetic aspects of drug interaction between Rifampicin and Efavirenz) Candidate: Abiy Habtewold Eyakem (Karolinska Institutet, Ethiopia) Dates: 10 September 2007- April 2013
	Title: Optimization of TB/HIV co-treatment in Ethiopian patients Candidate: Wondwossen Amogne (Karolinska Institutet, Ethiopia) Dates: 28 September 2008-May 2013
	Title: Optimization of HIV/TB co treatment in Tanzania: Pharmacokinetic and pharmacogenetic aspects of drug interaction between Rifampicin and Efavirenz in patients undergoing HIV/TB co treatment Candidate: Eliford Ngaimisi (Karolinska Institutet, Tanzania) Dates: 28 Septmber 2008-April 2013
	Title: Treatment outcome, Safety and Efficacy in Concomitant use of Efavirenz and Rifampicin in HIV and Tuberculosis patients Candidate: Sabina Mugusi (Karolinska Institute, Tanzania) Dates: 29 February 2008-21 November 2012
Publications:	1. Mugusi S, Ngaimisi E,. Janabi M, Minzi O, Bakari M, Riedel KD, Burhenne J, Lindquist L, Mugusi F, Sandstrom E. Aklillu E, Liver enzyme abnormalities and associated risk factors in HIV patients on Efavirenz-based HAART with or without Tuberculosis co-infection in Tanzania" *Plos One*. 2012; doi: 10.1371/journal.pone.0040180 2. Mugusi S, Ngaimisi E,. Janabi M, Mugusi F, Minzi O, Sasi P, Bakari M, Lindquist L, Aklillu E, Sandstrom E. Risk factors for mortality among HIV positive patients with and without active TB in Dar es Salaam, Tanzania. *Antiretroviral therapy* 2012;17:265-274 3. Yimer G, Amogne W, Habtewold A, Makonnen E, Ueda N, Suda A, Worku A, Haefeli WE, Burhenne J, Aderaye G, Lindquist L, Aklillu E. High plasma efavirenz level and

CYP2B6*6 are associated with efavirenz based HAART induced liver injury in treatment naïve HIV patients from Ethiopia: a prospective cohort study. *Pharmacogenomics J*. 2011; Aug 23. doi: 10.1038/tpj.2011.34
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3.1.3 PPK.DDK - HIV and TB medications

EDCTP Project Coordinator:	Concepta Merry (University of Cape Town, South Africa)
EDCTP Call Title:	Phase II-III trials of drug regimens that shorten or simplify current treatment options. Emphasis will be on novel regimens. In addition to efficacy and tolerability assessments, evaluation of pharmacokinetics and drug-drug interactions and drug absorption may be included. Proposals should include assessment of the proposed regimens in HIV- and/or HIV+ infected tuberculosis patients, including patients receiving anti-retroviral drugs (EDCTP Code 2004.01.T.d2).
EDCTP Project Title:	Determining the optimal doses of antiretroviral and antituberculous medications when used in combination for the treatment of HIV/TB in co-infected patients
EDCTP Project Code:	CT.2004.32011.003
EDCTP Project Start Date:	30 June 2006
EDCTP Project End Date:	6 July 2010
Collaborators:	• David J Back (University of Liverpool, UK) • David Marinus Burger (Radboud University Nijmegen, Netherlands) • Bill Burman (University of Colorado at Denver and Health Sciences Center, USA) • Linelle Campbell (South African Clinical Research Organisation (SACRA), South Africa) • Chifumbe Chintu (University Teaching Hospital, Zambia) • Peter Coakley (Makerere University, Uganda) • Eric Decloedt (University of Cape Town, South Africa) • Saye Khoo (University of Liverpool, UK) • Mohammed Lamorde (Trinity College, Ireland) • Gary Maartens (University of Cape Town, South Africa) • Helen McIlleron (University of Cape Town, South Africa) • Mirjam Oudijk (University Teaching Hospital, Zambia) • Mairin Ryan (Trinity College, Ireland) • Peter John Smith (University of Cape Town, South Africa) • Doug Wilson (University of KwaZulu-Natal, South Africa)
Trial 1:	
Site Principal Investigator(s):	Concepta Merry (South Africa)
Clinical Trial/Study Sponsor:	University of Cape Town (South Africa)
Trial/Study title:	Determining the optimal doses of antiretroviral and antituberculous medications when used in combination for the treatment of HIV/TB in co-infected patients
Goal:	To investigate the bi-directional interactions of efavirenz (EFV), nevirapine (NVP), lopinavir (LPV; with ritonavir) and ritonavir (RTV; with lopinavir) with rifampicin-based anti-TB therapy in South African adult and paediatric HIV-infected patients.
Primary Objective(s):	**Adult study:** 1. To compare PK of EFV, NVP, LPV and RTV in adult HIV-infected patients who are receiving rifampicin based ant-TB therapy with the PK profiles of EFV, NPV, LPV, and RTV in the same patients when they have completed anti-TB therapy 2. To compare the PK of rifampicin and isoniazid in patients receiving ARVs in accordance with national guidelines with historical population PK profiles of rifampicin and isoniazid in patients who do not require ARV therapy.

	Paediatric study: 1. To compare the trough levels of EFV, NVP, LPV and RTV in HIV-infected paediatric patients who are receiving rifampicin based anti-TB therapy with the PK profiles of EFV, NPV, LPV, and RTV in the same patients when they have completed anti-TB therapy.
Secondary Objective(s):	**Adult study:** 1. To develop the University of Cape Town as a regional reference centre for the conduct of clinical PK of HIV studies and the determination of ARV drug assays by building human laboratory capacity 2. To develop efficient methods appropriate to a resource-limited setting for estimation of EFV, NVP, LPV, and RTV concentrations 3. To determine the impact of covariate patient and drug factors on the PK of EFV, NPV, LPV, rifampicin and isoniazid. **Paediatric study:** 1. To test filter paper method developed in the adult study for the determination of EFV, NVP, LPV and RTV under field conditions, using 0.2ml of whole blood (obtained from a heel prick in children) 2. To determine the impact of covariate patient and drug factors on the pre-dose levels of EFV, NVP, LPV and RTV.
Clinical Trial/Study site(s):	• Groote Schuur Hospital, University of Cape Town (South Africa) • Red Cross Hospital, University of Cape Town (South Africa) • Tygerberg Hospital, Cape Town (South Africa) • PK-Laboratory Division of Pharmacology, University of Cape Town (South Africa)
Collaborating site(s):	• University of Liverpool (UK) • Radboud University Nijmegen (Netherlands) • SACRA (South Africa) • University Teaching Hospital (Zambia) • Makerere University (Uganda) • University of Cape Town (South Africa) • Trinity College Dublin (Ireland) • University of KwaZulu-Natal (South Africa)
Study design and population:	Non-randomised, open label study on adults and children with HIV/TB con-infection.
Number of subjects:	178
Product(s):	• Efavirenz (EFV) • nevirapine (NVP) • lopinavir (LPV) • ritonavir (RTV) • rifampicin
Manufacturer/Developer:	• DuPont Pharmaceuticals • Tübingen • Boehringer Ingelheim
Trial registration number(s):	ATM 2008060000852767
Status:	Completed
Results and Outcomes:	The key finding are that double dose of Kaletra does not overcome induction by rifampicin in HIV/TB infected children while double dose of Kaletra does appear to overcome induction by rifampicin in HIV/TB co-infected adults. The project has generated valuable data on the management of

	HIV/TB co-infected patients, built capacity both institutionally and for individuals in clinical pharmacokinetics and forged new collaborations north-south-south. A complementary study that has resulted from this study is a PhD project by Chao Zhang (funded by Wellcome Trust through PKPDia collaborative network). Integrated population PK models describing induction and inhibition interactions in children and adults receiving LPV/r-based ART and rifampicin-based antitubercular treatment.
PhD study:	Title: Antiretroviral Therapy – Pharmacological considerations in developing countries Candidate: Mohammed Lamorde (Infectious Diseases Institute, Faculty of Medicine, Makerere University, Kampala, Uganda) Dates: June 2008-15 September 2011
Publications:	1. McIlleron H, Ten Y, Nuttall J, Fairlie L, Rabie H, Cotton M, Eley B, Meyers T, Smith PJ, Merry C, Maartens G. Lopinavir exposure is insufficient in children given double doses of lopinavir/ritonavir during rifampicin-based treatment for tuberculosis. *Antiviral Therapy*, 2011;16(3):417-21. doi: 10.3851/IMP1757 2. Decloedt E, McIlleron Smith P, Merry C Orrell, C Maartens. The Pharmacokinetics of lopinavir in HIV-infected adults receiving rifampicin with adjusted doses of lopinavir/ritonavir tablets. *Antimirobial Agents and Chemotherapy* 2011 Jul;55(7):3195-200. doi: 10.1128/AAC.01598-10. Epub 2011 May 2 3. Maartens G, Decloedt E, Cohen K. Effectiveness and safety of antiretrovirals with rifampicin: critical issues for high burden countries. *Antiviral Therapy* 2009;14(8):1039-43 4. McIlleron H, Gous H. Pharmacokinetics of antiretroviral drugs in infancy. *Southern African Journal of HIV Medicine* 2009; 10:54-61 5. Zvada SP, Van Der Walt J, Smith PJ, Fourie PB, Roscigno G, Mitchison D, Simonsson USH, McIlleron HM. Effect of Four Different Meals Types on the Population Pharmacokinetics of a single 900 mg Dose of Rifapentine in Healthy Male Volunteers. *Antimicrob Agents Chemother*. 2010 Aug;54(8):3390-4. doi: 10.1128/AAC.00345-10. Epub 2010 Jun 1 6. Pepper DJ, Marais S, Wilkinson RJ, Bhaijee F, Maartens G, McIlleron H, De Azevedo V, Cox H, McDermid C, Sokhela S, Patel J, Meintjes G. The initiation of antiretroviral treatment at higher CD4 counts to reduce the burden of clinical deterioration during antituberculosis treatment in Africa. *BMC Infectious Diseases* 2010 Mar 30 ;10:83. doi: 10.1186/1471-2334-10-83 7. Ren Y, Nuttall JJC, Egbers C, Eley BS, Meyers TM, Smith PJ, Maartens G, McIlleron HM. Effect of Rifampicin on Efavirenz Pharmacokinetics in HIV-infected Children with Tuberculosis. *J Acquir Immune Defic Syndr* 2009. 50(5):439-43. 8. Decloedt, EH; Maartens, G; Smith, P; Merry, C; Bango, F; McIlleron, H. The Safety, Effectiveness and Concentrations of Adjusted Lopinavir/Ritonavir in HIV-Infected Adults on Rifampicin-Based Antitubercular Therapy, *PLOS ONE*, 2012, Vol 7 issue 3 9. Helen McIlleron, Hermien Gous. Pharmacokinetics of antiretroviral drugs in infancy. *The Southern African*

	Journal of HIV Medicine. Dec 2009, pp54-61 10. Oudijk, J. Mirjam ; McIlleron, Helen; Mulenga, Veronica; Chintu, Chifumbe; Merry, Concepta; Walker, A. Sarah; Cook, Adrian; Gibb, Diana M.; Burger, David M. Pharmacokinetics of nevirapine in HIV-infected children under 3 years on rifampicin-based antituberculosis treatment. *AIDS Official Journal of the International AIDS society*. 31 July 2012 - Volume 26 - Issue 12 - p 1523–1528.

3.1.4 Rifaquin

EDCTP Project Coordinator:	Amina Jindani (St. George's University of London, UK)
EDCTP Call Title:	Phase II-III trials of drug regimens for TB that shorten or simplify current treatment option
EDCTP Project Title:	A controlled clinical trial to evaluate high dose rifapentine and a quinolone in the treatment of pulmonary tuberculosis
EDCTP Project Code:	CT.2004.32011.002
EDCTP Project Start Date:	23 November 2006
EDCTP Project End Date:	31 December 2012
Collaborators:	• Salome Charalambous (Aurum Institute for Health Research, South Africa) • Gavin John Churchyard (Aurum Institute for Health Research, South Africa) • Heather Clouting (Medical Research Council (MRC), UK) • Elizabeth Corbett (Biomedical Research and Training Institute (BRTI), Zimbabwe) • Paul Craven (St. George's University of London, UK) • Zulmira Almeida Da Silva (Ministry of Health, Mozambique) • Janneke van Dijk (Medical Institute at Macha, Zambia) • Innocent Tichaona Gangaidzo (University of Zimbabwe) • Mark Hatherill (University of Cape Town, South Africa) • Gary Maartens (University of Cape Town, South Africa) • Helen McIlleron (University of Cape Town, South Africa) • Denis Mitchison (St. George's University of London, UK) • Mungofa, Stanley (Harare City Health Department, Zimbabwe) • Andrew Nunn (MRC, UK) • Paula Perdigao (Ministry of Health, Mozambique) • James Christopher Shepherd (BOTUSA, Botswana) • Peter John Smith (University of Cape Town, South Africa) • Michelle Tetlow (London School of Hygiene and Tropical Medicine (LSHTM), UK) • Simukai T. Zizhou (University of Zimbabwe)
Trial 1	
Site Principal Investigator(s):	Amina Jindani (UK)
Clinical Trial/Study Sponsor:	St Georges Hospital Medical School trading as St Georges University of London
Trial/Study title:	An international multicentre controlled clinical trial to evaluate high-dose rifapentine and a quinolone in the treatment of pulmonary tuberculosis
Goal:	To shorten the tuberculosis treatment duration or simplify treatment administration
Primary Objective(s):	1. To evaluate the effect of an increase in rifapentine dose size in reducing or eliminating the risk of rifamycin mono resistance (RMR) in relapse cultures in HIV positive patients 2. To evaluate the effect of an increase in Rifapentine dose size in decreasing the relapse rate so that it would be equivalent to the aret found in a control regimen of rifampicin/isoniazid 3. To assess whether moxifloxacin can substitute for isoniazid in treatment regimens.
Clinical Trial/Study site(s):	• SATVI Institute of Infectious Diseases & Molecular Medicine (South Africa) • BOTUSA, Gaborone (Botswana) • Harare City Health Department (Zimbabwe)

	• Medical/Malaria Institute at Macha, Macha Mission Hospital (Zambia) • Biomedical Research and Training Institute (Zimbabwe) • Provincial Medical Directorate Mashonaland East (Zimbabwe) • Aurum Insitute for Health Research (South Africa)
Collaborating site(s):	• Direcção de Saúde da Cidade de Maputo (Mozambique) • Harare City Health Department (Zimbabwe) • Biomedical Research and Training Institute (Zimbabwe) • Medical/Malaria Institute at Macha, Macha Mission Hospital (Zambia) • MRC Clinical trials Unit (UK) • SATVI, Institute of Infectious Diseases and Molecular Medicine (South Africa).
Study design and population:	Randomised, open label study on adults (18 years or over) with newly diagnosed, previously untreated pulmonary tuberculosis.
Number of subjects:	896
Product(s):	• Ethambutol • Isoniazid • Moxifloxacin • Pyrazinamide • Rifampicin (RIF) • Rifapentine
Manufacturer/Developer:	• Bayer • Sanofi-Aventis
Cofunders:	• Medical Research Council (MRC, UK) • Wellcome Trust (UK) • Sanofi-Aventis (France)
Sub-studies:	1. Population studies of INH, rifapentine and moxifloxacin blood levels will be carried out on samples of patients, only in South African centres 2. The rate of acetylation of INH, measured by NAT2 genotyping, will also be done on all failure/relapse patients as compared to a sample that go on to a cure.
Trial Registration number(s):	ISRCTN 44153044 ATMR2008060000861040
Status:	Completed
Results and Outcomes:	From Aug 2008 to Aug 2011, 827 patients were enrolled in South Africa (464), Zimbabwe (292), Botswana (56) and Zambia (15). 233 (28%) were HIV positive with a median CD4 count of 312/mm^3; 509 (62%) were male, and the median weight was 53 kg. The increase in proportion unfavourable results between the 4-month regimen and control was 12.6% (95% CI 5.9%, 19.2%) in the per protocol analysis and 11.8% (95% CI 3.8%,19.8%) in the ITT analysis. The difference between the 6-month regimen and control was -1.0% (95% CI -5.1%, 3.1%) in the per protocol analysis and -1.1% (95% CI -8 .0%, 5.7%) in the ITT analysis; all analyses were adjusted for centre. Forty six grade 3 or 4 adverse events during treatment were reported; six events were hepatic. Outcomes: The 6-month regimen with once-weekly 1200mg rifapentine and moxifloxacin in the continuation phase was non-inferior to control, but the 4 month regimen was significantly inferior to the control. Both regimens were safe and well tolerated.
Publications:	1. Zvada, SP; Denti, P; Geldenhuys, H; Meredith, S; van As, D; Hatherill, M; Hanekom, W; Wiesner, L; Simonsson, USH; Jindani, A; Harrison, T; McIlleron, HM. Moxifloxacin Population Pharmacokinetics in Patients with Pulmonary Tuberculosis and the Effect of Intermittent High-Dose

	Rifapentine. *Antimicrobial Agents and Chemotherapy*. Vol 56, Issue 8, pp 4471-4473.

3.1.5 PanACEA REMox I and II

EDCTP Project Coordinator:	Stephen Gillespie (University College London, UK)
EDCTP Call Title:	Phase II-III trials of drug regimens that shorten or simplify current treatment option
EDCTP Project Title:	Rapid Evaluation of Moxifloxacin in the treatment of sputum smear positive tuberculosis: REMoxTB (REMox I)
EDCTP Project Code:	CT.2004.32011.001
EDCTP Call Title:	Support of phase I, II and III clinical trials on new drugs and improved drug combinations for the treatment of tuberculosis
EDCTP Project Title:	Rapid Evaluation of Moxifloxacin in Tuberculosis (REMox II)
EDCTP Project Code:	IP.2007.32011.011
EDCTP Project Start Date:	21 October 2005
EDCTP Project End Date:	30 June 2014
Collaborators:	• Evans Amukoye (Kenya Medical Research Institute (KEMRI), Kenya) • Martin Boeree (Radboud University Nijmegen, Netherlands) • Salome Charalambous (Aurum Institute for Health Research, South Africa) • Gavin John Churchyard (Aurum Institute for Health Research, South Africa) • Francesca Miranda Conradie (University of the Witwatersrand, South Africa) • Rodney Dawson (University of Cape Town Lung Institute, South Africa) • Andreas Diacon, (Stellenbosch University, South Africa) • Jeannine Du Bois (Stellenbosch University, South Africa) • Anna Easton (University College London, UK) • Michael Hoelscher (Ludwig-Maximilians Universitat Munchen, Germany) • Gibson Kibiki (Kilimanjaro Clinical Research Institute (KCRI), Tanzania) • Shabir Lahki (University of Zambia (UNZA), Zambia) • Timothy McHugh (University College London, UK) • Peter Mwaba (University of Zambia (UNZA), Zambia) • Kim Narunsky (University of Cape Town, South Africa) • Andrew Nunn (Medical Research Council (MRC), UK) • Alphonse Okwera (Makerere University, Uganda) • Alex Pym (MRC, South Africa) • Andrea Rachow (Mbeya Medical Research Centre (MMRC), Tanzania) • Noel Elisifa Sam (KCRI), Tanzania) • Ian Matthias Sanne (University of the Witwatersrand, South Africa) • Afsatou Ndama Traoré (Albert Schweitzer Hospital, Gabon) • Alimuddin Zumla (University College London, UK)
Trial 1	**REMox I**
Site Principal Investigator(s):	• Stephen Gillespie (UK) • Andrew Nunn (UK) • Timothy McHugh(UK) • Sarah Meredith (UK) • Ali Zumla (UK)
Clinical Trial/Study Sponsor:	Global TB Alliance (USA)
Trial/Study title:	Controlled comparison of two moxifloxacin containing treatment shortening regimens in pulmonary tuberculosis
Goal:	To investigate the ability of moxifloxacin to substitute for either ethambutol or isoniazid.

Primary Objective(s):	To evaluate the appropriate role of the highly active fluoroquinolone moxifloxacin in shortening the duration of therapy using a novel trials methodology. This will be achieved by fulfilling the following objectives: 1. By trialling a regimen which replaces ethambutol with moxifloxacin to determine whether it can increase the proportion of patients culture negative at 2 months 2. By trialling a regimen which replaces isoniazid with moxifloxacin to determine whether it can increase the proportion of patients culture negative at 2 months.
Secondary Objective(s):	Capacity Building in sub-Saharan Africa to support future phase II and III clinical trials for TB treatment research.
Clinical Trial/Study site(s):	• Kibon'goto National Tuberculosis Hospital (Tanzania) • Tumaini University (Tanzania) • University Teaching Hospital, Lusaka (Zambia) • SAMRC Tuberculosis Programme, Durban (South Africa)
Collaborating site(s):	• University College London (UK) • Medical Research Council Clinical Trials Unit (UK) • University of Zambia (Zambia) • Kilimanjaro Christian Medical College (KCMC, Tanzania) • Triclinium Clinical Research (South Africa) • Medical Research Council (MRC, South Africa) • Pharmanet Development Group (United States)
Study design and population:	A randomised placebo-controlled, double-blind trial comparing two treatment-shortening regimens with the standard regimen (two months ethambutol, isoniazid, rifampicin and pyrazinamide followed by four months isoniazid and rifampicin) namely 1) two months moxifloxacin, isoniazid, rifampicin and pyrazinamide followed by two months moxifloxacin, isoniazid and rifampicin and 2) two months ethambutol, moxifloxacin, rifampicin and pyrazinamide followed by two months moxifloxacin and rifampicin for the treatment of adults with pulmonary tuberculosis.
Number of subjects:	Combined REMox I and REMox II (using the same protocol for the two projects) is 1900.
Product(s):	• Moxifloxacin • Ethambutol • Isoniazid • Pyrazinamide • Rifampicin (RIF)
Manufacturer/Developer:	• Bayer (Moxifloxacin) • Generic suppliers (Pyrazinamide, Rifampicin, Isoniazid, Ethambutol)
Cofunders:	• TB Alliance • Bayer • Sanofi-Aventis • Medical Research Council UK
Trial registration number(s):	NCT00864383 PACTR201110000124315
Status:	Ongoing
Results and Outcomes:	Recruitment reached the target of 1904 in January 2012. The follow-up study, REMox II, is detailed below.
Trial 2	**REMox II**
Site Principal Investigator(s):	• Gibson Kibiki, KCRI (Tanzania) • Noel Elisifa Sam, KCRI (Tanzania) • Rodney Dawson, UCT Lung Institute (South Africa) • Andreas Diacon, Task (South Africa) • Evans Amukoye, KEMRI (Kenya)) • Leonard Maboko, MMRC (Tanzania)

	• Ian Sanne, CHRU (South Africa) • Salome Charalambous, Aurum (South Africa)
Clinical Trial/Study Sponsor:	Global TB Alliance (USA)
Trial/Study title:	Rapid Evaluation of Moxifloxacin in Tuberculosis
Goal:	To generate data that will permit registration of one or two treatment-shortening regimens for the treatment of pulmonary TB.
Primary Objective(s):	1. To evaluate the efficacy, safety, and acceptability of two moxifloxacin-containing regimens 2. To determine whether substitution for ethambutol or isoniazid makes it possible to reduce the duration of chemotherapy 3. To present the data to international regulatory agencies to permit the regimens to be implemented internationally in resource-poor settings.
Secondary Objective(s):	1. To assess determinants of the pharmacokinetics of the TB drugs used in Regimen 1, Regimen 2, and Regimen 3 of the REMoxTB study 2. To assess possible relationships between the pharmacokinetics of the TB drugs in the REMoxTB study on the one hand and pharmacodynamic measures of efficacy, bacteriological response, and tolerability on the other hand. In this way, possible differences between treatment arms may be explained.
Clinical Trial/Study site(s):	• Kilimanjaro Christian Medical Centre, Moshi, Tanzania • UCT Lung Institute, University of Cape Town, South Africa • Task Applied Sciences, Stellenbosch, South Africa • Centre for Respiratory Disease Research (CRDR) at Kenya Medical Research Institute (KEMRI), Nairobi, Kenya • Mbeya Medical Research Centre (MMRC), Tanzania • Clinical HIV Research Unit (CHRU), Westdene, South Africa • The Aurum Institute, Tembisa, South Africa • University of Zambia and University Teaching Hospital, Lusaka, Zambia (site no longer active in study) • MRC Durban, South Africa (site no longer active in study)
Collaborating site(s):	• University College London (UCL) (UK) • Medical Research Council Clinical Trials Unit (MRC-CTU) (UK) • St Andrews University (UK)
Study design and population:	A randomised placebo-controlled double blind trial involving a treatment-shortening regimen comparing 2 months moxifloxacin, isoniazid, rifampicin, and pyrazinamide followed by 2 months moxifloxacin, isoniazid, and rifampicin with the standard regimen (2 months ethambutol, isoniazid, rifampicin, and pyrazinamide followed by 4 months isoniazid and rifampicin); a treatment-shortening regimen comparing 2 months ethambutol, moxifloxacin, rifampicin, and pyrazinamide followed by 2 months moxifloxacin and rifampicin with the standard regimen, for the treatment of adults with pulmonary TB.
Number of subjects:	Combined REMox I and REMox II (using the same protocol for the two projects) is 1900.
Product(s):	• Moxifloxacin • Ethambutol • Isoniazid • Pyrazinamide

	• Rifampicin (RIF)
Manufacturer/Developer:	• Bayer (Moxifloxacin) • Generic suppliers (Pyrazinamide, Rifampicin, Isoniazid, Ethambutol)
Cofunders:	• Medical Research Council (UK) • TB Alliance (USA) • Bill & Melinda Gates Foundation (USA) • Netherlands Organisation for Scientific Research (NOW, Netherlands)
Trial registration number(s):	NCT00864383 PACTR201110000124315
Sub-studies:	**QTc sub-study:** Although moxifloxacin has been in use for many years and has an excellent safety record, an additional sub-study to investigate the effect of all three regimens on QTc in the context of patients with low weight who are receiving the drug for up to 4 months. **Pharmacokinetic (PK) study:** A pharmacokinetic study of this potential interaction between rifampicin and moxifloxacin in the context of patients with tuberculosis.
Status:	Ongoing
Results and Outcomes:	Enrollment to the study has been completed with a total of 1931 patients randomised by 17 January 2012. All patients have now finished active treatment and continue in the follow-up phase.
Publications:	1. Phillips PP, Gillespie SH, Boeree M, Heinrich N, Aarnoutse R, McHugh T, Pletschette M, Lienhardt C, Hafner R, Mgone C, Zumla A, Nunn AJ, Hoelscher M. (2012) Innovative Trial Designs Are Practical Solutions for Improving the Treatment of Tuberculosis. *J Infect Dis*., Mar 23. PubMed PMID: 22448027 2. Coxon GD, Cooper CB, Gillespie SH, McHugh TD. (2012) Strategies and Challenges Involved in the Discovery of New Chemical Entities During Early-Stage Tuberculosis Drug Discovery. J Infect Dis., Mar 23 3. Singh KP, Brown M, Murphy ME, Gillespie SH. (2012) Moxifloxacin for tuberculosis. *Lancet Infect Dis*. Mar;12(3):176 4. Murphy ME, Singh KP, Laurenzi M, Brown M, Gillespie SH. (2012) Managing malaria in tuberculosis patients on fluoroquinolone-containing regimens: assessing the risk of QT prolongation. *Int J Tuberc Lung Dis*., Feb;16(2):144-9, i-iii. 5. Honeyborne I, McHugh TD, Phillips PP, Bannoo S, Bateson A, Carroll N, Perrin FM, Ronacher K, Wright L, van Helden PD, Walzl G, Gillespie SH. (2011) Molecular bacterial load assay, a culture-free biomarker for rapid and accurate quantification of sputum Mycobacterium tuberculosis bacillary load during treatment. *J Clin Microbiol*., Nov;49(11):3905-11. Epub 2011 Sep 7. PubMed PMID: 21900522; PubMed Central PMCID: PMC3209113 6. 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? *Clin Infect Dis*., May;52(9):e194-9 7. Gillespie SH, Singh K. (2011) XDR-TB, what is it; how is it treated; and why is therapeutic failure so high?, *Recent Pat Antiinfect Drug Discov*. May;6(2):77-83

	8. McNerney R, Maeurer M, Abubakar I, Marais B, McHugh TD, Ford N, Weyer K, Lawn S, Grobusch MP, Memish Z, Squire SB, Pantaleo G, Chakaya J, Casenghi M, Migliori GB, Mwaba P, Zijenah L, Hoelscher M, Cox H, Swaminathan S, Kim P, Schito M, Harari A, Bates M, Schwank S, O'Grady J, Pletschette M, Ditui L, Atun R, Zumla A. (2012) Tuberculosis Diagnostics and Biomarkers: Needs, Challenges, Recent Advances, and Opportunities. *J Infect Dis*., Apr 10. [Epub ahead of print] PubMed PMID: 22496353 9. Zumla A, Abubakar I, Raviglione M, Hoelscher M, Ditiu L, McHugh TD, Squire SB, Cox H, Ford N, McNerney R, Marais B, Grobusch M, Lawn SD, Migliori GB, Mwaba P, O'Grady J, Pletschette M, Ramsay A, Chakaya J, Schito M, Swaminathan S, Memish Z, Maeurer M, Atun R. (2012) Drug-Resistant Tuberculosis-Current Dilemmas, Unanswered Questions, Challenges, and Priority Needs. *J Infect Dis*., Apr 3. [Epub ahead of print] PubMed PMID: 22476720 10. Burki, T (2012) PanACEA: a new approach to tuberculosis research; Volume 12, Issue 3, Pages 184-185 11. Friedrich, SO, Rachow, A, Saathoff, E, Singh, K, Mangu, CD, Dawson, R, Phillips, PPJ. Venter, A, Bateson, A, Boehme, CC, Heinrich, N, Hunt, RD, Boeree, MJ, Zumla, A, McHugh, TD, Gillespie, SH, Diacon, AH, Hoelscher, M on behalf of the Pan African Consortium for the Evaluation of Anti-tuberculosis Antibiotics (PanACEA) (2013) Assessment of the sensitivity and specificity of Xpert MTB/RIF assay as an early sputum biomarker of response to tuberculosis treatment. *The Lancet Respiratory Medicine*, 1(6), pages 462-470, doi:10.1016/S2213-2600(13)70119-X 12. 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 Respir Med* 1: 786-92, http://dx.doi.org/10.1016/ S2213-2600(13)70231-5 13. Rojas-Ponce, G, Rachow, A, Guerra, D, Mapamba, D, Joseph, J, Mlundi, Marimoto, S, Ntinginya, NE, Mangu, C, Framhein, A, Butler, Kohlenberg, A, Ngatemelela, D, Froeschl, G, Maboko, L, Hoelscher, M, Heinrich, N (2013) A continuously monitored colorimetric method for detection of *Mycobacterium tuberculosis* complex in sputum. *Int J Tuberc Lung Dis* 17(12): 1607-1612
Press releases:	TB Alliance press release EDCTP press release

3.1.6 PanACEA-HIGHRIF

EDCTP Project Coordinator:	Martin Boeree (Radboud University Nijmegen, Netherlands)
EDCTP Call Title:	Support of phase I, II and III clinical trials on new drugs and improved drug nations for the treatment of tuberculosis
EDCTP Project Title:	Rapid evaluation of high-dose rifamipicin and other rifamycins in tuberculosis
EDCTP Project Code:	IP.2007.32011.012
EDCTP Project Start Date:	11 June 2009
EDCTP Project End Date:	31 December 2014
Collaborators:	• Robert Edward Aarnoutse (Radboud University Nijmegen, Netherlands) • Salim Abdulla (Ifakara Health Research and Development Centre, Tanzania) • Hans-Peter Beck (Swiss Tropical Institute, Switzerland) • Boeree, Martin (Radboud University Nijmegen, Netherlands) • Gavin Churchyard (Aurum Institute for Health Research, South Africa) • Rodney Dawson (University of Cape Town Lung Institute, South Africa) • Andreas Henri Diacon (Stellenbosch University, South Africa) • Stephen Gillespie (University College London, UK) • Gibson Kibiki (Kilimanjaro Christian Medical Centre (KCMC), Tanzania) • Timothy McHugh (University College London, UK) • Alphonse Okwera (Makerere University, Uganda) • Georgette Plemper van Balen (Radboud University Nijmegen, Netherlands) • Noel Elisifa Sam (KCMC, Tanzania) • D. van Soolingen (National Institute for Public Health and the Environment (RIVM), Netherlands)
Trial 1	
Site Principal Investigator(s):	• Andreas Henri Diacon (South Africa) • Rodney Dawson (South Africa)
Clinical Trial/Study Sponsor:	Radboud University Nijmegen Medical Centre (Netherlands)
Trial/Study title:	A Phase IIA Dose Ranging Trial to Evaluate the Safety, Tolerability, Extended Early Bactericidal Activity and Pharmacokinetics of Higher Doses of Rifampicin in Adult Subjects with Newly Diagnosed, Uncomplicated, Smear-Positive, Pulmonary Tuberculosis.
Goal:	Study 1 is a phase I/II maximum tolerability dosage (MTD) trial for rifampicin administered as a single drug and when combined with regular TB drugs in TB patients. In this MTD study a multiple dose rising approach is chosen to assess the safety/tolerability, pharmacokinetics and early bactericidal activity of increasing doses of rifampicin administered alone and with other TB drugs during a short period of 1 and 2 weeks respectively.
Primary Objective(s):	1. To establish the incidence and severity of adverse events of increasing dosages of rifampicin administered as a single drug and when combined with isoniazid, pyrazinamide and ethambutol in patients with newly diagnosed, uncomplicated, smear-positive pulmonary TB 2. To establish the maximum tolerated dose for rifampicin administered in increasing doses as a single drug and when combined with isoniazid, pyrazinamide and

	ethambutol in patients with newly diagnosed, uncomplicated, smear-positive pulmonary TB.
Secondary Objective(s):	1. To assess the early bactericidal activity of increasing doses of rifampicin when administered as a single drug 2. To describe the steady-state pharmacokinetics of increasing doses of rifampicin when administered as a single drug and when combined with isoniazid, pyrazinamide and ethambutol 3. To assess possible relationships between pharmacokinetic parameters of rifampicin on the one hand and adverse events and bactericidal activity on the other hand (pharmacodynamics of rifampicin).
Clinical Trial/Study site(s):	TASK applied Science (South Africa) University of Cape Town Lung Institute, Cape Town (South Africa)
Collaborating site(s):	• Radboud University (The Netherlands) • Ifakara Health Research and Development Centre (Tanzania) • Aurum Institute for Health Research (South Africa) • Stellenbosch University (South Africa) • St Andrews University (UK) • University College London (UK) • Makerere University (Uganda) • Kilimanjaro Christian Medical Centre (KCMC) (Tanzania) • National Institute for Public Health and the Environment (RIVM) (The Netherlands)
Study design and population:	• An open-label, prospective, two-centre, Phase IIA, maximum tolerability dosage (MTD) study conducted in consecutive groups • Open-label, one-arm, two-period, and fixed-order pharmacokinetic interaction study. For both: Adults (18-65 years), newly diagnosed, previously untreated, smear-positive TB.
Number of subjects:	68
Product(s):	Rifampicin
Manufacturer/Developer:	Sanofi-Aventis, Paris (France)
Cofunders:	• Netherlands Organisation for Scientific Research (NWO, Netherlands) • Radboud University Nijmegen (Netherlands) • Swiss Tropical and Public Health Institute (Switzerland) • Prince Leopold Institute of Tropical Medicine (Belgium) • Medical Research Council South Africa (MRC, South Africa)
Trial registration number(s):	PACTR201104000281203
Status:	Ongoing
Results and Outcomes:	The group have successfully completed the enrolment of 68 participants in the dose escalation study. The safety results of the patients have been extensively reviewed by the Trial Steering Committee for all dosing steps. With 35 mg rifampicin/kg still being safe and tolerable an important deliverable is obtained, but the search for the maximum tolerated dose of rifampicin has not yet been completed.
Trial 2	
Site Principal Investigator(s):	• Gibson Kibiki (Tanzania) • Klaus Reither (Tanzania)
Clinical Trial/Study	Radboud University Nijmegen Medical Centre, Nijmegen,

Sponsor:	Netherlands
Trial/Study title:	Pharmacokinetics and pharmacodynamics of high versus standard dose rifampicin in patients with pulmonary tuberculosis in Tanzania (High RIF Study).
Goal:	To evaluate the safety/tolerability and pharmacokinetics of 900 mg and 1200 mg of rifampicin combined with other TB drugs during a period of two months. Study 2 is a small exploratory Phase II study to evaluate the safety/tolerability and pharmacokinetics of 900 mg and 1200 mg of rifampicin combined with other TB drugs during a period of two months. This Phase II study reflects a cautious approach for the sake of patients' safety, in which application of high dose rifampicin for 2 months period is first evaluated for rather modest dose increases of rifampicin.
Primary Objective(s):	1. To determine the effect of a higher than standard dose of rifampicin on the pharmacokinetics of rifampicin in patients with smear-positive pulmonary tuberculosis in Tanzania 2. To determine the effect of a higher than standard dose of rifampicin on the occurrence of adverse events in the same population 3. To explore the effect of a higher than standard dose of rifampicin on the bacteriological response of Mycobacterium tuberculosis, evaluated by sputum culture conversion at two months and Serial Sputum Colony Forming Units Count (SSCC), in the same population.
Secondary Objective(s):	1. To compare the accuracy of surrogate markers (SSCC and RNA) with the standard two month sputum conversion marker in patients with smear-positive pulmonary tuberculosis in Tanzania 2. To document the occurrence of mixed Mycobacterium tuberculosis strain infections in the same patient population and its influence on treatment response.
Clinical Trial/Study site(s):	• Kilimanjaro Christian Medical College, Moshi with its field site Kibong'oto National TB Hospital, Sanya Yuu (Tanzania) • Ifakara Health Research and Development Centre, Bagamoyo (Tanzania)
Collaborating site(s):	Kibong'oto National TB Hospital, Sanya Yuu (Tanzania)
Study design:	Double blind, randomised, controlled, three arm, phase II clinical trial on adults (18-65 years) with newly diagnosed, previously untreated, smear-positive TB.
Number of subjects:	150
Product(s):	Rifampicin
Manufacturer/Developer:	Sanofi-Aventis (France)
Cofunders:	• Netherlands Organisation for Scientific Research (NWO, Netherlands) • Radboud University Nijmegen (Netherlands) • Swiss Tropical and Public Health Institute (Switzerland) • Prince Leopold Institute of Tropical Medicine (Belgium) • Medical Research Council South Africa (MRC, South Africa)
Trial registration number(s):	NCT00760149 PACTR2009060001493909
Status:	Ongoing
Results and Outcomes:	Study 1 was completed however is planned to expand based upon the initial trial outcomes. This trial aimed to investigate the maximum tolerable dosage (MTD) of rifampicin compared to standard treatment (10 mg/kg or approximately 600mg daily). The MTD study administered 20, 25, 30 and 35 mg/kg of rifampicin. The study team found that despite administering a

	dose up to 3.5 fold increase in rifampicin compared to standard treatment, the MTD has not yet been found. The primary endpoint was to determine the incidence of adverse events and to identify the MTD. Based upon the common terminology criteria for adverse events (CTCAE) grading scale, only minimal grade 3 and 2 events occurred. No grade 4 or 5 events were reported. A secondary outcome was that the higher dosages of rifampicin (30 and 35 mg/kg) showed improved early bactericidal activity (EBA) over a 14 day period. The conclusion of this study was that the increase from 10 to 35mg/kg was found to be safe and tolerated, with a suggestion that higher dosages were more effective in treating tuberculosis infection. As the MTD for rifampicin has not yet been determined, the study team is now seeking additional funds to continue this study.
PhD studies:	Title: Exploratory phase II study about laboratory analyses Candidate: Charles Mtahbo (Radboud University, Nijmegen, Netherlands) Dates: completion date of December 2013
	Title: Method validation and Pharmacokinetics Candidate: Hadija Semvua (Muhimbili University, Tanzania) Dates: completion date of December 2013
Other/Sub-studies:	Multi-arm multi-stage trial to identify regimens to include in a phase III trial for shorter treatment of tuberculosis. Objectives: The general objective is to identify arms which are significantly more efficient than the control regimen in terms of reducing bacterial load in sputum, measured by time to culture conversion. Secondary objectives are: • To assess the relative efficacy of the experimental four-drug combinations for the treatment of pulmonary tuberculosis within the first twelve weeks of treatment, and select the most efficient experimental treatment regimen for further development • To assess the frequency of acquired drug resistance among the experimental four-drug combinations. • To assess the frequency, severity, and type of adverse events (AEs), AE-related treatment discontinuations, and changes in ECG • To describe the steady-state pharmacokinetics of the experimental new drugs and/or doses used in the experimental regimens and to assess possible relationships between pharmacokinetic parameters of the various drugs, and • To describe relationships between pharmacokinetic parameters and pharmacodynamic indices on the one hand and efficacy and safety endpoints on the other hand.
Publications:	1. 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-e199. doi: 10.1093/cid/cir184 2. Boeree, MJ, Plemper van Balen, G, Aarnoutse, RA. (2011) High-dose rifampicin: how do we proceed? *International Journal of Tuberculosis and Lung Disease*. PMID 21740683

3. Phillips, PP, Gillespie, SH, Boeree, MJ, Heinrich, N, Aarnoutse, R, McHugh, T, Pletschette, M, Lienhardt, C, Hafner, R, Mgone, C, Zumla, A, Nunn, AJ, Hoelscher, M. (2012) Innovative Trial Designs Are Practical Solutions for Improving the Treatment of Tuberculosis. *J Infect Dis*. Mar 23. PubMed PMID: 22448027.
4. Burki, T (2012) PanACEA: a new approach to tuberculosis research, The Lancet Infectious Diseases; Volume 12, Issue 3, Pages 184-185
5. Friedrich, SO, Rachow, A, Saathoff, E, Singh, K, Mangu, CD, Dawson, R, Phillips, PPJ. Venter, A, Bateson, A, Boehme, CC, Heinrich, N, Hunt, RD, Boeree, MJ, Zumla, A, McHugh, TD, Gillespie, SH, Diacon, AH, Hoelscher, M on behalf of the Pan African Consortium for the Evaluation of Anti-tuberculosis Antibiotics (PanACEA) (2012) Assessment of the sensitivity and specificity of Xpert MTB/RIF assay as an early sputum biomarker of response to tuberculosis treatment. *The Lancet Respiratory Medicine,* 1(6), pages 462-470, doi:10.1016/S2213-2600(13)70119-X
6. 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 Respir Med* 1: 786-92, http://dx.doi.org/10.1016/ S2213-2600(13)70231-5
7. Rojas-Ponce, G, Rachow, A, Guerra, D, Mapamba, D, Joseph, J, Mlundi, Marimoto, S, Ntinginya, NE, Mangu, C, Framhein, A, Butler, Kohlenberg, A, Ngatemelela, D, Froeschl, G, Maboko, L, Hoelscher, M, Heinrich, N (2013) A continuously monitored colorimetric method for detection of *Mycobacterium tuberculosis* complex in sputum. *Int J Tuberc Lung Dis* 17(12): 1607-1612

3.1.7 PanACEA-SQ109

EDCTP Project Coordinator:	Michael Hoelscher (Ludwig-Maximilians Universitat Munchen, Germany)
EDCTP Call Title:	Support of phase I, II and III clinical trials on new drugs and improved drug combinations for the treatment of tuberculosis
EDCTP Project Title:	Evaluation of a novel TB drug (SQ109) to shorten and simplify TB treatment
EDCTP Project Code:	IP.2007.32011.013
EDCTP Project Start Date:	16 June 2009
EDCTP Project End Date:	15 June 2013
Collaborators:	• Akim Ayola Adegnika (Leiden University, Netherlands) • Gavin Churchyard (Aurum Institute for Health Research, South Africa) • Rodney Dawson (University of Cape Town Lung Institute, South Africa) • Keertan Dheda (University College London, UK) • Andreas Henri Diacon (Stellenbosch University, South Africa) • Martin Grobusch (University of the Witwatersrand, South Africa) • Sonja Henne (Ludwig-Maximilians Universitat Munchen, Germany) • Grey Horwith (Sequella Inc., USA) • Leonard Maboko (Mbeya Medical Research Programme, Tanzania) • Ulrich Mansmann (Ludwig-Maximilians Universitat Munchen, Germany) • Peter Mwaba (University of Zambia (UNZA), Zambia) • Alphonse Okwera (Makerere University, Uganda) • Michael Ramharter (University of Tübingen, Germany) • Klaus Reither (Ifakara Health Research and Development Centre, Tanzania) • Alimuddin Zumla (University College London, UK)
Trial 1	
Site Principal Investigator(s):	• Andreas Diacon (South Africa) • Rodney Dawson (South Africa)
Clinical Trial/Study Sponsor:	University of Munich (Germany)
Trial/Study title:	A Phase 2A Trial to evaluate the extended early bactericidal activity, safety, tolerability and Pharmacokinetics of of SQ109 in adult subjects with newly-diagnosed , uncomplicated, smear-positive, pulmonary tuberculosis (N=90)
Goal:	The overall objective of the SQ109 trial is to add a novel drug that has the potential to shorten the duration of TB treatment, simplify the treatment regimen, and decrease disease recurrence by replacing EMB in the intensive treatment phase.
Primary Objective(s):	1. To evaluate the safety, tolerability, efficacy, and pharmacokinetics of three oral dose levels of SQ109 alone and in combination with standard dose rifampicin 2. To assess safety, rolerability, and preliminary efficacy of isoniazid, rifampicin, pyrazinamide, and SQ109 (HRZSQ) 3. To compare of isoniazid, rifampicin, pyrazinamide, and SQ109 (HRZSQ) with isoniazid, rifampicin, pyrazinamide, and ethambutol (HRZE).
Secondary Objective(s):	Rate of change of logCFU in sputum over three time periods, time to sputum culture positivity
Clinical Trial/Study site(s):	• Task Applied Sciences (South Africa) • University of Cape Town (South Africa)

Collaborating site(s):	• University of Munich (Germany) • University College of London (UK) • University of Stellenbosch (South Africa) • Sequela Inc.(USA)
Study design and population:	A two-centre, partially blinded, randomised, parallel-group clinical trial. Five groups will receive SQ109 alone or with Rif and a sixth (control) group will receive standard dose RIF for 14 days. Study subjects are adults (18 years and older) with newly diagnosed, previously untreated pulmonary TB
Number of subjects:	90
Product(s):	SQ109
Manufacturer/Developer:	Sequella Inc. (USA)
Cofunders:	• Klinikum der Universitat Munchen (Germany) • Institute for Medical Bioinformatics (Germany) • Medical Research Council (UK) • Bill & Melinda Gates Foundation (USA) • Sequella (USA) • Federal Ministry of Education and Research (BMBF, Germany) Netherlands Organisation for Scientific Research (NWO, Netherlands)
Trial registration number(s):	NCT01218217 (The EBA study) PACTR201009000252144
Sub-studies:	Early Bactericidal Activity (EBA)
Status:	Ongoing
Results and Outcomes:	
PhD studies:	Title: Bactericidal assay for therapeutic management of patients with pulmonary tuberculosis from Tanzania. (WBA/PBA Study) Candidate: Stellah Mpagama (KCRI, Tanzania) Dates: February 2012-January 2014
	Title: Direct comparison of different sputum derived biomarkers of antituberculosis drug activity in early bactericidal activity (EBA) studies Candidate: Xavier Abdulkarim Kayifire (Stellenbosch University, South Africa) Dates: March 2012-December 2014
MSc studies:	Title: MSc in Clinical Trials (distance learning) Candidate: Denis Lyakurwa (KCMC/Muhimbili University, Tanzania) Dates: October 2011-August 2013
	Tite: MSc in Clinical Trials (distance learning) Candidate: Jackline Odhiambo (KEMRI, Kenya) Dates: September 2011-October 2013
	Title: Determination of the Mechanism of Action of SQ109 in Mycobacterium tuberculosis (MTB) Candidate: Bayanika Manunu (Stellenbosch University, South Africa) Dates: July 2011-October 2013
	Title: MSc in Infectious Diseases (distance learning) Candidate: Liliana Rutaihwa (IHI-BRTC, Tanzania) Dates: June 2011-July 2014
Publications	1. Burki, T (2012) PanACEA: a new approach to tuberculosis research, The Lancet Infectious Diseases; Volume 12, Issue 3, Pages 184-185 2. Friedrich, SO, Rachow, A, Saathoff, E, Singh, K, Mangu, CD, Dawson, R, Phillips, PPJ. Venter, A, Bateson, A, Boehme, CC, Heinrich, N, Hunt, RD, Boeree, MJ, Zumla, A, McHugh, TD,

	Gillespie, SH, Diacon, AH, Hoelscher, M on behalf of the Pan African Consortium for the Evaluation of Anti-tuberculosis Antibiotics (PanACEA) (2012) Assessment of the sensitivity and specificity of Xpert MTB/RIF assay as an early sputum biomarker of response to tuberculosis treatment. The Lancet Respiratory Medicine, 1(6), pages 462-470, doi:10.1016/S2213-2600(13)70119-X 3. 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 Respir Med* 1: 786-92, http://dx.doi.org/10.1016/ S2213-2600(13)70231-5 4. Rojas-Ponce, G, Rachow, A, Guerra, D, Mapamba, D, Joseph, J, Mlundi, Marimoto, S, Ntinginya, NE, Mangu, C, Framhein, A, Butler, Kohlenberg, A, Ngatemelela, D, Froeschl, G, Maboko, L, Hoelscher, M, Heinrich, N (2013) A continuously monitored colorimetric method for detection of *Mycobacterium tuberculosis* complex in sputum. *Int J Tuberc Lung Dis* 17(12): 1607-1612

3.1.8 PanACEA MAMS study

EDCTP Project Coordinators:	Martin Boeree (Radboud University Nijmegen Medical Centre (RUNMC), The Netherlands) Stephen Gillespie (University of St Andrews, UK) Michael Hoelscher (Ludwig-Maximilians Universitat Munchen, Germany)
EDCTP Call Title:	Support of phase I, II and III clinical trials on new drugs and improved drug combinations for the treatment of tuberculosis
EDCTP Project Title:	Multi-arm multi-stage trial to identify regimens to include in a phase III trial for shorter treatment of tuberculosis.
EDCTP Project Code:	IP.2007.32011.011 IP.2007.32011.012 IP.2007.32011.013
EDCTP Project Start Date:	16 June 2012
EDCTP Project End Date:	31 December 2014
Collaborators:	• Robert Aarnoutse (Radboud University Nijmegen Medical Centre, The Netherlands) • Gibson Kibiki (Tumaini University, Kilimanjaro Christian Medical Centre, Tanzania) • Andreas Diacon (Task Applied Science, South Africa) • Jeannine du Bois (Task Applied Science, South Africa) • Rodney Dawson (University of Cape Town Lung Institute, South Africa) • Gavin Churchyard (Aurum Institute for Health Research, South Africa) • Nomagugu Ndlovu (Aurum Institute for Health Research, South Africa) • Salim Abdulla (Ifakara Health Research and Development Centre, Bagamoyo Branch, Tanzania) • Alphonse Okwera (Makerere University and Mulago Hospital Kampala, Uganda) • Leonard Maboko (Mbeya Medical Research Centre, Tanzania) • Nyanda Elias Ntinginya (Mbeya Medical Research Centre, Tanzania) • Timothy McHugh (University College London, UK) • Andrew Nunn (MRC clinical Trials Unit/University College London, UK) • Patrick Philips (MRC clinical Trials Unit/University College London, UK) • Dick van Soolingen (National Insitiute for Public Health and Environment (RIVM) • Gary Horwith (Sequella Inc, US) • Lisa Beth Ferstenberg (Sequella Inc, US) • Karla Mellet (University of the Witwatersrand) • Lilian Tina Minja (Ifakara Health Research and Development Centre) • Georgette Plemper van Balen (Radboud University Nijmegen Medical Centre, The Netherlands) • Sonja Henne (Klinikum of the University of Munich (LMU), Germany) • Norbert Heinrich (Klinikum of the University of Munich (LMU), Germany) • Anna Maria Mekota (Klinikum of the University of Munich (LMU), Germany)

Trial 1	
Site Principal Investigator(s):	• Nyanda Elias Ntinginya (Tanzania) • Lilian Tina Minja (Tanzania) • Gibson Kibiki (Tanzania) • Andreas Diacon (South Africa) • Jeannine du Bois (South Africa) • Rodney Dawson (South Africa) • Karla Mellet (South Africa) • Nomagugu Ndlovu (South Africa)
Clinical Trial/Study Sponsor:	Ludwig-Maximilians Universitat Munchen
Trial/Study title:	Multi-arm multi-stage trial to identify regimens to include in a phase III trial for shorter treatment of tuberculosis.
Goal:	The purpose of this multiple arm, multiple stage (MAMS), phase 2, open label, randomized, controlled clinical trial is to evaluate four treatment regimens including SQ109, two increased doses of rifampicin, and moxifloxacin in adult subjects with newly diagnosed, smear-positive pulmonary tuberculosis.
Primary Objective(s):	The primary objective is to evaluate whether one or more of four experimental regimens based on SQ109, moxifloxacin and "high-dose" rifampicin given for twelve weeks is superior to standard treatment, as assessed by time to sputum culture conversion to negative in liquid media.
Secondary Objective(s):	1. To assess the relative efficacy of the experimental regimens compared to standard treatment of pulmonary tuberculosis 2. To assess the frequency of acquired drug resistance among the experimental combinations. 3. To assess frequency, severity and type of adverse events (AEs) and AE-related treatment discontinuations, as well as ECG alterations. 4. To describe the steady-state pharmacokinetics (PK) of the experimental new drugs and/or doses used in the experimental regimens and to assess possible relationships between pharmacokinetic parameters of the various drugs, and 5. To describe relationships between pharmacokinetic parameters and pharmacodynamic indices on the one hand, and the efficacy and safety endpoints on the other hand.
Clinical Trial/Study site(s):	The Aurum Institute for Health Research (South Africa) TASK Applied Science (South Africa) Centre for Tuberculosis Research Innovation (South Africa) Wits Health Consortium (South Africa) Ifakara Health Institute (Tanzania) NIMR-Mbeya Medical Research Centre (Tanzania) Kilimanjaro Clinical Research Institute (Tanzania)
Collaborating site(s):	• Radboud University Nijmegen Medical Centre (RUNMC) • St Andrews University • Klinikum of the University of Munich (LMU) • MRC clinical Trials Unit (UK) • University College London (UK)
Study design	A maximum of 372 adult (≥ 18 years of age) patients with newly diagnosed, smear positive pulmonary TB. Up to 62 per experimental treatment arm will be enrolled and randomized prospectively to five treatment arms. In the case of unforeseen delays, it may be necessary to recruit more participants than

	planned into the control arm (see sample size considerations).
Product(s):	Rifampicin (Svizera) Rifampicin containing fixed dose combinations (Svizera) Moxifloxacin (Bayer) SQ109 (Sequella) Vitamin B6 (Svizera)
Manufacturer/Developer:	Svizera (The Netherlands) Bayer (Germany) Sequella (US)
Trial registration number(s):	NCT01785186 PACTR201205000383208
Status:	Ongoing
Results and Outcomes:	
Publications:	

3.1.9 TB Vac prep Ethiopia/THYB-03

EDCTP Project Coordinator:	Abraham Aseffa (Armauer Hansen Research Institute (AHRI), Ethiopia)
EDCTP Call Title:	Capacity building and site development for the conduct of phase III trials of TB vaccines in high risk populations
EDCTP Project Title:	Capacity building for the conduct of ICH-GCP level TB vaccine trials in high risk populations in Ethiopia and East Africa
EDCTP Project Code:	CT.2005.32080.003
EDCTP Project Start Date:	10 August 2007
EDCTP Project End Date:	31 December 2010
Collaborators:	• Markos Abebe (Armauer Hansen Research Institute (AHRI), Ethiopia) • Ripley Ballou (GlaxoSmithKline, UK) • Peter Bang (Statens Serum Institut, (SSI), Denmark) • Joe Cohen (GlaxoSmithKline, UK) • Jaap van Dissel (Leiden University, Netherlands) • Mark Doherty (Statens Serum Institut, (SSI), Denmark) • Patrice Dubois (ImmunoVac Consulting, Belgium) • Howard Engers (AHRI, Ethiopia) • Gibson Kibiki (Kilimanjaro Christian Medical Centre (KCMC), Tanzania) • Opokua Ofori-Anyinam (GlaxoSmithKline, UK) • Tom Ottenhoff (Leiden University, Netherlands) • Herrimanana Henri Ramarokoto (Institut Pasteur de Madagascar) • Voahangy Rasolofo (Institut Pasteur de Madagascar) • John Shao (KCMC, Tanzania) • Ezera Shimeles (AHRI, Ethiopia) • Jean-Louis Soares (Institut Pasteur de Madagascar) • Liya Wassie Dubale (AHRI, Ethiopia) • Lawrence Yamuah (AHRI, Ethiopia)
Study/Trial 1	
Site Principal Investigator(s):	• Abraham Aseffa (Ethiopia) • Jemal Hussein (Ethiopia)
Clinical Trial/Study Sponsor:	SSI (Denmark)
Trial/Study title:	A Safety and Immunogenicity Trial With an Adjuvanted TB Subunit Vaccine (Ag85B-ESAT-6 + IC31) THYB-03
Goal:	1. To evaluate the safety profile of an adjuvanted TB subunit vaccine administered in different antigen/adjuvant formulations at 0 and 2 months 2. To determine the immunogenicity profile of an adjuvanted TB subunit vaccine administered in different antigen/adjuvant formulations at 0 and 2 months.
Primary Objective(s):	Strengthening the capacity of AHRI and its Ethiopian collaborators to carry out the required laboratory and data management activities to satisfy ICH-GCP conduct of Phase I, II and III TB vaccine trials.
Secondary Objective(s):	Strengthening the capacity of existing AHRI partners in East Africa (Madagascar and Tanzania) to produce the basic laboratory information and data required for supporting TB vaccine research in their respective countries.
Clinical Trial/Study site(s):	The Armauer Hansen Research Institute (AHRI, Ethiopia)
Collaborating site(s):	• AHRI (Ethiopia) • Institut Pasteur (IPM, Madagascar) • Kilimanjaro Christian Medical College (KCMC, Tanzania) • GlaxoSmithKline Biologicals (GSK, UK) • Statens Serum Institute (SSI, Denmark

	• Leiden University (Netherlands) • Immunovac Consulting (Belgium)
Study design and population:	Phase I, open label randomised controlled trial to assess safety and efficacy. ADULTS (18-40 years); males N=39
Product(s):	ESAT-6/Ag85B
Manufacturer/Developer:	• SSI produces ESAT-6/Ag85B • Intercell A/S produces IC31adjuvant
Cofunders:	• Statens Serum Institut (Denmark) • Leiden University (Netherlands)
Trial Registration number(s):	NCT01049282
Status:	Completed
Results and Outcomes:	The project was successful in building capacity for clinical trials at AHRI, Institut Pasteur in Madagascar and at KCMC in Tanzania. At AHRI, the capacity was built with hands on running of a phase I TB vaccine trial (ThyB 03) in collaboration with SSI. Laboratory infrastructure was improved with improved capacity for flow cytometric assays with FACSCanto. The GCP team has developed much experience in the course of the phase I trial and learned to work on a new phase II trial protocol writing. At KCMC, data management capacity was improved and laboratory skills for TB enhanced through training by a team from AHRI. Similarly, IP Madagascar benefited from lab assay training by Immunovac on flow cytometric assays and on GCLP. AHRI organized an ethics training for IP Madagascar staff. Several PhD and Masters students were trained at AHRI, Tanzania and at Madagascar. The links between the institutions were strengthened as a result leading to additional newtowrking in similar projects. At Addis Ababa, AHRI strengthened its links with the Ministry of Health and the regulatory authorities as well as the ethics committees through a number of communications and joint activities. The interaction between the SSI and AHRI scientists has benefitted the site and facilitated skills transfer particularly in the immunogenicity assays for the vaccine trial. Close interaction between Tanzania, Malagasy and Ethiopian laboratory researchers, including a two year stay of two AHRI researchers at KCMC on a Masters project, led to an excellent south-south networking which is now further enriched through additional opportunities of collaboration.
PhD studies:	Candidate: Wude Mihret (Addis Ababa University, Ethiopia)
	Candidate: Liya Wassie (Addis Ababa University, Ethiopia)
	Candidate: Kidist Bobsha (Addis Ababa University, Ethiopia)
MSc studies:	Title: MSc in Clinical Research Candidate: Tewodros Tariku (Addis Ababa University, Ethiopia)
	Title: MSc in Clinical Research Candidate: Wassihum Wodajo (Addis Ababa University, Ethiopia)
	Title: MSc in Clinical Research Candidate: Radeye Abeje (Addis Ababa University, Ethiopia)
	Title: MSc Clinical Trials Candidate: Meseret Habtamu (Tumani University, Tanzania)
	Title: MSc in Clinical Trials Candidate: Demis Arga (Tumani University, Tanzania)
	Title: MSc in Clinical Trials Candidate: Tesfamaruam Mebrahtu (Addis Continental School of Public Health/Gondar, Ethiopia)
	Title: MSc in Clinical Trials Candidate: Student: Sebe Mamo (Addis Continental School of

	Public Health/Gondar, Ethiopia)
Publications:	1. Ottenhoff, TH, Doherty, TM, van Dissel, JT, Bang, P, Lingnau, K, Kromann, I, Andersen, P. (2010) First in humans: a new molecularly defined vaccine shows excellent safety and strong induction of longlived Mycobacterium tuberculosis-specific Th1-cell like responses. *Human Vaccines*, Dec 6 (12), 1007-15, 2. Jaap T. van Dissel, Sandra M. Arend, Corine Prins, Peter Bang, Pernille Nyholm Tingskov, Karen Lingnau, Jan Nouta, Michèl R. Klein, Ida Rosenkrands, Tom H. M. Ottenhoff, Ingrid Kromann, T. Mark Doherty and Peter Andersen. Ag85B-ESAT-6 adjuvanted with IC31® promotes strong and long-lived Mycobacterium tuberculosis specific T cell responses in naïve human volunteers. *Vaccine*. 2010 Apr 30;28(20):3571-81.

3.1.10 Van't Hoog-TB Vac prep Kenya

EDCTP Project Coordinator:	Anja van't Hoog (University of Amsterdam, Netherlands)
EDCTP Call Title:	Capacity building and site development for the conduct of phase III trials of TB vaccines in high risk populations
EDCTP Project Title:	Prospective epidemiological studies of TB in neonates and adolescents in Karemo Division, Siaya district, Western Kenya, in preparation for future clinical trials
EDCTP Project Code:	CT.2005.32080.002
EDCTP Project Start Date:	13 June 2007
EDCTP Project End Date:	31 December 2011
Collaborators:	• Martinus Willem Borgdorff (KNCV Tuberculosis Foundation, Netherlands) • Vicky Cardenas (Aeras Global Tuberculosis Foundation, USA) • Daniela Cirillo, (San Raffaelle del monte Tabor foundation – Milan, Italy) • Parasuram Dhulipalla (Aeras Global Tuberculosis Foundation, USA) • Macaya Julie Douoguih (Aeras Global Tuberculosis Foundation, USA) • Lawrence James Geiter (Aeras Global Tuberculosis Foundation, USA) • Markus Gmeiner (Vienna School of Clinical Research, Austria) • Toni Hawkridge (Aeras Global Tuberculosis Foundation, USA) • Gregory Hussey (University of Cape Town, South Africa) • Kayla Laserson (Centers for Disease Control and Prevention (CDC), USA) • Katherine Leigh Feidler (Aeras Global Tuberculosis Foundation, USA) • Hassan Mahomed (University of Cape Town, South Africa) • Videlis Nduba (Kenya Medical Research Institute (KEMRI), Kenya) • Elizabeth Onyango-Okoth (Ministry of Health, Kenya) • Juliana Otieno (Ministry of Health, Kenya) • Jen Page (Aeras Global Tuberculosis Foundation, USA) • Suzanne Verver (KNCV Tuberculosis Foundation, Netherlands)
Study/Trial 1	
Site Principal Investigator(s):	• Videlis Nduba (Kenya) • Anja van't Hoog (Netherlands) • Kayla Laserson (USA)
Trial/Study title:	A Prospective Epidemiological Cohort Study to Evaluate the Incidence of Tuberculosis in Infants in Western Kenya A Prospective epidemiological study of TB in adolescents in Siaya district, Western Kenya, in preparation for future vaccine trials
Goal:	Cohort studies to develop capacity and prepare for TB vaccine trials
Primary Objective(s):	Neonates study aims to: 1. Estimate the one year incidence of tuberculosis disease as diagnosed by two sputum smears positive for AFB and/or a positive Mycobacterial culture 2. Determine all-cause and TB-specific mortality, through vital events monitoring and verbal autopsies; out-migration and cohort retention 3. Develop a system of reporting home deliveries and

	provision of BCG vaccination within 96 hours of birth 4. Monitor incidence of BCG-related adverse events 5. Assess community knowledge and attitudes about current practices regarding BCG vaccination. The adolescent study aims to: 1. Determine the optimal way to access an adolescent population 2. Determine one-year incidence of TB disease as diagnosed by two sputum smears positive for AFB and/or a positive Mycobacterial culture 3. Determine the prevalence of TB infection and disease 4. Estimate the annual risk of infection with M. tuberculosis as evidenced by the tuberculin skin test (TST) 5. Assess community knowledge and attitudes about current practices regarding BCG vaccination and TB 6. Determine the rate of hospitalization and mortality events through record review and verbal autopsy 7. Determine out-migration and cohort retention.
Secondary Objective(s):	To build capacity to: 1. Develop a system of reporting home deliveries and provision of BCG vaccination within 96 hours of birth 2. Monitor incidence of BCG-related adverse effects 3. Assess community knowledge and attitudes about current practices regarding BCG vaccination 4. Determine all cause mortality and TB specific mortality, through vital events monitoring and verbal autopsies.
Clinical Trial/Study site(s):	Karemo Division, Siaya district (Kenya)
Collaborating site(s):	• KNCV Tuberculosis Foundation (Netherlands) • Ministry of Health (Kenya) • KEMRI, Kenya • University of Cape Town (South Africa) • Center for Disease Control and Prevention (CDC, USA) • Vienna School of Clinical Research (Austria) • San Raffaelle del monte Tabor foundation (Italy)
Study design:	Prospective cohort study
Number of subjects:	5004 adolescents and 2900 infants
Cofunders:	• Netherlands Organisation for Scientific Research (NWO, Netherlands) • KNCV Tuberculosis Foundation (Netherlands) • San Raffaelle del monte Tabor foundation (Italy) • Austrian Federal Ministry of Science (Austria)
Status:	Completed
Results and Outcomes:	**Infant Cohort Study:** Following screening of 3223 infants, 2900 infants were enrolled in the study and BCG vaccinated. 60% of infants were born at home and 40% were born at health facilities. 401 (16.3%) were born to HIV infected mothers, and 2.6% tested HIV+ve at 6 weeks of age. Disclosure counselling was done and 47/73 (64%) infants referred and followed up to begin ART as per WHO and National recommendations; 26 out of 73 had died before disclosure. Through four monthly follow up visits and unscheduled (sick visits) 922 (31.8%) TB suspects were identified. 128 (13.9%) had a history of contact, 590(64%) had a hospitalisation criteria and 196 (21.3%) had TB symptoms. Of these 732 (79.6%) were investigated for TB in the newly renovated Case Verification Ward. Two early morning gastric aspirates and two induced

	sputum samples were collected on consequent mornings. Chest radiographs, Mantoux tests, HIV testing and Clinical assessments were done to determine TB cases. 45 TB cases were started on anti TB treatment in conjunction with the National Programme. This gives an incidence rate of 1.0 per 1000 person years (95% CI 0.75-1.36) for definite, probable and possible TB combined. 160 (5.5%) participants were identified to have Latent TB infection based on positive mantoux test, negative culture and normal chest radiographs. 24990 ancillary or unscheduled visits were conducted where free health care was provided at the study clinic. There were 203/2900(57/1000 person years) deaths. This is almost half the infant mortality in the study area (119/1000 live births) 10.8% were neonatal deaths. Pneumonia, malaria, diarreal disease were the leading immediate causes of death accounting for 43.1% of deaths. Study closeout visits have been completed. **Adolescent Cohort Study:** A total of 5541 adolescents were approached to participate in the study of which 5004 (90.3%) were enrolled. Out of 5004 adolescents enrolled, 2579 (51.5%) were male, mean age 14 years (SD 1.9). Based on screening criteria at enrolment, 1775 (35.5%) were identified as TB suspects due to either a household contact 144 (2.9%), symptoms of TB 515 (10.3%) and/or a positive TST 1544/4808 (32.1%); with 87.3% of TB suspects having only one criterion for investigation. All the TB suspects were offered and agreed to a HIV test and 21/1775 (1%) tested HIV positive. Fifteen culture confirmed PTB cases were identified and 24 probable PTB based on clinical and radiological criteria reflecting a prevalence estimate of 300/100,000 (definite) and 779/100,000 (definite and probable) PTB respectively. Of the 5004 adolescents, 4965 adolescents without TB at baseline were followed up for incident TB. During follow up 23 TB cases were found with a corresponding incidence density of 3.9 (95% CI, 2.4-5.8) events per 1000 person years of observation (PYO). After adjustments were done, being male (P=0.0045, HR 0.91 95% CI, 0.86-0.96), having a BCG scar (P=<.0001, HR 2.04 95% CI, 1.88-2.21) and school going (P=<.0001, HR 1.70 95% CI, 1.51-1.92) remained the strongest predictors of TB incidence
PhD studies:	Title: Epidemiology of tuberculosis in adolescents in western Kenya Candidate: Videlis Nduba (University of Amsterdam, Netherlands) Dates: Completed December 2013
	Title: Tuberculosis incidence among HIV-infected adults and overall health care utilization among target populations in the Health and Demographic Surveillance Population in western Kenya: Implications for TB vaccine trials Candidate: Godfrey Bigogo (University of Amsterdam, Netherlands) Dates: Completed December 2013
	Title: Infectious disease modeling/epidemiology of tuberculosis in infants and care seeking in self reported adult TB patients in western Kenya Candidate: Lazarus Odeny (University of Amsterdam, Netherlands)

	Dates: Completed December 2013
MSc studies:	Title: MA Project Planning and Management Candidate: Joseph Opole (University of Nairobi, Kenya) Dates: October 2008-December 2010
	Title: MSc in Clinical Trials Candidate: Walter Mchembere (Maseno University, Kenya) Dates: June 2008-December 2012
	Title: Msc in Clinical Trials Candidate: Peter Myamthimba (LSHTM, UK) Dates: December 2013
Publications:	

3.1.11 TB Vac prep Uganda

EDCTP Project Coordinator:	Philippa Musoke (Makerere University, Uganda)
EDCTP Call Title:	Capacity building and site development for the conduct of phase III trials of TB vaccines in children under 1 year of age
EDCTP Project Title:	Towards conducting phase III trials of novel TB vaccines in Ugandan infants and adolescents
EDCTP Project Code:	CT.2005.32090.003
EDCTP Project Start Date:	28 August 2007
EDCTP Project End Date:	31 January 2012
Collaborators:	• Sabrina Bakeera-Kitaka (Makerere University, Uganda) • Robert Colebunders (Prince Leopold Institute of Tropical Medicine (ITM), Belgium) • Vinod K. Diwan (Karolinska Institute, Sweden) • Willem Hanekom (University of Cape Town, South Africa) • Moses Lutaakome Joloba (Ministry of Health, Uganda) • Gunilla Kallenius (Karolinska Institute, Sweden) • Noah Kiwanuka (Medical Research Council Programme on AIDS - Uganda Virus Research Institute (MRC/UVRI), Uganda) • Asli Kulane (Karolinska Institute, Sweden) • Markus Maeurer (Karolinska Institute, Sweden) • Arnaud Marchant (Université Libre de Bruxelles, Belgium) • Harriet Mayanja-Kizza (Makerere University, Uganda) • Keith McAdam (Makerere University, Uganda) • Joris Menten (ITM, Belgium) • Philippa Musoke (Makerere University) • Patrick Nabongo (Makerere University) • Margaret Nakakeeto Kijambu (Makerere University) • Stefan Peterson (Karolinska Institute, Sweden) • Stefan Svenson (Swedish Institute for Infectious Disease Control (SMI), Sweden) • Suzanne Verver (KNCV Tuberculosis Foundation, Netherlands) • Anne Wajja (Makerere University, Uganda)
Study/Trial 1	
Site Principal Investigator(s):	Philippa Musoke (Uganda)
Clinical Trial/Study Sponsor:	Infectious Diseases Institute (IDI), Makerere University (Uganda)
Trial/Study title:	Epidemiological cohort study
Goal:	To build capacity in Uganda to ultimately conduct phase III trials of novel tuberculosis (TB) vaccines, in infants <1 year of age and adolescents.
Primary Objective(s):	1. To determine the incidence of TB disease in infants. Endpoint: Proportion of infant population with clinical TB disease over a 1 year period 2. To determine the prevalence and the 18 months incidence of TB disease among adolescents 12-16year old. The endpoint of the study is to determine the proportion of the adolescent population with clinical incident TB disease over the 18 month period.
Secondary Objective(s):	1. To determine the longitudinal kinetics of the immune response induced by newborn BCG vaccination. Endpoint: Longitudinal changes in multiple markers of the BCG-induced T cell response 2. To determine the annual risk of infection among adolescent 12-16 year old. Endpoint: Proportion of the

	adolescent population with a positive TST in the different age groups 3. To compare tuberculin skin testing (TST) to novel immunological assays to diagnose TB. Endpoint: Proportion of the adolescent population with clinical TB disease and positive TST and/or positive immunological assays 4. To determine infant and adolescent mortality rates and causes of mortality. Endpoint: Proportion of infant and adolescent population (12 -16 years) that dies, over a period of 2 years, and proportional cause of mortality 5. To determine knowledge, attitudes and practices (KAP) about TB, and willingness to participate in TB vaccination trials, and to increase TB awareness in the community. Endpoint: Qualitative community concepts and quantification of pertinent qualitative findings 6. To determine rates of cohort retention, and causes of loss to follow up. Endpoint: Proportion of enrolled infant and adolescent population that have completed 1 year follow-up of observation, and proportional causes of loss to follow-up.
Clinical Trial/Study site(s):	Iganga/Mayuge Demographic Surveillance Site in Eastern Uganda
Collaborating site(s):	• Infectious Diseases Institute (IDI), Makerere University College of Health Sciences (Uganda) • Mycobacteriology (BSL-3) Lab (MYCO-LAB) – Department of Medical Microbiology, Makerere University College of Health Sciences (Uganda) • The School of Public Health, Makerere University College of Health Sciences (Uganda) • The National TB Reference Laboratory (NTRL)-Wandegeya (Uganda) • South African Tuberculosis Vaccine Initiative (SATVI, South Africa) • Swedish Institute for Infectious Disease Control (SMI, Sweden) • Karolinska Institute (Sweden) • Prince Leopold Institute of Tropical Medicine (Belgium) • The Institute for Medical Immunology (Belgium) • The KNCV Tuberculosis Foundation (Netherlands)
Study design:	Prospective cohort tudy
Number of subjects:	2500 subjects in the Infant Cohort Study 5000 subjects in the Adolescent Cohort Study 100 subjects in the immunology study
Cofunders:	• Swedish International Development Cooperation Agency (SIDA, Sweden) • Karolinska Institute (Sweden) • Prince Leopold Institute of Tropical Medicine (Belgium) • Aeras Global TB Vaccine Foundation (USA)
Status:	Completed
Results and Outcomes:	Primary outcomes of the study were: 1. To determine the incidence of TB disease in infants. Endpoint: Proportion of infant population with clinical TB disease over a 1 year period – The study showed a low incidence of TB disease in this population. Only one (1) culture positive case of MTB (definite TB) was found throughout the study follow up. However using the SATVI algorithm which classifies cases into definite, probable and possible TB, there were

	27 probable TB cases and therefore the incidence rate (combining 1 definite and 27 probable cases) is 62 per 10,000 person years. Another 35 cases were classified as possible TB. Overall, 38 participants were treated for TB mostly based on clinical or radiological assessment.and these included 1 definite case, 2 probable TB cases and 35 possible TB cases 2. To determine the prevalence and the 18 months incidence of TB disease among adolescents 12-16 year old: Endpoint: Proportion of the adolescent population with clinical incident TB disease over the 18 month period – Eight culture confirmed cases of TB were found among adolescents at baseline resulting in a prevalence of 160/100,000 (95% CI, 69-315). During follow up, a total of 14 cases of TB of which one was clinical extra-pulmonary TB and the 13 culture confirmed MTB cases of TB in an average of 1.1 person years of follow up was found resulting in an incidence
PhD study:	Title: Vaccine induced immunity in nine-month old infants following BCG vaccination at birth or at 6 weeks of age Candidate: Fredrick Lutwama (University of Cape Town, South Africa) Dates: June 2008-March 2013
Publications:	1. Buregyeya E, Kulane A, Colebunders R, Wajja A, Kiguli J, Mayanja H, Musoke P, Pariyo G, Mitchell EM (2011) Tuberculosis knowledge, attitudes and health-seeking behaviour in rural Uganda. *International Journal of Tuberculosis Lung Disease*; 15 Jul (7):938-42. 2. Asiimwe BB, Bagyenzi GB, Ssengooba W, Mumbowa F, Mbowa G, Wajja W, Mayanja-Kiiza H, Musoke P, Kallenius G, Joloba ML (2013) Species and genotypic diversity of non-tuberculous mycobacteria isolated from children investigated for pulmonary tuberculosis in rural Uganda. *BMC Infectious Diseases*, 18 Feb, 13:88, doi: 10.1186/1471-2334-13-88. 3. Ssengooba W, Wajja A, Bugumirwa E, Mboowa G, Namaganda C, Nakayita G, Kateete DP, Waako J, Verver S, Musoke P, Mayanja-Kizza H, Joloba ML (2012) An Early Morning Sputum Sample Is Necessary for the Diagnosis of Pulmonary Tuberculosis, Even with More Sensitive Techniques: A Prospective Cohort Study among Adolescent TB-Suspects in Uganda. *Tuberculosis Research and Treatment*, Article ID 970203, 6 pages, doi:10.1155/2012/970203. 4. Sekadde MP, Wobudeya E, Joloba ML, Ssengooba W, Kisembo H, Bakeera-Kitaka S, Musoke P (2013) Evaluation of the Xpert MTB/RIF test for the diagnosis of childhood pulmonary tuberculosis in Uganda: a cross-sectional diagnostic study. *BMC Infect Dis.* Mar 12;13:133 5. Ssengooba W, Kiwanuka N, Kateete DP, Katamba A, Joloba ML (2012) Incremental yield of serial sputum cultures for diagnosis of tuberculosis among HIV infected smear negative pulmonary TB suspects in Kampala, Uganda. *PLoS One*;7(5):e37650.

3.1.12 THYB-04

EDCTP Project Coordinator:	Peter Andersen (Statens Serum Institut, (SSI), Denmark)
EDCTP Call Title:	Call for support of clinical trials, capacity building and networking in tuberculosis vaccines development
EDCTP Project Title:	Conduct of ICH-GCP level phase II TB vaccine trials in high risk populations in Africa
EDCTP Project Code:	IP.2007.32080.001
EDCTP Project Start Date:	25 March 2009
EDCTP Project End Date:	24 March 2014 (1 November 2014 – PhD Martha Zewdie)
Collaborators:	• Peter Aaby (Bandim Health Project, Guinea-Bissau) • Markos Abebe (Armauer Hansen Research Institute (AHRI), Ethiopia) • Abraham Aseffa (AHRI, Ethiopia) • Peter Bang (SSI, Denmark) • Ahmed Bedru (AHRI, Ethiopia) • Jaap van Dissel (Leiden University, Netherlands) • Mark Doherty (SSI, Denmark) • Howard Engers (AHRI, Ethiopia) • Asfawossen Gebreyohannis (AHRI, Ethiopia) • Victor Gomes (Bandim Health Project, Guinea Bissau) • Jemal Hussain (AHRI, Ethiopia) • Ingrid Kromann (SSI, Denmark) • Ruth Leekassa (AHRI, Ethiopia) • Tom Ottenhoff (Leiden University, Netherlands) • Liya Wassie Dubale (AHRI, Ethiopia) • Christian Wejse (University of Aarhus, Denmark) • Lawrence Yamuah (AHRI, Ethiopia)
Study/Trial 1	
Site Principal Investigator(s):	Hennie Geldenhuys (South Africa)
Clinical Trial/Study Sponsor:	Statens Serum Institute (SSI, Denmark)
Trial/Study title:	A phase II, randomised, double-blind, trial to evaluate the immunogenicity and safety of 2 doses of an adjuvanted TB subunit vaccine (Ag85B-ESAT-6 + IC31) using 2 different vaccination schedules in healthy adolescents (THYB-04)
Goal:	To test the hypothesis that the vaccine is safe and immunogenic at a dose and in a human population resembling that in which the final product will be used.
Primary Objective(s):	To evaluate the immunogenicity and safety of a TB subunit vaccine administered in volunteers at 0 and 2 months. The description of the immunogenicity profile will be based on the magnitude of production of IFN after stimulation with mitogen or antigen. The relative change from baseline will be visualised using plots. The relative change from baseline to the end of the study will be quantified using regression techniques allowing for within subject correlation.
Seconday Objective(s):	To evaluate additional immunogenicity outcomes of a TB subunit vaccine administered in volunteers at 0 and 2 months. Frequency and patterns of specific type-1 cytokines in CD4 and CD8 T cells will be described after shortterm stimulation of whole blood with overlapping peptides of Ag85B peptides, ESAT-6, H1 protein, and BCG (measured by WBA-ICS).
Clinical Trial/Study site(s):	1. Armauer Hansen Research Institute (AHRI) Addis Ababa, Ethiopia (no longer THYB-04 clinical trial site as per September 2011) 2. Nazaret/Adama Regional Hospital(Nazaret/Ethiopia) (no

	longer THYB-04 clinical trial site as per September 2011) 3. Debre Zeit Hospital (Debre Zeit/Ethiopia) (no longer THYB-04 clinical trial site as per September 2011) 4. SATVI South Africa
Collaborating site(s):	• Statens Serum Institute (SSI, Denmark) • Armauer Hansen Research Institute (AHRI, Ethiopia) • Leiden University Medical Centre (LUMC, Netherlands) • Projecto de Saúde de Bandim/SSI (Guinea-Bissau) • Bandim Health Project/ Aarhus University Hospital, Århus (Denmark)
Study design and population:	Phase II multicentre double-blinded randomised controlled trial; ADOLESCENTS (12-18 years); TST positive healthy individuals N= 240
Product(s):	• ESAT-6/Ag85B • adjuvant IC31
Manufacturer/Developer:	• SSI produces ESAT-6/Ag85B and IC13 • Intercell A/S developed IC31adjuvant
Cofunders:	• Danish International Development Agency (Denmark) • Leiden University Medical Centre (Netherlands)
Trial registration number(s):	DOH-27-0612-3947 (SANCTR)
Status:	Completed
Results and Outcomes:	Recruitment at SATVI started September 2012. As of 28 March 2013, 358 patients were screened and 178 were enrolled.
PhD studies:	Title: Analysis of regulation of immune responses in Tuberculosis Candidate: Martha Zewdie (SSI, Denmark/AHRI, Ethiopia) Dates: 1 January 2011-Q3 2014
	Title: PREDicting Tuberculosis among TB suspects, Improving triage and Nutritional support to Alter Mortality, PREDINAM Candidate: Frauke Rudolph (Bandim Health Project, Guinea Bissau) Dates: 1 September 2009-31 January 2013
	Title: Isoniazid or Rifampicin and Isoniazid Preventive Therapy for children exposed to Tuberculosis – the IRIPT trial Candidate: Grethe Lemvik (Bandim Health Project, Guinea Bissau) Dates:1 March 2010-28 February 2014
Post-Doc studies:	Title: Implementation of IPT in an low resource setting Candidate: Victor Gomes (Bandim Health Project, Guinea Bissau) Dates: 1 April 2011-31 March 2014
	Title: Evolution of immune response during TB treatment Candidate: Markos Abebe (AHRI, Ethiopia) Dates: 2010-March 2014
Study/Trial 2	
Site Principal Investigator(s):	Grethe Lemvik (Guinea Bissau)
Clinical Trial/Study Sponsor:	Statens Serum Institute (SSI, Denmark)
Trial/Study title:	Isoniazid or Rifampicin and Isoniazid Preventive Therapy for children exposed to Tuberculosis – the IRIPT trial
Goal:	To determine the best preventive therapy for TB exposed children
Primary Objective(s):	To compare the adherence of 9 months of INH (9I) versus 4 months of INH+RIF (4IR)
Secondary Objective(s):	To assess the TB-incidence and mortality related to TB and TB-exposure among children<15 years of age in an urban area of Guinea-Bissau

Clinical Trial/Study site(s):	Bandim Health Project (Guinea Bissau)
Collaborating site(s):	• SSI (Denmark) • AHRI (Ethiopia) • Leiden University Medical Centre (LUMC) (Netherlands) • Projecto de Saúde de Bandim/SSI (Guinea-Bissau) • Bandim Health Project/Aarhus University Hospital, Århus (Denmark)
Study design:	Open-label cluster-randomised clinical trial
Product(s):	Isoniazid and Rifampicin
Manufacturer/Developer:	International Dispensary Association, Holland
Cofunders:	SSI (Denmark)
Trial Registration number(s):	PACTR201101000273931
Status:	Ongoing: Closed to recruitment: follow up continuing
Results and Outcomes:	Recruitment is currently ongoing
Study/Trial 3	
Site Principal Investigator(s):	Frauke Rudolf (Guinea Bissau)
Clinical Trial/Study Sponsor:	Statens Serum Institute (SSI, Denmark)
Trial/Study title:	PREDicting Tuberculosis among TB suspects, Improving triage and Nutritional support to Alter Mortality, PREDÌNAM
Goal:	To improve the case management of pulmonary tuberculosis (PTB) suspects and confirmed PTB patients by using simple measures and interventions applicable in low resource settings.
Primary Objective(s):	To lower mortality in PTB suspects by securing early consideration of PTB in the diagnostic process and using a diagnostic algorithm applicable in a low resource setting.
Secondary Objective(s):	To compare risk assessment in the current PTB suspect cohort to identification of high risk patients after implementation of the suPAR quicktest.
Tertiary Objective(s):	To reduce the complexity of the current version of the TBscore by using Principal Component Analysis.
Clinical Trial/Study site(s):	Bandim Health Project (Guinea Bissau)
Collaborating site(s):	• Statens Serum Institute (SSI), Copenhagen, Denmark • Armauer Hansen Research Institute (AHRI), Addis Ababa, Ethiopia • Leiden University Medical Centre (LUMC) Leiden, Netherlands • Projecto de Saúde de Bandim/SSI, Guinea-Bissau • Bandim Health Project/ Aarhus University Hospital, Århus, Denmark
Study design:	Observational follow-up cohort study on PTB suspects
Product(s):	suPARnostic quick test
Manufacturer/Developer:	Virogates
Cofunders:	SSI (Denmark)
Trial Registration number(s):	PACTR201101000273931
Status:	Ongoing
Results and Outcomes:	The total number of included patients is now 1445. Out of those 1015 should have a 1 year follow-up and as of March 2013 930 have.
Study/Trial 4	
Site Principal Investigator(s):	Martha Zewdie (Ethiopia)
Trial/Study title:	Analysis of regulation of immune responses in Tuberculosis
Goal:	Assessment of the "quality" of the memory immune response during TB treatment, latent infection and after vaccination

	allowing us to compare memory in a failed natural immune response (TB disease) with a rotective natural immune response (control of infection leading to latency) with the immune response generated by vaccination.
Primary Objective(s):	1. Measure magnitude and duration of primary endpoints in vaccine study cohorts (IFN gamma production by ELISA/ELISpot) 2. Identify the role of effector, memory and Treg cell subsets in the induction of a robust immune response in healthy adults given a new candidate TB vaccine 3. Evaluate the role of different subsets of T cells during latent and active TB infection before and after chemotherapy 4. Evaluate the difference in effector and regulatory immune cells between active TB patients, latently infected individuals, and healthy endemic controls 5. Assess the efficacy of real time PCR in identifying and distinguishing T cell subsets by comparison with flow cytometry.
Clinical Trial/Study site(s):	• Armauer Hansen Research Institute (AHRI, Ethiopia)
Cofunders:	SSI (Denmark)
Status:	Ongoing
Results and Outcomes:	Recruiting
Publications:	

3.1.13 TB-021

EDCTP Project Coordinator:	Helen McShane (University of Oxford, UK)
EDCTP Call Title:	Call for support of clinical trials, capacity building and networking in tuberculosis vaccines development
EDCTP Project Title:	A proof-of-concept Phase IIb clinical trial to evaluate the protective efficacy of a booster MVA85A vaccination administered to healthy, HIV infected adult in South Africa, Senegal and The Gambia
EDCTP Project Code:	IP.2007.32080.002
EDCTP Project Start Date:	27 August 2009
EDCTP Project End Date:	31 December 2014
Collaborators:	• Nathaniel Brittain (University of Oxford, UK) • Christiane A.J. Huygen (Pasteur Institute – Brussels, Belgium) • Farba Karam (University Cheikh Anta DIOP de Dakar (UCAD), Senegal) • Souleymane Mboup (UCAD, Senegal) • Paul Milligan (London School of Hygiene and Tropical Medicine (LSHTM), UK) • Robert Wilkinson (University of Cape Town, South Africa)
Study/Trial 1	
Site Principal Investigator(s):	Robert Wilkinson (South Africa) Souleymane Mboup (Senegal)
Clinical Trial/Study Sponsor:	University of Oxford (UK)
Trial/Study title:	A phase II, proof-of-concept, randomised, double-blind, placebo-controlled study to evaluate the protective efficacy against TB disease, safety, and immunogenicity of MVA85A/AERAS-485 in healthy, HIV-infected adults
Primary Objective(s):	To use an HIV-infected adult cohort to evaluate the safety of MVA85A/AERAS-485 compared to control subjects who receive placebo, and to provide proof of concept for efficacy. To provide capacity building within sub-Saharan Africa, which will allow the successful conduct of a Phase IIb, randomised controlled proof-of-concept trial evaluating the safety of MVA85A/AERAS-485 administered to HIV-infected adults.
Secondary Objective(s):	1. To evaluate the efficacy of MVA85A/AERAS-485 in the prevention of TB disease compared to control subjects who receive placebo in HIV-infected, African adult subjects without active TB disease. 2. To evaluate CD4+ lymphocyte counts and HIV-1 viral load before and after administration of MVA85A/AERAS-485 compared to placebo. 3. To evaluate the efficacy of MVA85A/AERAS-485 in the prevention of TB disease in subjects receiving ART at baseline compared to subjects receiving ART at baseline but who receive placebo. 4. To evaluate the efficacy of MVA85A/AERAS-485 in the prevention of TB disease in subjects who received isoniazid preventive therapy compared to control subjects who also received isoniazid preventive therapy but who receive placebo. 5. To evaluate the immunogenicity of MVA85A/AERAS-485 compared to placebo as described by the ex vivo IFN-γ ELISPOT assay. 6. To evaluate the immunogenicity of MVA85A/AERAS-485 compared to placebo as described by flow cytometric

	intracellular cytokine staining of CD4+ and CD8+ T cells after stimulation with a peptide pool of mycobacterial antigens. 7. To identify potential immunological correlates of protection from tuberculosis in subjects vaccinated with MVA85A/AERAS-485. 8. To evaluate the QuantiFERON (QFN) conversion rate at final study assessment in MVA85A/AERAS-485 recipients compared to control subjects without a diagnosis of tuberculosis during the trial.
Clinical Trial/Study site(s):	• Centre Hospitalier Universitaire Le Dantec, Dakar (Senegal) • Khayelitsha site B and GF Jooste Hospital, Cape Town (South Africa)
Collaborating site(s):	• University of Oxford (UK) • LSHTM (UK) • University of Cape Town (South Africa) • Centre Hospitalier Universitaire Le Dantec, Dakar (Senegal) • Pasteur Institute, Brussels (Belgium)
Study design and population:	Phase IIb safety and efficacy trial; proof of concept double-blinded randomised placebo-controlled trial; ADULTS (≥18 years); Healthy, HIV-infected individuals N=650
Product(s):	• Candin (Allermed Labs, USA) - placebo • MVA85A (IDT GmbH / Oxford) / AERAS – 485 (Impfstoffwerk Dessau- • Tornau (IDT) Biologika GmBH, DE
Manufacturer/Developer:	• IDT • UoT OETC
Cofunders:	• DfID UK • Aeras • Scientific Institute of Public Health (SIPH) Belgium
Trial registration number(s):	NCT01151189
Status:	Ongoing
Results and Outcomes:	Recruitment completed in April 2013; last participant visit June 2014
PhD studies:	Title: Incidence and patterns of TB among HIV-infected participants of MVA85a/AERAS 485 phase II clinical trial in Senegal Candidate: Birahim Pierre Ndiaye (Cheikh Anta Diop University, Senegal) Dates: September 2010-2014
MSc studies:	Title: MSc at LSHTM by distance learning Candidate: Aderonke Odutola
	Title: Clinical epidemiology of HIV associated TB in Khayelitsha, South Africa Candidate: Tolullah Oni (Imperial College London, UK)
Postdoc study:	Candidate: Kerryn Matthews (UCT, South Africa)
Publications:	1. Oni T, Tsekela R, Kwaza B, Manjezi L, Bangani N, Wilkinson KA, Coetzee D, Wilkinson RJ. A Recent HIV Diagnosis Is Associated with Non-Completion of Isoniazid Preventive Therapy in an HIV-Infected Cohort in Cape Town. *PLoS One*. 2012;7(12):e5AE2489. doi: 10.1371/journal.pone.0052489. Epub 2012 Dec 20. 2. Pepper DJ, Marais S, Bhaijee F, Wilkinson RJ, De Azevedo V, et al. Assessment at Antiretroviral Clinics during TB Treatment Reduces Loss to Follow-Up among HIV-Infected Patients. (2012) *PLoS ONE* 7(6): e37634. doi:10.1371/journal.pone.0037634

	3. Vordermeier HM, Hewinson RG, Wilkinson RJ, Wilkinson KA, Gideon HP, et al. Conserved Immune Recognition Hierarchy of Mycobacterial PE/PPE Proteins during Infection in Natural Hosts. (2012) *PLoS ONE* 7(8): e40890. doi:10.1371/journal.pone.0040890

3.1.14 AERAS 402/Crucell Ad35

EDCTP Project Coordinator:	Mark Hatherill (University of Cape Town, South Africa)
EDCTP Call Title:	Call for support of clinical trials, capacity building and networking in tuberculosis vaccines development
EDCTP Project Title:	A Multicentre Phase II Trial of a New TB Vaccine in African Infants
EDCTP Project Code:	IP.2007.32080.003
EDCTP Project Start Date:	25 May 2009
EDCTP Project End Date:	30 March 2014
Collaborators:	• Benon Asiimwe, (Makerere University, Uganda) • Christian Burri (Swiss Tropical Institute, Switzerland) • Robert Colebunders (Prince Leopold Institute of Tropical Medicine (ITM), Belgium) • Vinod K. Diwan (Karolinska Institute, Sweden) • Katrina Downing (University of Cape Town, South Africa) • Bernard Erima (Makerere University, Uganda) • Willem Hanekom (University of Cape Town, South Africa) • Anja van 't Hoog (University of Amsterdam, Netherlands) • Gabriela Schreyer (ienna School of Clinical Research, Austria) • Moses Lutaakome Joloba (Ministry of Health, Uganda) • Gunilla Kallenius (Karolinska Institute, Sweden) • Asli Kulane (Karolinska Institute, Sweden) • Kayla Laserson (Centers for Disease Control and Prevention (CDC), USA) • Markus Maeurer (Karolinska Institute, Sweden) • Hassan Mahomed (University of Cape Town, South Africa) • Harriet Mayanja-Kizza (Makerere University, Uganda) • Jose Muñoz Gutierrez (Hospital Clinic of Barcelona, Spain) • Philippa Musoke (Makerere University, Uganda) • Videlis Nduba (Kenya Medical Research Institute (KEMRI), Kenya) • George Pariyo (Makerere University, Uganda) • Stefan Peterson (Karolinska Institute, Sweden) • Jahit Sacarlal (Manhiça Health Research Center, Mozambique) • Stefan Svenson (Swedish Institute for Infectious Disease Control (SMI), Sweden) • Suzanne Verver (KNCV Tuberculosis Foundation, Netherlands) • Eric Wobudeya (Makerere University, Uganda)
Study/Trial 1	
Site Principal Investigator(s):	• Mark Hatherill(Cape Town) • Jahit Sacarlal (Manhica) • Videlis Nduba (Kenya) In addition, Glenda Gray (NIH site - PHRU, Baragwanath, Johannesburg, South Africa), Mark Cotton (NIH site – KID-CRU, Stellenbosch, South Africa) and Sandy Pillay (NIH site – Durban) are NIH site Principal Investigators on this study.
Clinical Trial/Study Sponsor:	Aeras (USA)
Trial/Study title:	A phase II, double-blind, randomised, placebo-controlled, multicentre, proof-of-concept study to evaluate the safety and efficacy of AERAS-402 in BCG-vaccinated, HIV-uninfected infants without evidence of tuberculosis
Goal:	This is the first Phase II study of AERAS-402 in infants. The first

	dose of AERAS-402 will be administered to infants of at least 16 weeks of age who have already been vaccinated with BCG. A second dose will be administered 28 days after the first dose and, in the expanded safety phase of the study, a third dose will be administered 280 days after the first dose. The rationale for dose selection in the expanded safety phase will be based on safety experience and immunogenicity data from a prior Phase I infant trial and from the dose-finding phase in this study. In the dose-finding phase of this study, the immune responder rate, measured by ICS on Study Day 56 was 30-50% in recipients of the selected high dose. Additional assays using ELIspot and ELISA will be conducted on samples from recipients who received the high dose.
Primary Objective(s):	1. To evaluate the safety profile of AERAS-402 in infants 2. To evaluate the efficacy of AERAS-402 in the prevention of TB in infants based on TB case definition endpoint #1 as described in the protocol In Protocol version 7.0 the objectives were revised to remove those related to efficacy, immune correlates of protection and immunogenicity by whole blood ICS assay devlopeed by UCT. These changes were made based on the decision by the sponsor to modify the study to be a safety study, due to the low immunogenicity, by both ICS and ELISpot, of 2 doses of AERAS-402 seen in the previous study (C-018-402) and in subjects in this study (C-029-402) through Study Day 56. The second primary objective was therefore removed in version 7.0.
Secondary Objective(s):	1. To select a dosing regimen of AERAS-402 for testing in infants 2. To evaluate the immunogenicity of AERAS-402 compared to controls as described by flow cytometric intracellular cytokine staining (ICS) of CD4 and CD8 T cells producing one, two or three cytokines (IFN-γ, TNF-α, and/or IL-2) simultaneously after stimulation with a peptide pool of mycobacterial peptides 3. To evaluate the proportion of on-study IFN-γ release assay (IGRA) conversions, measured using QuantiFERON-TB Gold In-Tube test, in infants that received AERAS-402 compared to controls 4. To evaluate the efficacy of AERAS-402 in the prevention of TB in infants based on TB case definition endpoints #2 and #3 as specified in the protocol.
Clinical Trial/Study site(s):	• Kisumu, Siaya district (Kenya) • Manhiça (Mozambique) • Worcester (South Africa) • The NIH funded sites that are taking part in C-029-402 are Perinatal HIV Research Unit (PHRU, South Africa); Baragwanath, Johannesburg (South Africa); KID-CRU, Stellenbosch (South Africa); Sandy Pillay (NIH site in Durban, South Africa)
Collaborating site(s):	• ITM (Belgium) • Swiss Tropical and Public Health Institute (STI, Switzerland) • Swiss Agency for Development and Cooperation (SDC, Switzerland) • Karolinska Institutet (Sweden) • KNCV Tuberculosis Foundation (Netherlands) • University of Cape Town (South Africa) • KEMRI (Kenya) • CRESIB (Mozambique)

	• Infectious Diseases Institute (IDI) Makarere University, Kampala (Uganda) • Mulago Hospital, Kampala (Uganda)
Study design and population:	Phase II proof-of-concept multi-centre double-blinded randomised placebo-controlled trial; INFANTS (16-26 weeks); BCG vaccinated, HIV- infants with no evidence of TB N=487
Product(s):	AERAS-402/Crucell Ad35
Manufacturer/Developer:	• Crucell B.V. • Aeras
Cofunders:	• Instituto de Salud Carlos III, Madrid (Spain) • Aeras (USA) • Vienna School of Clinical Research (VSCR, Austria) • SDC (Switzerland)
Trial registration number(s):	NCT 01198366 PACTR201203000306280
Status:	Ongoing/Amended
Results and Outcomes:	A total of 487 infants were enrolled into the Aeras C-402-029 study, 285 (58%) at the KEMRI/CDC (Kenya), 166 (34%) at SATVI (South Africa) and 14 (3%) at CISM (Mozambique) sites. An additional 22 infants were enrolled at an NIH sponsored site. Group 5 enrolment at KEMRI/CDC, SATVI as well as one other NIH site began in January 2012 and continued through April 2012. 281 subjects were enrolled in the safety cohort, at KEMRI (141=50%), at SATVI (118 = 42%) and 1 NIH Site (22 – 7%). The last subject completed the Day 56 follow-up visit on June 28, 2012. The Data Monitoring Committee (DMC) for the C-402-029 study met on 12 October 2012 to review the available C-029-402 data. The DMC noted no patterns of safety concern and no safety signals were identified. The DMC advised that the C-029-402 study could proceed to dose 3 injections of Group 5 as per Protocol version 6.0. Administration of the 3rd dose in Group 5 commenced in the last quarter of 2012. Following per protocol review of immunogenicity data from Groups 1-4, it was recommended that the study should convert to a safety and immunogenicity trial only. Accordingly, amended protocol V7.0 reduced the period of efficacy follow-up. Infants in Group 4 and Group 5 at the SATVI site are receiving end of study letters and having final study visits during July 2013. Database lock is expected in Q3 2013.
PhD studies:	Title: Phenotypic analysis of MTB antigen specific T-cells and the evaluation of new point of care TB diagnostic tests Candidate: Helen Buteme (KI, Sweden) Supervisors: Gunilla Kanellius, Moses Joloba, Markus Maeurer
	PhD in Epidemiology Candidate: Steve Wandiga (KEMRI/CDC, Kenya) Supervisor: Prof. Christian Heumann
Post Doctoral studies:	-In-vitro cytokine response to Mycobacterium tuberculosis Uganda genotype strain in human monocyte derived macrophages -Characterization of isolates from the Iganga-Mayuge district. Candidate: Benon Asiime
	Topic: Identification of immune correlates of risk of childhood TB disease, following BCG vaccination Candidate: Brian Abel
	Topic: Identification of immune correlates of risk of childhood TB

	disease, following BCG vaccination (cont. of Dr Brian Abel's work) Candidate: Adam Penn-Nicholson
MSc studies:	Title: Integration of HIV services in TB treatment in Uganda Candidate: Faith Keneko (deceased)
	Title: Prevalence and factors associated with hepatotoxicity in HIV infected patients on anti-tuberculosis therapy in Mulago Hospital Candidate: Mark Okwir
	Title: Diagnostic accuracy of the Genexpert system among children with possible/probable tuberculosis at Mulago Hospital Candidate: Moorine Sekadde
	Title: MSc in Clinical Trials via distant learning at the LSHTM Candidate: Grace Kiringa
	Title: MSc in Laboratory Science/Microbiology at the Kenya Medical Research Institute, KEMRI/CDC programme Candidate: Benson Muchiri (discontinued)
	Title: MSc in Clinical Trials part time (LSHTM) Candidate: Paul Mwaka
	Title: MSc Clinical Trials part time (LSHTM) Candidate: Samuel Gurrion Ouma
	Title: MA Project Planning & Management Candidate: Hyrine Matheka
Other/Sub-studies:	ITHACA study
Study/Trial 2	
Site Principal Investigator(s):	• Jahit Sacarlal • Kizito Gondo • Jose Muňoz
Trial/Study title:	Determination of the minimum incidence rate of tuberculosis in infants and children in Manhiça District, Mozambique
Goal:	This is a prospective study aiming to assess the incidence of TB among children under 3 years in the DSS population during a period of one year
Primary Objective(s):	To estimate the annual minimum incidence rate of TB disease in children under 3 years in the Manhiça area
Secondary Objective(s):	1. To describe the clinical characterisation and outcome of tuberculosis in children under 3 years 2. To describe the timing and coverage of BCG vaccination (including scarring patterns) in TB suspects under 3 years 3. To compare the bacteriologic yield of fluorescence microscopy compared to culture in gastric aspirates and induced sputa samples of TB suspects under 3 years 4. To assess the rate of co-infection with HIV in TB suspects and TB cases under 3 years 5. To assess the rate of co-infection with helminths in TB suspects and TB cases under 3 years.
Clinical Trial/Study site(s):	Manhiça District (Mozambique)
Status:	Ongoing
Results and Outcomes:	Recruitment ended on the 17 October 2012 with a total of 823 TB suspects and 103 TB contacts admitted to the study. All patients have been followed up for a 7 month period (until May 2013). Data analysis and manuscript writing to proceed in Q3 2013/Q12014. An ancillary study named "Prevalence of Nontuberculous Mycobacteria in TB suspects under the age of three" is taking place at the site.
Publications:	1. Fletcher HA, Keyser A, Bowmaker M, Sayles PC, Kaplan G, Hussey G, Hill AV, Hanekom WA. Transcriptional profiling of mycobacterial antigen-induced responses in infants vaccinated with BCG at birth. *BMC Med Genomics*. 2009

Feb 24; 2:10. doi: 10.1186/1755-8794-2-10
2. Hawkridge T, Mahomed H. Prospects for a new, safer and more effective TB vaccine. *Paediatr Respir Rev*. 2011 Mar;12(1):46-51. doi: 10.1016/j.prrv.2010.09.013. Epub 2010 Oct 14. Review
3. Kagina BM, Abel B, Scriba TJ, Hughes EJ, Keyser A, Soares A, Gamieldien H, Sidibana M, Hatherill M, Gelderbloem S, Mahomed H, Hawkridge A, Hussey G, Kaplan G, Hanekom WA; other members of the South African Tuberculosis Vaccine Initiative. Specific T cell frequency and cytokine expression profile do not correlate with protection against tuberculosis after bacillus Calmette-Guérin vaccination of newborns. *Am J Respir Crit Care Med*. 2010 Oct 15;182(8):1073-9. doi: 10.1164/rccm.201003-0334OC. Epub 2010 Jun 17.
4. Mahomed H, Fourie PB. Clinical trials of TB vaccines: harmonization and cooperation. *Tuberculosis* (Edinb). 2012 Mar;92 Suppl 1:S21-4. doi: 10.1016/S1472-9792(12)70008-2.
5. Sekadde MP, Wobudeya E, Joloba ML, Ssengooba W, Kisembo H, Bakeera-Kitaka S, Musoke P: Evaluation of the Xpert MTB/RIF test for the diagnosis of childhood pulmonary tuberculosis in Uganda: a cross-sectional diagnostic study. *BMC Infect Dis*, 13:133. doi:10.1186/1471-2334-13-133
6. Asiimwe BB, Bagyenzi GB, Ssengooba W, Mumbowa F, Mboowa G, Wajja A, Mayanja-Kiiza H, Musoke PM, Wobudeya E, Kallenius G *et al*: Species and genotypic diversity of non-tuberculous mycobacteria isolated from children investigated for pulmonary tuberculosis in rural Uganda. *BMC Infect Dis*, 13:88. doi:10.1186/1471-2334-13-88

3.1.15 Aurum 102/THYB-05

EDCTP Project Coordinator:	Gavin Churchyard (Aurum Institute for Health Research, South Africa)
EDCTP Call Title:	Call for support of clinical trials, capacity building and networking in tuberculosis vaccines development
EDCTP Project Title:	Phase II Double-Blind, Randomized, Placebo-Controlled Study to Evaluate the Safety and Immunogenicity of H1, an adjuvanted TB subunit vaccine in HIV-infected, BCG-vaccinated Adults With CD4+ Lymphocyte Counts Greater Than 350 Cells/mm3
EDCTP Project Code:	IP.2009.32080.002
EDCTP Project Start Date:	30 September 2010
EDCTP Project End Date:	29 March 2013
Collaborators:	• Bang, Peter (Statens Serum Institut, (SSI), Denmark) • Borgdorff, Martinus Willem (KNCV Tuberculosis Foundation, Netherlands) • Burri, Christian (Swiss Tropical Institute, Switzerland) • Charalambous, Salome (Aurum Institute for Health Research, South Africa) • Daubenberger, Claudia (Swiss Tropical Institute, Swtizerland) • Hawkridge*, Toni (Aeras, USA) • Kromann, Ingrid (SSI, Denmark) • Kufa, Tendesayi (Aeras, USA) • Lwilla, Fred Israel (Ifakara Health Research and Development Centre, Tanzania) • Mashamaite, Sello (Aurum Institute for Health Research, South Africa) • Reither, Klaus (Ifakara Health Research and Development Centre, Tanzania) • Verver, Suzanne (KNCV Tuberculosis Foundation, Netherlands)
Study/Trial 1	
Site Principal Investigator(s):	• Klaus Reither (BRTC/IHI, Tanzania) • Nicolene Gardiner (Aurum, Denmark)
Clinical Trial/Study Sponsor:	Statens Serum Institute (SSI, Denmark)
Trial/Study title:	Phase II double-blind, randomised, placebo-controlled study to evaluate the safety and immunogenicity of H1, an adjuvanted TB subunit vaccine (Ag85B-ESAT-6 + IC31), in HIV-infected, BCG-vaccinated adults with CD4+ lymphocyte counts greater than 350 Cells/mm^3
Goal:	To test the hypothesis that the vaccine is safe and immunogenic at a dose and in a human population resembling that in which the final product will be used.
Primary Objective(s):	1. To evaluate the safety of H1/IC31®, an adjuvanted TB subunit vaccine administered to HIV-infected adult subjects with no evidence of active TB disease. 2. To determine the immunogenicity of H1/IC31® in HIV-infected adult subjects with no evidence of TB disease.
Secondary Objective(s):	1. To assess cellular immunity induced by H1 in HIV-infected, BCG-vaccinated adult subjects. 2. Exploratory Objective: To evaluate innate and adaptive immune response to H1/IC31® in HIV-infected adults using transcriptomics, multi-colour flow cytometry, multi-plex luminex assays and quantitative real time PCR.
Clinical Trial/Study site(s):	• Ifakara Health Institute/Bagamoyo Research Centre, Bagamoyo Tanzania)

	• The Aurum Institute (Johannesburg, South Africa
Collaborating site(s):	• The Aurum Institute (South Africa) • Aeras Global TB Vaccine Foundation (South Africa) • KNCV Tuberculosis Foundation (The Netherlands) • Swiss Tropical Institute (Switzerland) • Ifkara Health Institute (Tanzania) • Statens Serum Institut (Denmark) • University of Amsterdam-Academic Medical Centre (The Netherlands)
Study design and population:	Phase II double-blinded randomised placebo-controlled trial; ADULTS (≥18 years); HIV-infected, BCG-vaccinated individuals with CD4+ counts >350 Cells/mm3 N=48 (24 at each site)
Product(s):	Ag85B-ESAT-6 [50 Pg](H1) + adjuvant [500 nmol KLK and 20 nmol ODN1a] (IC31) Control: Tris buffer (FL), (10mM Tris + 169mM NaCl, pH 7.4)
Manufacturer/Developer:	SSI (Denmark)
Cofunders:	• Swiss Tropical and Public Health Institute, Switzerland • SIDA, Sweden • Swiss National Science Foundation (SNSF), Switzerland
Trial registration number(s):	PACTR201105000289276 DOH-27-0611-3538
PhD studies:	PhD Immunology Title: Flow cytometry based immunomonitoring in TB and malaria vaccine trials Candidate: Maxmillian Mpina (AMC UvA, Netherlands) Dates: January 2011-December 2013
	PhD Epidemiology Title: Incidence of tuberculosis among HIV-infected persons with CD4 Counts greater than 350 cells/µl attending primary care clinics in Ekurhuleni North Sub-District in South Africa Candidate: Tendesayi Kufa (UvA, Netherlands) Dates: September 2011-September 2014
	PhD Epidemiology Title: Impact of HIV, malaria and Helminths co-infections on innate and adaptive immune responses in East African volunteers Candidate:Nicole Lenz (Swiss TPH, Switzerland) Dates: January 2011-December 2013
MSc studies:	MSc Epidemiology (protocol development) Title: Estimating TB incidence among HIV-infected antiretroviral therapy naïve persons with early HIV disease in Tanzania Candidate: Khadija Said (IHI) [Swiss TPH, Switzerland]) Dates: March 2013-June 2014
	MSc Immunogology Title: Cellular immunogenicity of H1/IC31® tuberculosis vaccine in HIV infected adults Candidate: Teson Lukindo (IHI) [Nelson Mandela African Institute of Science and Technology Arusha Tanzania] Dates: November 2011-November 2013
	Title: Targeted transcriptome analysis for characterisation of H1/IC31 induced adaptive immune response in HIV infected adults Candidate: Tobias Schindler (Swiss TPH, Switzerland) Dates: April 2013-March 2014
Sub-studies:	**Bagamoyo** Retrospective cohort study of TB incidence regardless of prior IPT use based on review of medical records combined with a

	prospective assessment of the TB status Approximately 1400 participants will be enrolled (on paper) over 1 year (in 2008) to meet the sample size requirements and will be once followed-up during the observation period of one year. Objectives: • To describe among HIV-infected adults with a CD4 count>350 cells/mm^3 living in Bagamoyo district – The incidence of TB overall and restricted to 18 to 45 year olds – The risk factors associated with TB, such as age, sex, CD4 category, history of TB, IPT use Status: Ongoing. Delay as product label had to be redone to conform to enrolment numbers. **Johannesburg** A prospective study of TB incidence among HIV infected participants with CD4 counts >350 cells/Pl. To be eligible participants have to be 18 years or older, had a CD4 count>350 cell/pl within one year preceding enrolment and living within the catchment area of the facilities from which enrolment is taking place. Objectives: • To describe among HIV-infected adults with a CD4 count greater than 350 cells/mm^3 living in the Ekurhuleni districts of Johannesburg – The incidence of TB overall and restricted to 18 to 45 year olds – Assess prevalence of TB among this group to determine what proportion would be excluded from a trial – The risk factors associated with TB incidence, such as age, sex, CD4 category, history of TB, IPT use, district, facility, history of diabetes and occupation. Status: Pending protocol approval. GSK to fund GeneXpert tests)
Status:	Completed
Results and Outcomes:	**Primary Objective** The trial enrolled 48 participants and 47 of them completed both vaccinations. In the 48 enrolled participants, 441 AEs were reported. 55 Study defined local AEs (pain, tenderness, erythema, induration or nodules), 84 study defined systemic AEs (malaise, myalgia, headache, nausea, vomiting, arthralgia, fatigue, chills and fever) and 303 non-study defined AEs were reported. The frequency of IFN-γ, TNF-A and IL-2 producing CD4+ cells when stimulated with Ag85B, ESAT-6, H1 or BCG were similar between arms at baseline and were greater in the H1/IC31® vaccine versus placebo arm when stimulated with Ag85B, H1 ESAT-6, H1 or BCG. Similarly IL-17 producing CD4+ cells when stimulated with Ag85b, ESAT-6, H1 or BCG were similar between arms at baseline and were greater in the H1/IC31® vaccine versus placebo arm when stimulated with Ag85B only. At visit 9(day 70) there was no evidence of a difference in frequencies of IFN-γ, TNF-A-a, IL-2 and IL-17+ producing CD8+ T-cells between study arms for any of the antigens.

	Through intracellular cytokine staining performed on whole blood, the H1/IC31 vaccine was associated with a durable response in vaccine recipients at visit 10 (day 182) compared to visit 9 (day 70). CD4+ and CD8+ T-cell expression (frequency and MFI) of Ki67 was similar by study arm. At visit 9(day 70) there was no evidence of a difference in cell expression (frequency and MFI) of Ki67. The vaccine was well tolerated and safe in HIV-infected adults with CD4+ counts greater than 350cells/mm3. In terms of immunogenicity the vaccine, EliSPOT results were excluded for analysis and ELISA assays were not performed due to high background IFN-γ in negative controls. Possible reasons for the high background rate include that HIV-infected participants are known to have higher background stimulation rates than HIV-uninfected persons and secondly the specimens may have been contaminated when shipped from Bagamoyo to SATVI, South Africa. However, differences in IFN-γ production were assessed through intracellular cytokine staining performed on stimulated whole blood and H1/IC31 was associated with durable response with similar responses in vaccine recipients at visit 10 (study day 182) compared to visit 9 (study day 70). **Secondary objective:** Effect of the H1/IC31® TB vaccine in HIV-infected adults on: • CD4+ lymphocyte counts; No significant effect on CD4+ counts. • HIV viral loads; No significant effect on HIV Viral loads. Results from the **exploratory objective** are still pending
Publications:	1. Kufa T, Chihota V, Charalambous S, Verver S, Churchyard GJ. Willingness to participate in trials and to be vaccinated with new tuberculosis vaccines. Public Health Action 2013,3(1): 31–37. 2. Rustomjee R, McClain B, Brennan MJ, McLeod R, Chetty-Makkan CM, McShane H, et al. 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) 2013 Mar;93(2):136-42. 3. Rustomjee R, McLeod R, Hanekom W, Steel G, Mahomed H, Hawkridge A, et al. Key issues in the clinical development and implementation of TB vaccines in South Africa. Tuberculosis (Edinb) 2012 Sep;92(5):359-64.

3.1.16 TB NEAT

EDCTP Project Coordinator:	Keertan Dheda (University of Cape Town, South Africa)
EDCTP Call Title:	Call for applications to support clinical trials, capacity building and networking in new and improved diagnostics for tuberculosis (TB)
EDCTP Project Title:	Evaluation of multiple novel and emerging technologies for TB diagnosis, in smear-negative and HIV-infected persons, in high burden countries (the TB-NEAT study)
EDCTP Project Code:	IP.2009.32040.009
EDCTP Project Start Date:	17 May 2010
EDCTP Project End Date:	30 November 2014
Collaborators:	• Mark Nicol (National Laboratory Service and UCT, South Africa) • Peter Mwaba (University Teaching Hospital, Zambia) • Lynn Zijenah (University of Zimbabwe, Zimbabwe) • Peter Mason (Biomedical Research and Training Institute, Zimbabwe) • Andrea Rachow (NIMR-MMRP, Tanzania) • Alexander Pym (KwaZulu-Natal Research Institute for Tuberculosis and HIV (K-RITH), South Africa) • Alimuddin Zumla (University College London (UCL), UK) • Bram van Ginneken (Radboud University, Netherlands) • Michael Hoelscher (Klinikum der Universität München, Germany) • Markus Maeurer (MTC, Karolinska Institute, Sweden) • Catharina Boehme (Foundation for Innovative Diagnostics (FIND), Switzerland)
Study/Trial 1	**Point-of-treatment GeneXpert MTB/RIF Assay**
Site Principal Investigator(s):	• Keertan Dheda (South Africa) • Mark Patrick Nicol (South Africa) • Alexander Pym (South Africa) • Peter Mwaba (Zambia) • Lynn Sodai Zijenah (Zimbabwe) • Andrea Rachow (Tanzania)
Clinical Trial/Study Sponsor:	Institute of Infectious Disease and Molecular Medicine, University of Cape Town (South Africa)
Trial/study title	A randomised controlled trial of point-of-treatment GeneXpert MTB/RIF Assay for the diagnosis of TB at primary care clinics in high HIV prevalence resource limited settings.
Goal	To evaluate whether one sputum GeneXpert MTB/RIF assay performed at point-of-treatment will improve TB diagnosis and the time-to-treatment for HIV-infected and un-infected patients with TB presenting to primary level TB clinics in high HIV prevalent settings.
Primary Objective(s):	1. To determine the differences in time-to-treatment initiation between the point-of-treatment Xpert® MTB/RIF Assay and microscopy-centre based same day smear microscopy 2. To compare the performance outcomes of one point-of-treatment sputum GeneXpert® MTB/RIF Assay compared to two same-day standard fluorescence smear microscopy for TB diagnosis in primary level clinics 3. To determine the incremental diagnostic yield of a single point-of-treatment Xpert® MTB/RIF Assay over two sputum fluorescence smears using MGIT Liquid culture as the reference standard 4. To examine the feasibility of the point-of-treatment GeneXpert® MTB/RIF Assay performed by non-technical

	research personnel 5. To evaluate the cost-effectiveness of using a single point-of-treatment GeneXpert® MTB/RIF Assay for primary clinic-based TB diagnosis.
Clinical Trial/Study site(s)	• University of Cape Town (South Africa) • National Health Laboratory Service and University of Cape Town (South Africa) • Medical Research Council (South Africa) • University Teaching Hospital (Zambia) • NIMR-Mbeya Medical Research Programme (MMRP) (Tanzania • University of Zimbabwe College of Health Sciences, Harare, Zimbabwe
Collaborating site(s)	• University College London (UK) • Radboud University (Netherlands) • Klinikum der Universität München (Germany) • MTC, Karolinska Institute (Sweden)
Study design	The study will be a multicentre patient-level randomised controlled trial comparing a single sputum GeneXpert MTB/RIF Assay performed at point-of-treatment with same-day standard fluorescent smear microscopy for TB diagnosis at the primary level of care. Liquid MGIT culture will be used as the "classic" TB reference standard.
Study population and number of expected recruits	ADULT 18 and over, 300 patients per site
Investigational product(s)/Manufacturer/ Developer: (if applicable)	Xpert MTB/Rif assay (Cepheid, Sunnyvale, California USA)
Cofunders	• Foundation for Innovative New Diagnostics (FIND, Switzerland) • Swedish International Development Cooperation Agency (SIDA, Sweden) • German Ministry for Education and Research (BMBF, Germany) • Computer-Aided Detection of Tuberculosis (CAD4TB, Netherlands); • Evaluation of transrenal-DNA detection to diagnose tuberculosis (TB trDNA) - a FP6-funded project from the University College London (UCL, UK) • MRC (UK) • Active Diagnosis of Active TB [ADAT, EU-funded consortium between Zambia, Tanzania, UCL and Ludwig Maximilian University of München (LMU, Germany) • Netherlands-African partnership for capacity development and clinical interventions against poverty-related diseases (NACCAP, Netherlands)
Trial Registration Number	NCT01554384
Status:	Completed
Results and Outcomes:	
Study/Trial 2	**Determine TB® Point-of-care urine LAM prospective cohort**
Site Principal Investigator(s):	• Keertan Dheda (South Africa) • Jonny Peter (South Africa) • Grant Theron (South Africa) • Peter Mwaba (Zambia) • Lynn Sodai Zijenah (Zimbabwe) • Andrea Rachow (Tanzania) • Peter Mwaba (Zambia) • Duncan Chandra (Zambia)

	• Lynn Zijenah (Zimbabwe) • Michael Hoelscher (NIMR-MMRP) • Andrea Rachow (NIMR-MMRP)
Clinical Trial/Study Sponsor:	Institute of Infectious Disease and Molecular Medicine, University of Cape Town (South Africa)
Trial/Study title:	A randomized control trial of the point-of-care urine LAM lateral flow strip test – Determine TB® - for HIV co-infected patients at primary care TB clinics
Goal:	To assess the LAM lateral flow strip test when combined with smear microscopy (LAM or smear positive) will significantly improve the rapid diagnosis of TB and the proportion of patients starting TB treatment with 24 hours compared to smear microscopy alone in HIV-infected patients.
Primary Objective(s):	1. To compare the performance outcomes of the Determine TB® urine LAM lateral flow test in combination with same-day sputum smear microscopy (so treatment based on LAM or smear in that order) versus same-day sputum smear microscopy alone, for TB diagnosis in HIV-infected patients in primary care TB clinics 2. To determine the time-specific proportion of patients on TB treatment and differences in time-to-treatment initiation between the Determine TB® urine LAM lateral flow test/ same-day sputum microscopy versus same-day sputum microscopy alone for TB diagnosis in HIV-infected patients. 3. To evaluate the cost-effectiveness of each strategy for TB diagnosis in HIV-infected patients at primary TB clinics.
Clinical Trial/study site(s)	• University of Cape Town (South Africa) • South African MRC (South Africa) • University Teaching Hospital (Zambia) • University of Zimbabwe College of Health Sciences (Zimbabwe) • NIMR-MMRP (Tanzania)
Collaborating site(s):	• University College London (UK) • Radboud University (Netherlands) • Klinikum der Universität München (Germany) • MTC, Karolinska Institute (Sweden)
Study design:	The study involves two phases. The 1st phase will be a prospective cohort study to evaluate the Determine TB urine LAM lateral flow test specificity. The 2nd phase will be a multicentre patient-level randomised controlled trial comparing a point-of-care Determine TB® urine LAM lateral flow strip test together with same-day standard fluorescent smear microscopy for TB diagnosis in HIV-infected patients at primary care level. Liquid MGIT culture will be used as the TB reference standard.
Study population and number of expected recruits:	Adult (18 and older) HIV-positive patients with suspected TB, 500 recruits per site
Product(s):	Urine LAM lateral flow strip test (Determine TB®) Xpert® MTB/RIF Assay
Manufacturer/Developer:	Inverness Medical Professional Diagnostics Cepheid, Sunnyvale, California USA
Cofunders:	• Foundation for Innovative New Diagnostics (FIND; Switzerland) • Swedish International Development Cooperation Agency (SIDA) • Sweden) • German Ministry for Education and Research (BMBF; Germany) • Computer-Aided Detection of Tuberculosis (CAD4TB;

	Netherlands) • Evaluation of transrenal-DNA detection to diagnose tuberculosis (TB trDNA) - a FP6-funded project from the University College London (UCL) UK) • Medical Research Council (MRC) UK • Active Diagnosis of Active TB [ADAT, EU-funded consortium between Zambia, Tanzania, UCL and Ludwig Maximilian University of Munich (LMU; Germany); • Netherlands-African partnership for capacity development and clinical interventions against poverty-related diseases (NACCAP; Netherlands)
Status:	Complete
Results and Outcomes:	This study was a go/no go decision based on the performance of the LAM strip for TB detection when using urine collected from the Xpert RCT. The strip test showed good performance on approximately 600 urines and, based on this, the group have decided to proceed with phase 2, which involves patient recruitment.
Study/Trial 3	**Determine TB® Point-of-care urine LAM RCT**
Site Principal Investigator(s):	• Keertan Dheda (South Africa) • Jonny Peter (South Africa) • Grant Theron (South Africa) • Peter Mwaba (Zambia) • Lynn Sodai Zijenah (Zimbabwe) • Andrea Rachow (Tanzania) • Peter Mwaba (Zambia) • Duncan Chandra (Zambia) • Lynn Zijenah (Zimbabwe) • Michael Hoelscher (NIMR-MMRP) • Andrea Rachow (NIMR-MMRP)
Clinical Trial/Study Sponsor:	Institute of Infectious Disease and Molecular Medicine, University of Cape Town (South Africa)
Trial/Study title:	A randomised controlled trial to evaluate the impact of using a point of-care urine LAM strip test for TB diagnosis amongst hosptialized HIV-infected patients in resource-poor settings
Goal:	The purpose of this study will be to determine the impact of the urine LAM strip test on mortality in hospitalized HIV-infected patients with suspected TB when LAM is used as a POC test to guide rapid treatment initiation
Primary Objective(s):	To examine whether the urine LAM strip test, when combined with standard TB diagnostics (smear microscopy and culture), will significantly improve TB treatment-related outcomes (TB-related mortality, morbidity and length of hospital stay) in HIV-infected hospitalized patients when compared to standard TB diagnostics alone.
Clinical Trial/study site(s)	• University of Cape Town (South Africa) • University Teaching Hospital (Zambia) • University of Zimbabwe College of Health Sciences (Zimbabwe) • NIMR-MMRP (Tanzania)
Collaborating site(s):	• University College London, London, UK; • Radboud University, Nijmegen Medical Center, Nijmegen, Netherlands • Klinikum der Universität München, Department of Infectious Diseases & Tropical Medicine, Munich, Germany • MTC, Karolinska Institute, Stockholm, Sweden
Study design:	Randomised controlled trial (RCT)
Study population and number of expected	Adult (18 and older) HIV-positive patients with suspected TB, 300 recruits per site

recruits:	
Product(s):	Urine LAM lateral flow strip test (Determine TB®) Xpert® MTB/RIF Assay
Manufacturer/Developer:	Inverness Medical Professional Diagnostics Cepheid, Sunnyvale, California USA
Cofunders:	• Foundation for Innovative New Diagnostics (FIND, Switzerland) • Swedish International Development Cooperation Agency (SIDA, Sweden) • German Ministry for Education and Research (BMBF, Germany) • Computer-Aided Detection of Tuberculosis (CAD4TB, Netherlands) • Evaluation of transrenal-DNA detection to diagnose tuberculosis (TB trDNA) - a FP6-funded project from the University College London (UCL, UK) • Medical Research Council (MRC, UK • Active Diagnosis of Active TB [ADAT, EU-funded consortium between Zambia, Tanzania, UCL and Ludwig Maximilian University of Munich (LMU, Germany); • Netherlands-African partnership for capacity development and clinical interventions against poverty-related diseases (NACCAP, Netherlands)
Trial Registration Number	NCT01770730
Status:	Ongoing
Results and Outcomes:	
Study/Trial 4	**Paediatrics study**
Site Principal Investigator(s):	• Heather Zar (South Africa) • Mark Nicol (South Africa)
Clinical Trial/Study Sponsor:	Institute of Infectious Disease and Molecular Medicine, University of Cape Town (South Africa)
Trial/Study title:	Diagnosis of Tuberculosis in HIV-infected children – development of microbiological and immunological strategies
Goal:	To evaluate the utility of new TB diagnostics in children
Primary Objective(s):	Aim 1: Microbiological approach 1. To improve the rapid diagnosis (within 1 day) of TB disease in HIV-infected children by investigating the sensitivity and specificity of the following diagnostic techniques (using culture-proven TB as the gold-standard): – Loop-mediated isothermal amplification (LAMP, Eiken/FIND, Geneva, Switzerland) of respiratory and non-respiratory samples – A novel fully automated real-time PCR-based test (Xpert™ MTB, Cepheid/FIND) for the detection of MTB DNA and associated rifampicin resistance – Antigen capture ELISA for detection of mycobacterial lipoarabinomannan (LAM, FIND) in urine 2. To improve the yield and speed of microscopy and culture-based diagnosis of TB disease in HIV-infected children – To determine the optimum specimen collection protocol by comparing the yield from repeated induced sputum and nasopharyngeal aspirates (NPA) – To determine whether microscopic observation drug susceptibility (MODS) assay provides more rapid culture and drug-susceptibility results than conventional (mycobacterial growth indicator [MGIT]) culture. Aim 2: Immunological approach

	1. To determine the incremental value of the addition of MTB-specific enzyme linked immunospot (ELISpot) assay (T-SPOT.TB, Oxford Immunotec, Oxford, U.K.) to clinical diagnostic algorithms for the diagnosis of TB disease in HIV-infected children. Children with culture confirmed TB and a control group in whom TB has been excluded will represent gold standard positive and negative. The effect of age and degree of immune depletion on ELISpot responses and TST will also be investigated 2. To determine whether ELISpot (T-SPOT.TB) using cells from a site-specific clinical specimen (e.g. pleural or cerebrospinal fluid) confers increased sensitivity over ELISpot using peripheral blood for the diagnosis of extrapulmonary TB in HIV-infected children.
Clinical Trial/study site(s)	• Red Cross War Memorial Children's Hospital (RCH), Cape Town (South Africa) • New Somerset Hospital (NSH), Cape Town (South Africa) • Nolungile Clinic, Site C, Khayelitsha (South Africa)
Collaborating site(s):	• Childrens Hospital of Melbourne (Australia) • McGill University (Canada)
Study design:	Prospective study of the diagnostic value of novel tests for TB in HIV-infected children with suspected pulmonary or extrapulmonary TB presenting to pediatric hospitals in Cape Town, South Africa, a high HIV and high TB prevalence area.
Study population and number of expected recruits:	Children (up to 15 years old), clinically suspected of having pulmonary TB or extrapulmonary TB (TB meningitis or pleural TB or pericardial TB or abdominal TB RCH and NSH: 500 HIV-infected children compared to 200 HIV-uninfected children with suspected TB. Khayelitsha (site C): 400 children with suspected TB
Product(s):	Xpert MTB/Rif assay
Manufacturer/Developer:	Cepheid, Sunnyvale, California USA
Cofunders:	• Foundation for Innovative New Diagnostics (FIND, Switzerland) • Swedish International Development Cooperation Agency (SIDA, Sweden) • German Ministry for Education and Research (BMBF, Germany) • Computer-Aided Detection of Tuberculosis (CAD4TB, Netherlands) • Evaluation of transrenal-DNA detection to diagnose tuberculosis (TB trDNA) - a FP6-funded project from the University College London (UCL, UK) • Medical Research Council (MRC, UK • Active Diagnosis of Active TB [ADAT, EU-funded consortium between Zambia, Tanzania, UCL and Ludwig Maximilian University of Munich (LMU, Germany) • Netherlands-African partnership for capacity development and clinical interventions against poverty-related diseases (NACCAP, Netherlands)
Status:	Ongoing
Results and Outcomes:	
PhD studies:	Title: Predictive value of quantitative T cell responses for progression to active TB in HIV co-infected individuals Candidate: Duncan Chandra (University Teaching Hospital Lusaka, Zambia) Dates: February 2012-December 2015
	Title: Population specific risks for TB infection and the variable performance characteristics of novel diagnostic technologies

	Candidate: Richard Nellis Van Zyl-Smit (UCT, South Africa) Dates: January 2010-December 2011
	Title: An evaluation of immunodiagnostic tests for tuberculosis infection and determinants of TB infection in a population of healthcare workers in the Western Cape, University of Cape Town, South Africa Candidate: Shahieda Adams (UCT, South Africa) Dates: January 2010-January 2014
	Title: Sputum induction, and novel emerging technologies to improve TB diagnosis, in a high HIV prevalence primary care setting (SINET study) Candidate: Jonny Peter (UCT, South Africa) Dates: January 2010-January 2014
	Development and Evaluation of Point-Of-Care Diagnostics for Tuberculosis Candidate: Veronica Allen (UCT, South Africa) Dates: June 2009-August 2012
	Title: Improvement and development of microbiological TB detection methods in resource constrained settings Candidate: Gabriel Rojas-Ponce (NIMR-MMRP) Dates: September 2010-August 2013
	Title: Automatic detection of tuberculosis in radiographs using active learning Candidate: Laurens Hogeweg (Radboud University, Netherlands) Dates: November 2008-August 2013
	Title: Automatic detection of tuberculosis in radiographs Candidate: Pragnya Maduskar (Radboud University, Netherlands) Dates: November 2010-November 2014
MSc studies:	Title: Evaluation and validation of TB-BEAD Diagnostic assay in both smear positive and negative TB Suspects Candidate: Jennifer Allen (MRC Durban, South Africa) Dates: January 2010-Decmeber 2012
	Title: Performance outcomes of LED technology (Lumin) for microscopic detection of mycobacteria in a high HIV seroprevalence setting in Africa Candidate: Cuthbert Musarurwa (University of Zimbabwe College of Health Sciences) Dates:
Postdoc studies:	Grant Theron (UCT, South Africa)
	Brandie Young-Gqama (UCT, South Africa)
	Justin O'Grady (UCL, South Africa)
	Samana Schwank (UCL, South Africa)
	Widaad Zemanay (UCT, South Africa)
Other/Sub-studies:	Proteomics study "A mass spectral proteomic analysis of human urine samples for the discovery and qualification of new tuberculosis diagnostic biomarkers – a TB-NEAT substudy" IGRA HCW study "Scientific protocol for a study to evaluate immunodiagnostic tests for Tuberculosis infection and determinants of TB infection in a population of health care workers in the Western Cape of South Africa" Sputum Induction study "Utility of sputum induction, and new and emerging technologies to improve the diagnostic yield, in a high HIV prevalence primary care setting (SINET study)"

	Xpert negative study "Specificity of GeneXpert MTB/RIF® in culture-negative TB suspects"
Publications:	1. Theron, G, Peter, J, van Zyl-Smit, R, Mishra, H, Streicher, E, Murray, S, Dawson, R, Whitelaw, A, Holescher, M, Sharma, S, Pai, M, Warren, R, Dheda, K. (2011) Evaluation of the XpertMTB/RIF Assay for theDiagnosis of Pulmonary Tuberculosis in a High HIV Prevalence Setting. Am J Respir Crit Care Med, 184: 132-140, doi: 10.1164/rccm.201101-0056OC 2. 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. doi: 10.7448/IAS.15.3.17364 3. 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. The Lancet 2013, doi:10.1016/S0140-6736(13)62073-5 4. 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. The Lancet Respiratory Medicine, 2600(13), 5–7. doi:10.1016/S2213-2600(13)70120-6 5. 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. The Lancet Global Health, 1(2), e97-e104.

3.1.17 TB CHILD

EDCTP Project Coordinator:	Fred Lwilla (Ifakara Health Research and Development Centre, Tanzania)
EDCTP Call Title:	Call for applications to support clinical trials, capacity building and networking in new and improved diagnostics for tuberculosis (TB)
EDCTP Project Title:	Evaluation of new and emerging diagnostics for childhood tuberculosis in high burden countries (TB CHILD)
EDCTP Project Code:	IP.2009.32040.007
EDCTP Project Start Date:	17 May 2010
EDCTP Project End Date:	16 May 2013
Collaborators:	• Klaus Reither (Swiss Tropical and Public Health Institute Switzerland and Ifakara Health Research and Development Centre, Tanzania) • Levan Jugheli (Ifakara Health Research and Development Centre, Tanzania) • Salim Abdoulla (Ifakara Health Research and Development Centre, Tanzania) • Christian Burri (Swiss Tropical and Public Health Institute, Switzerland) • Francesco Aloi (San Raphael of St. Francis Hospital Nsambya, Uganda) • Hans-Peter Beck (Swiss Tropical Institute, Switzerland) • Catharina Boehme (Foundation for Innovative New Diagnostics (FIND), Switzerland) • Claudia Daubenberger (Swiss Tropical and Public Health Institute, Switzerland) • Martin Nsubuga (San Raphael of St. Francis Hospital Nsambya, Uganda) • Petra Clowes (MMRP, Tanzania) • Nyanda Elias (MMRP, Tanzania) • Enrico Girardi (National Institute for Infectious Diseases Lazzaro Spallanzani, Italy) • Delia Goletti (National Institute for Infectious Diseases Lazzaro Spallanzani, Italy) • Angela Cannas (National Institute for Infectious Diseases Lazzaro Spallanzani, Italy) • Daniela Maria Cirillo (San Raphael of St. Francis Hospital Nsambya, Italy) • Christof Gedmacher (LMU München, Germany) • Michael Hoelscher (LMU München, Germany) • Mahavir Singh (Lionex GmbH, Germany) • Francis Drobniewski (Health Sciences Research Ltd, UK)
Study/Trial 1	**Study A: Trial for early evaluation in adults**
Chief Trial investigator	Klaus Reither (Tanzania)
Site Principal Investigator(s):	• Nahya Salim Masoud (Tanzania) • Martin Nusubuga/ Franscesco Aloi (Uganda) • Nyanda Elias/Petra Clowes (Tanzania)
Clinical Trial/Study Sponsor:	Ifakara Health Institute (Tanzania)
Goal:	Developing sustainable, collaborative research capacity for the diagnosis of childhood TB in parts of sub-Saharan Africa and on the effective, efficient conduct of clinical trials on new or improved diagnostics for pediatric tuberculosis
Primary Objective(s):	1. To assess performance characteristics (sensitivity, specificity, positive and negative predictive value, diagnostic likelihood ratios) of new TB diagnostics in

	sputum smear-positive or sputum smear-negative/culture-positive adults and adult controls, and the appropriateness of the new test for further systematic evaluation in children 2. To assess reproducibility of test results 3. To investigate the influence of clinical characteristics on the test performance 4. To establish a specimen bank of adequately stored clinical materials from well-characterised patients for future analysis.
Clinical Trial/Study site(s):	• Bagamoyo Research and Training Centre / Ifakara Health Institute, and • NIMR-Mbeya Medical Research Programme (Tanzania) • San Raphael of St. Francis Hospital Nsambya (Uganda)
Collaborating site(s):	• Swiss Tropical and Public Health Institute (Switzerland) • Klinikum of the University of Munich (LMU) (Germany) • Italian National Institute for Infectious Diseases (Italy) • Fondazione Centro San Raffaele del Monte Tabor (Italy) • Foundation for Innovative New Diagnostics (FIND) (Switzerland) • Stellenbosch University (South Africa) • Health Sciences Research Ltd (UK) • LIONEX GmbH (Germany)
Study design:	Case-control evaluation study Adult patients suspected of having pulmonary TB will be prospectively recruited. The study is expected to recruit: sputum smear-positive and smear-negative/ Xpert MTB positive or culture-positive adult pulmonary TB cases, and additionally healthy non-TB controls. These groups will be utilised for the early evaluation studies on those new emerging diagnostic approaches in order assess test accuracy and reproducibility and probably to refine the methodology for application in children.
Number of subjects	Adults; TB cases: 180; Healthy controls: 120
Product(s):	• LHSD Rapid test to detect LAM in sputum or urine • Diagnostic potential of IP10 and other biomarkers in blood and urine • T cell activation markers on Mycobacterium tuberculosis (MTB) specific T cells (TAM-IGRA) • Lab-on-chip based new platform (In-checkTM) for the molecular diagnosis • Newly developed TB diagnostics
Manufacturer/Developer:	• LIONEX, Braunschweig, Germany • Not applicable • Not applicable • STMicroelectronics, Geneva, Switzerland • Not applicable
Cofunders	• State Secretariat for Education and Research SER / Swiss National Science Foundation (Switzerland) • Bundesministerium für Bildung und Forschung (BMBF, Germany) • FIND (Switzerland) • Italian Ministry of Foreign Affairs – Italian Directorate for Development Cooperation (Italy) • Fondazione Centro San Raffaele del Monte Tabor (Italy) • Aispo-Nsambya Hospital (Uganda/Italy) • LMU-Klinikum Der Universitat Munchen (Germany) • Swiss Agency for Development and Cooperation (SDC, Switzerland)
Status	Completed

Results and Outcomes	
Study/Trial 2	**Study B: New diagnostics for childhood TB**
Chief Trial investigator	Klaus Reither (Tanzania)
Site Principal Investigator(s):	• Nahya Salim Masoud (Tanzania) • Martin Nusubuga/ Franscesco Aloi (Uganda) • Nyanda Elias/Petra Clowes (Tanzania)
Clinical Trial/Study Sponsor:	Ifakara Health Institute (Tanzania)
Trial/Study title:	New diagnostics for childhood TB
Goal:	Developing sustainable, collaborative research capacity for the diagnosis of childhood TB in parts of Sub-Saharan Africa and on the effective, efficient conduct of clinical trials on new or improved diagnostics for pediatric tuberculosis
Primary Objective(s):	1. To assess new TB diagnostic modalities regarding sensitivity, specificity, positive and negative predictive value, as well as diagnostic likelihood ratio, in comparison to well-defined diagnostic classification groups for childhood TB 2. To investigate the influence of clinical characteristics and disease diversity on the test performance 3. To test reproducibility of test results 4. To obtain operational feasibility data and assess staff and training requirements for promising new tests 5. To assess the requirements for quality assurance and safety issues for each new test 6. To explore the identification of a resource-stratified diagnostic algorithm by integrating various clinical variables, risk factors and relevant laboratory results 7. To establish a specimen bank of adequately stored clinical reference materials from well-characterised patients for future analysis.
Clinical Trial/Study site(s):	• Bagamoyo Research and Training Centre / Ifakara Health Institute (Tanzania) • NIMR-Mbeya Medical Research Programme (Tanzania) • Saint Raphael of St. Francis, Nsambya Hospital, Kampala (Uganda)
Collaborating site(s):	• Swiss Tropical and Public Health Institute (Switzerland) • Klinikum of the University of Munich (LMU, Germany) • Italian National Institute for Infectious Diseases (Italy) • Fondazione Centro San Raffaele del Monte Tabor (Italy) • Foundation for Innovative New Diagnostics (FIND, (Switzerland) • Stellenbosch University (South Africa) • Health Sciences Research Ltd (UK) • LIONEX GmbH (Germany)
Study design:	This is the central study of the project. The study will comprehensively assess the ability of new tests/approaches, identified in adult early evaluation studies, to reliably diagnose TB in children. Diagnostic accuracy, operational feasibility and appropriateness of the candidate tests/approaches for routine health care service implementation will be evaluated.
Study population:	Children (between 6 weeks and 14 years old) with suspected TB N=600
Product(s):	• LHSD Rapid test to detect LAM in sputum or urine • Loop-mediated isotermal amplification (LAMP) • GeneXpert • Diagnostic potential of IP10 and other biomarkers in blood and urine • T cell activation markers on Mycobacterium tuberculosis

	(MTB) specific T cells (TAM-IGRA) • Mtb DNA extraction from stool • Lab-on-chip based new platform (In-checkTM) for the molecular diagnosis • Ustar TB IAD Kit (Biotech) • Pari eFlowrapid nebulizer • Newly developed TB diagnostics
Manufacturer/Developer:	• LIONEX, Braunschweig, Germany • Eiken Chemical Co. Ltd., Tokyo, Japan • Cepheid, Sunnyvale, USA • STMicroelectronics, Geneva, Switzerland • Biotech, China • Pari pharma, Germany
Cofunders:	• State Secretariat for Education and Research SER / Swiss National Science Foundation (Switzerland) • Bundesministerium für Bildung und Forschung (BMBF, Germany) • FIND (Switzerland) • Italian Ministry of Foreign Affairs – Italian Directorate for Development Cooperation (Italy) • Fondazione Centro San Raffaele del Monte Tabor (Italy) • Aispo-Nsambya Hospital (Uganda/Italy) • LMU-Klinikum Der Universitat Munchen (Germany) • Swiss Agency for Development and Cooperation (SDC, Switzerland)
Status:	Completed
Results and Outcomes	
PhD studies:	Title: Evaluation of XpertTMTM MTB/RIF (GeneXpert, Cepheid) AND Ustar® IAD TB (Biotech) on cytological aspirates for diagnosis of extrapulmonary tuberculosis in children compared to established FNA methodologies and subsequent genotyping of mycobacterial isolates Candidate: Maira Bholla (Aga Khan Hospital, Kenya) Dates: March 2011-March 2015
	Title: Serum microRNAs as biomarkers for active and latent tuberculosis infection in immunocompetent and immunodeficient hosts Candidate: Grace Mwangoka (Ifakara Health Institute, Tanzania) Dates: October 2010-October 2014
MSc studies:	Title: MSc Applied Microbiology, University Dar es Salaam; Thesis title: Prevalence and Environment sources of Atypical Mycobacteria among Tuberculosis suspects Candidate: Sarah Mswata (Ifakara Health Institute, Tanzania) Dates: June 2010-June 2012
	Title: Active case finding among household contacts of patients with sputum smear positive tuberculosis in Mbeya Tanzania, Liverpool School of Tropical Medicine Candidate: Nyanda Elias Ntinginya (Mbeya Medical Research Programme, Tanzania) Dates: September 2010-September 2011
Other/Sub-studies:	Ancillary study: Molecular characterization of M.tuberculosis strains from Bagamoyo and Dar es Salaam ('genotyping')
Publications:	1. Miotto, P, Mwangoka, G, Valente, IC, Norbis, L, Sotgiu, G, Bosu, R, Ambrosi, A, Codecasa, LR, Goletti, D, Matteelli, A, Ntinginya, EN, Aloi, F, Heinrich, N, Reither, K, Cirilli, DM (2013) miRNA Signatures in Sera of Patients with Active Pulmonary Tuberculosis, *PloS ONE,* 8(11): e80149 2. Ntinginya, EN, Squire, SB, Millington, KA, Mtafya, B, Saathoff, E, Heinrich, N, Rojas-Ponce, G, Kowuor, D, Maboko,L, Reither, K, Clowes, P, Hoelsche M, Rachow, A (2012) Performance of

	the Xpert® MTB/RIF assay in an active case-finding strategy: a pilot study from Tanzania, *Int J Tuberc Lung Dis*, 16(11): 1468-1470

3.1.18 AE TBC

EDCTP Project Coordinator:	Gerhard Walzl (Stellenbosch University, South Africa)
EDCTP Call Title:	Call for applications to support clinical trials, capacity building and networking in new and improved diagnostics for tuberculosis (TB)
EDCTP Project Title:	The evaluation of Mycobacterium tuberculosis specific host cytokine signatures in whole blood culture supernatants as diagnostic biomarkers for active TB infection
EDCTP Project Code:	IP.2009.32040.011
EDCTP Project Start Date:	16 June 2010
EDCTP Project End Date:	15 December 2013
Collaborators:	• Claudia Giehl (European Reasearch & Project Office GmbH (EURICE), Germany) • Amelia Crampin (Karonga Prevention Study (KPS), Malawi) • Hazel Dockrell (London School of Hygiene and Tropical Medicine (LSHTM), UK) • Rawleigh Howe (Armauer Hansen Research Institute (AHRI), Ethiopia) • Desta Kassa (Ethiopian Health and Nutrition Research Institute (EHNRI), Ethiopia) • Stefan H.E.Kaufmann (Max Planck Institute for Infection Biology (MPIIB), Germany) • Harriet Mayanja-Kizza (CWRU Research Collaboration (UCRC), Uganda) • Jayne Sutherland (MRC, The Gambia) • Tom Ottenhoff (Leiden University Medical Centre (LUMC), Netherlands) • Ida Rosenkrands (Statens Serum Institute (SSI), Denmark) • Marieta Van der Vyver (University of Namibia (UNAM), Namibia)
Study/Trial 1	
Site Principal Investigator(s):	• Gerhard Walzl (South Africa) • Jayne Sutherland (The Gambia) • Rawleigh Howe (Ethiopia) • Desta Kassa (Ethiopia) • Harriet Mayanja-Kizza (Uganda) • Mia Crampin (Malawi) • Marieta Van der Vyver (Namibia)
Clinical Trial/Study Sponsor:	Stellenbosch University (South Africa)
Trial/Study title:	The evaluation of Mycobacterium tuberculosis specific host cytokine signatures in whole blood culture supernatants as diagnostic biomarkers for active TB infection
Goal:	The overall goal of the project is to develop a point of care test for diagnosis of active TB that will be based on an overnight culture of whole blood in the presence of Mtb antigens and the measurement of a combination of up to three markers (EGF, IL-1α and MIP-1β) by lateral flow upconverting phosphor technology.
Primary Objective(s):	To evaluate the performance of the combination of levels of EGF, IL-1α and MIP-1β in WBA supernatants, measured by lateral flow upconverting phosphor test strips to enable the accurate diagnosis of active tuberculosis in a rapid field-friendly assay. Such a test would be a significant improvement over current tests as it would not require advanced laboratory capacity, as it would provide a result within 24 hours and as it may enable diagnosis of active disease in patients with

	paucibacillary or extrapulmonary disease.
Secondary Objective(s):	1. To evaluate improvements of the overnight whole blood assay by: – Investigating WBA supernatants by Luminex multiplex cytokine technology to identify additional host markers with good diagnostic ability to differentiate between active and latent TB – Investigating the performance of novel infection phase specific Mtb proteins – Investigating the performance of the novel tests discussed above to diagnose TB in clinical situations where bacteriologic confirmation is difficult, including in HIV infection and in extrapulmonary TB 2. To establish a comprehensive bio bank for diagnostic marker discovery
Clinical Trial/Study site(s):	• Stellenbosch University (South Africa) • Medical Research Council (The Gambia) • Armauer Hansen Research Institute (Ethiopia) • Makerere University (Uganda) • Karonga Prevention Study/LSHTM, (Malawi) • University of Namibia (Namibia) • Ethiopian Health and Nutrition Research Institute (Ethiopia)
Collaborating site(s):	• Max Planck Society for the Advancement of Science/Max Plank Institute for Infection Biology (Germany) • LUMC (The Netherlands) • LSHTM (UK) • European Research & Project Office GmbH (Eurice) (Germany) • Statens Serum Institute (Denmark)
Study design and population:	Group I: Patients with suspected TB (HIV-uninfected adults, >14 to 65; N=800) will be recruited and followed up for 6 months at primary health care clinics at the African consortium institutions. Confirmation of disease status will be performed by clinical (symptom questionnaire, physical examination), radiological (chest X-rays) and laboratory measures (sputum smear and culture, confirmation by speciation). Participants will be followed up once at month six to ascertain treatment response and thereby increase diagnostic certainty. The project expects to enrol 300 active TB cases and 500 participants without active TB and this group will include people with LTBI and acute and chronic lung infections not due to TB as well as non-infectious conditions, like chronic obstructive pulmonary disease (COPD). Group II: Patients with suspected TB (HIV-positive adults, >14 to 65; N=400) as above but with HIV infection. The study expects to enrol 200 active TB cases and 200 participants without active TB and this group will include people with LTBI and acute and chronic lung infections not due to TB, all with HIV infection. Database and sample bank: All clinical and laboratory data will be entered into i) site-specific databases and ii) a central consortium database. Samples will be stored at site-specific bio banks but sample information will also be entered into the central database. Samples will be collected to establish a bio bank for future discovery of diagnostic biomarkers.
Product(s):	Commercial in vitro interferon gamma (IFN-γ) release assays (IGRAs): QuantiFERON® TB Gold In-Tube

	T SPOT.TB
Manufacturer/Developer:	• Cellestis, Victoria (Australia) • Oxford Immunotec, Abington (UK)
Cofunders:	• Stellenbosch University (South Africa) • Makarere University (Uganda) • Max Planck Institute (Germany) • Leiden University (Netherlands) • LSHTM (UK) • European Research and Project Office GmbH (Germany) • BMBF (Germany) • NACCAP (Netherlands) • MRC (UK)
Status:	Completed
Results and Outcomes	First patient in: 9 November 2010
PhD studies:	Gene expression and cytokine pattern of pulmonary tuberculosis patients and their contacts in Ethiopia Candidate: Adane Mhiret Bekele (Stellenbosch University, South Africa) Dates: April 2009-December 2012
	Candidate: Wegene Tamene (Ethiopia)
MSc studies:	Title: Innate immune responses in protection against MTB infection Candidate: Khutso Phalane (Stellenbosch University, South Africa) Dates: January 2011-December 2012
	Title: Diagnostic potential of memory T cell subtypes in MTB infection Candidate: Paulin Essone Ndong (Stellenbosch University, South Africa) Dates: January 2011-December 2012
	Title: The evaluation of MTB specific host cytokine signatures in whole blood culture supernatants as diagnostic biomarkers Candidate: Josephina Nolongo (University of Namibia) Dates: March 2011-October 2012
	Title: The profile of antiretroviral drug resistance mutations at baseline and at time of failure of antiretroviral therapy in tuberculosis co-infected Human Immunodeficiency Virus-1 patients in Ethiopia Candidate: Gebremedhin Gebremichael (LSHTM, UK)
	Title: Mycobacterium tuberculosis specific cytokine profile in childhood Tuberculosis in Ethiopia Candidate: Yodit Alemayehu (LSHTM, UK)
	Title: Cytokines as markers to detect active tuberculosis in patients attending the tuberculosis clinic at Mulago Hospital Candidate: Anna Ritah Namuganga (Makerere University, Uganda)
	Title: Evaluation of clinical and radiological predictors of TB disease recurrence Candidate: Grace Muzanye (LSHTM, UK) Dates: August 2011-August 2014
Post-doc studies:	Novel Chegou (Stellenbosch University, South Africa)
	Maria Esterhuyse (Max Planck Institute for Infection Biology, Germany)
Other/Sub-studies:	Global transcriptome analyses of blood leukocytes Maria Esterhuyse (post-doctoral fellowship)
Publications:	1. Chegou, NN, Hoek, KG, Kriel, M, Warren, RM, Victor, TC, Walzl, G. (2011) Tuberculosis assays: past, present and future. *Expert Rev Anti Infect Ther*. 9(4):457-469, doi: 10.1586/eri.11.23. 2. Walzl, G, Ronacher, K, Hanekom, W, Scriba, TJ, Zumla, A. (2011) Immunological biomarkers of tuberculosis. *Nat Rev*

Immunol. 11(5):343-54, doi: 10.1038/nri2960.
3. Chegou, NN, Black, AG, Loxton, AG, Stanley, K, Essone, PN, Klein, MR, Parida, SK, Kaufmann, SHE, Doherty, TM, Friggen, AH, Franken, KL, Ottenhoff, TH, Walzl, G. (2012) Potential of novel Mycobacterium tuberculosis infection phase-dependent antigens in the diagnosis of TB disease in a high burden setting. *BMC Infectious Diseases* 12(10), doi: 10.1186/1471-2334-12-10
4. Cliff, JM, Lee, JS, Constantinou, N, Cho, JE, Clark, TG, Ronacher, K, King, EC, Luckey, PT, Duncan, K, Van Helden, PD, Walzl, G, Dockrell, HM (2013) Distinct phases of blood gene expression pattern through tuberculosis treatment reflect modulation of the humoral immune response. *Journal of Infectious Diseases,* 207(1) , 18-29, doi: 10.1093/infdis/jis499. Epub 2012 Aug 7
5. Esterhuyse, MM, Linhart, HG, Kaufmann, SHE (2012) Can the battle against tuberculosis gain from epigenetic research? *Trends in Microbiology,* 20(5) 220-6, doi: 10.1016/j.tim.2012.03.002. Epub 2012 Mar 30
6. Corstjens, PLAM, de Dood, CJ, van der Ploeg-van Schip, JJ, Wiesmeijer, KC, Riuttamaki, T, van Meijgaarden, KE, Spencer, JS, Tanke, HJ, Ottenhoff, THM, Geluk, A (2011) Lateral flow assay for simultaneous detection of cellular- and humoral immune responses. *Clinical Biochemistry,* 44(14-15), 1241-1246, doi: 10.1016/j.clinbiochem.2011.06.983.Epub 6 July 2011.

3.1.19 NEAT - MDRTB

EDCTP Project Coordinator:	Luis Eduardo Cuevas (Liverpool School of Tropical Medicine (LSTM), UK)
EDCTP Call Title:	EDCTP Strategic Primer Grants
EDCTP Project Title:	Paving the way for clinical trials for the community-based treatment of MDR-TB through innovative approaches to screen and monitor patients with TB
EDCTP Project Code:	SP.2011.41304.021
EDCTP Project Start Date:	1 December 2013
EDCTP Project End Date:	30 November 2014
Collaborator(s)	• Saddiq Tsimiri Abdurrahman (Federal Ministry of Health, Nigeria) • Silvia Blanco (University of Addis Ababa, Ethiopia) • Daniel Datiko (University of Hawassa, Ethiopia) • Jose Antonio Dominguez (University Hospital Germans Trias i Pujol, Spain) • Lovett Lawson (Zankli Medical Centre, Nigeria) • Joshua Olusegun Obasanya (Federal Ministry of Health, Nigeria) • Christophe Sola (Institut de Genetique et Microbiologie, France)
Study	Paving the way for clinical trials for the community-based treatment of MDR-TB through innovative approaches to screen and monitor patients with TB
Study/Trial 1	NEAT-MDRTB
Site Principal Investigator(s):	• Luis Eduardo Cuevas (UK) • Lovett Lawson (Nigeria) • Daniel Datiko (Ethiopia)
Study title:	Evaluation of an automated platform (TBDx) for reading and grading FM smears
Goal:	To evaluate a diagnostic platform that could improve the large scale screening of patients with symptoms of TB.
Primary Objective(s):	To evaluate the sensitivity, specificity and accuracy of the TBDx platform. To evaluate whether TBDx combined with selective use of Xpert could be used as part of an algorithm to identify cases with TB.
Secondary objective(s):	To evaluate whether the TBDx could be used to develop a screening system to serve several reference hospitals for the diagnosis of TB.
Study site(s):	Zankli Medical Centre, (Abuja, Nigeria)
Collaborating site(s):	• Federal Ministry of Health (Nigeria) • LSHTM (UK) • University Hospital Germans Trias i Pujol (Spain) • Institut de Genetique et Microbiologie (France)
Study design:	Prospective, cross sectional study of consecutive patients with symptoms of TB being screened at participating district hospitals of the FCT Abuja. All patients are requested to provide two sputum specimens on the spot for analysis. Sputum is screened using TBDx, manual FM, Xpert and culture. Analysis will compare • TBDx and manual FM (head to head) • TBDx plus selected manual reading or smears graded as scanty (diagnostic algorithm 1) • TBDx plus selected Xpert testing of smears graded as scanty (diagnostic algorithm 2). Culture will be considered the reference standard. The same samples will be used to obtain genotype and DST testing (see sub-study 2). Biomedical samples: samples with DNA.
Study population:	Adults with symptoms of TB. Sample size for the initial evaluation (objectives 1 and 2) is 1600 participants. A further 1600 participants will be recruited for the secondary objective.
Cofunders:	• Medical Research Council (UK) • Centre de Recerca en Salut Internacional de Barcelona (CRESIB, Spain) • LSHTM (UK)

	• Institut de Genetique et Microbiologie (IGEPE, France) • Zankli Medical Centre (Nigeria) • University of Addis Ababa (Ethiopia) • Federal Ministry of Health (Nigeria) • Spanish National Research Council (CSIC, Spain)
Status:	Ongoing
Study/Trial 2	Feasibility and acceptability of community-based treatment of MDR-TB
Site Principal Investigator(s):	• Luis Eduardo Cuevas, (LSHTM, UK) • Daniel Datiko (University of Hawassa, Ethiopia)
Trial/Study title:	Feasibility and acceptability of community-based treatment of MDR-TB
Goal:	Provide essential information on the feasibility and acceptability of community-based treatment of MDR-TB in Nigeria and Ethiopia and identify the services that are needed to support treatment adherence.
Primary Objective(s):	Assess the feasibility and acceptability of schemes that facilitate community-based treatment of TB, as a surrogate for the treatment of MDR-TB in the community
Clinical Trial/Study site(s):	University of Hawassa, Hawassa, Ethiopia Zankli Medical Centre, Abjua, Nigeria
Collaborating site(s):	• University of Addis Ababa (Ethiopia) • LSHTM (UK) • University of Hawassa (Ethiopia) • University Hospital Germans Trias i Pujol (Spain) • Zankli Medical Centre (Nigeria) • Institut de Genetique et Microbiologie (France)
Study design:	Observational study Qualitative in-depths interviews and focus group discussions of patients, program managers and community leaders to explore the acceptability and feasibility of providing treatment to patients in the community and to identify the ancillary services that are needed to ensure patients are able to adhere to treatment. Prospective descriptive study of a cohort of patients receiving treatment for TB and of patients receiving the continuation phase MDR-TB treatment (after discharge from hospital) to document adherence, problems encountered and support services needed (as informed by qualitative studies) No biological specimens retained.
Status:	Ongoing
Results and outcomes:	Recruitment to start in October 2013
Other/Sub-studies (including cohorts/epidemiological studies:	Title: MDR-TB among new and retreatment cases and molecular epidemiology of *Mycobacterium tuberculosis* Study purpose and objectives: Establish the patterns of drug resistance in newly diagnosed and retreatment TB patients and the molecular epidemiology of *M. tuberculosis*. Primary Objective: Establish the patterns of drug resistance in newly diagnosed and retreatment TB patients to obtain baseline information for the planning of subsequent trials. Secondary Objective: To describe the genetic diversity of *M. tuberculosis*. To assess the feasibility of using smears to establish drug sensitivity patterns of *M. tuberculosis*
Publications:	

3.1.20 PredART

EDCTP Project Coordinator:	Graeme Ayton Meintjes (Univeristy of Cape Town, South Africa)
EDCTP Call Title:	Strategic Primer Grants
EDCTP Project Title:	Preventing tuberculosis-associated immune reconstitution inflammatory syndrome in high-risk patients: a randomised placebo-controlled trial of prednisone
EDCTP Project Code:	SP.2011.41304.074
EDCTP Project Start Date:	15 December 2012
EDCTP Project End Date:	15 December 2014
Collaborators:	• Lutgarde Lynen (Institute of Tropical Medicine (ITM), Antwerp, Belgium) • Robert J. Wilkinson (Imperial College London, UK and University of Cape Town, South Africa) • Gary Maartens (University of Cape Town, South Africa) • Robert Colebunders (ITM, Belgium) • Christiana Noestlinger (ITM, Belgium) • Harry van Loen (ITM, Belgium) • Joris Menten (ITM, Belgium) • Jozefien Buyze (ITM, Belgium) • Charlotte Schutz (University of Cape Town, South Africa) • Edwin Wouters (University of Antwerp, Belgium) • William J. Burman (University of Colorado, USA) • Raffaella Ravinetto (ITM, Belgium) • Shaheed Mattee (Ubuntu HIV-TB clinic, Khayelitsha, South Africa) • Funeka Bango (Ubuntu HIV-TB clinic, Khayelitsha, South Africa) • Friedrich Thienemann (University of Cape Town, South Africa) • Jan Kuehne (Ubuntu HIV-TB clinic, Khayelitsha, South Africa)
Study/Trial	
Site Principal Investigator(s):	• Graeme Meintjes (South Africa)
Clinical Trial/Study Sponsor:	University of Cape Town (South Africa)
Trial/Study title:	Preventing tuberculosis-associated immune reconstitution inflammatory syndrome in high-risk patients: a randomised placebo-controlled trial of prednisone
Project Acronym:	PredART
Primary Objective(s):	7. To determine whether a 4-week course of prednisone in patients starting antiretroviral therapy (ART) within 30 days of starting treatment for tuberculosis (TB) and a CD4 count ≤ 100/μL reduces the incidence of paradoxical TB-IRIS, without an excess of adverse events. The trial is powered to determine a reduction in TB-IRIS events.
Secondary Objective(s):	Secondary efficacy endpoints: 1. Time to IRIS event 2. Severity of IRIS events (defined by the following: need for hospitalisation for IRIS, C-reactive protein, and neurological involvement) 3. Duration of TB-IRIS event (from onset of symptoms/signs to resolution of TB-IRIS symptoms/signs) 4. Mortality attributed to TB and TB-IRIS 5. All-cause mortality 6. Composite endpoint of death, hospitalization, or hepatotoxicity (using the protocol-specified definition of Grade 3 or 4 increase in ALT or bilirubin).

	7. Other (non-TB) IRIS events 8. Quality of life assessment (measured using PROQOL-HIV, EQ-5D-3L, HIV symptom index and Karnofsky score) 9. Adverse events and severe adverse events ascribed to TB treatment, ART or co-trimoxazole. This will include a pre-specified analysis of drug-induced liver injury and drug rash. This assessment will include the number of treatment interruptions for drug adverse events. 10. Discontinuation of either ART or TB treatment for > 5 days due to adverse events 11. Number of hospitalizations and total days hospitalized Safety and tolerability endpoints: 1. Corticosteroid-associated adverse events, classified by severity and relation to study drug. These will include hypertension, hyperglycaemia, hypomania/mania, depression, acne, epigastric pain, upper gastro-intestinal bleeding, Cushingoid features, new oedema and avascular bone necrosis 2. Laboratory safety data: glucose, full blood count and electrolytes 3. Other infections (AIDS-related, bacterial, fungal and viral) and malignancies (Kaposi's sarcoma) 4. All grade 1, 2, 3 and 4 adverse events (clinical and laboratory using the ACTG grading system)
Clinical Trial/Study site(s):	• Khayelitsha Site B Ubuntu HIV/TB clinic (South Africa)
Study design:	Randomised double blind placebo-controlled trial; two arms parallel (prednisone and placebo); phase 3; efficacy and safety trial.
Study population:	ADULTS (≥18 years); Patients starting ART while on treatment for TB with CD4 count ≤ 100 cells/µL. N= 240
Product(s):	• Prednisone
Manufacturer:	• Gulf Drug Company
Cofunders:	Department of Science and Technology (South Africa): ESASTAP programme
Trial Registration number(s):	PACTR201304000511413
Status:	Ongoing
Results and Outcomes:	
Publications:	

3.1.21 PROMISE TB

EDCTP Project Coordinator:	Philippe van de Perre (Montpellier University Hospital Centre (CHU), France)
EDCTP Call Title:	EDCTP Strategic Primer Grants
EDCTP Project Title:	**PRO**Moting **I**nfant health and nutrition in **S**ub-Saharan Africa – **E**valuation of Innovative **T**u**B**erculosis diagnostic tests **(PROMISE-TB)**
EDCTP Project Code:	SP.2011.41304.070
EDCTP Project Start Date:	1 February 2013
EDCTP Project End Date:	31 December 2014
Collaborator(s)	• Stephane Blanche (Necker Hospital, France) • Stephane Canaa (CNRS, France) • Chipepo Kankasa (University Teaching Hospital, Zambia) • Thorkild Tylleskar (University of Bergen, Norway)
Study/Trial 1	PROMISE-TB
Site Principal Investigator(s):	Kankasa, Chipepo (Zambia)
Clinical Trial/Study Sponsor:	French National Agency for Research on AIOS and Viral Hepatitis (ANRS, France)
Trial/Study title:	
Goal:	The main objective is to assess the performance of innovative immunological tests (either alone or in combination) for the diagnosis of active TB among HIV-infected and HIV-unifected children: 1. Immunoenzymatic assays measuring circulating antibodies directed against MTB lipolytic enzymes 2. Multicytokine release assay.
Primary Objective(s):	The key deliverables are to obtain tests that proved accurate to diagnose paediatric active TB (and therefore to prompt treatment) among immuno-competent and immune-compromised Zambian children.
Secondary Objective(s):	• To estimate the intrinsic performance of alternative commercial TB diagnosis tests (GeneXpert, LAM, and IGRA) in African children infected by HIV or unifected by HIV. • To build the laboratory capacity of the HIV paediatric centre of excellence in Lusaka (Zambia).
Clinical Trial/Study site(s):	University Teaching Hospital (UTH, Zambia)
Collaborating site(s):	• Necker Hospital (France) • CNRS (France) • Montpellier University Hospital Centre (CHU, France) • University of Bergen (Norway)
Study design:	Diagnostic accuracy study
Number of subjects:	200 subjects
Product(s):	Diagnostic analysis, Innovative immunological test to detect characteristic MTB proteins and lipids in blood samples
Cofunders:	• ANRS (France) • University of Montpellier (France) • Comité National d'Éthique pour la Recherche du Gabon (CNER, France) • UTH (Zambia) • University of Bergen (Norway)
Status:	Ongoing
Results and Outcomes:	
Publications:	

3.1.22 Diacon

EDCTP Project Coordinator:	Andreas Henri Diacon (Stellenbosch University, South Africa)
EDCTP Call Title:	Strategic Primer Grants
EDCTP Project Title:	β-lactams against TB: Teaching new tricks to an old dog
EDCTP Project Code:	SP.2011.41304.076
EDCTP Project Start Date:	3 October 2013
EDCTP Project End Date:	28 February 2015
Collaborators:	• Esperança Sevene, Manhiça Foundation, Mozambique • David Barros, GlaxoSmithKline, Madrid, Spain • Jose Muñoz Gutierrez, Barcelona Centre for International Health Research (CRESIB), Spain • Chistoph Lange, Research CenterBorstel
Study/Trial	
Site Principal Investigator(s):	Andreas Henri Diacon (Stellenbosch University, South Africa)
Clinical Trial/Study Sponsor:	Task Foundation NPC (South Africa)
Trial/Study title:	β-lactams against TB: Teaching new tricks to an old dog
Primary Objective(s):	1. To generate robust early bactericidal activity (EBA) data in tuberculosis patients with drugsensitive strains of M. tuberculosis (single drug) that will be the basis for future clinical trialsfor ß-lactams and explore the feasibility of developing faropenem as an antituberculosis oralagent. 2. To generate capacity in Africa through the development of EBA in African sites.
Clinical Trial/Study site(s):	Task Clinical Research Centre, Cape Town, South Africa
Study design:	Phase IIa single-centre proof of concept trial with two experimental arms and a control arm as follows: **Experimental arm 1**: 1 g meropenem + 125 mg clavulanic acid (CA), three times daily intravenously for 1 week followed by 2 weeks faropenem per os (dosing TBD) **Experimental arm 2:** 2 g meropenem + 125 mg clavulanic acid (CA), three times daily intravenously for 1 week followed by 2 weeks faropenem per os (dosing TBD) **Control arm:** Per os dosing of Rifafour for 1 week followed by 2 weeks faropenem per os (dosing TBD) Primary endpoint will be daily rate of change of colony-forming units of MTB in sputum or the prolongation of time to positivity (TTP) in liquid culture.
	ADULTS (18-65 years); Treatment-naïve, sputum smear-positive patients with drug sensitive pulmonary tuberculosis. N=53
Product(s):	• Faropenem • Meropenem/CA • Rifafour®e275
Manufacturer:	
Cofunders:	• Borstel Research Center (Germany) • Barcelona Center for International Health Research (Spain) • Federal Ministry of Education and Research (Germany) • GlaxoSmithKline (Spain) • Task Applied Science (South Africa) • Department of Science and Technology (South Africa) • Hospital Clínic de Barcelona – Researcher at Barcelona

	Centre for International Health Research (CRESIB)
Trial Registration number(s):	Not yet registered
Sub-studies:	• The first sub-study will further evaluate a novel diagnostic test for TB. Diagnosis of TBin sputum is challenging in a number of cases especially in HIV co-infected patientsand children. Specific Mycobacterium complex (MTC)-DNA is excreted in urine and canbe detected by a novel urine test. This sub-study will evaluate the test in patientswith TB in the initial phase of treatment. Urine samples will be taken at time pointsspecified in the events table, immediately frozen and sent to Research Center Borstel.Analysis of the kinetics of transrenal *M. tuberculosis* specific nucleic acid will be doneat the Research Center in collaboration with scientists from Africa • A second substudy will measure mycobacterial RNA in sputum. Sputum will be storedin Trizol and at minus 80 degrees for subsequent mycobacterial RNA extraction.Quantitative real-time PCR will be used to quantify mycobacterial RNA and its declineover the first days of treatment.
Status:	Ongoing
Results and Outcomes:	
Publications:	

3.1.23 PanBIOME

EDCTP Project Coordinator:	Stephen Gillespie (University of St Andrews, UK)
EDCTP Call Title:	Strategic Primer Grants
EDCTP Project Title:	Molecular Biomarkers in MAMS trial (MBMAMS)
EDCTP Project Code:	SP.2011.41304.008
EDCTP Project Start Date:	3 January 2013
EDCTP Project End Date:	3 January 2015
Collaborators:	• Michael Barer (University of Leicester, UK) • Martin Boeree (Radboud University, The Netherlands) • Goeffrey Chipungu (University of Malawi, Malawi) • Liz Corbett, LSHTM (UK) • Geraint Davies (University of Liverpool, UK) • Michael Hoelcher (Ludwig-Maximilians Universitat Munchen) • Isabella Honeyborne (University College London) • Ilesh Jani (Instituto Nacional de Saúde, Mozambique) • Margaret Khonga (University of Malawi, Malawi) • Gibson Kibiki (Kilimanjaro Clinical Research Institute, Tanzania) • Timothy McHugh (University College London, UK) • Nyanda Ntinginya (Mbeya Medical Research Centre, Tanzania)
Study/Trial	
Site Principal Investigator(s):	Stephen Gillespie (UK)
Clinical Trial/Study Sponsor:	University of St Andrews
Trial/Study title:	PanBIOME
Primary Objective(s):	To collect a series of sequential samples to test candidate biomarkers
Secondary Objective(s):	Evaluation of candidate biomarkers in comparison to standard clinical trial endpoints: solid and liquid culture
Clinical Trial/Study site(s):	Mbeya Medical Research Centre (Tanzania) Kilimanjaro Clinical Research Institute (Tanzania) Instituto Nacional de Saúde (Mozambique) University of Malawi (Malawi)
Collaborating site(s):	• University of Leicester (UK) • Radboud University (The Netherlands) • LSHTM (UK) • (University of Liverpool, UK) • (Ludwig-Maximilians Universitat Munchen) • (University College London)
Study design:	Technology evaluation
Number of subjects:	Of the proposed 373 patients to be recruited into the MAMS study (see section 3.1.8), 100 are expected to be recruited into PANBIOME in Moshi and Mbeya.
Cofunders:	Sequella Foundation (US) University of St Andrews (UK) Global Health Initiative (US) Global Alliance for TB Drug Development (US) IMI PreDiCT-TB (Belgium)
Status:	Ongoing
Results and Outcomes:	Pending
Publications:	

3.1.24 PZA-RTBA

EDCTP Project Coordinator:	Michael Hoelscher (Ludwig-Maximilians Universitat Munchen, Germany)
EDCTP Call Title:	Strategic Primer Grants
EDCTP Project Title:	Epidemiology of PZA resistance in TB Clinical trials in Africa – an essential prerequisite for evaluating novel TB drug combinations
EDCTP Project Code:	SP.2011.41304.008
EDCTP Project Start Date:	5 December 2012
EDCTP Project End Date:	4 December 2014
Collaborators:	• Abraham Alabi (Albert Schweitzer, Gabon) • Matthew Bates (University Teaching Hospital, Zambia) • Martin Boeree (Radboud University, The Netherlands) • Daniela Cirillo (Ospedale San Raffaele, Italy) • Francesca Conradie (University of the Witwatersrand, South Africa) • Stephen Gillespie (University of St Andrews, UK) • Gibson Kibiki (Kilimanjaro Clinical Research Institute, Tanzania) • Bertrand Lell (Albert Schweitzer Hospital, Gabon) • Solomon Mohammed (Jimma University, Ethiopia) • Stefan Niemann (Research Centre Borstel, Germany) • Nyanda Elias Ntinginya (NIMR-MMRC) • Justin O'Grady (University College London, UK) • Andrea Rachow (Ludwig-Maximilians Universitat Munchen, Germany) • Elvira Richter (Research Centre Borstel, Germany) • Sabine Ruesch-Gerdes (Research Centre Borstel, Germany) • Ian Matthias Sanne (University of the Witwatersrand, South Africa) • Sofia Omar Viegas (Instituto Nacional de Saúde, Mozambique)
Study/Trial	
Site Principal Investigator(s):	Michael Hoelscher
Clinical Trial/Study Sponsor:	Department of Infectious Diseases and Tropical Medicine, LMU, Munich
Trial/Study title:	Epidemiology of PZA resistance in TB Clinical trials in Africa – an essential prerequisite for evaluating novel TB drug combinations (PZA-RTBA)
Primary Objective(s):	To assess the epidemiology of phenotypic and genotypic PZA-resistance in up to 900 Tb strains collected from TB patients recruited into TB clinical trials in Western-, Southern and Eastern- Africa, including Lambarene, Gabon; Maputo, Mozambique; Lusaka, Zambia; Mbeya and Moshi, Tanzania; Jimma, Ethiopia; Johannesburg RSA.
Secondary Objective(s):	1. To establish the genotypic PZA resistance pattern at the study sites in Africa, by sequencing the pncA and RpsA gene region 2. To contribute to the TB Diagnostic Forum database with PZA mutation pattern to ensure that also strains circulating outside South Africa are considered. 3. To train African scientists in sequencing techniques in Borstel using their own samples. 4. To develop a capacity development plan for sites with a high PZA resistance prevalence to be able to assess PZA resistance in 3 days. Either through a newly developed molecular assay (e.g. High Resolution Melting (HRM)

	developed by NIH consortium) or by introducing sequencing capability.
Clinical Trial/Study site(s):	NIMR-MMRC, Mbeya (Tanzania) KRCI, Moshi (Tanzania INS/Cispoc Maputo, Mozambique WITS, Johannesburg, South Africa Albert Schweitzer Hospital, Lambarene, Gabon University Teaching Hospital, Lusaka, Zambia Jimma University, Jimma, Ethiopia
Collaborating site(s):	• Radboud University Nijmegen (The Netherlands) • Research Center Borstel (Germany) • University College London (UK) • University of St Andrews, St Andrews (UK) • Ospedale St Raffaele (Italy)
Study design:	Cross-Sectional at most sites, the sites in Mbeya, Moshi and Johannesburg do perform TB strain collection within the MAMS-TB-trials
Number of subjects:	TB patients participating in different TB clinical trials at all collaborating research sites
Cofunders:	BMBF (Germany) DZIF (Germany) CIH-Munich (Germany) University of St. Andrews (UK) NIH (US)
Status:	Ongoing
Results and Outcomes:	Pending
Publications:	

4 Malaria

Table 4-1: Malaria clinical trials

Click on underlined text to link to project profiles and additional information.

Grantee Grant Code Acronym	Disease area	Phase	Clinical Trial Registration Numbers	Product(s)	Manufacturer/ Developer	Study population	Status
ABDULLA SP.2011.41304.047 P27ACTB	MALARIA VACCINES	I	NCT01949909	P27A (active ingredient: PFF0165c); Adjuvant: Alhydrogel or GLA-SEP27A doses	Almac, Nova Laboratories, Brenntag, IDRI	ADULTS (18-45 years); N=56	Ongoing
BYAKIKA KIBWIKA TA.2009.40200.020 EPQUACT	MALARIA TREATMENT	II	PACTR201110000321348	Quinine, Artesunate, Artemether-lumefantrine, Dihydroartemisinin-piperaquine		ADULTS and CHILDREN (6 months- 60 years); N=404	Ongoing
CISSE TA.2005.40200.004	MALARIA TREATMENT	IV	NCT00529620	Sulfalene-pyrimethamine, Amodiaquine, Dihydroartemisinin, Piperaquine, Sulfadoxine pyrimethamine		CHILDREN (2 months-5 years); N=1,833	Completed
D'ALESSANDRO CT. 2004. 31060.001 4ABC	MALARIA TREATMENT	III	NCT00393679 & PACTR20090100009 11750	Amodiaquine-artesunate, Dihydroartemisinin-piperaquine, Artemether-lumefantrine, Lapdap (Chlorproguanil-Dapsone) + artesunate	Sanofi-Aventis, Sigma-Tau, Glaxo SmithKline, Novartis	CHILDREN with uncomplicated malaria (6-59 months); N=4,112	Completed
D'ALESSANDRO IP.2007.31080.001 PREGACT	MALARIA TREATMENT	III	NCT00852423 & PACTR20100800024 8160	Artesunate-amodiaquine, Dihydroartemisinin-piperaquine, Artesunate-mefloquine, Artemether-lumefantrine	Sanofi-Aventis, Sigma-Tau, Farmanguinhos, Novartis	PREGNANT WOMEN (>15 years old) +INFANTS; N=3,480	Ongoing
DJIMDE IP.2007.31060.002 WANECAM	MALARIA TREATMENT	IIIb/IV	PACTR20110500028 6876	Amodiaquine-artesunate, Dihydroartemisinin-piperaquine, Artemether-lumefantrine, Artesunate-pyronaridine	Sanofi-Aventis, Sigma-Tau, Novartis, Shin Poong Pharm	CHILDREN with uncomplicated malaria (6 months-5 years old) & ADULTS; N=4,722	Ongoing
DJIMDE TA.2004.40200.002	MALARIA TREATMENT	IV	n/a				Completed

KREMSNER CT.2004. 31070.001 SMAC-II	MALARIA TREATMENT	II	NCT00522132	Artesunate (IV)	WRAIR, Sigma-Tau	CHILDREN with severe malaria (6 months-10 years); N=197	Completed
KREMSNER CT.2004. 31070.001 SMAC-III	MALARIA TREATMENT	III	PACTR201102000277177	Artesunate (IV and IM)	Guillin Pharm.	CHILDREN with severe malaria (≤14 years); N=1,047	Completed but data analysis ongoing
LEROY IP.2008.31100.001 MVVC/VAC040	MALARIA VACCINES	I	NCT01379430	ChAd63 ME-TRAP; MVA ME-TRAP	CBF, IDT Biologika, GmbH	ADULTS; N=30	Completed
LEROY IP.2008.31100.001 MVVC/VAC041	MALARIA VACCINES	I	NCT01373879	ChAd63 ME-TRAP; MVA ME-TRAP	CBF, IDT Biologika, GmbH	CHILDREN (2-6 years) and ADULTS; N=52	Completed
LEROY IP.2008.31100.001 MVVC/VAC042	MALARIA VACCINES	I	NCT01450293	ChAd63 ME-TRAP; MVA ME-TRAP	CBF, IDT Biologika, GmbH	INFANTS (10 weeks-12 months); N=72	Ongoing
LEROY IP.2008.31100.001 MVVC/VAC046	MALARIA VACCINES	II	NCT01635647	ChAd63 ME-TRAP; MVA ME-TRAP	CBF, IDT Biologika, GmbH	ADULTS; N=120	Ongoing
LEROY IP.2008.31100.001 MVVC/VAC047	MALARIA VACCINES	II	NCT01658696	ChAd63 ME-TRAP; MVA ME-TRAP	CBF, IDT Biologika, GmbH	ADULTS; N=120	Ongoing
LEROY IP.2008.31100.001 MVVC/VAC050	MALARIA VACCINES	II	NCT01666925	ChAd63 ME-TRAP; MVA ME-TRAP	CBF, IDT Biologika, GmbH	CHILDREN; N=700	Ongoing
LEROY SP.2011.41304.025 MVVC2- Phase I	MALARIA VACCINES	I	pending (MVVC2)	ChAd63 ME-TRAP; MVA ME-TRAP; R21 + MF59	CBF, Novartis	ADULTS and CHILDREN; N=60	Not registered yet
LEROY SP.2011.41304.025 MVVC2- Phase II	MALARIA VACCINES	I	pending (MVVC2)	ChAd63 ME-TRAP; MVA ME-TRAP; R21 + MF59	CBF, Novartis	ADULTS and CHILDREN; N=120	Not registered yet
MENENDEZ IP.2007.31080.002 MiPPAD	MALARIA TREATMENT	IV	NCT00811421 & PACTR2010020001813440	Mefloquine, Sulphadoxine-pyrimethamine	Hoffman-La, Roche, UCB Pharma, Carreras/Bonals	PREGNANT WOMEN (>15 years old) +INFANTS; N=4,716	Ongoing
MENENDEZ IP.2007.31080.002 MiPPAD	MALARIA TREATMENT	IV	PACTR2010020001429343	Mefloquine, Sulphadoxine-pyrimethamine, Cotrimoxazole, Placebo	Hoffman-La Roche, UCB Pharma, Carreras/Bonals	PREGNANT WOMEN (HIV-positive, >15 years old)+INFANTS; N=1,070	Ongoing

MWAPASA IP.2007.31060.003 ADAPT ADJUST	MALARIA TREATMENT	IV	PACTR201303000506302	Dihydroartemisinin-piperaquine		CHILDREN, Patients with uncomplicated *P. falciparum* malaria; N=200	Ongoing
MWAPASA IP.2007.31060.003 ADAPT ARV-ACT Theme 1, Phase 1, Step 1	MALARIA TREATMENT	III	PACTR201003000187129 3	Amodiaquine-artesunate Dihydroartemisinin-piperaquine Artemether-lumefantrine; Antiretroviral drug combinations [3TC-d4T-NVP, Trioimune, Cipla; 3TC-AZT-EFV (combivir plus efavirenz); 3TC-AZT-NVP (combivir plus NVP); TDF-3TC-AZT-LPV/r (tenofovir, combivir plus lopinavir/ritonavir)]	Sanofi-Aventis, Sigma-Tau, Novartis	ADULTS, HIV+ individuals receiving ART; N= 84	Completed
MWAPASA IP.2007.31060.003 ADAPT ARV-ACT Theme 1, Phase 1, Step 2	MALARIA TREATMENT	III	PACTR201003000197140 9	Amodiaquine-artesunate Dihydroartemisinin-piperaquine Artemether-lumefantrine; Antiretroviral drug combinations [3TC-d4T-NVP, Trioimune, Cipla; 3TC-AZT-EFV (combivir plus efavirenz); 3TC-AZT-NVP (combivir plus NVP); TDF-3TC-AZT-LPV/r (tenofovir, combivir plus lopinavir/ritonavir)]	Sanofi-Aventis, Sigma-Tau, Novartis	ADULTS, HIV+ individuals receiving ART; N=209	Ongoing
MWAPASA IP.2007.31060.003 ADAPT ARV-ACT Theme 1, Phase 2	MALARIA TREATMENT	IV	PATCR201311000659400	Amodiaquine-artesunate Dihydroartemisinin-piperaquine Artemether-lumefantrine; Antiretroviral drug combinations [3TC-d4T-NVP, Trioimune, Cipla; 3TC-AZT-EFV (combivir plus efavirenz); 3TC-AZT-NVP (combivir plus NVP); TDF-3TC-AZT-LPV/r (tenofovir, combivir plus lopinavir/ritonavir)]	Sanofi-Aventis, Sigma-Tau, Novartis	ADULTS (15-65 years), HIV+ individuals receiving ART; N=489	Ongoing
NDIAYE TA.2010.40200.032	MALARIA TREATMENT	IV	NCT01449045	Sulfadoxine-pyrimethamine, Amodiaquine, Artemether-lumefantrine		CHILDREN (3 months-10 years); N=4,554	Completed
OBONYO TA.2011.40200.059	MALARIA TREATMENT	III	PACTR201209000419241	Clindamycin, quinine, artemether-lumefantrine		CHILDREN (6 months - 5 years); N=384	Ongoing
OGUTU SP.2011.41304.062 PfSPZ Challenge Study	MALARIA VACCINES	I	PACTR201211000433272	Aseptic, purified, cryopreserved P. falciparum sporozoites (PfSPZ) [Investigational New Drug 14267: PfSPZ Challenge is	Sanaria Inc.	ADULTS (18-40 years); N=28	Completed

				currently filed with the US Food and Drug Administration (FDA)]			
PHIRI TA.2008.40200.016 MALARID	MALARIA TREATMENT	IV	PACTR201005000214168 2	Ferric ammonium citrate, Placebo	Malawi Pharmacies	CHILDREN (4-24 months); N=245	Ongoing
STRUB-WOURGAFT MS.2009.10800.004	MALARIA TREATMENT	IV	PACTR201202000278282	Artesunate-mefloquine, Artemether-lumefantrine		CHILDREN (6 months-5 years); N=940	Ongoing
TER KUILE IP.2007.31080.003 IPTp–SP	MALARIA TREATMENT	IV	NCT01084213	Sulfadoxine-pyrimethamine, Artemether-lumefantrine	Novartis	PREGNANT WOMEN+INFANT (>16 years old); N=5,000	Ongoing
TER KUILE IP.2007.31080.003 IPTp–SP	MALARIA TREATMENT	III	PACTR201103000280319 & ISRCTN69800930	Sulfadoxine-pyrimethamine, Dihydroartemisinin-piperaquine, Artemether-lumefantrine, Artesunate-amodiaquine, mefloquine-artesunate	Durbin PLC, Sigma-Tau	PREGNANT WOMEN+INFANT (>16 years old); N=1,675	Ongoing
THEISEN IP.2007.31100.001 GMZ2-IP Mal Vac	MALARIA VACCINES	II	PACTR201006000203353 7	GMZ2: GLURP + MSP3 hybrid	SSI	CHILDREN; N=1,847	Ongoing
THEISEN IP.2007.31100.001 GMZ2-IP Mal Vac	MALARIA VACCINES	I	NCT00703066	GMZ2: GLURP + MSP3 hybrid	SSI	CHILDREN (1-5 years); N=30	Completed
TIONO TA.2009.40200.019	MALARIA TREATMENT	IV		Clindamycin, Quinine, Artemether-lumefantrine		CHILDREN (6 months-5 years); N=6,191	Ongoing
VAN GEERTRUYDEN MS.2010.10800.004 QuinACT	MALARIA TREATMENT	III	NCT01374581	Sulphadoxine-Pyrimethamine, Mefloquine		PREGNANT WOMEN (HIV-, step1; HIV+, step 2)+INFANT; N=5,786	Ongoing

4.1 Integrated projects and clinical trials

4.1.1 4ABC study

EDCTP Project Coordinator:	Umberto D'Alessandro (Prince Leopold Institute of Tropical Medicine, Belgium)
EDCTP Call Title:	Support of phase II-III drug trials for uncomplicated malaria using novel artemisinin-based combination drugs
EDCTP Project Title:	Evaluation of 4 artemisinin-based combinations for treating uncomplicated malaria in African children
EDCTP Project Code:	CT.2004.31060.001
EDCTP Project Start Date:	5 December 2005
EDCTP Project End Date:	30 June 2010
Collaborators:	• Abdel Babiker (Medical Research Council (MRC), UK) • Francis Bajunirwe (Mbarara University of Science and Technology, Uganda) • Quique Bassat (Centre de Recerca en Salut Internacional de Barcelona (CRESIB), Spain) • Julia Critchley (University of Liverpool, UK) • Carrol Gambie (University of Liverpool, UK) • Paul Garner (University of Liverpool, UK) • Jean Pierre van Geertruyden (Prince Leopold Institute of Tropical Medicine (ITM), Belgium) • Raquel Gonzales (Manhiça Health Research Center (CISM), Mozambique) • Philippe Jean Guerin (Epicentre, France) • Robert T Guiguemdé (Centre Muraz, Burkina Faso) • Jean Paul Guthmann (Epicentre, France) • Moses Kamya (Makerere University, Uganda) • Corine Karema (Programme National de Lutte contre le Paludisme, Rwanda) • Bertrand Lell (University of Tübingen, Germany) • Eusebio Macete (CISM, Mozambique) • Sónia Machevo (CISM, Mozambique) • Pierre Blaise Matsiegui (Albert Schweitzer Hospital, Gabon) • Clara Menendez (Hospital Clinic of Barcelona, Spain) • Martin Meremikwu (University of Calabar, Nigeria) • Modest Mulenga (Tropical Diseases Research Centre, Zambia) • Theonest Mutabingwa (National Institute for Medical Research (NIMR), Tanzania) • Lawrence Mwananyanda (Tropical Diseases Research Centre, Zambia) • Carolyn Nabasumba (Mbarara University of Science and Technology, Uganda) • Nathan Bakyaita Nsubuga (Makerere University, Uganda) • Piola, Patrice (Epicentre Uganda, Uganda) • Claude Rwagacondo (Programme National de Lutte contre le Paludisme, Rwanda) • Caroline Sabin (University College London, UK) • Francisco Saute (CISM, Mozabique) • Ambrose Talisuna (Ministry of Health, Uganda) • Halidou Tinto (Centre Muraz, Burkina Faso) • Innocent Valea (Centre Muraz, Burkina Faso) • Paula Williamson (University of Liverpool, UK) • Adoke Yeka (Makerere University, Uganda)
Site Principal Investigator(s):	• Umberto D'Alessandro (Antwerpen, Belgium) • Halidou Tinto (Bobo Dioulasso, Burkina Faso)

	• Pierre Matsiegui (Libreville, Gabon) • Sonia Machevo (Manhiça, Mozambique) • Martin Meremikwu (Cross River State, Nigeria) • Corine Karema (Kigali, Ruanda) • Patrice Piola (Kampala, Uganda) • Moses Kamya (Kampala, Uganda) • Carolyne Nabasumba (Mbarara, Uganda) • Modest Mulenga (Ndola, Zambia)
Clinical Trial/Study Sponsor:	Prince Leopold Institute of Tropical Medicine, Antwerp (Belgium)
Trial/Study title:	Evaluation of 4 artemisinin-based combinations for treating uncomplicated malaria in African children
Goal:	The main objective is to compare the safety and efficacy of 4 artemisinin-based combinations (ACT) [amodiaquine-artesunate (AQ+AS), dihydroartemisinin-piperaquine (DHAPQ), artemether-lumefantrine (AL) and chlorproguanil/dapsone plus artesunate (CDA) for single and repeat treatments of uncomplicated malaria in children. Safety was determined by registering and grading adverse events and by laboratory, and vital signs evaluations. Their incidence was compared between the different study arms.
Primary Objective(s):	1. PCR unadjusted treatment failure (TF28U): all treatment failures detected during the active follow up, regardless of genotyping (time frame: day 28) 2. PCR adjusted treatment failure up to day 28 (TF28A): all early failures before day 14 plus the recurrent parasitaemias detected at day 14 or later and classified by genotyping as recrudescence (time frame: day 28).
Secondary Objective(s):	1. PCR unadjusted treatment failure up to day 63 (TF63U): TF28U plus all cases of recurrent parasitaemia (symptomatic or asymptomatic) detected between day 29 and day 63 by passive follow up, regardless of genotyping (time frame: day 63) 2. PCR adjusted treatment failure for the whole period of passivesurveillance (TFAPS): TF28A plus all episodes of recurrent parasitaemia identified as recrudescence by genotyping (time frame: day 28) 3. Fever clearance time 4. Asexual parasite clearance time 5. Gametocytaemia (prevalence and density) at day 7, 14, 21 and 28 after treatment (for both active follow-ups) (time rame: 28 days) 6. Hb changes day 3, 7, 14 and 28 (first and second follow up) (time frame: 28 days) 7. Clinical malaria after first active follow-up (time frame: 28 days) 8. Clinical malaria after second active follow-up (time frame: Up to 7 months) 9. Time frame (TF) second clinical episode (D28 and D63) (time frame: 63 days) 10. Changes in the frequency of mutations in the dihydrofolate reductase (DHFR) gene at day 0 first follow-up and day re-appearance of parasitaemia (for patients treated with CDA - Note that CDA arm was discontinued on 17.02.2008 because of safety concerns). 11. Safety profiles including significant changes in relevant laboratory values (time frame: up to 7 months).
Clinical Trial/Study site(s):	• Nanoro (Burkina Faso) • Afokang and Pamol (Nigeria)

	• Fougamou and Lambaréné (Gabon) • Mbarara, Jinja and Tororo (Uganda) • Rukara and Mashesha (Rwanda) • Ndola (Zambia) • Manhiça (Mozambique)
Collaborating site(s):	• Institute of Tropical Medicine, Antwerp (Belgium) • Liverpool School of Tropical Medicine and University of Liverpool (UK) • Centre Muraz/IRSS, Bobo-Dioulasso (Burkina Faso) • University of Calabar, Calabar (Nigeria) • Tropical Diseases Research Centre, Ndola (Zambia) • University Hospital Tuebingen, Tübingen (Germany) Albert Schweitzer Hospital, Lambaréné (Gabon) • Uganda Malaria Surveillance Project (Uganda) • Mbarara University of Science and Technology, Mbarara (Uganda) • Programme National Lutte contre le Paludisme, Kigali (Rwanda) • Center for International Health Research, University of Barcelona, Barcelona (Spain) • Manhiça Health Research Centre, Manhiça (Mozambique)
Study design:	Phase III randomised, controlled, open-label study Randomised controlled trial, comparing 4 combinations of artesunate derivatives: **Arm 1:** Intervention with amodiaquine-artesunate (ASAQ) consisting of a fix-dose combination tablet containing artesunate-amodiaquine in three different dosages, to be used according to patient age and weight: 25mg/67.5mg; 50mg/135mg; 100mg/270mg (other name of ASAQ is Coarsucam by Sanofi-Aventis). **Arm 2:** Intervention with dihydroartemisinin-piperaquine (DHAPQ) consisting of DHAPQ tablets contain either 20/160mg or 40/320mg of dihydroartemisinin (DHA) and piperaquine phosphate (PQ) respectively. To be noted: since the batches of the study drug DHAPQ expired at the end of October 2008 and the unavailability of a new batch of DHAPQ from the manufacturer, the recruitment in the DHAPQ arm had to be discontinued on 30 October 2008. A formal amendment was submitted to all the concerned ECs and competent authorities (other names for DHAPQ is Eurartekin by Sigma-Tau). **Arm 3:** Intervention with artemether-lumefantrine (AL) consisting of tablets containing 20 mg of Artemether and 120 mg of Lumefantrine (other names for AL are Coartem and Riamet by Novartis) **Arm 4:** Intervention with Lapdap (Chlorproguanil-Dapsone) + artesunate (AS) consisting of Lapdap tablets contain 15/18.75mg or 80/100mg of Chlorproguanil Hydrochloride and Dapsone, respectively. Arsumax® tablets contain 50mg Artesunate (other names of CDA are Lapdap by GSK and Arsumax by Sanofi-Aventis and Guilin Pharmaceutical). TO BE NOTED: following GlaxoSmithKline decision to discontinue the clinical development of the fixed-doses combination of Lapdap (Chlorproguanil-Dapsone) and artesunate, the Lapdap plus Artesunate arm was immediately discontinued in this study, on 17 February 2008. A formal amendment was approved by

	several ethics and regulatory authorities by June 2008.
Study population:	4,116 children 6-59 months old with uncomplicated *P. falciparum* malaria
Product(s):	• Amodiaquine-artesunate (ASAQ) • Dihydroartemisinin-piperaquine (DHAPQ) • Artemether-lumefantrine (AL) • Lapdap (Chlorproguanil-Dapsone) + artesunate (AS) (CDA)
Manufacturer/Developer:	• Sigma-Tau • Sanofi-Aventis • Glaxo SmithKline • Novartis
Cofunders:	• Medicines for Malaria Venture [MMV] (Switzerland) • Carlos III Health Institute (Spain) • Medical Research Council [MRC] (UK) • Prince Leopold Institute of Tropical Medicine, (Belgium) • GlaxoSmithKline Foundation, Department for International Development [DFID] (UK)
Trial Registration number(s):	NCT 00393679
Status:	Completed
Results and Outcomes:	The results from this study have shown that AL, ASAQ, and DHAPQ had excellent efficacy up to day 63 post-treatment. However, the risk of recurrent infections was significantly lower, even in areas of high transmission, for DHAPQ, followed by ASAQ, and then AL. CDA treatment was withdrawn early in course of the study for safety reasons (high risk of developing severe anaemia in glucose-6 phosphate dehydrogenase deficient individuals). Furthermore, the study showed that CDA had the lowest efficacy of the four ACTs. This large multicentre trial covered seven African countries with different malaria endemicities and has generated information that will assist national malaria control programmes in sub-Saharan Africa in choosing the most appropriate ACTs for their specific setting. AL and ASAQ are already included in the antimalarial drug policies of many sub-Saharan African countries. Importantly, the data also showed that DHAPQ is a new option for the treatment of uncomplicated malaria with the added value of its long lasting prophylaxis in comparison to the other two ACTs. These results have contributed to the recent registration of DHAPQ by EMEA. This project is an excellent model of a strong North-South partnership, involving 10 sites in 7 African countries (Burkina Faso, Gabon, Mozambique, Nigeria, Rwanda, Uganda and Zambia) in partnership with 5 European institutions (Belgium, United Kingdom, Germany, France and Spain) as well as the product development partnership, Medicines for Malaria Venture (MMV).
PhD studies:	Title: The best approach for retreating patients with recurrent malaria in the era of ACT Candidate: Adoke Yeka (ITM, Belgium) Dates: 5 December 2005-4 April 2013
	Title: Antimalarial treatment policies in Africa: How to improve the existing strategies? The experience of Burkina Faso Candidate: Innocent Valéa Yeka (Institute of Tropical Medicine, Antwerp, Belgium) Dates: 5 December 2005-27 May 2013

	Title: The value of individual patient data for mixed treatment comparison meta-analysis Candidate: Sarah Donegan (University of Liverpool, UK) Dates: January 2006-23 September 2011
Other/Sub-studies:	Efficacy of quinine, artemether-lumefantrine and dihydroartemisinin-piperaquine for recurrent uncomplicated malaria in Ugandan children
Publications:	1. D'Alessandro, U. Artemisinin combination therapies (ACTs) for uncomplicated malaria in African children: The 4ABC trial, preliminary results. *Tropical Medicine and International Health* 2010; 15(8): S13. 2. D'Alessandro U on behalf of The Four Artemisinin-Based Combinations (4ABC) Study Group. A Head-to-Head Comparison of Four Artemisinin-Based Combinations for Treating Uncomplicated Malaria in African Children: A Randomised Trial. *PLoS Med.* 2011; 8(11): e1001119 3. Donegan S, Williamson P, D'Alessandro U, Smith CT. Assessing the consistency assumption by exploring treatment by covariate interactions in mixed treatment comparison meta-analysis: individual patient-level covariates versus aggregate trial-level covariates. *Statistics in Medicine* 2012; 31(29):3840-3857. 4. Donegan S, Williamson P, D'Alessandro U, Garner P, Smith CT. Combining individual patient data and aggregate data in mixed treatment comparison meta-analysis: Individual patient data may be beneficial if only for a subset of trials. *Statistics in Medicine* 2012; 32(6): 914-930. Doi: 10.1002/sim.5584. 5. Ravinetto RM, Talisuna AO, De Crop M, van Loen H, Menten J, Van Overmeir C, Tinto H, Gonzalez R, Meremikwu M, Nabasuma C, Ngoma GM, Karema C, Yeka A, Chaponda M, Van geertruyden JP, D'Alessandro U. Challenges of non-commercial multicentre North-South collaborative clinical trials. *Tropical Medicine and International Health* 2013; 18(2): 237-241. Doi:10.1111/tmi.12036 6. Yeka A, Tibenderana J, Achan J, D'Alessandro U Talisuna AO. Efficacy of Quinine, Artemether-Lumefantrine and Dihydroartemisinin-Piperaquine as Rescue Treatment for Uncomplicated Malaria in Ugandan Children. *PLoS ONE* 2013; 8(1): e53772. Doi:10.1371/journal.pone.0053772

4.1.2 SMAC-II and III (Dose Optimisation Study)

EDCTP Project Coordinator:	Peter G. Kremsner (University of Tübingen, Germany)
EDCTP Call Title:	Support of Phase II-III (dose optimization) drug trials for the treatment of severe malaria using artemisinin compounds
EDCTP Project Title:	Artesunate for severe malaria in African children
EDCTP Project Code:	CT.2004.31070.001
EDCTP Project Start Date:	3 July 2006
EDCTP Project End Date:	5 April 2013
Collaborators:	• Tsiri Agbenyega (University of Science and Technology-Kwame Nkrumah, Ghana) • Kalifa Bojang (Medical Research Council Laboratories, The Gambia) • Markus Gmeiner (Vienna School of Clinical Research, Austria) • Saadou Issifou (Albert Schweitzer Hospital, Gabon) • Christa Janko (Vienna School of Clinical Research, Austria) • Maryvonne Kombila (Cambodian University of Health Sciences, Gabon) • Sanjeev Krishna (St. George's University of London, UK) • James Mwenechanya (Queen Elizabeth Central Hospital, Malawi) • Charles Newton (Kenya Medical Research Institute (KEMRI), Kenya) • Gabriele Schreyer (Vienna School of Clinical Research, Austria) • Terrie Taylor (Queen Elizabeth Central Hospital, Malawi)
Study/Trial 1	**SMAC-II (artesunate study in severe malaria)**
Site Principal Investigator(s):	• Peter Kremsner (Tuebingen, Germany & Lambaréné, Gabon) • Saadou Issifou (Lambaréné, Gabon) • Maryvonne Kombila (Libreville, Gabon) • Terrie Taylor (Blantyre, Malawi)
Clinical Trial/Study Sponsor:	Medicines for Malaria Venture, Geneve (Switzerland)
Trial/Study title:	Phase II Randomised, Double-Blind Study of the Efficacy, Safety, Tolerability, and Pharmacokinetics of Intravenous Artesunate in Children With Severe Malaria
Goal:	The overall goal of the study is to compare the efficacy, safety and tolerability of the standard 5-dose iv regimen with a simplified 3-dose iv regimen of Artesunate in children with severe malaria.
Primary Objective(s):	To evaluate the effectiveness of 2 intravenous artesunate dosing regimens (2.4 mg/kg initially and at 12, 24, 48, and 72 hours or 4.0 mg/kg initially and at 24 and 48 hours) in clearing *P. falciparum* parasites in children with severe malaria.
Secondary Objective(s):	1. To compare the tolerability and safety of the 2 intravenous artesunate dosing regimens 2. To evaluate differences in the pharmacokinetic profile of intravenous artesunate by patient age and clinical presentation.
Clinical Trial/Study site(s):	• Albert Schweitzer Hospital, Lambaréné (Gabon) • Université de Medecine et Science de la Santé, Libreville (Gabon) • Queen Elizabeth Central Hospital, Blantyre (Malawi)
Collaborating site(s):	• School of Medical Sciences, University of Sciences and Technology, Kumasi (Ghana) • Kenya Medical Research Institute (KEMRI), Kilifi (Kenya) • MRC Laboratories, Banjul (The Gambia)

	• University of Tübingen, Tübingen (Germany) • Vienna School of Clinical Research, Vienna (Austria) • St George's Hospital Medical School, London (UK)
Study design:	A double-blind, multicentre, randomised, parallel-group study of the antimalarial activity and safety of 2 intravenous artesunate regimens (2.4 mg/kg initially and at 12, 24, 48, and 72 hours or 4.0 mg/kg initially and at 24 and 48 hours) in children with severe *P. falciparum* malaria. The study will also evaluate the pharmacokinetic profile of artesunate in pediatric patients. Patients will be randomised to 1 of 2 cohorts. Cohort 1: artesunate 2.4 mg/kg on admission, and at 12, 24, 48, and 72 hours (12 mg/kg total dose); or Cohort 2: artesunate 4 mg/kg on admission, and at 24 and 48 hours (12 mg/kg total dose), normal saline will be administered as a placebo at 12 and 72 hours in order to maintain the study blind. As soon as the patient is able to receive oral medication and no signs and symptoms of severe malaria are present, but not before the last pharmacokinetic sample is taken (approximately 50 hours after the start of therapy), a single dose of sulfadoxine/pyrimethamine will be administered to ensure parasitological cure. Randomisation will be balanced at each study site in a 1:1 ratio for each artesunate regimen. Patient participation will be for at least 28 days following the first dose of study drug. Patients will be hospitalized for at least 4 days (day 0, 1, 2, and 3). The patient will return to the study site for study visits on days 7, 14, and 28. If adverse events reported during the study are unresolved by day 28, patients will be followed for an additional 30 days or until resolution of the event or determination that no further medical management is deemed necessary. Similarly, the investigator will instruct the patient to return to the study site if any untoward event occurs within 30 days of completing the study drug.
Study population:	CHILDREN with severe malaria (6 months-10 years) 200 patients planned, 182 patients analysed (ITT population); 93 patients analysed in cohort 1 89 patients analysed in cohort 2
Product(s):	Artesunate
Manufacturer/Developer:	WRAIR
Cofunders	• Medicines for Malaria Venture (MMV, Switzerland) • Federal Ministry of Education and Research (BMBF, Germany)
Trial Registration number(s):	NCT00522132
Status:	Completed
Results and Outcomes:	The results of the phase II studies showed that treatment of severe malaria can be simplified to a 3-dose regimen (given at 0, 24 and 48 h) with a total dose of 12 mg/kg artesunate intravenously administered instead of the conventional 5-dose regimen of intravenous artesunate (given at 0, 12, 24, 48 and 72 hours).

	If outcome is positive, the results of the ongoing phase III studies investigating further simplification of the treatment of severe malaria by administering artesunate in a simplified 3-dose regimen intramuscularly rather than intravenously have potential for cost saving and improved severe malaria management in resource limited settings. These results will inform policy and evidence-based future changes in malaria treatment guidelines by WHO for malaria endemic countries. The study timelines were from September 2007 to December 2008.
PhD study	Title: Efficacy, Safety and Tolerability of two different regimen of intravenous Artesunate therapy in children with severe malaria Candidate: Matthias Duscha (University of Tuebingen, Germany) Dates:
Publications:	1. Kremsner, PG, Taylor T, Issifou S, Kombila M, Chimalizeni Y, Kawaza K, Bouyou Akotet MK, Duscha M, Mordmuller B, Kösters K, Humberg A, Scott Miller R, Weina P, Duparc S, Möhrle J, Kun JFJ, Planche T, Teja-Isavadham P, Simpson J, Köhler C, Krishna S. A simplified intravenous artesunate regimen for severe malaria. *Journal of Infectious Diseases*, 2012; 205: 312-9
Study/Trial 2	**SMAC-Dose Optimization Study (Artesunate Follow-Up Study for severe malaria in children)**
Site Principal Investigator(s):	• Peter Kremsner (Tuebingen, Germany & Lambaréné, Gabon) • Saadou Issifou (Lambaréné, Gabon) • Maryvonne Kombila (Libreville, Gabon) • Terrie Taylor (Blantyre, Malawi) • Tsiri Agbenyega (Kumasi, Ghana) • Charles Newton (Kilifi, Kenya) • Bernhards Ogutu (Kisumu, Kenya) • Kalifa Bojang (Banjul, The Gambia) • Sanjeev Krishna (London, UK)
Clinical Trial/Study Sponsor:	Universitätsklinikum Tübingen, Tübingen (Germany)
Trial/Study title:	Phase III Comparative, Open-Label, Dose and Regimen Optimisation Follow-up Study of Intravenous and Intramuscular Artesunate in African Children With Severe Malaria
Goal:	The overall goal of the study is to compare the efficacy, safety and tolerability of 3-dose regimens: iv artesunate and im artesunate simplified dosing regimens (4 mg/kg artesunate at 0, 24 and 48 hours; 12 mg/kg total dose) and the standard iv treatment dosing regimen (2.4 mg/kg artesunate at 0, 12, 24, 48 and 72 hours; 12 mg/kg total dose).
Primary Objective(s):	The primary objective of the study is to evaluate the non-inferiority of iv artesunate and im artesunate simplified dosing regimens (4 mg/kg artesunate at 0, 24 and 48 hours; 12 mg/kg total dose) to the standard im treatment dosing regimen (2.4 mg/kg artesunate at 0, 12, 24, 48, 72 hours; 12 mg/kg total dose) in clearing parasitaemia in children with severe malaria.
Secondary Objective(s):	1. To compare the tolerability and safety of the 3 artesunate dosing regimens 2. To evaluate differences in the pharmacokinetic profile of parenteral artesunate by patient age and clinical presentation (total of 300 patients to be studied).

	Exploratory Analysis: 1. To assess non-invasive oto-acoustic tests linked to disease 2. To assess predictability of fatal malaria by means of the Lambaréné-Organ-Dysfunction Score (LODS) 3. To analyze genetic polymorphisms in humans and parasites linked to disease and treatment 4. To assess in vitro drug sensitivity of clinical study isolates.
Clinical Trial/Study site(s):	• Albert Schweitzer Hospital, Lambaréné (Gabon) • Université de Médecine et Science de la Santé, Libreville (Gabon) • Queen Elizabeth Central Hospital, Blantyre (Malawi) • School of Medical Sciences, University of Sciences and Technology, Kumasi (Ghana) • Kenya Medical Research Institute (KEMRI), Centre for Geographical Medicine (Coast), Kilifi (Kenya) • Kenya Medical Research Institute (KEMRI), Kondele Childrens Hospital, Kisumu (Kenya) • MRC Laboratories, Banjul (The Gambia)
Collaborating site(s):	• Vienna School of Clinical Research, Vienna (Austria) • St George's Hospital Medical School, London (UK) • Institut für klinische Pharmakologie, Stuttgart (Germany) • University of Innsbruck (Austria)
Study design:	An open label, multicenter, parallel-group, three arm follow-up study to compare the antimalarial activity and safety of 3 artesunate dosing regimens in children with severe *P. falciparum* malaria: iv artesunate 4 mg/kg initially, and at 24 and 48 (12 mg/kg total dose); im artesunate 4 mg/kg initially, and at 24 and 48 hours (12 mg/kg total dose), im artesunate 2.4 mg/kg initially, and at 12, 24, 48 and 72 hours (12 mg/kg total dose). The study will also evaluate the pharmacokinetic profile of artesunate in pediatric patients. Patients will be randomised to 1 of 3 cohorts. Cohort 1: iv artesunate 4 mg/kg initially, and at 24 and 48 hours (12 mg/kg total dose); or Cohort 2: im artesunate 4 mg/kg initially, and at 24 and 48 hours (12 mg/kg total dose), or Cohort 3: im artesunate 2.4 mg/kg initially, and at 12, 24, 48, and 72 hours (12 mg/kg total dose). Patient participation will be for at least 28 days following the first dose of study drug. Patients will be hospitalized for at least 3 days. The patient will return to the study site for study visits on Days 7, 14, and 28. If adverse events reported during the study are unresolved by day 28, patients will be followed for an additional 30 days or until resolution of the event or determination that no further medical management is deemed necessary. Similarly, the investigator will instruct the patient to return to the study site if any untoward event occurs within 30 days of completing the study drug. Artesunate treatment will be completed with another antimalarial, e.g. sulfadoxine-pyrimethamine (25 mg/kg and 1.25 mg/kg) at discharge. Adjunctive therapy, including fluids, glucose and blood will follow SMAC standards based on WHO guidelines for the treatment of severe malaria.

	In case of initial treatment failure with intravenous or intramuscular artesunate or a severe drug reaction to artesunate, parenteral quinine will be given to treat severe malaria, if patients had previous quinine therapy (within 12 hours), continue administering 8mg quinine base/kg every 8 hours, if no previous quinine therapy, give loading dose of 16 mg/kg and continue with normal regimen). Recurrent malarial infection within 28 days will be treated with artemether/lumefantrine. The study timelines were from December 2010 to April 2013 (Recruitment period from July 2011 until September 2012).
Study population:	CHILDREN with severe malaria (≤14 years), N=1,047. 348 patients planned per cohort approx. 300 patients to be included in PK-& genetic polymorphism-analysis approx. 200 patients to be included in auto-acoustic tests approx. 200 patients to included in in vitro-sensitivity assay
Product(s):	Artesunate
Manufacturer/Developer:	Guillin Pharmaceuticals, Shanghai (China)
Cofunders:	Federal Ministry of Education and Research (BMBF, Germany)
Trial Registration number(s):	PACTR201102000277177
Status:	Ongoing
Results and Outcomes:	All study sites completed recruitment in early October 2012 (Lambaréné, Libreville, Kumasi, Banjul, Kisumu and Kilifi). Study is in close-out phase, analysis expected for March 2013
Other/Sub-studies:	• PK- and exploratory analysis will not be performed on the whole study population but only in selected centers on a limited number of patients: – PK: 300 patients to be analysed from the population recruited in Lambaréné, Kumasi and Kisumu. – Genetic Polymorphisms: 300 patients to be analysed from the population recruited in Lambaréné, Kumasi and Kisumu. – Oto-acoustic tests: 200 patients to perform these tests from the populations recruited in Lambaréné, Kumasi and Kisumu. – In vitro-sensitivity: 200 patients to be analysed from the population recruited in Lambaréné.
Publications:	In progress

4.1.3 PREGACT

EDCTP Project Coordinator:	Umberto D'Alessandro (Prince Leopold Institute of Tropical Medicine, Belgium)
EDCTP Call Title:	Support of clinical trials, capacity building and networking in malaria in pregnancy
EDCTP Project Title:	Safe and Efficacious Artemisinin-based Combination Treatments for African Pregnant Women With Malaria
EDCTP Project Code:	IP.2007.31080.001
EDCTP Project Start Date:	6 February 2009
EDCTP Project End Date:	30 September 2014
Collaborators:	• Sharleen Braham (Prince Leopold Institute of Tropical Medicine (ITM), Belgium) • Victor Chalwe (Tropical Diseases Research Centre, Zambia) • Yves Claeys (ITM, Belgium) • Jean Pierre van Geertruyden (ITM, Belgium) • Jenny Hill (University of Liverpool, UK) • Christa Janko (Vienna School of Clinical Research, Austrial) • Gertrude Kalanda (University of Malawi) • Linda Kalilani-Phiri (University of Malawi) • Charles Mangani (University of Malawi) • Christine Manyando (Tropical Diseases Research Centre, Zambia) • Joris Menten (ITM, Belgium) • Modest Mulenga (Tropical Diseases Research Centre, Zambia) • Theonest Mutabingwa (National Institute for Medical Research (NIMR), Zambia) • Reuben Ndindi (University of Malawi) • Vysaul Nyirongo (Malawi-Liverpool-Wellcome Trust Research Programme, Malawi) • Rafaella Ravinetto (ITM, Belgium) • Stephen Rulisa (University Central Hospital of Kigali, Rwanda) • Henk Schallig (Royal Tropical Institute (KIT), Netherlands) • Gabriele Schreyer (Vienna School of Clinical Research, Austria) • Harry Tagbor (University of Science and Technology-Kwame Nkrumah, Ghana) • Christian Tahita (Institut de Recherche en Sciences de la Santé, Burkina Faso) • Feiko ter Kuile (University of Liverpool, UK) • Halidou Tinto (Centre Muraz, Burkina Faso) • Maminata Traore (Centre Muraz, Burkina Faso) • Peter J de Vries (ICRH-International Centre of Reproductive Health, Netherlands)
Site Principal Investigator(s):	• Umberto D'Alessandro (Antwerpen, Belgium) • Halidou Tinto, Marc Tahita, Maminata Traoré (Bobo Dioulasso, Burkina Faso) • Harry Tagbor (Kumasi, Ghana) • Linda Kalilani-Phiri & Victor Mwapasa (Blantyre, Malawi) • Modest Mulenga & Michael Nambozi (Nchlenge, Zambia)
Clinical Trial/Study Sponsor:	Institute of Tropical Medicine, Antwerp (Belgium)
Trial/Study title:	Safe and Efficacious Artemisinin-based Combination Treatments for African Pregnant Women With Malaria
Goal:	To determine the safety and efficacy of 4 ACTs (amodiaquine-artesunate or AQAS, dihydroartemisinin-piperaquine or DHAPQ;

	artemether-lumefantrine or AL, Mefloquine-artesunate or MQAS) when administered to pregnant women with *P. falciparum* infection during the second and the third trimester and collect explanatory variables for treatment failure (PCR-corrected) and for recurrent parasitaemia. Safety will be determined by registering adverse events and grading, laboratory, and vital signs evaluations. Their incidence will be compared between the different study arms. The primary hypothesis tested is the clinical equivalence (pair-wise non-inferiority) of the 4 treatment regimens with clinical equivalence defined as difference in treatment failure rates (PCR corrected) of 5% or less.
Primary Objective(s):	1. To compare the efficacy of AL, AQAS, MQAS and DHAPQ in terms of – Treatment failure (see definition below) by 63 days after start of treatment with or without genotyping – Time to treatment failure (PCR adjusted and unadjusted) during 63 days of active follow-up after treatment – Asexual parasite clearance time – Gametocytaemia (prevalence and density) at day 7, 14, 21, 28 and 63 after treatment, and gametocyte carriage (gametocyte-weeks) – Haematological recovery by 14, 28, 42 and 63 days post-treatment and at delivery – Preventing placenta *P. falciparum* malaria – Birth weight measured within 72 hrs of delivery 2. To describe the safety profile of AL, AQAS, MQAS and DHAPQ in terms of – Tolerability – Incidence of serious and non-serious adverse events until delivery
Secondary Objective(s):	1. To determine the relation between drug pharmacokinetics (partner drug) and response to treatment 2. To assess the in-vitro susceptibility of *P. falciparum* isolates collected before treatment and at time of recurrent infection to several drugs, including the partner drug tested, and to correlate their IC50 to treatment response.
Clinical Trial/Study site(s):	• Nanoro & Nazoanga (Burkina Faso) • Ejisu Sekyere East & Juaben Government Hospital, and Effiduase Government Hospital in the Sekyere East district, Ashanti Region (Ghana) • Madziabango & Mpemba Health Centers, Blantyre (Malawi) • St. Paul's' Hospital, Nchelenge Kashikishi & Kambwali Health Centers (Zambia)
Collaborating site(s):	• Institute of Tropical Medicine, Antwerp (Belgium) • Liverpool School of Tropical Medicine, Liverpool (UK) • Centre Muraz/IRSS, Bobo-Dioulasso (Burkina Faso) • Kwame Nkrumah University of Science and Technology, Kumasi (Ghana) • University of Malawi College of Medicine, Blantyre (Malawi) • Central University Hospital of Kigali, Kigali (Rwanda) • Tropical Diseases Research Centre, Ndola (Zambia) • Seattle Institute for Biomedical and Clinical Research & National Institute for Medical Research, Morogoro (Tanzania) • Vienna School of Clinical Research (Austria) • Institute of Tropical Medicine (KIT) & Academic Medical Center, Amsterdam (Netherlands)
Study design:	Phase IIIb randomised, controlled, open label study

	Randomised controlled trial, comparing 4 combinations of artesunate derivatives (DHAPQ, MQAS, AQAS and AL), to be tested in each country by a 3-arm trial using a "balanced incomplete block design". **Arm 1 (experimental): three-day treatment with dihydroartemisinin-piperaquine (DHAPQ)** DHAPQ tablets are green film coated intended for oral use and contain 20/160mg or 40/320mg of dihydroartemisinin (DHA) and piperaquine phosphate (PQ) respectively. In this trial the 40/320mg for adults will be used (other name of DHAPQ is Eurartesim and was developed by Sigma Tau in partnership with Medicines for Malaria Venture). **Arm 2 (experimental): three-day treatment with artesunate-mefloquine (MQAS)** MQAS will be provided as a fixed-dose ACT. There are 2 strengths (AS25+MQ55mg and AS100+MQ220mg) and dosing regimen is calculated according to 12 mg/kg AS and 24mg/kgMQ total dose over three days. Pregnant women will receive 2 tablets/day for 3 days. It is developed by Farmanguinhos with the Drugs for Neglected Diseases Initiative (DNDi). **Arm 3 (active comparator): three-day treatment with artesunate-amodiaquine (AQAS)** AQAS, developed by DNDi with Sanofi-Aventis and manufactured by Sanofi-Aventis, has been pre-qualified by the WHO in 2008 and is available in several African countries, including those involved in this trial. AQAS tablets are round, yellow on one side and white-slightly yellow on the other, with a breaking bar, AS engraved on one side and either 25, 50 or 100 on the other side. Tablets to be used in this trial are those 100mg/270mg AS/AQ, containing 100 mg of artesunate, 352.640 mg of amodiaquine hydrochloride corresponding to 270mg of amodiaquine base (other name of AQAS is Winthrop®). **Arm 4 (active comparator): three-day treatment with artemether-lumefantrine (AL)** AL (tablets containing a FDC of 20 mg of artemether and 120 mg of lumefantrine) is manufactured by Novartis and has been extensively used in Africa for the treatment of uncomplicated malaria. AL was registered in Switzerland in 1999, has since received marketing authorisation in several endemic and non-endemic countries and it is WHO pre-qualified (other name of AL is Coartem®, Riamet).
Study population:	3,480 pregnant women and their infants
Product(s):	• Dihydroartemisinin-piperaquine • Artesunate-mefloquine • Artesunate-amodiaquine • Artemether-lumefantrine
Manufacturer/Developer:	• Sigma-Tau • Farmanguinhos (with the mediation from DNDi) • Sanofi-Aventis • Novartis
Cofunders:	• Medical Research Council (MRC, UK) • Austrian Federal Ministry of Science (Austria)

	• Netherlands Organisation for Scientific Research (NWO), (Netherlands) • Liverpool School of Tropical Medicine (UK) • Prince Leopold Institute of Tropical Medicine (Belgium) • Bill & Melinda Gates Foundation (USA)
Trial Registration number(s):	NCT 00852423 PACTR 201008000248160
Status:	Ongoing
Results and Outcomes:	Summary of achievements (from February 2010 until March 2013) 1. In Clinical trials: • Phase III studies (main trial): – Recruitment is completed in 3 out of the 4 recruiting sites, i.e. Malawi, Zambia and Burkina Faso and in Ghana is about 65% of their total sample size. So far, 3,205 patients have been enrolled from a total sample size of 3,480 (and 2,664 deliveries have been recorded) – The delay in recruitment in Ghana during this reporting period is mainly due to the temporary suspension of the trial by the local Food and Medicine Board (from April to October 2012, coinciding with the peak of the malaria season in the area). Therefore, the recruitment period for this collaborating centre will need to be extended until August/September 2013, which in consequence the last follow-up visit of the last newborn will take place by August/September 2014. An additional recruitment center has been identified in order to allow completion of the trial within the NCE period (September 2014). • Three sub-studies: – Sub-study 1: Malaria signs and symptoms in pregnancy (Nanoro, BF). Six hundred pregnant women have been enrolled, 200 with suspected clinical malaria and 400 as controls. Analysis is in progress; however, active screening to early detect and treat malaria infection should be performed in all pregnant women attending a health facility – Sub-study 2: Malaria endemicity in Nchelenge District (ZM). This ancillary study was done between February 2012 and March 2012 and 782 children (under 10 years old meeting the inclusion/exclusion criteria) were enrolled in the study – Sub-study 3: Malaria in pregnancy in Rwanda (RW). Study site(s) preparations completed. Recruitment is scheduled to start in April 2013. 2. In capacity development: – There have been minor infrastructure upgrades during this period. Infrastructure upgrade, including a dedicated space was created for the performance of the trial in Ruhuha (Rwanda) – GCLP workshop, Antwerp, Belgium, February 2012. – Placenta histopathology, individual training for Dr Mubikayi, Barcelona August 2012 – GCP course (19-21 September 2012, Malawi) was attended by one study nurse – Project Management in Clinical and Epidemiological Research (24-26 September 2012, Malawi) was attended by two study nurses – One MSc student completed his master in February 2012. The second master student is expected to

	complete in July 2014 – Two PhDs are expected to finish by November 2013 and the other two are expected to finish by July/December 2014. 3. In networking: – Biweekly Trial Steering Committee meetings (TSC) and 3 DSMB meetings in February, June and October 2012 – PREGACT investigator's meeting was held at ASTMH, Atlanta, November 2012 – Malaria in pregnancy Consortium meeting was also held at ASTMH, Atlanta, November 2012 – One article published at AJTMH (2012) JAMA and one publication at International Innovation Journal (2011). Setbacks: The major setback of these studies is the accumulated delays in starting and temporarily interrupting recruitment in Ghana; firstly, because difficulties in obtaining the ethical approval and secondly, because the GCP inspection from the Ghanaian Food and Medicine Board (FMB), from April to October 2012. As consequence, completion of the follow up until delivery will be only possible by August 2014. Thereafter, they will need to finalise the database and the statistical analysis.
PhD studies:	Title: Antimalarial treatment safety and efficacy in pregnant women Candidate: Michael Nambozi (University of Antwerp, Belgium) Dates: July 2010-July 2014
	Title: Antimalarial treatment safety and efficacy in pregnant women Candidate: Marc Tahita (University of Antwerp, Belgium) Dates: June 2010-December 2014
	Title: The role of drugs in the control of malaria in pregnancy Candidate: Christine Manyando (University of Gent, Belgium & TDRC, Zambia) Dates: 1 January 2012-1 December 2013
	Title: Placental malaria in an area of low transmission, effects on incidence, diagnostic procedures and immune status Candidate: Steven Rulisa (University of Amsterdam) Dates: 1 March 2009-1 December 2013
MSc studies:	Title: How does the risk of morbidity and mortality in HIV-exposed infants who are breast fed compare with morbidity and mortality in HIV-exposed infants who receive replacement feeding? Candidate: Sebastian Hachizovu (MPH, Diseases Control, Institute of Tropical Medicine, Antwerp, Belgium) Dates: 2009-2010
	Title: Master in Public Health: Epidemiology and Clinical Research Candidate: Biébo Bihoun (Université Catholique Louvain (UCL) Belgium) Dates: September 2012-July 2014
Other/Sub-studies:	**Malaria signs and symptoms in pregnancy** Site Principal Investigator: Halidou Tinto Title: Clinical signs and symptoms of *P. falciparum* malaria infection (patent and sub-patent) in pregnant women living in an area of high seasonal transmission Purpose: Determine the clinical presentation of malaria during

	pregnancy Study site: Nanoro (Burkina Faso) Synopsis: A hospital-based descriptive study aiming at describing the clinical presentation of P. falciparum malaria among pregnant women will be carried out in rural Burkina Faso. All women attending Nanoro Hospital, either the routine ANC or the outpatient will be asked to participate to the study. After having obtained the informed verbal consent, age, parity, gestational age and signs and symptoms suggestive of malaria will be recorded by the maternity staff onto a standardized questionnaire. The axillary temperature and a blood sample (capillary) for parasitaemia, PCV and later genotyping will be collected on all included women. Women with a positive blood slide for malaria will be treated with oral quinine for 7 days for those in the first trimester and with ACT in the second and third trimester. Women with complicated malaria will be admitted to the maternity ward and treated with parenteral quinine followed by SP. Anaemia will be treated according to the national guidelines with oral ferrous sulphate and folic acid for one month. This study will provide information on the clinical presentation of malaria during pregnancy. Therefore, it may identify signs and symptoms in women to be treated with an ACT. **Malaria endemicity in Nchelenge District** Site Principal Investigator: Michael Nambozi Title: Defining the Malaria Burden in Nchelenge District using the WHO Malaria Indicators Survey Purpose: To characterise the malaria endemicity in Nchelenge district Primary Objective(s): To assess the prevalence of malaria infection and anaemia in among children less than 10 years Secondary Objective(s): To assess: 1. The knowledge of children's care takers on malaria and relative control measures; 2. The relationship between individual knowledge and interventions' use and the risk of infection and anaemia. Study site: Nchelenge (Zambia) Synopsis: This is a cross-sectional survey to be carried out in the rural communities of Kashikishi and Nchelenge (total population of 43,105); the sampling unit will be the household (defined as all the persons who occupy a housing unit) where all children < 10 will be included in the survey. A blood sample for Hb measurement and detection of malaria infection will be collected by finger prick on each study individual. Households will be selected according to pre-defined, computer-generated list of random numbers. This study will provide information on the malaria endemicity in the site where PREGACT is carried out. **Malaria in pregnancy in Rwanda** Site Principal Investigator: Steven Rulisa

	Title: Placental malaria in an area of low transmission, effects on incidence, diagnostic procedures and immune status Purpose Primary Objective(s): To determine the burden of malaria in pregnancy, either acute or placental infection, and to establish the best method to identify pregnancy-related malaria in Rwanda and to establish the degree of protective immunity against malaria in pregnancy over successive pregnancies. Secondary Objective(s): 1. To determine the incidence of placental malaria via placental biopsy. 2. To determine if there are any immunological markers present in pregnant women that might give an indication of protection in subsequent pregnancies. 3. To determine the association between low birth weight and pre-maturity to maternal malaria. Study sites: Muhima Hospital (Kigali) and Bugesera Hospital and Ruhuha Health Centre in Bugesera District located in eastern Province (Rwanda) Synopsis: In Rwanda, not much is known about malaria in pregnancy. A report from 2005 has described a 13.5% prevalence of malaria in pregnant women but up to date data on the prevalence of placental malaria is not available. However, in recent years malaria transmission has changed (it has decreased) and therefore it can be expected that the incidence of placental malaria has also changed, but this has not been documented yet. In addition, the protective immunity against malarial infections may have decreased, possibly resulting in more acute illness to the mother. It is not known if Rwandese women still have immunity against malaria in pregnancy or that even in this relatively low malaria transmission country immunity can still be build up during successive pregnancies or that immunity has totally weaned. Regardless of the immune status of the women and the prevalence of malaria in pregnancy, it is important to diagnose it because of the potential negative effects that can be expected in both women and their offspring. We seek to document malaria burden including proportion of pregnant mothers with anaemia and the immune status of the mothers as well as the effect of maternal malaria on foetal outcomes. This data is required to effectively plan interventions to improve maternal and foetal health.
Publications:	1. D'Alessandro U. Combating malaria in pregnancy. *International Innovation Journal* 2012 June Issue, 41-43 2. Kattenberg JH, Tahita CM, Versteeg IAJ, Tinto H, Coulibaly MT, D'Alessandro U, Schallig HDFH, Mens PF. Evaluation of Antigen Detection Tests, Microscopy, and Polymerase Chain Reaction for Diagnosis of Malaria in Peripheral Blood in Asymptomatic Pregnant Women in Nanoro, Burkina Faso, *Am. J. Trop. Med. Hyg.* 2012; 87(2): 251-256.

4.1.4 MiPPAD

EDCTP Project Coordinator:	Clara Menéndez Santos (Hospital Clinic of Barcelona, Spain)
EDCTP Call Title:	Support of clinical trials, capacity building and networking in malaria in pregnancy
EDCTP Project Title:	Evaluation of alternative antimalarial drugs to sulfadoxine-pyrimethamine for intermittent preventive treatment in pregnancy (IPTp) in the context of insecticide treated nets
EDCTP Project Code:	IP.2007.31080.002
EDCTP Project Start Date:	28 November 2008
EDCTP Project End Date:	27 November 2014
Collaborators:	• Salim Abdulla (Ifakara Health Research and Development Centre, Tanzania) • Azucena Bardaji Alonso (Hospital Clinic of Barcelona, Spain) • Valerie Briand (Institut de Recherche pour le Développement (IRD), France) • Michel Cot (IRD, France) • Gilles Cottrell (IRD, France) • Meghna Desai (Centers for Disease Control and Prevention (CDC), USA) • Andre Garcia (IRD, France) • Raquel González Álvarez (Hospital Clinic of Barcelona, Spain) • Abdunoor Mulokozi Kabanywanyi (Ifakara Health Research and Development Centre 2, Tanzania) • Simon Kariuki (Kenya Medical Research Institute (KEMRI), Kenya) • Abraham Katana (KEMRI, Kenya) • Ghislain Koura (Université d'Abomey-Calavi, Benin) • Eusebio Macete (Manhiça Health Research Center, Mozambique) • Sonia Machevo (Hospital Clinic of Barcelona, Spain) • Inacio Mandomando (Manhiça Health Research Center, Mozambique) • Ahlin Achille Massougbodji (Université d'Abomey-Calavi, Benin) • Kephas Otieno (KEMRI, Kenya) • Smaila Ouedraogo (IRD, France) • Peter Ouma (KEMRI, Kenya) • Golbahar Pahlavan (Hospital Clinic of Barcelona, Spain) • Ian Pattison (Vienna School of Clinical Research (VSCR), Austria) • Michael Ramharter (University of Tübingen, Germany) • Gabriele Schreyer (VSCR, Austria) • Esperança Sevene (Eduardo Mondlane University, Mozambique) • Laurence Slutsker (CDC, USA) • Muriel Vray (Institut Pasteur, France)
Study/Trial 1	**IPTp-SP versus IPTp-MQ (in HIV non-infected women receiving LLITNS)**
Site Principal Investigator(s):	• Clara Menéndez Santos (Barcelona, Spain & Manhiça, Mozambique) • Achille Massougbodji (Cotonou, Benin) • Ghyslain Mombo -Ngoma(Lambaréné, Gabon) • Eusebio Macete (Manhiça, Mozambique) • Salim Abdulla (Ifakara, Tanzania)
Clinical Trial/Study Sponsor:	Fundació Clínic per a la Recerca Biomèdica (FCRB), Barcelona

	(Spain)
Trial/Study title:	Evaluation of the Safety and Efficacy of Mefloquine as Intermittent Preventive Treatment of Malaria in Pregnancy
Goal:	The study aims to evaluate the safety, tolerability and efficacy of Mefloquine (MQ) as an alternative to Sulfadoxine-Pyrimethamine (SP) in Intermittent Preventive Treatment in pregnancy (IPTp) in the context of Insecticide Treated Nets (ITN) used in different malaria endemic settings in Africa.
Primary Objective(s):	To compare the safety, tolerability and efficacy of MQ to SP as IPTp for the prevention of malaria in pregnancy for the mother and her infant.
Secondary Objective(s):	1. To compare MQ tolerability given as full dose with a split dose administered over 2 days 2. To evaluate the efficacy of CTX in the prevention of malaria infection in pregnant women 3. To compare immune status of HIV infected women receiving CTX + IPTp-MQ to those receiving CTX + IPTp-placebo 4. To assess the safety of study drugs in the development of infants.
Clinical Trial/Study site(s):	• Allada, Sekou and Attogon (Benin) • Fougamou and Lambaréné (Gabon) • Manhiça and Maragra (Mozambique) • Makole and Chambwino (Tanzania)
Collaborating site(s):	• Barcelona Centre for International Health Research (CRESIB) & Hospital Clinic de Barcelona, Barcelona (Spain) • Université d'Abomey-Calavi, Cotonou (Benin) • Albert Schweitzer Hospital, Lambaréné (Gabon) • Manhiça Health Research Centre, Manhiça (Mozambique) • Ifakara Health Institute (IHI) • Ifakara (Tanzania) • Vienna School of Clinical Research (VSCR) • Vienna (Austria) • Institut de Recherche pour le Developpement, Paris (France) • Institute of Tropical Medicine & University of Tuebingen, Tuebingen (Germany)
Study design:	Trial 1: phase IV randomised, controlled, open-label study Comparing IPTp-SP versus IPTp-MQ in HIV non-infected women receiving LLITNS. This is a randomised open-label superiority 3 arms trial to compare 2-dose MQ versus 2-dose SP for IPTp in the prevention of the adverse effects of malaria during pregnancy and to compare MQ tolerability of 2 different MQ administration regimens. The three arms of the study will be: 1. IPTp with SP + LLITNs (Active Comparator) HIV-negative pregnant women receiving 2 doses of IPTp (500mg of sulfadoxine and 25 mg of pyrimethamine) at the 1st and 2nd Antenatal Clinic visit in the context of long lasting Insecticide Treated Nets (LLITNs). 2. IPTp with MQ given as full dose + LLITNs (Experimental) HIV-negative pregnant women receiving 2 full doses of IPTp (15 mg/Kg) on 1 day at the 1st and 2nd Antenatal Clinic visit in the context of LLITNs. 3. IPTp with MQ given as a split dose + LLITNs (Experimental) HIV-negative pregnant women receiving 2 doses of MQ as IPTp split dose over 2 days (15mg/kg) at the 1st and

	2nd ANC visit in the context of LLITNs. This trial is being conducted in four sites in Benin, Gabon, Tanzania and Mozambique. It thus involves regions from Western, Eastern, Central and Southern sub-Saharan Africa where malaria transmission is stable but displays distinctly varying characteristics according to the site.
Product(s):	• Mefloquine (MQ) • Sulfadoxine-pyrimethamine (SP)
Manufacturer/Developer:	• Hoffman-La Roche • Sterop • UCB Pharma (GSK manufacturer)
Status:	Ongoing
Results and Outcomes:	See below for details (recruitment completed)
Study/Trial 2	**IPTp-MQ versus IPTp- placebo (in HIV infected women receiving CTX and LLITNs)**
Site Principal Investigator(s):	• Eusebio Macete (Manhiça, Mozambique) • Meghna Desai and Peter Ouma (Kisumu, Kenya) • Salim Abdulla (Ifakara, Tanzania)
Clinical Trial/Study Sponsor:	Fundació Clínic per a la Recerca Biomèdica (FCRB), Barcelona (Spain)
Trial/Study title:	Evaluation of the Safety and Efficacy of Mefloquine as Intermittent Preventive Treatment of Malaria in Pregnancy
Goal:	The study aims to evaluate the safety, tolerability and efficacy of Mefloquine (MQ) as Intermittent Preventive Treatment in pregnancy (IPTp) in HIV-infected women receiving cotrimoxazole in the context of Insecticide Treated Nets (ITN).
Primary Objective(s):	To determine the safety and efficacy of IPTp with mefloquine among HIV infected women receiving cotrimoxazole (CTX) prophylaxis for opportunistic infections.
Secondary Objective(s):	1. To compare MQ tolerability given as full dose with a split dose administered over 2 days 2. To evaluate the efficacy of CTX in the prevention of malaria infection in pregnant women 3. To compare immune status of HIV infected women receiving CTX + IPTp-MQ to those receiving CTX + IPTp-placebo 4. To assess the safety of study drugs in the development of infants.
Clinical Trial/Study site(s):	• Kisumu (Kenya), Manhiça and Maragra (Mozambique) • Dodoma, Makole and Chambwino (Tanzania)
Collaborating site(s):	• Barcelona Centre for International Health Research (CRESIB) & Hospital Clinic de Barcelona, Barcelona (Spain) • Kenya Medical Research Institute & Centers for Disease Control and Prevention (CDC), Kisumu (Kenya) • Manhiça Health Research Centre, Manhiça (Mozambique) • Ifakara Health Institute (IHI), Ifakara (Tanzania).
Study design:	Trial 2: phase IV randomised, double-blind Comparing IPTp-MQ versus IPTp- placebo in HIV-infected women receiving CTX and LLITNs. This is a randomised double-blind superiority clinical trial to compare the efficacy of MQ as IPTp with placebo-IPTp in HIV-infected pregnant women receiving CTX prophylaxis. 1. CTX+IPTp-Placebo+LLITNs (Experimental) HIV-positive pregnant women receiving 3 doses of IPTp (placebo) at the 1st, 2nd and 3rd Antenatal Clinic visit in the context of LLITNs.

	2. CTX + IPTp-MQ+ LLITNs (Experimental) HIV-positive pregnant women receiving 3 doses of IPTp (15 mg/Kg MQ) at the 1st and 2nd Antenatal Clinic visit in the context of LLITNs. This trial is being conducted in 3 sites from south eastern sub-Saharan Africa (Kenya, Mozambique and Tanzania), where HIV prevalence in pregnant women ranges from 10 to 30%.
Product(s):	• Mefloquine (MQ) • MQ Placebo • Cotrimoxazole (CTX)
Manufacturer/Developer:	• Hoffman-La Roche • Carreras/Bonals • UCB Pharma (GSK manufacturer)
Cofunders:	• Carlos III Health Institute (Spain), University of Tübingen (Germany) • German Aerospace Center [Deutsches Zentrum fuer Luft- und Raumfahrt – DLR] (Germany) • Institut de Recherche pour le Développement [IRD] (France) • Austrian Federal Ministry of Science (Austria) • Malaria in Pregnancy Consortium (UK)
Trial Registration number(s):	NCT 00811421 PACTR 2010020001813440 PACTR 2010020001429343
Status:	Ongoing
Results and Outcomes:	Summary of the major achievements (from November 2008 until February 2014) for both trials: 1. In Clinical trials: • Both trials finalised recruitment and mother follow-up during Y4. • For Trial 1: Evaluation of the Safety and Efficacy of Mefloquine as Intermittent Preventive Treatment of Malaria in Pregnancy (in HIV non-infected women receiving LLITNS): Child follow-up data-collection from sites was finalized during this period as planned (Q4, Y5). – Child follow-up data-collection from sites was finalized during this period as planned (Q4, Y5). – Data cleaning prior to analysis has been delayed significantly. Manuscript submission of Mother data is estimated for Q1,Y6. – Finalization of Child data cleaning initially planned for Q4, Y5 is estimated during Q1, Y6 and manuscript submission by Q3, Y6. • For Trial 2: Evaluation of the Safety and Efficacy of Mefloquine as Intermittent Preventive Treatment of Malaria in Pregnancy (in HIV infected women receiving CTX and LLITNs): – Child follow-up and data collection were finalized during this period (Q3, Y5). – Data cleaning has been laborious due also in part to the demobilisation of study staff. – Manuscript submission of HIV-positive Mother data shall be done with that of the HIV-negative data. – Cleaning of Child data is estimated during Q1, Y6 and

	manuscript submission by Q3, Y6. 2. In Capacity Development, Training and Infrastructure: • There have not been any infrastructure upgrades during this final period. A CRF storage unit has been budgeted for the next period • The MSc student is expected to be completed by December 2014 • The PhD is expected to finish by December 2014. 3. In Networking: – The outcome following the WHO Malaria Policy Advisory Committee (MPAC) meeting in December 2013 was the release of the updated *WHO Malaria Policy Advisory Committee (MPAC) recommendations have been published in the Malaria journal:* http://www.malariajournal.com/content/12/1/456/abstract – Fourth Statistics Working Group Meeting, 4-6 June 2013, Barcelona, Spain, 2 participants per site – Fourth MiPPAD Annual Investigators' Meeting, 12-14 June 2013, Barcelona, Spain, 2 participants per site – Fifth Malaria in Pregnancy Consortium Meeting, 3-5 October 2013, Durban, South Africa, participation of MiPPAD site PIs.One DSMB meeting took place during this reporting period (February 2012, Barcelona, ES) The major setbacks of these studies have been the long regulatory processes in several study sites which has had a knock on effect in starting recruitment and the need to request for a no-cost extension to MiP Consortium and EDCTP. In particular, in the case of Kenya and Mozambique, the creation of new regulatory bodies, respectively the Kenya Pharmacy and Poison Board and the Ministry of Health Departamento Farmacéutico, have caused additional delays in securing import permit for study drugs. As consequence the new planned timelines for recruitment initiation were set to Q1-Q2 of 2010.
Study population and total number of subjects (clinical trials only):	PREGNANT WOMEN (HIV-positive, >15 years old)+ INFANTS N=5,783 Trial 1: 4,716 subjects Trial 2: 1,070 subjects
PhD study:	Title: Safety profile of antimalarial drugs during pregnancy in the evaluation framework of alternative antimalarial drugs to sulfadoxine-pyrimethamine in Sub-saharan Africa Candidate: Dominic Mosha (University of Basel, Swiss Tropical Institute, Switzerland and CRESIB, Spain) Dates: March 2012-June 2014
MSc study:	Title: Effect of cotrimoxazole alone or in combination with mefloquine on antibodies to variant surface antigens (VSAs) in pregnant women in Western Kenya (Kenya Medical Research Institute/Center for Global Health Research, Kisumu, Kenya) Candidate: Kephas Otieno (KEMRI/CDC, Kenya) Dates: March 2011-December 2015
Other/Sub-studies:	The Ancillary studies approved to date by the MiPPAD ExCom are listed below: **1. *APEC*** Site Principal Investigator: Smaïla Ouédraogo, Achille Massougbodji Title: *Aetiology of anaemia in pregnancy and consequences on*

	the infants in a malaria endemic area Purpose: To determine the etiological factors of anemia in pregnancy and the consequences on the mothers and infants in terms of morbidity (specifically anemia) and growth, in a malaria endemic area. Study site: Benin Synopsis: Anemia during pregnancy is an important issue in developing countries, mainly in Sub-Saharan Africa where 5-10% and more than 50% of women develop severe and moderate anemia during pregnancy, respectively. Severe anemia seems to increase mortality and morbidity in mothers, but little is known on its risk factors and especially on its impact on the health of both fetuses and infants. Malaria and iron deficiency are important and wellknown risk factors for anemia during pregnancy. It is estimated that 26% of severe anemia among pregnant women is attributable to malaria and around 50% is iron deficiency anemia (IDA) compared with less than 1% in developed countries where diets and iron supplementation are better adapted to the needs of the women. During pregnancy, there is a significant increase in the amount of iron required to increase the red cell mass, expand the plasma volume and to allow for the growth of the fetal-placental unit; in Sub-Saharan Africa the need of iron is often not covered. Other risk factors include helminthiases, genetic disorders such as sickle cell disease or G6PD deficiency, micronutrients deficiency (folic acid), undernutrition. However little is known on their real contribution to the development of the disease. The goal of this study is to determine the etiological factors of anemia in pregnancy and the consequences on the mothers and infants in terms of morbidity (specifically anemia) and growth, in a malaria endemic area 2. **EPOPEE** Site Principal Investigator: Valérie Briand Title: EPOPEE (Évaluation du POids de naissance comme facteur Prédictif de l'État de santé de l'Enfant). Birth weight as a predictor for child health Purpose: The **EPOPEE** project aims to assess low birth weight (LBW) as a predictor for child health in the first two years of life. Primary Objective(s): To assess the impact of low birth weight on child infectious morbidity (focusing on malaria, diarrhea and respiratory infections) and growth Secondary Objective(s): To determine the respective proportion of prematurity and intrauterine growth retardation (IUGR) as underlying physiopathological mechanism for LBW; To assess the impact of the different types of low birth weight (IUGR and prematurity) on child morbidity and growth ; To estimate the effect of maternal and fetal risk factors for each type of LBW, as well as their population attributable risk; To assess the direct and indirect (through LBW) impact of malaria in pregnancy on child morbidity and growth;

	To evaluate the reliability and usefulness of other indicators related to birth weight - than LBW - to predict child health. Study site: Benin Synopsis: Birth weight is one of the main determinants of infant and child morbidity and mortality. While the deleterious consequences of low birth weight (LBW, defined as <2 500gr) have been well documented in developed countries, there is less literature coming from developing countries. In these countries, LBW newborns have been shown to be at higher risk for dying, for having infectious diseases (mainly diarrhea and respiratory infections) and growth impairment. However, these findings are based on studies where child (in particular, nutritional status), maternal (schooling, decision-making-power, mother's child-care) and household-level factors (hygiene practices, economic resources, size and structure) have seldom been taken into account. The EPOPEE study aims to assess the independent effect of birth weight on infectious morbidity and growth while adjusting for these factors. Also, children will be categorized according to the underlying mechanism for LBW (prematurity or intra-uterine growth restriction). For each type of LBW, maternal and fetal determinants, as well as consequences on child health will be assessed. Finally, other indicators related to birth weight – than LBW – will be evaluated as predictors for infant morbidity and growth. These results may help estimating the long-term impact of interventions that are recommended during pregnancy to reduce birth weight deficiency. **3. TOLIMMUNPAL** Site Principal Investigator: André Garcia Title: Environmental, biological and genetic factors involved in the immune tolerance related to malaria: consequences for the protection of pregnant women and young children TOLIMMUNPAL for TOLérance IMMUNitaire PALudisme Purpose To explore the determining factors of malaria-related immune tolerance and to understand its consequences in terms of protection strategies for pregnant women and newborns Primary Objective(s): To identify the main determinants responsible for variable susceptibility to plasmodial infection between birth and 2 years of life, in the following domains: a. Ecologic (entomological transmission, children's living conditions, etc.) b. Biologic (child's immune response development, mother's infection during pregnancy and mother's specific immune response, child's and mother's nutritional status, etc.) c. Genetic (polymorphisms of genes involved in the control of immune response) To confirm that, taking into account previous risk factors, immune tolerance is involved in this susceptibility and to propose a conceptual (functional) hypothesis to explain the pathway by which immune tolerance plays this role. Study sites: Benin Synopsis: Pregnant women and children are the main risk populations for malaria. Pregnancy associated malaria (PAM) due to *P. falciparum*, can induce placenta malaria (PM). Children

	born to mothers with PM seem to have an increased risk of early *P. falciparum* infection and it has been conjectured that PM may alter infant's immune response and cause immune tolerance (IT) inducing immune mechanisms such that parasites escape from anti-malaria immunity. We argue that all infections occurring during pregnancy affect the child's acquisition anti-malaria immunity and cause IT, not only through PM. The expression of HLA-G by pathogen-infected cells has been proposed as efficient immune escape strategy. However, correlation between HLA-G expression and level of antibodies in *Plasmodium*-infected individuals is unknown. Our program is based on the hypothesis that, in *P. falciparum* infection occurring in pregnant women, expression of HLA-G molecules is up-regulated and soluble HLA-G production by mother's immune cells will be induced, leading to the inhibition of maternal B cell response. This will result in transmission deficiency of anti-plasmodium antibodies, from the mother to the child, responsible for an increased susceptibility. Certain HLA-G genetic variants are associated with different levels of soluble HLA-G. It is possible that the mechanism leading to IT in children could be under genetic control.
Publications:	1. Ouédraogo S, Bodeau-Livinec F, Briand V, Huynh BT, Koura GK, Accrombessi MM, Fievet N, Massougbodji A, Deloron P, Cot M Malaria and gravidity interact to modify maternal haemoglobin concentrations during pregnancy. *Malaria Journal* 2012; 11:348. Doi: 10.1186/1475-2875-11-348. 2. Ouédraogo S, Koura GK, Bodeau-Livinec F, Accrombessi MM, Massougbodji A, Cot M. Maternal anaemia at first antenatal visit: prevalence and risk factors in a malaria endemic area in Benin. *American Journal of Tropical Medicine & Hygiene* 2012; 87(3):418-24. Doi: 10.4269/ajtmh.2012.11-0706 3. Ouédraogo S, Koura GK, Bodeau-Livinec F, Accrombessi MM, Massougbodji A, Cot M. Maternal Anemia in Pregnancy: Assessing the Effect of Routine Preventive Measures in a Malaria-Endemic Area. *American Journal of Tropical Medicine & Hygiene* 2013; 88(2): 292-300. Doi: 10.4269/ajtmh.12-0195. 4. 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. 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* 2013; 56(6):e68-75. Doi: 10.1093/cid/cis976 5. 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 and Becker K. Transmission of Staphylococcus aureus between mothers and infants in an African setting. *Clinical Microbiology and Infection* 2013. Article first published online : 18 Nov 2013, DoI: 10.1111/1469-0691.12417

4.1.5 IPTp-SP

EDCTP Project Coordinator:	Feiko ter Kuile (University of Liverpool, UK)
EDCTP Call Title:	Support of clinical trials, capacity building and networking in malaria in pregnancy
EDCTP Project Title:	Scheduled intermittent screening and treatment in pregnancy (ISTp) versus intermittent preventive treatment with sulphadoxine-pyrimethamine (IPTp-SP) in women protected by insecticide treated nets for the control of malaria in pregnancy in west Africa and Malawi
EDCTP Project Code:	IP.2007.31080.003
EDCTP Project Start Date:	18 December 2008
EDCTP Project End Date:	17 December 2013
Collaborators:	• Francis Akor (Medical Research Council (MRC) Laboratories, The Gambia) • Kalifa Bojang (MRC Laboratories, The Gambia) • Chandramohan, Daniel (London School of Hygiene and Tropical Medicine (LSHTM), UK) • Manuela Claite (LSHTM, UK) • Christine Clerk (Navrongo Health Research Centre, Ghana) • Sheick Oumar Coulibaly (University of Ouagadougou, Burkina Faso) • Stephanie Dellicour (Liverpool School of Tropical Medicine, UK) • Ogobara Doumbo (University of Bamako, Mali) • Annemieke van Eijk (University of Liverpool, UK) • Brian Faragher (University of Liverpool, UK) • Exnevia Gomo (University of Malawi) • Brian Greenwood (LSHTM, UK) • Jenny Hill (University of Liverpool, UK) • Abraham Hodgson (Navrongo Health Research Centre, Ghana) • Gertrude Kalanda (University of Malawi) • Linda Kalilani-Phiri (University of Malawi) • Kassoum Kayentao (University of Bamako, Mali) • Pascal Magnussen (University of Copenhagen, Denmark) • Paul Milligan (LSHTM, UK) • Gerarld Mwapasa (University of Malawi) • Ian Pattison (Vienna School of Clinical Research (VSCR), Austria) • Sanie Samuel Sogoyan Sesay (MRC Laboratories, The Gambia) • Esperança Sevene (Eduardo Mondlane University, Mozambique) • Jacek Skaribnski (Centers for Disease Control and Prevention (CDC), USA) • Steve Ward (University of Liverpool) • John Williams (Navrongo Health Research Centre)
Study design:	This grant involves two clinical trials and a SP drug resistance sub-study: A phase IIIb, two arm multi-centre randomised controlled superiority trial conducted at three sites in southern Malawi with high levels of SP resistance and high ITN coverage. Phase IV, two-arm, multi-centre, open, randomised, controlled, non-inferiority trial comparing two malaria control strategies in pregnancy in West Africa. A sub-study that explores the relationship between the level of SP resistance in the population (of pregnant women) and the

	effectiveness of IPTp-SP in reducing adverse effect of malaria at birth.
Study/Trial 1	**IPTp-Mon study**
Site Principal Investigator(s):	• Kassoum Kayentao (Malaria Research and Training Centre, Mali) • Sheick O. Coulibaly and B. Kayoute (Université de Ouagadougou CNRFP, Burkina Faso) • Pascal Magnussen (University of Copenhagen, Denmark) • Linda Kalilani (College of Medicine, Malawi) • Daniel Chandramohan and Brian Greenwood (LSHTM, UK) • Harry Tagbor (LSHTM, UK/Ghana) • Feiko ter Kuile (LSTM, UK)
Clinical Trial/Study Sponsor:	• Liverpool School of Tropical Medicine (LSTM, UK) • London School of Hygiene & Tropical Medicine (LSHTM, UK)
Trial/Study title:	Monitoring the impact of Sulphadoxine-Pyrimethamine Resistance on the the Effectiveness of Intermittent Preventive Treatment (IPT) for the Control of Malaria in Pregnancy
Goal:	To explore the relationship between the level of SP resistance in the population (of pregnant women) and the effectiveness of IPTp-SP in reducing the adverse effects of malaria at birth.
Primary Objective(s):	1. To determine the relationship between the degree of SP resistance in the population as assessed by molecular markers and its impact on the ability of IPTp with SP to clear existing infections, prevent new infections and prevent the adverse malaria associated morbidity 2. To design a practical operational tool to monitor SP effectiveness that can be used outside of research settings.
Secondary Objective(s):	1. To characterize the degree of resistance of P. falciparum to SP in the population using molecular markers in dihydrofolate reductase (DHFR) and dihydropteroate synthase (DHPS) 2. To determine the efficacy of SP IPTp in clearing peripheral parasitaemia in asymptomatic parasitaemic pregnant women 3. To determine the effectiveness of SP IPTp in preventing placental malaria, maternal anaemia and low birth weight, by comparing these among women who have received 2 or more versus less than 2 doses of IPTp based on their antenatal clinic records 4. To determine which parasite genotypes recrudesce, cause new infections, and persist in the placenta in women receiving IPTp-SP 5. To model the pharmacodynamic relationship between drug levels, parasite SP resistance genotype, recrudescence, and new infection and to validate the model using the pooled data from the different study sites 6. To use the pooled experience and 'rich' *in-vivo* data from the weekly follow-up to determine the potential validity of a 'sparse' 'population' sampling methodology for future therapeutic *in-vivo* follow-up studies.
Clinical Trial/Study site(s):	• Blantyre district (Malawi) • Ziniare (Burkina Faso) • Navrongo (Ghana) • San and Kita (Mali)
Collaborating partners(s):	• Liverpool School of Tropical Medicine (LSTM, UK) • London School of Hygiene & Tropical Medicine (LSHTM, UK) • University of Copenhagen (Denmark) • Université de Ouagadougou (Burkina Faso)

	• Navrongo Health Research Centre (Ghana) • College of Medicine (Malawi) • Medical Research and Training Centre (Mali) • Manhica Health Research Centre (Mozambique) • Centres for Disease Control and Prevention (CDC, USA) • University of Melbourne (Australia)
Study design:	A multi-centre, multi-country study conducted in several sites in sub-Saharan Africa where malaria is endemic and where IPTp with SP is used in the control of malaria in pregnancy. The study is designed to determine the frequency of molecular markers and the in-vivo response in each site. It is also designed to determine the effect of different doses of IPTp on the presence of placental malaria. In each study site, there will be three parts to this study, each of which will be conducted simultaneously, in the same study area: 1. Molecular markers of SP resistance To characterize the degree of resistance to SP in the population, the prevalence of molecular markers of SP resistance (DHFR and DHPS anti-folate resistance mutations in P. falciparum) will be measured in parasites collected from both pregnant women and a random sample of patients with clinical malaria attending outpatient clinics 2. In vivo assessment of parasitological response to IPTp-SP To determine the efficacy of IPTp-SP in pregnant women in clearing existing infections or preventing new infections, a prospective in vivo study will be conducted in women presenting for antenatal care (ANC). Women will receive IPTp-SP according to national guidelines and be followed weekly for 42 days to assess the parasitological response (therapeutic efficacy) and their ability to prevent new infections. Parasites will be genotyped to distinguish between recrudesce and reinfection and for markers of SP resistance. Drug levels will be measured using nested populations pharmacokinetics studies 3. Assessment of IPTp-SP effectiveness on birth parameters A cross-sectional study at delivery of the impact of IPTp-SP on the prevalence of peripheral malaria, placental malaria, maternal anaemia and low birth weight in primi- and secundigravidae. Diagnostic and speciating PCR will be conducted to determine sub-patent infections, and PCR will be conducted to characterise the presence of molecular markers of SP resistance.
Product(s):	Sulfphadoxine-pyrimethamine (SP)
Manufacturer/Developer:	Durbin PLC (UK)
Cofunders	• Liverpool School of Tropical Medicine (UK) • London School of Hygiene & Tropical Medicine (LSHTM, UK) • MRC (UK), University of Copenhagen (Denmark) • Austrian Federal Ministry of Science (Austria) • Bill & Melinda Gates Foundation (USA)
Status:	Ongoing
Results and Outcomes:	Field work completed, molecular assays ongoing (see below for further details)
Total number of subjects (clinical trials only):	256 per site (in-vivo module), and up to 1,100 deliveries per site (3 study sites)
Study/Trial 2	**ISTp-Malawi**
Site Principal	• Linda Kalilani-Phiri (Blantyre, Malawi)

Investigator(s):	• Feiko ter Kuile (LSTM, UK)
Clinical Trial/Study Sponsor:	Liverpool School of Tropical Medicine (LSTM, UK)
Trial/Study title:	Scheduled intermittent screening and treatment in pregnancy (ISTp) versus intermittent preventive treatment with sulphadoxine-pyrimethamine (IPTp-SP) in women protected by insecticide treated nets (ITNs) for the control of malaria in pregnancy in Malawi: a randomised controlled trial
Goal:	To evaluate whether Scheduled intermittent screening and treatment in pregnancy is a suitable alternative strategy to Intermittent Preventive Therapy for the control of malaria in pregnancy in areas with high SP resistance.
Primary Objective(s):	To compare the efficacy of scheduled intermittent screening with malaria rapid diagnostic tests (RDTs) and treatment of RDT-positive women with dihydroartemisinin-piperaquine (ISTp-DP) with intermittent preventive treatment with sulphadoxine-pyrimethamine (IPTp-SP) in the second and third trimesters on adverse birth outcome and malaria infection at term among HIV-negative women protected by insecticide–treated bed nets.
Secondary Objective(s):	To determine if ISTp-DP has greater efficacy than IPTp-SP in terms of placental malaria (in G1 and G2), maternal malaria infection at delivery, mean birth weight, low birth weight (<2,500 grams), gestational age, mean gestational age at birth, pre-term birth (<37 weeks), small for gestational age, mean maternal haemoglobin at birth; anaemia (Hb ≤ 11 g/dL) at birth, moderate to severe anaemia (Hb ≤ 8g/dL); stillbirths; neonatal deaths; clinical malaria episodes during the second and third trimesters of pregnancy; third trimester mean maternal haemoglobin, anaemia (Hb ≤ 11 g/dL) and moderate to severe anaemia (Hb ≤ 8g/dL); severe cutaneous skin reaction in the mothers; other serious adverse events in the mothers; minor adverse events in the mothers by day three after study drugs given; congenital malformation at birth and by day 28; neonatal jaundice at day one or day seven; incidence of anaemia, and clinical malaria in babies up to the age of eight weeks.
Clinical Trial/Study site(s):	Three trial sites in Blantyre District (Malawi)
Collaborating partner(s):	• Liverpool School of Tropical Medicine (LSTM, UK) • London School of Hygiene & Tropical Medicine (LSHTM, UK) • Vienna School of Clinical Research (VSCR, Austria) • College of Medicine (Malawi) • Manhiça Health Research Centre (Mozambique)
Study design and population:	Phase IIIb, two arm multi-centre randomised controlled superiority trial to be conducted at three sites in southern Malawi with high levels of SP resistance and high ITN coverage. • Arm 1 (IPTp-SP): 3 or 4-dose regimen of IPTp with SP. • Arm 2 (ISTp-DP): 3 or 4-scheduled doses of ISTp and treatment with ACTs if participants are found to be positive by a rapid diagnostic test (RDT). Participants are randomly allocated to receive either at least three doses of IPTp with SP or at least three scheduled screenings with an RDT and treatment with DHA-PQ if they are RDT-positive. All participants are given an insecticide-treated bed net if they do not already have one. Women enrolled in the trial make at least three scheduled visits to the clinic spread over the second and third trimesters at least four weeks apart to receive the study intervention approximately mirroring the appointment schedule for 'focussed

	antenatal care' in Malawi which consists of four scheduled visits. Newborns are seen at approximately seven days and six weeks after delivery, to assess the health of the infant. The study is open label as it will not be possible to blind the participants to their allocation, although where possible laboratory staffs undertaking trial-related diagnostic tests are blinded. Participants are HIV-negative pregnant women. They are screened for eligibility and enrolled at 16 to 29 weeks gestation. The study aims to recruit 1655 participants and started in the 2nd quarter of 2011 and will recruit for a period of 18 to 24 months, with a further six months follow-up.
Product(s):	• Sulphadoxine-pyrimethamine (SP) • Dihydroartemisinin-piperaquine (DHA-PQ or DP) • Artemether-lumefantrine • Artesunate-amodiaquine • mefloquine-artesunate
Manufacturer/Developer:	• Durbin PLC (UK) (SP) • Sigma-Tau, Italy (DHA-PQ)
Cofunders:	• Liverpool School of Tropical Medicine (UK) • Austrian Federal Ministry of Science (Austria) • Bill & Melinda Gates Foundation (USA)
Trial Registration number(s):	ISRCTN69800930 PACTR201103000280319
Status:	Ongoing
Results and Outcomes:	Recruitment completed in April 2013 (for further details see below)
Total number of subjects (clinical trials only):	1,665
Study/Trial 3	**IST – IPTp study West Africa**
Site Principal Investigator(s):	• Harry Tagbor (Ghana) • Abraham Hodgson (Ghana) • Kassoum Kayentao (MRTC, Mali) • Sheick O. Coulibaly (Université de Ouagadougou CNRFP, Burkina Faso) • Kalifa Bojang (The Gambia) • Daniel Chandramohan and Brian Greenwood (LSHTM, UK) • Feiko ter Kuile (LSTM, UK) • Pascal Magnussen (University of Copenhagen, Denmark)
Clinical Trial/Study Sponsor:	London School of Hygiene & Tropical Medicine (LSHTM, UK)
Trial/Study title:	A trial of intermittent preventive treatment with sulfadoxine-pyrimethamine versus intermittent screening and treatment of malaria in pregnancy in west Africa
Goal:	The goal of this project is to determine whether in pregnant women who sleep under a long lasting insecticide treated bed net, screening and treatment at each scheduled antenatal clinic visit is as effective in protecting them from anaemia, low birth weight and placental infection as SP-IPTp.
Primary Objective(s):	To determine the optimum method of controlling malaria in pregnancy in women who sleep under an LLIN in areas of seasonal malaria transmission.
Secondary Objective(s):	1. To determine if scheduled screening and treatment during antenatal clinic visits is as effective in protecting against low birth weight, anaemia and malaria infection of the placenta as a standard SP-IPTp in primigravidae and secundigravidae who sleep under a long lasting ITN. 2. To evaluate the cost-effectiveness of delivering the two

	strategies measured as the cost per cases of maternal anaemia and antenatal malaria averted.
Clinical Trial/Study site(s):	• Ziniare (Burkina Faso) • Navrongo (Ghana) • San and Kita (Mali) • Basse (The Gambia)
Collaborating partner(s):	• London School of Hygiene & Tropical Medicine (LSHTM, UK) • Liverpool School of Tropical Medicine (LSTM, UK) • Vienna School of Clinical Research (VSCR, Austria) • University of Copenhagen (Denmark) • Université de Ouagadougou (Burkina Faso) • Medical Research Council Laboratories (The Gambia) • Navrongo Health Research Centre (Ghana) • College of Medicine (Malawi) • Medical Research and Training Centre (Mali) • Manhiça Health Research Centre (Mozambique)
Study design and population:	Phase IV, two-arm, multi-centre, open, randomised, controlled, non-inferiority trial comparing two malaria control strategies in pregnancy is proposed. The study groups are as follows: • Arm 1 (SP-IPTp SP according to WHO recommendations): women receive at least two doses of SP during their pregnancy, one at each of the recommended ante-natal visits during the 2nd and 3rd trimester. Women in this arm are the reference group • Arm 2 (IST using RDTs): scheduled intermittent screening by RDT and treatment of those who are RDT positive during ante-natal clinic visits in the 2nd and 3rd trimester. All study women are provided with an LLIN at their first attendance at the ANC and given instructions on how to use it. Random home visits are made to check on net usage during the pregnancy.
Product(s):	• Sulphadoxine-pyrimethamine (SP) • Artemether-lumefantrine
Manufacturer/Developer:	Novartis (Switzerland)
Cofunders:	• Liverpool School of Tropical Medicine (UK) • London School of Hygiene & Tropical Medicine (LSHTM, UK) • MRC (UK) • University of Copenhagen (Denmark) • Austrian Federal Ministry of Science (Austria) • Bill & Melinda Gates Foundation (USA)
Trial Registration number(s):	NCT 01084213
Status:	Ongoing
Results and Outcomes:	Recruitment completed for all three studies. Summary of major achievements (from 18 December 2008 until 17 December 2012) 1. In Clinical Trials • SP-resistance studies (Observational study): – All field work for the in vivo and delivery module components is completed in Malawi, Mali and Burkina Faso, totalling 4,383 pregnancies. Molecular assays are ongoing (70% completed) – Results indicated sustained effectiveness of IPTp-SP in Burkina Faso and Mali, but reduced effectiveness in Malawi where saturation of the quintuple DHFR/DHPS mutations has occurred, confirming high-grade SP resistance. There was no indication that the additional

DHPS-581 mutation was associated with harm (which was a concern raised by previous NIH funded research from high-grade resistance region in north Tanzania). Two manuscripts in preparation.
  - The country specific clinical impact analysis and meta-analysis are ongoing.
- Trial 1b ISTp-Malawi:
  - An additional recruitment center was identified in order to allow completion of the trial; therefore three recruitment sites, two in Blantyre District and one in Chikwawa District, Malawi
  - 100% of multigravidae and 98% of G1/G2 recruited by 1 Mar 2013. At current rate, last patient-in will be completed by March 2013. Last follow-up will be completed by October 2013. Success rate of follow-up consistently of 90%. From these, 70% have delivered
  - Data analysis plan has been discussed with DSMB and is now finalised. Approximately, half of the data is cleaned completed (pending PCR results), the other half involved active participants and is ongoing.
- Trial 2 ISTp-west Africa:
  - ISTp Economics (Malawi Trial 1b)
  - ISTp Acceptability (Malawi Trial 1b)
  - Econ ISTp-IPTp west Africa (Trial 2)
  - Data analysis approved by DSMB. Lab work to be completed by mid-2013 and all data analysis expected to be completed by the end of 2013.
- Three sub-studies:
  - Follow-up of all study women is completed; 5,356 women were recruited into the trial and 4,559 followed until delivery.
  - Success rate of follow-up consistently of 85%.
  - Data analysis approved by DSMB. Lab work to be completed by mid-2013 and all data analysis expected to be completed by the end of 2013.

2. In capacity Development, Training and Infrastructure:

- There have been minor infrastructure upgrades during this period. Two extensions to the Chikwawa antenatal facilities have constructed, one of which is completed (please see provided pictures).
- GCP refresher course (24-26 September 2012, Malawi) attended by two nurses and one data officer.
- Support course for the data managers.
- Two MSc students completed their masters in February 2012. However, an additional MSc student, Mwayi Madanitsa, has registered and begun an online Masters in Epidemiology at the LSHTM, UK (due for completion in June 2014).
- One PhD is expected to finish by December 2013 and a second PhD student is expected to finish by March 2014.

3. In Networking:

- Trial 1b:
  - Investigators meeting in Blantyre, Malawi in February 2013.
- Trial 2:
  - MiP Consortium EC/IC meeting and a Trial 2 Steering Committee meeting were held at ASTMH, Atlanta, November 2012
  - Investigators meeting in Atlanta, USA, November 2012.

	Preliminary results of the SP resistance study and the above meta-analysis were shared with the WHO Expert Reviw Group (ERG) meeting in July 2012. In addition, the results of the 2 vs. 3 dose meta-analysis have been communicated via press releases from LSTM and JAMA journal. One article published at JAMA and two manuscripts in preparation. Setbacks: • For Trial 1b, recruitment was planned to be completed by December 2012; however, this is now to be happening in March 2013 • For Trial 2, the team detected that the quality of placental histology slides prepared at 3 of the 4 centers were poor. Thus, placenta blocks from these sites had to be sent to Ghana for new slides to be prepared. This is now ongoing but has caused a delay in completing the database for analysis. • In capacity building, the expected completion dates for the third MSc and for one PhD students will be after the end date of the grant, which is end of December 2013.
Total number of subjects (clinical trials only):	4,500
PhD studies:	Title: Optimisation of the existing regimen of intermittent preventive treatment with sulfadoxine-pyrimethamine for the prevention of malaria in pregnancy and assessing the impact of sulfadoxine-pyrimethamine resistance in west-Africa Candidate: Kassoum Kayentao (Liverpool School of Tropical Medicine, Liverpool, UK & Medical Research and Training Centre, University of Bamako, Mali) Dates: March 2009-March 2014
	Title: The Diagnosis of malaria in pregnancy in west-Africa Candidate: John Williams (London School of Hygiene and Tropical Medicine, London, UK & Navrongo Health Research Centre, Navrongo, Ghana) Dates: October 2010-December 2013
MSc studies:	Title: MBA (distance learning) Candidate: Mamkumba Sanneh (Affiliation, The Gambia) Dates: February 2012 (Completed)
	Title: Master Clinical trials (distance learning) Candidate: Gerald Mwapasa Dates: February 2012 (Completed)
Other/Sub-studies:	Economic: to determine the cost-effectiveness of ISTp-DP versus IPTp-SP from a societal perspective and to use the cost data to populate a model of the economic burden of malaria in pregnancy. To model the economic cost of scale-up and affordability. Acceptability and implementability: to explore the implementability, acceptability, feasibility and potential for scale-up of ISTp in Malawi.
Publications:	1. Kayentao K, Garner P, van Eijk AM, Naidoo I, Roper C, Mulokozi A, MacArthur JR, Luntamo M, Ashorn P, Doumbo OK, ter Kuile FO. Intermittent preventive therapy for malaria during pregnancy using 2 vs. 3 or more doses of sulfadoxine-pyrimethamine and risk of low birth weight in Africa: systematic review and meta-analysis. *JAMA* 2013; 309: 594-604.

4.1.6 WANECAM

EDCTP Project Coordinator:	Abdoulaye Djimdé (Malaria Research & Training Center, Mali)
EDCTP Call Title:	Support of clinical trials, capacity building and networking in malaria treatment
EDCTP Project Title:	An integrated approach to clinical trials, capacity building and networking in West Africa (WANECAM)
EDCTP Project Code:	IP.2007.31060.002
EDCTP Project Start Date:	15 September 2009
EDCTP Project End Date:	15 September 2014
Collaborators:	• Abdoul Habib Beavogui (Centre National de Formation et de Recherche en Santé Rurale (CNFRSR) de Mafèrinyah, Guinea) • Anders Björkman (Karolinska Institute, Sweden) • Steffen Borrmann (University of Heidelberg, Germany) • David Joseph Conway (London School of Hygiene and Tropical Medicine, LSHTM, UK) • Esperance Coulibali (Centre national de recherche de Formation sur le Paludisme (CNRFP), Burkina Faso) • Adama Dao (University of Bamako, Mali) • Alexandre Delamou (CNFRSR de Mafèrinyah, Guinea) • Mamadou Malal Diallo (CNFRSR de Mafèrinyah, Guinea) • Dapa Diallo (University of Bamako, Mali) • Alassane Dicko (University of Bamako, Mali) • Ogobara Doumbo (University of Bamako, Mali) • Kassoum Kayentao (University of Bamako, Mali) • Aminatou Kone (University of Bamako, Mali) • Issa Ouedraogo Nebie (CNRFP, Burkina Faso) • Oumou Niare (University of Bamako, Mali) • Jean-Bosco Ouedraogo (Institut de Recherche en Sciences de la Santé, Burkina Faso) • Stephane Picot (University of Lyon, France) • Issaka Sagara (University of Bamako, Mali) • Sodiomon Sirima (CNRFP, Burkina Faso) • Colin Sutherland (LSHTM, UK) • Mahamadou Aly Thera (University of Bamako, Mali) • Alfred Tiono (CNRFP, Burkina Faso) • Boubacar Traore (University of Bamako, Mali) • Jean Baptiste Yaro (Medical Research Council Laboratories, The Gambia)
Site Principal Investigator(s):	• Sodiomon B. Sirima (Ouagadougou, Burkina Faso) • Issiaka Soulama (Ouagadougou, Burkina Faso) • Jean-Bosco Ouedraogo (Bobo-Dioulasso, Burkina Faso) • Issaka Sagara (Bamako, Mali) • Abdoul H. Beavogui (Conakry, Republic of Guinea)
Clinical Trial/Study Sponsor:	University of Bamako (Mali)
Trial/Study title:	A phase IIIb/IV randomised, multi-centre, open label, parallel 3-arm clinical study to assess the safety and efficacy of repeated administration of pyronaridine-artesunate, dihydroartemisinin-piperaquine or artemether-lumefantrine or artesunate-amodiaquine over a two-year period in children and adult patients with acute uncomplicated Plasmodium sp. Malaria
Goal:	The aim of this study are to compare the efficacy and the safety of repeated ACT therapy over a period of 2 years (pyronaridine-artesunate or dihydroartemisininpiperaquine are compared to either artesunate-amodiaquine or artemetherlumefantrine) in children and adults.

Primary Objective(s):	The primary objective of this clinical study is to compare the incidence rate of uncomplicated malaria episode in children and adults treated with repeated ACT therapy over a period of 2 years. In this 3 arm study PA and DHA-PQP is compared to either ASAQ or AL (depending on the site location). PA and DHA-PQP will not be formally compared.
Secondary Objective(s):	1. To compare PCR corrected and uncorrected ACPR at D28 and D42 (as defined by WHO 2009 protocol) between the ACT treatment arms 2. To compare re-infection and recrudescence rates over 42 days between the ACT treatment arms 3. To compare FCT and PCT between the ACT treatment arms 4. To compare gametocytes carriage and density between the ACT treatment arms 5. To compare time to the second infection and re-infections between treatments arms 6. To assess and compare safety of the three ACTs in repeated therapy.
Clinical Trial/Study site(s):	• Bougoula Hameau and Kolle (Mali) • Niankoloko-Banfora and Sakaby-Bobo Dioulasso (Burkina Faso), Maferinyah (Republic of Guinea)
Collaborating site(s):	• University of Bamako & Malaria Research and Training Center, Bamako (Mali) • Centre National de Recherche et de Formation sur le Paludisme (CNRFP), Ouagadougou (Burkina Faso) • IRSS, Bobo-Dioulasso (Burkina Faso) • Centre National de Formation et de Recherche en Santé Rurale (CNFRSR) de Mafèrinyah, Conakry (Republic of Guinea) • Medical Research Council (MRC) Gambia, Fajara (The Gambia) • University of Heidelberg (Germany) • Université Claude Bernard Lyon 1, Lyon (France) • Karolinska University Hospital, Stockholm, (Sweden) • London School of Hygiene & Tropical Medicine (LSHTM), London (UK)
Study design:	The study is designed as a comparative, randomised, multicentre, open label, parallel 3 arm study to assess the safety and efficacy of repeated ACT therapy over a period of 2 years in uncomplicated Plasmodium sp. malaria in children and adults. Patients are to be followed for 2 years starting from the first enrolment with the randomised study drug. In each site, eligible subjects are randomised into 3 treatments arms: • Arm 1: dihydroartemisinin-piperaquine (DHA-PQP), • Arm 2: pyronaridine tetraphosphate/artesunate (pyramax, PA), • Arm 3: either artemether-lumefantrine (AL) or artesunate-amodiaquine (ASAQ) (as first line ACT treatment). The total sample size is 4,722 patients. Depending on the study site, DHA-PQP or PA will be compared to either ASAQ (Bougoula-Hameau in Mali; Niankoloko-Banfora in Burkina Faso and Maferinyah in Guinea) or AL (Kolle in Mali and Sakaby-Bobo Dioulasso in Burkina Faso). The total number of patients being randomized in each study drug (PA, DHA-PQP

	or comparator drug) is 1,344. The comparator drug (AL or ASAQ) is regarded in this study as one, although for Mali and Burkina Faso, the comparator will be either ASAQ or AL depending on the study site. This is because, in these 2 countries, both drugs are used as the first line treatments for uncomplicated malaria. No direct comparison will be done between DHA-PQP and PA. This is because, in these 2 countries, both drugs are used as the first line treatments for uncomplicated malaria. No direct comparison will be conducted between DHA-PQP and PA.
Study population:	CHILDREN with uncomplicated malaria (6 months-5 years old) & ADULTS N=4,722
Product(s):	Pyramax: pyronaridine tetraphosphate/artesunate (PA) combined tablet or granule for oral administration. Eurartesim: dihydroartemisinin-piperaquine (DHA-PQP) combined tablet for oral administration. ASAQ-Winthrop/Coarsucam: artesunate-amodiaquine (ASAQ) combined tablet for oral administration. Coartem or Coartem-D: artemether-lumefantrine (AL) combined tablet or dispersible tablet for oral administration.
Manufacturer/Developer:	• Novartis • Sanofi-Aventis • Sigma Tau • Shin Poong Pharmaceutical
Cofunders:	• MRC (UK) • SIDA (Sweden) • BMBF (Germany) • University Claude Bernard Lyon (France) • MRTC (Mali) • CNRFP (Burkina Faso) • IRSS (Burkina Faso) • CNFRSR (Republic of Guinea) • Medicines for Malaria Venture (MMV, Switzerland)
Trial Registration number(s):	PACTR201105000286876
Status:	Ongoing
Results and Outcomes:	This project will develop a sub-region composed of Burkina Faso, Guinea and Mali capable of state of the art clinical studies. Recruiting started on 25 October 2011 in Mali and is now ongoing in all three collaboting countries, i.e Mali, Burkina Faso and Republic of Guinea. Summary of major achievements (from 15 September 2009 until 15 December 2012) 1. In Clinical Trials • Study subjects recruitment started in Sotuba, Mali, in October 2011 and is currently ongoing in all 6 trial sites, i.e. 3 study sites in Mali, 2 in Burkina Faso and 1 in the Republic of Guinea. The sample size was increased from 4,032 to 5,376 subjects (i.e. 448 patients in each study arm) because safety requirements, i.e. inclusion criteria of only recruit adults for the Pyramax arm and to evaluate a minimum of 20 patients receiving at least one repeat dose of Pyramax before enrolling children (≥ 2 years-old with a

	weight of at least 15 Kg) in the study. • A database for the clinical trials has been implemented and data entry is ongoing. 2. In capacity Development, Training and Infrastructure • Several ethics and GCP refresher courses, microscopy certification training, training in data management, training in financial management, etc. were provided in an ongoing basis either on-site or during network-wide meetings. Site upgrades have been completed in all trial participating sites. Details are provided below: 3. Mali: the study site in Kolle is now fully powered with solar panels, which has considerably minimised the consumption of petrol in the site. • A new building facility funded by Vac4all (lead by Prof. O. Doumbo) shares the infrastructure with the WANECAM team and vice versa. The vaccine project also equipped three sister sites in villages around the Bougoula study site of the WANECAM project, which are being used by the WANECAM team for patient recruitment – as the vaccine recruitment is completed. As consequence, and using MMV funding, the WANECAM purchased an additional Toyota Pick-up that is used to shuttle patients from these 3 villages to Bougoula-Hameau, the main WANECAM site. Therefore, the Bougoula-Hameau centre has now 3 Toyota Pick-ups (each one funded by the different funding agencies, i.e. EDCTP, MMV and Va4all). • Refurbishment of a new dispensary in the village of Samanko, which is 4 Km from the Kolle site in Mali. A Nissan pick-up was purchased from MMV's funding to shuttle patients from Samanko to the main study site in Kolle 4. Burkina Faso (CNRFP): renovation of an insectarium in Niangoloko/Banfora field site is ongoing. • Complementary clinical, laboratory and pharmacy procedures were written and implemented in the study site. An external quality control program was also established with the WWARN through the Malaria Molecular External Quality Assessment Program (M2EQAP) for molecular biology laboratory analysis 5. Burkina Faso (IRSS): in Sakaby, the rooms where the clinicians receive the study participants have been refurbished with installation of air conditioners. The inpatient department has been extended with the building of a new hall containing 3-4 beds. The hall contains a new consultation room (for the patients under follow up) and a space for the slides reading. In between, a large space is dedicated for a waiting space for children & parents and can occasionally serve as a meeting space (weekly meeting). • In August 2012, the team in IRSS received the biochemistry machine and the UPS 6. Guinea: all laboratory and clinical equipment was successfully installed and tested. • The Guinean Ministry of Health provided 12 desktop computers to the Centre in Maferinyah. The installation of solar panels in the Maferenya site is underway (with financial support from MMV).

	7. Networking activities • Several Networking activities including North-South, South-South and North-North Networking activities have been carried out during this reporting period, including the Second Investigators Meeting held in Conakry (Guinea, 31 May-3 June 2012), where overall 44 participants from Heidelberg, Switzerland, Gambia, Guinea, Mali and Burkina Faso and MMV were present at this meeting. In addition, a Principal Investigators Meeting was held in Philadelphia in December 2011 at the 60th Annual Meeting of American Society of Tropical Medicine & Hygiene (ASTMH) • Establishment of various 'Interest Groups' to address specific research topics and the terms of reference within the Network. These are the following: – Group 1: Infectivity and transmission, led by Colin Sutherland (LSTMH, UK) – Group 2: Pharmacogenomics, molecular markers, led by Pedro Gill (KI, Sweden) – Group 3: Pharmacokinetics and Parasite genotyping, led by Steffen Borrmann (Heidelberg, Germany) – Group 4: In vitro/Ex-vivo studies, led by Stephane Picot (Lyon, France) – Group 5: Immunology, led by Issa Nebie (CNRFP, Burkina-Faso) Two publications were accepted by the *Am. J. Trop. Med. Hyg.* during the reporting period under evaluation. Seven oral/poster presentations and/or abstracts were presented in international conferences and included in books abstracts. WANECAM network website is under development (www.wanecam.org) Network memberships: West African Network for Clinical Trials of Anti Malarial drugs (Kick-off meeting 23-25 Feb 2010) and World Wide Antimalarial Drug Resistance Network (WWARN).
PhD studies:	Title: Phase IIIb Comparative, Open, Randomised, Multi-Centre, Study of the Efficacy, Safety and Impact on malaria incidence of repetitive treatment with four artemisinin based combination therapies for uncomplicated falciparum malaria: Artesunate-Pyronaridine Dihydroartemisinin-Piperaquine, Artesunate-Amodiaquine, and Artemether-Lumefantrine. Candidate: Issaka Sagara (Universite de Marseille, France) Dates: October 2010 – December 2014
PhD studies: MSc studies:	Title: A pilot study of the efficacy of artesunate in the treatment of uncomplicated malaria in Bougoula-Hameau, Sikasso, Mali Candidate: Aminatou Kone (Karolinska Institute, Sweden) Dates: September 2009-December 2014
	Title: Pharmacodynamic-pharmacokinetic analysis of the effect of artemisinin-based combination therapies on recurrent episodes of uncomplicated *P. falciparum* malaria Candidate: Mamadou Tekete (Heidelberg University, Germany) Start date: September 2009-December 2014
	Title: Epidemiology, Clinical Research Candidate: Esperance Ouedraogo (Vienna School of Clinical Research, Vienna, Austria) Dates: February 2011-July 2012

MSc studies: Other/Sub-studies:	Title: International Master of Medical & Veterinary Entomology Candidate: Moussa Sylla (Guinea) Supervisor: Abdoul H. Beavogui (University of Bobo Dioulasso, Burkina Faso) Dates: September 2009-December 2012
	Title: Molecular Parasitology and Medical Entomology Candidate: Elizabeth Diawara (University of Bamako, Mali) Training Institution: University of Bamako, Mali Dates: July 2009-December 2013
	Baseline malaria epidemiology and normal references ranges for biological parameters in Maferya, Guinea. Objectives: The primary objective of this study is to measure the age specific incidence disease in children during the two consecutive years to estimate the malaria burden and provide data for sample size calculation for future trials in these age groups. The secondary objectives are to monitor the efficacy of first line antimalarial treatment (ASAQ), to determine the normal references values for biological parameters in this population and to assess the year to year variation in frequency of infection and disease and transmission intensity. Study Design: This is an observational study to determine the burden of malaria in children of 3 months to 45 years of age. Subjects will be identified during a census. After obtaining community consent, eligible subjects will be invited to participated and screened after informed consent is obtained. A total of three cross sectional surveys will be carried out each year for two consecutive years (at the beginning and end of the transmission season and middle of the dry season). During these surveys, blood will be collected for malaria smears and haemoglobin measurement using Hemocue. Subjects will be enrolled at the beginning of transmission season each year and will be followed passively for 12 months. During the follow up, subjects with fever of history or fever will receive a clinical examination and finger pricks for malaria smears and determination of haemoglobin, cases diagnosed with malaria will be treated according to National Malaria Control Program (NMCP) guidelines. Diagnosis and treatment of other conditions will be performed as determined by the treating clinician.
Publications:	1. Beshir KB, Hallett RL, Eziefula AC, Bailey R, Watson J, Wright SG, Chiodini PL, Polley SD, Sutherland CJ. Measuring the efficacy of anti-malarial drugs in vivo: quantitative PCR measurement of parasite clearance (2010). *Malaria Journal*; 9:312. Doi: 10.1186/1475-2875-9-312 2. Ferreira PE, Holmgren G, Veiga MI, Uhlén P, Kaneko A, et al. PfMDR1: Mechanisms of Transport Modulation by Functional Polymorphisms (2011). *PLoS ONE* 6(9): e23875. doi:10.1371/journal.pone.0023875 3. Maiga AW, Fofana B, Sagara I, Dembele D, Dara A, Traore OB, Toure S, Sanogo K, Dama S, Sidibe B, Kone A, Thera MA, Plowe CV, Doumbo OK, Djimde AA. No Evidence of Delayed Parasite Clearance after Oral Artesunate Treatment of Uncomplicated Falciparum Malaria in Mali (2012). *Am. J. Trop. Med. Hyg.*, 87(1), 23–28. Doi: 10.4269/ajtmh.2012.12-0058 4. Sagara I, Fofana B, Gaudart J, Sidibe B, Togo A, Toure S,

Sanogo K, Dembele D, Dicko A, Giorgi R, Doumbo OK, Djimde AA. Repeated Artemisinin-Based Combination Therapies in a Malaria Hyperendemic Area of Mali: Efficacy, Safety, and Public Health Impact (2012). *Am. J. Trop. Med. Hyg*., 87(1), 50–56. Doi: 10.4269/ajtmh.2012.11-0649

5. Piedade R, Schaeffeler E, Winter S, Asimus S, Schwab M, Ashton M, Burk O, Gil JP. PXR Variants and Artemisinin Use in Vietnamese Subjects: Frequency Distribution and Impact on the Interindividual Variability of CYP3A Induction by Artemisinin (2012). *Antimicrobial Agents and Chemotherapy*, 56(4), 2153-2157. Doi: 10.1128/AAC.06009-11
6. Kone A, Mu J, Maiga H, Beavogui AH, Yattara O, Sagara I, Tekete MM, Traore OB, Dara A, Dama S, Diallo N, Kodio A, Traoré A, Björkman A, Gil JP, Doumbo OK, Wellems TE, Djimde AA. Quinine Treatment Selects the pfnhe–1 ms4760–1 Polymorphism in Malian Patients with Falciparum Malaria (2013). *The Journal of Infectious Diseases*, 207:520–527. Doi: 10.1093/infdis/jis691
7. Beshir KB, Sutherland CJ, Sawa P, Drakeley CJ, Okell L, Mweresa CK, Omar SA,Shekalaghe SA, Kaur H, Ndaro A, Chilongola J, Schallig HD, Sauerwein RW, Hallett RL, Bousema T. Residual Plasmodium falciparum Parasitemia in Kenyan Children After Artemisinin-Combination Therapy Is Associated With Increased Transmission to Mosquitoes and Parasite Recurrence. *J. Infect. Dis.* 2013 ;208(12):2017-24. doi: 10.1093/infdis/jit431

4.1.7 ADAPT

EDCTP Project Coordinator:	Victor Mwapasa (Malawi-Liverpool-Wellcome Trust Research Programme, Malawi)
EDCTP Call Title:	Support of clinical trials, capacity building and networking in malaria treatment
EDCTP Project Title:	Special populations and label expansion studies with the fixed dose combinations artemether-lumefantrine, amodiaquine-artesunate, and dihydroartemisinin-piperaquine in Zambia, Malawi and Mozambique
EDCTP Project Code:	IP.2007.31060.003
EDCTP Project Start Date:	14 July 2009
EDCTP Project End Date:	31 December 2014
Collaborators:	• Michael Boele van Hensbroek (University of Amsterdam, Netherlands) • Mike Chaponda (Tropical Diseases Research Centre, Zambia) • Umberto D'Alessandro (Prince Leopold Institute of Tropical Medicine (ITM), Belgium) • Fraction Dzinjalamala (University of Malawi) • Brian Faragher (University of Liverpool, UK) • Jean Pierre van Geertruyden (ITM, Belgium) • Exnevia Gomo (University of Malawi) • Raquel González Álvarez (Hospital Clinic of Barcelona, Spain) • Nayra Gutierrez (Manhiça Health Research Center, Mozambique) • Gertrude Kalanda (University of Malawi) • Neelam Kaul (Vienna School of Clinical Research (VSCR), Austria) • Saye Khoo (University of Liverpool, UK) • Heinrich Klech (VSCR, Austria) • David Lalloo (University of Liverpool, UK) • José Machado Almeida (Manhiça Health Research Center, Mozambique) • Jane Mallewa (Malawi-Liverpool-Wellcome Trust Research Programme, Malawi) • Inacio Mandomando (Manhiça Health Research Center, Mozambique) • Clara Menendez (Hospital Clinic of Barcelona, Spain) • Modest Mulenga (Tropical Diseases Research Centre, Zambia) • Denise Suzanne Naniche (Hospital Clinic of Barcelona, Spain) • Feiko ter Kuile (University of Liverpool, UK) • Dianne Terlouw (University of Liverpool, UK) • Steve Ward (University of Liverpool, UK) • Sarah Ann White (Malawi-Liverpool-Wellcome Trust Research Programme, Malawi)
Study/Trial 1	**ARV – ACT trial**
Site Principal Investigator(s):	Victor Mwapasa (Malawi)
Clinical Trial/Study Sponsor:	Liverpool School of Tropical Medicine (LSTM, UK)
Trial/Study title:	Pharmacokinetic studies of interactions between Artemisinin-based Combination Therapies and Antiretroviral Therapies in Malawi - ARV – ACT trial (Theme 1)
Goal:	To reduce malaria-associated morbidity and mortality in HIV positive individuals by determining the most appropriate ACT

	treatment in this group of individuals based on safety and efficacy.
Primary Objective(s):	To identify and describe any pharmacokinetic interactions between ACTs and ARVs and assess the safety of co-administering these drugs in malaria-negative HIV-infected adults.
Secondary Objective(s):	1. To compare the pharmacokinetic parameters (Area Under time-concentration Curve [AUC0-t], maximum concentration [Cmax], time to maximum concentration [tmax], terminal elimination half life [t1/2]) of lumefantrine and dihydroartemisinin in HIV-infected adults taking artemether-lumefantrine plus 3TC-d4T-NVP, 3TC-d4T-EFV or AZT-3TC-TDF-LPV/r and HIV-infected adults taking artemether-lumefantrine only 2. To compare the pharmacokinetic parameters (Cmax, AUC0-t, tmax and t1/2) of dihydroartemisinin, amodiaquine and the amodiaquine metabolite; desethylamodiaquine in HIV-infected adults taking artesunate-amodiaquine plus 3TC-d4T-NVP or AZT-3TC-TDF-LPV/r and HIV-infected adults taking artesunate-amodiaquine only. Note: Interactions with EFV-containing ART will not be assessed because of previous evidence of serious adverse reactions, as discussed in the background section 3. To compare the pharmacokinetic parameters (Cmax, AUC0-t, tmax and t1/2) of piperaquine, and dihydroartemisinin in HIV-infected adults taking dihydroartemisinin-piperaquine plus 3TC-d4T-NVP, 3TC-d4T-EFV or AZT-3TC-TDF-LPV/r and HIV-infected adults taking dihydroartemisinin-piperaquine only 4. Describe the tolerability and incidence of clinical and sub-clinical adverse events upon co-administration of the ACT/ART drug combinations, described in objectives #1 to #3 above.
Study design:	Phase IIIb studies. Interventional. Single centre, open-label, dose-escalation, drug-drug interaction pharmacokinetic study. The study, conducted at MLW (Malawi) only, is being implemented in the following two steps: • In Phase 1 Step 1, half adult doses of the ACTs were administered in HIV positive malaria-negative individuals on steady-state ART and a control group of HIV positive individuals who are not on ART. This step served as a safety evaluation step in drug interaction studies, checking for unexpected clinical toxicities or interactions. Blood samples for data-rich pharmacokinetic assays were collected over a 28 day period alongside real time clinical, biochemical and haematological monitoring for severe adverse events. Pharmacokinetic parameters including AUC, Cmax, Tmax and t1/2 were determined and compared with existing historical data to establish the nature and extent of any drug interaction • In Phase 1 Step 2: (in study arms with no significant adverse events or high drug levels in step 1), data-rich pharmacokinetic studies of full dose ACT are currently being undertaken over a 28 day period in HIV positive malaria negative individuals on steady-state ART and a control group of HIV positive individuals who are not on ART. Close monitoring adverse events will be undertaken. These initial data-rich PK studies of interactions between ART

	and different ACT options in HIV infected malaria-negative individuals (Phase 1) are being conducted at MLW (Malawi) only. They will be followed by multicentre efficacy and safety studies of the selected ACTs with suitable PK profiles (Phase 2). This component of the study will be conducted at MLW (Malawi), TDRC (Zambia) and CISM (Mozambique). The study participants are receiving the following nationally recommended ART regimes: • 3TC (150mg) -d4T (30mg)-NVP (200mg), 1 tablet 12-hourly. Most of the study participants will be receiving this regimen. However, some study participants receiving nevirapine-based ART, may have already been switched to 3TC (150mg) -AZT (300mg) twice daily because of d4T toxicity. • 3TC (150mg) –d4T (30mg) 12-hourly plus Efavirenz (EFV; 600mg) once daily. Some of the study participants receiving EFV-based ART may have been switched to 3TC (150mg) -AZT (300mg) every 12 hours because of d4T toxicity. • 3TC (150mg) -AZT (300mg) every 12 hours plus Tenofovir (TDF; 300mg) once daily plus Lopinavir (200mg)/ritonavir (50mg) 2 tablets every 12 hours.
Clinical Trial/Study site(s):	ART Clinic at Queen Elizabeth Central Hospital (QECH, Blantyre Malawi), Ndola, (Zambia), and Manhiça (Mozambique)
Collaborating site(s):	• Malawi-Liverpool-Wellcome Trust Clinical Research Programme and Department of Medicine, College of Medicine (Malawi) • Manhiça Health Research Center (CISM), Manhiça, (Mozambique) • Tropical Diseases Research Centre, Ndola (Zambia) • Liverpool School of Tropical Medicine, Liverpool (UK) • University of Liverpool, Liverpool (UK) • Institute of Tropical Medicine (ITM), Antwerp (Belgium) • Vienna School of Clinical Research (VSCR), Vienna (Austria) • Amsterdam Medical Centre(AMC), Amsterdam (Netherlands) • Barcelona Centre for International Health Research (CRESIB)/Hospital Clinic, Barcelona (Spain)
Number of subjects:	Stage 1, step 1, N=84 Stage 1, step 2, N=209 Stage 2, N= 490
Product(s):	Artemether-Lumefantrine (AL), (Coartem®, Novartis) Artesunate-Amodiaquine, (Coarsucam™, Sanofi-Aventis) DHA-piperaquine, (Euratesim®), Sigma Tau) Antiretroviral drug combinations: 3TC-d4T-NVP, Trioimune, Cipla), 3TC-AZT-EFV (combivir plus efavirenz, 3TC-AZT-NVP (combivir plus NVP) TDF-3TC-AZT-LPV/r (tenofovir, combivir plus lopinavir/ritonavir).
Manufacturer/Developer:	• Novartis • Sanofi-Aventis • Sigma Tau
Cofunders:	• Carlos III Health Institute (Spain) • MRC UK (UK) • Austrian Federal Ministry of Science (Austria)
Trial Registration number(s):	ATMR 2010030001871293 (Phase I, step 1 study) ATMR 2010030001971409 (Phase I, step 2 study)
Status:	Ongoing
Results and Outcomes:	In October 2011, the team presented preliminary results from Phase 1 Step 1 to the DSMB and at the Sixth EDCTP forum. In February 2012, the DSMB recommended progression of 9 of 11

	study arms from Phase 1 Step 1 to Step 2. By 13th July 2012, it was completed enrolment of participants in 5 of the 9 Phase 1 Step2 study arms and performed a significant number of PK assays. Nevertheless, in February 2012, the DSMB requested the collection of additional data in two of the study arms in Phase 1 Step 1, before it could consider recommending progression to Step 2. In addition, in May 2012 the DSMB recommended enrolment of study participants in three (3) additional study arms that were not originally planned for in order to ascertain causes of some of the haematological abnormalities we are observing in some study arms. The enrolment of participants in these additional arms has significant cost-implications. There have been deviations in the study timelines, as follows: • Enrollment of 1st study participant was delayed from 8 October 2009 to 11 August 2010 • Completion of follow up of study participants in Phase 1 Step 1 was delayed from 31 December 2009 to 24 July 2011 • DSMB recommendation to progress from Phase 1 Step 1 to Step 2 was delayed from 30 April 2010 to 7 February 2012 • Start of Phase 1 Step 2 was delayed from 1 July 2010 to 1 March 2012. In summary, planned study activities are delayed by up to 20 months. In view of the delays described above, the timelines have changed as follows: • End of enrolment in Phase 1 Step 2 is expected on 30 October 2012 from the originally planned date of 15 February 2011. • Completion of PK assays for Phase 1 Step 2 is expected by 31 December 2012. • Commencement of Phase 2 will be delayed to July 2013 from the originally planned date of 1 October 2011. • Completion of Phase 2 is expected by December 2014 from the originally planned date of 30 June 2013.
Study/Trial 2	**ADJUST**
Site Principal Investigator(s):	Dianne Terlouw (Malawi)
Clinical Trial/Study Sponsor:	LSTM (UK)
Trial/Study title:	Programmatic age- and weight based dosing regimens for artemether-lumefantrine and dihydroartemisinin-piperaquine.
Goal:	To design and field test age-based dosing regimens for AL and DHA-PPQ, in order to generate an evidence-base for translation of weight-based dose recommendations to programmatic dosing regimens.
Primary Objective(s):	1. To apply a newly developed modelling tool established by LSTM to determine the optimal age-based dosing regimen for AL and DHA-PIP 2. To determine the dosing accuracy, population pharmacokinetics, safety and effectiveness of the new age-based regimens compared against programmatic weight-based regimens.
Study design:	Objective 1. Statistical modelling: a new modelling tool developed by scientists at the LSTM, DNDi and TDR/WHO is used to develop practical age-based dose regimens that would

	result in the smallest number of patients with malaria receiving ACT doses above or below the therapeutic range. This objective is completed. Objective 2. Interventional: these modelled age-based regimens will be compared in a regulatory trial against the existing weight-based regimen for their dosing accuracy and safety and effectiveness in Malawi (N=400). This part is ongoing and it is expected to be completed by 30 April 2014. Study population: Children ≥ 4 months and adults. Individuals dosed by age and weight will receive the same tablet burden (number of tablets) in 5 categories. The study will therefore focus enrolment of children and adolescents who are at the extremes of their weight or age category (i.e. the heaviest and lightest children per category, at an age around the age cut-offs when a dose increase step is conducted) as this is the group where a differential treatment effect is likely to occur. Anticipated sample size is under review as part of the development of the optimal population PK schedule. Initial estimates assumed Ar-Lu n = ~600, DHA-PPQ n = ~600. Justification: most weight-based regimens consist of 5 weight categories. We will compare drug levels in between individuals dosed by age and weight within the 5 dosing categories, as well as a 6th group of large adults (≥ 70 kg).
Clinical Trial/Study site(s):	Blantyre and Chikhwawa (Malawi)
Collaborating site(s):	• Malawi-Liverpool-Wellcome Trust Clinical Research Programme and Department of Medicine, College of Medicine (Malawi) • Liverpool School of Tropical Medicine, Liverpool (UK) • University of Liverpool, Liverpool (UK) • Vienna School of Clinical Research (VSCR), Vienna (Austria)
Product(s):	Artemether-Lumefantrine (AL), (Coartem®, Novartis) DHA-piperaquine, ((Euratesim®), Sigma Tau)
Cofunders:	• MRC (UK) • Austrian Federal Ministry of Science (Austria)
Status:	Ongoing
Results and Outcomes:	In progress
PhD studies:	Title: Review and development of statistical methodologies for handling missing observations in comparative and non-comparative anti-malarial efficacy and pharmacokinetic /pharmacodynamic studies Candidate: Mavuto Mukaka (Registered at the LSTM, UK) Dates: 1 December 2009-30 November 2013
	Title: Interaction between HIV and malaria: implications for public health and medical decision making Candidate: Victor Chalwe (Institute of Tropical Medicine, Antwerp, Belgium) Dates: 1 December 2009-September 2011 (discontinued)
MSc studies:	Title: MSc in Computer Science focussed on Data Management Candidate: Rueben Dickman Ndindi (University of Edinburg, UK) Dates: September 2010-November 2011 (Completed)
	Title: MPH in Public Health Disease Control Candidate: Sebastian Hachizovu (Institute of Tropical Medicine, Antwerp, Belgium) Dates: August 2009-September 2010 (Completed)
Publications:	In progress

4.1.8 FosClin

EDCTP Project Coordinators:	Saadou Issifou (Albert Schweitzer Hospital, Gabon) Peter Kremsner (University of Tübingen, Germany)
EDCTP Call Title:	Support of clinical trials, capacity building and networking in malaria treatment
EDCTP Project Title:	Development of fosmidomycin and clindamycin in a fixed dose combination, for the treatment of acute uncomplicated plasmodium falciparum malaria. Clinical Trial terminated because data from another study demonstrated low efficacy in children under the age of three years.
EDCTP Project Code:	IP.2008.31060.003
EDCTP Project Start Date:	29 January 2010
Clinical trial termination date:	15 July 2011
PhD study (Ongoing):	Title: Resistance phenotyping and transmission kinetics of clinical *P. falciparum* isolates under fosmidomycin treatment Candidate: José Francisco Fernandes

4.1.9 GMZ2

EDCTP Project Coordinator:	Michael Theisen (Statens Serum Institut (SSI), Denmark)
EDCTP Project Call:	Calls for support of integrated projects on clinical trials, capacity building and networking
EDCTP Project Title:	Fostering research capacity, networking and project management through phase I-IIB clinical trials of candidate malaria vaccine GMZ2.
EDCTP Project Code:	IP.2007.31100.001
EDCTP Project End Date:	19 January 2009
EDCTP Project End Date	18 January 2014
Collaborators:	• Frank Atuguba (Navrongo Health Research Centre, Ghana) • Kalifa Bojang (Medical Research Council Laboratories, The Gambia) • Dawit Ejigu (Statens Serum Institut (SSI), Denmark) • Saadou Issifou (Albert Schweitzer Hospital, Gabon) • Fred Kironde (Makerere University, Uganda) • Elie Mavoungou (Albert Schweitzer Hospital, Gabon) • Benjamin Mordmüller (Albert Schweitzer Hospital, Gabon) • Mark Kaddumukassa (Makerere University, Uganda) • Sodiomon Sirima (Centre national de recherche de Formation sur le Paludisme (CNRFP), Burkina Faso) • Alfred Tiono (CNRFP, Burkina Faso) • Brenda Okech (Statens Serum Institut (SSI), Denmark) • Ismaela Abubakar (Medical Research Council Laboratories, The Gambia) • Ulysse Ateba (Albert Schweitzer Hospital, Gabon) • Bouyoukou Aurore Hounkpatin (Albert Schweitzer Hospital, Gabon)
Site Principal Investigator(s):	• Sodiomon Sirima (Burkina Faso) • Saadou Issifou (Gabon) • Fred Kironde (Uganda) • Frank Atuguba (Ghana)
Clinical Trial/Study Sponsor:	Statens Serum Institut (SSI), Denmark
Trial/Study title:	**Phase IB** A phase I, randomised, controlled, double-blind, single-centre trial to evaluate the safety and immunogenicity of 30 µg and 100 µg of the GMZ2 vaccine in Gabonese children aged 1-5 years. **Phase IIB** A phase II, randomised, controlled, double-blind, multi-centre trial to evaluate the efficacy, safety, and immunogenicity of the GMZ2 vaccine in Gambian, Gabonese, Burkinabe and Ugandan children aged 1-5 years.
Goal:	To develop an effective malaria vaccine that is safe, effective, and can be integrated into the expanded programme on immunisation in African countries.
Primary Objective(s):	**Phase IB** • To evaluate the safety and reactogenicity of three doses of 30 µg and 100µg GMZ2 adsorbed on aluminium hydroxide, in comparison with three doses of the control vaccine (rabies), in healthy Gabonese children aged 1-5 years. **Phase IIB** • To evaluate the efficacy of three doses of GMZ2 vaccine adsorbed on aluminium hydroxide, in comparison with three doses of the control vaccine, in healthy Gambian,

	Gabonese, Burkinabe and Ugandan children aged 1-5 years.
Secondary Objective(s):	**Phase IB** 1. To assess the humoral immune response to the vaccine antigens GMZ2, LURP and MSP3 by measuring the IgG and IgG isotypes by ELISA and antigen specific memory B-cell by ELISPOT 2. To assess the cellular immune response by measuring the T-cell reactivity after stimulation with medium, SEB (positive control), GMZ2, GLURP, or MSP3. Cytokine profiles will be analyzed in the supernatants of short term cultures after 24 and 48 hours of stimulation using Th1/Th2 Cytometric Bead Arrays. **Phase IIB** 1. To evaluate the safety and reactogenicity of three doses of GMZ2 adsorbed on aluminium hydroxide, in comparison with three doses of the control vaccine, in healthy Gambian, Gabonese, Burkinabe and Ugandan children aged 1-5 years 2. To assess the humoral immune response to the vaccine antigens GMZ2, GLURP and MSP3 by measuring the IgG and IgG isotypes by ELISA and antigen specific memory B-cell by ELISPOT in a subset of participants 3. To assess the cellular immune response by measuring the T-cell reactivity after stimulation with medium, SEB (positive control), GMZ2, GLURP, or MSP3. IFN-γ production will be measured on single cell level by intracellular cytokine staining of T-cells in a sub-sample of participants. Cytokine profiles will be analyzed in the supernatants of short term cultures after 24 and 48 hours of stimulation using Th1/Th2 Cytometric Bead Arrays 4. To evaluate the protective efficacy of GMZ2 vaccine on anaemia and severe anaemia as defined by haemoglobin cut-offs at 10mg/dl and 5mg/dl respectively.
Clinical Trial/Study site(s):	• MRU Lambaréné (Gabon) • CNRFP (Burkina Faso) • Makarere University (Uganda) • Navrongo Medical Research Centre (NMRC, Ghana)
Collaborating site(s):	• Medical Research Council Laboratories (The Gambia) • Staten Serum Institut (Denmark) • Albert Schweitzer Hospital (Gabon) • Makerere University (Uganda) • Centre national de recherche de Formation sur le Paludisme (CNRFP) (Burkina Faso) • Navrongo Health Research Centre (NHRC), Ghana • University of Tübingen (Germany)
Study design:	Phase IB: Double-blind, randomised, and controlled trial Phase IIB: Double-blind, randomised, controlled, Multi-centre trial
Study population:	Phase IB: CHILDREN (1-5 years) N=30 Phase IIB: CHILDREN N=1847
Product:	GMZ2: GLURP + MSP3 hybrid
Manufacturer/Developer:	SSI (Denmark)
Cofunders	• University of Tübingen (Germany) • Statens Serum Institut (Denmark) • European Vaccine Initiative (EVI, Germany)

	• Federal Ministry of Education and Research (BMBF, Germany) • Department for International Development (DFID, UK)
Trial Registration number(s):	ATMR2010060002033537
Status:	Ongoing
Results and Outcomes:	The results of baseline studies provided guidance for the sample size of phase IIb. The recruitment target was reached by September 2011. The 1847 enrolled children are being followed-up. Three vaccinations were given at day 0, 28 and 56 and the follow-up duration for the ongoing Phase IIb trial was 24 months after 1st vaccination. The last visits for the last participants were conducted in June 2013 and the results analysis is ongoing.
PhD studies:	Title/topic: Humoral Immune Responses and Immunological Memory against Plasmodium Falciparum Malaria Antigens Candidate: Mark Kaddumukasa (Makerere University, Uganda) Dates: November 2010- September 2013
	Title/topic: Protective role of IgG and FcγR in malaria Candidate: Tiendrebeogo Régis Wendpayangde (CNRFP, Burkina Faso) Dates: 1 November 2011-1 November 2014
MSc study:	Title/topic: MSc Professional IT (Databases) Candidate: Abubakar Ismaela (MRC, The Gambia) Dates: September 2010 -September 2013
Publications:	1. B. Mordmüller et al. Safety and immunogenicity of the malaria vaccine candidate GMZ2 in malaria-exposed, adult individuals from Lambaréné, Gabon. *Vaccine* 28 (2010) 6698–6703 2. Belard S, Issifou S, Hounkpatin AB, Schaumburg F, Ngoa UA, et al. (2011) A Randomised Controlled Phase Ib Trial of the Malaria Vaccine Candidate GMZ2 in African Children. *PLoS ONE* 6(7): e22525. doi:10.1371/journal.pone.0022525

4.1.10 MVVC

EDCTP Project Coordinator:	Odile Leroy (European Vaccine Initiative (EVI), Germany)
EDCTP Project Call:	Calls for support of integrated projects on clinical trials, capacity building and networking
EDCTP Project Title:	Integrating capacity building and networking in the design and conduct of Phase I and II clinical trials of viral vectored candidate malaria vaccines in East and West African children and infants (Vectored Malaria Vaccines)
EDCTP Project Code:	IP.2008.31100.001
EDCTP Project Start Date:	18 December 2009
EDCTP Project End Date:	17 December 2013
Collaborators:	• Muhammed Olanrewaju Afolabi (Medical Research Council (MRC) Laboratories, The Gambia) • Phillip Bejon (University of Oxford, UK) • Kalifa Bojang (MRC Laboratories, The Gambia) • Badara Cisse (University Cheikh Anta DIOP de Dakar (UCAD), Senegal) • Adrian Hill (University of Oxford, UK) • Ya Jankey Jagne (MRC Laboratories, The Gambia) • Issa Ouedraogo Nebie (Centre national de recherche de Formation sur le Paludisme (CNRFP), Burkina Faso) • Alfredo Nicosia (Okairos s.r.l, Italy) • Ogwang, Caroline (Kenya Medical Research Institute (KEMRI), Kenya) • Sodiomon Sirima (CNRFP, Burkina Faso) • Jean Baptiste Yaro (CNRFP, Burkina Faso) • Nicola Viebig (European Vaccine Initiative (EVI), Germany)
Site Principal Investigator(s):	• Kalifa Bojang (The Gambia) • Caroline Ogwang (Kenya) • Sodiomon Sirima (Burkina Faso) • Badara Cisse (Senegal)
Clinical Trial/Study Sponsor:	University of Oxford (UK)
Trial/Study title:	Trial 1: The VAC040 trial: phase Ib, dose escalation trial to assess tolerability and immunogenicity of the malaria vectored vaccine candidates AdCh63 ME-TRAP and MVA ME-TRAP in Kenyan adults Trial 2: The VAC041 trial: phase Ib, age de-escalation trial, to assess the safety, tolerability and immunogenicity of the malaria vectored vaccine candidates AdCh63 ME-TRAP and MVA ME-TRAP in Gambian adults and children (2-6 years) Trial 3: The VAC042 trial: phase Ib, age de-escalation trial, to assess the safety, tolerability and immunogenicity of the vaccine candidates in Gambian infants (5-12 months) Trial 4: The VAC046 trial: phase IIb, to evaluate the efficacy of the vaccination strategy against natural P. falciparum in Kenyan adults Trial 5: The VAC047 trial: phase IIb, to evaluate the efficacy of the vaccination strategy against natural P. falciparum in Senegalese adults Trial 6: The VAC050 trial: phase Ib/IIb, to assess the protective efficacy against clinical malaria in infants and

	children, in Burkina Faso
Goal:	To integrate capacity building and networking in the design and conduct of Phase I and II clinical trials of viral vectored candidate malaria vaccines.
Primary Objective(s):	1. Demonstration of the safety and immunogenicity of a new adenovirus encoding malaria antigens in adults and young children in sub-Saharan Africa 2. Demonstration of the safety and immunogenicity of an adenovirus prime MVA boost regime encoding malaria antigens in adults and young children in sub-Saharan Africa 3. Assessment of the safety, immunogenicity and efficacy of this new prime-boost regime in protection against clinical malaria in 5-17 month old children followed for 12 months at multiple sites in East and West Africa.
Secondary Objective(s):	Vaccine safety and immunogenicity; efficacy as measured by other measures of malaria infection and disease: e.g. parasite density, other definitions of clinical disease, anaemia, cross-sectional parasite rates.
Clinical Trial/Study site(s):	• The phase I trial in Kenyan adults and children was conducted at the KEMRI coastal research unit at Kilifi, Kenya • The phase I study in Gambians was conducted at the Sukuta site near to Banjul in The Gambia • The phase IIb trials are conducted at KEMRI (Kenya), Gwediawaye (Senegal) and at the CNRFP Banfora site in Burkina Faso.
Collaborating site(s):	• CNRFP (Burkina Faso) • KEMRI Wellcome Trust Centre, Kilifi (Kenya) • Farafenni and Sukuta Field Stations (The Gambia) • Université Cheikh Anta Diop (UCAD, Senegal) • The European Vaccine Initiative (EVI, Germany) • University of Oxford (UOXF, UK) • Okairòs s.r.l. (Italy) • Vienna School of Clinical Research (Austria)
Study design:	Randomised, controlled, double-blind phase IIb efficacy trial
Study population:	VAC040 trial: ADULTS, N=30 VAC041 trial: CHILDREN (2-6 years) and ADULTS, N=52 VAC042 trial: INFANTS (10 weeks-12 months), N=72 VAC046 trial: ADULTS, N=120 VAC047 trial: ADULTS, N=120 VAC050 trial: INFANTS (5-17 months) and CHILDREN, N=700
Product(s):	Adenovirus ME-TRAP and MVA ME-TRAP
Manufacturer/Developer:	Impfstoffwerke Dessau-Tornau (Germany)
Cofunders:	• Swedish International Development Cooperation Agency (SIDA, Sweden) • Medical Research Council (UK) • Department of Foreign Affairs (Ireland) • Kenya Medical Research Institute (KEMRI, Kenya) • University of Oxford (UK) • Okairos s.r.l (Italy) • Vienna School of Clinical Research (Austria) • CNRFP (Burkina Faso) • Medical Research Council Laboratories (The Gambia) • Austrian Federal Ministry of Science (Austria) • EVI (Germany) • UCAD (Senegal)
Trial Registration number(s):	The VAC040 trial: NCT01379430 The VAC041 trial: NCT01373879

	The VAC042 trial: NCT01450293 The VAC046 trial: NCT01666925 The VAC047 trial: NCT01658696 The VAC050 trial: NCT01635647 Other reg. numbers: Phase Ib trial in Kenyan adults: ATMR2010020001771828 Phase Ib trial in Gambian adults: PACTR201008000221638
Status:	Ongoing
Results and Outcomes:	The VAC040 trial is now completed. The VAC041 trial enrolled 36 children aged 2-6 years, 12 in the placebo group and 24 in the vaccine group receiving staggered doses of ChAd63ME-TRAP and MVA ME-TRAP at day 0 and day 56. It was conducted between 18 January and 22 December 2011. The trial is completed and a paper has been published. The VAC042 trial enrolled 48 infants in October 2011 and followed them up until January 2013. The close-out visit was condicted in February 2013 and a manuscript on the results from this study is being prepared. In the VAC046 trial, 120 healthy adult males were enrolled in March 2012 and are being followed up until Janauary 2013. The database cleaning for lock-up was done at the end of Jan 2013. In the VAC047 trial, recruitment of 120 participants for VAC047 has been completed and follow up is ongoing. The VAC050 trial, was initiated in October 2012 with the first subject first visit in December 2012 for the phase-I lead-in study (30 children). The phase IIb efficacy study, which will enrol 700 participants, started in March 2013. Both adult and pediatric studies showed a good safety profile at the doses tested. The studies have concluded that ChAd63-MVA ME-TRAP is a safe and highly immunogenic vaccine regimen in adults with prior exposure to malaria. These findings have supported further evaluation of ChAd63/MVA.ME-TRAP vaccines in the ongoing efficacy trials now being conducted in Kenya, Senegal and Burkina Faso.
Total number of subjects (clinical trials only):	In total, 1084 participants in phase I and II trials
PhD studies:	Title/topic: Evaluation of alternative informed consent procedures in clinical trials conducted in The Gambia Candidate: Muhammed Afolabi (MRC, The Gambia) Dates: September 2011-September 2014.
	Title: Malaria burden in the first two years of life Candidate: David Kangoye (CNRFP, Burkina Faso) Date: September 2011-June 2014
	Title: Evolution of malaria morbidity from 2000 to 2011: Identification and Characterization of malaria hot spots in Keur Soce health and demographic surveillance site system Candidate: Mansour Ndiath (UCAD, Senegal) Date: October 2010-December 2013
MSc studies:	Title: Optimization of operational research processes in Keur Soce health Candidate: Massamba Syll (UCAD, Senegal) Date: Started in October 2010
	Title: Seasonal variation of malaria infection in a stable malaria transmission area in Burkina Faso/ Trial Protocol Development”

	at the Vienna School of Clinical Research (Austria) Candidate: Jean Baptiste Yaro (CNRFP, Burkina Faso) Date: Completed in July 2012
	Title: MSc training at the London School of Hygiene and Tropical Medicine Candidate: Ya Jankey Jagne (MRC, The Gambia) Date: September 2012-September 2013
PostDoc study:	Title: B cell memory and immunity to malaria Candidate: Francis Ndungu (KEMRI, Kenya) Date: August 2011-December 2013
Other sub-studies	Baseline Study in Burkina Faso: Assessing malaria morbidity during the first two years of life and age-specific sero-prevalence of adenovirus type Ad5, Ad35 and ChAd63, potential malaria vectored vaccine candidates in two settings of seasonal malaria transmission. Study sample: 750 enrolled participants Baseline Study UCAD: Malaria morbidity during the first two years of life and age-specific seroprevalence of adenovirus type Ad5, Ad35 and ChAd63, potential malaria vectors vaccines candidates in two settings of seasonal malaria transmission. Study sample: 766 enrolled participants
Publications:	1. Ogwang C, Afolabi M, Kimani D, Jagne YJ, Sheehy SH, et al. (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. doi:10.1371/journal.pone.0057726 2. Ndungu FM, Olotu A, Mwacharo J, Nyonda M, Apfeld J, Mramba LK, Fegan GW, Bejon P, Marsh K. Memory B cells are a more reliable archive for historical antimalarial responses than plasma antibodies in no-longer exposed children. *Proc Natl Acad Sci U S A*. 2012 May 22;109(21):8247-52. Epub 2012 May 7. 3. Illingworth J, Butler NS, Roetynck S, Mwacharo J, Pierce SK, Bejon P, Crompton PD, Marsh K and Ndungu FM. Chronic Exposure to Plasmodium falciparum is associated with phenotypic evidence of B and T-cell exhaustion. *J Immunol*. 2013 Feb 1;190(3):1038-47. doi: 10.4049/jimmunol.1202438. Epub 2012 Dec 21. 4. Ibison F, Olotu A, Muema DM, Mwacharo J, Ohuma E, Kimani D, Marsh K, Bejon P and Ndungu FM. Lack of Avidity Maturation of Merozoite Antigen-Specific Antibodies with Increasing Exposure to Plasmodium falciparum Amongst Children and Adults Exposed to Endemic Malaria in Kenya. *PLoS One*. 2012;7(12):e52939. doi:10.1371/journal.pone.0052939. Epub 2012 Dec 26. 5. Ndungu FM, Mwacharo J, Kimani D, Kai O, Moris P, Jonger E, Vekemans J, Olotu A, Bejon P. A Statistical Interaction Between Circumsporozoite Protein-Specific T cell and Antibody Responses and Risk of Clinical Malaria Episodes Following Vaccination with RTS,S/AS01E. *PLoS One*. 2012;7(12):e52870. doi:10.1371/journal.pone.0052870. Epub 2012 Dec 27. 6. Bakshi S and Imoukhuede EB. Malaria Vectored Vaccines Consortium (MVVC). *Human Vaccines* 6:6, 4-5; June 2010. 7. Imoukhuede EB. Vaccine Ventures, International Innovation. *Healthcare*, May 2012, issue 15.

4.1.11 MVVC2

EDCTP Project Coordinator:	Egeruan Babatunde Imoukhuede (European Vaccine Initiative (EVI), Germany)
EDCTP Call Title:	Strategic Primer Grants
EDCTP Project Title:	Field Trials of a New Combination Malaria Vaccine in West African Adults and Children (MVVC 2)
EDCTP Project Code:	SP.2011.41304.025
EDCTP Project Start Date:	1 December 2012
EDCTP Project End Date:	31 October 2014
Collaborators:	• Muhammed Olanrewaju Afolabi (Medical Research Council Laboratories, The Gambia) • Kwaku Poku Asante (Kintampo Health Research Center, Ghana) • Phillip Bejon (University of Oxford, UK) • Badara Cisse (University Cheikh Anta DIOP de Dakar (UCAD), Senegal) • Giuseppe Del Giudice (Novartis International AG, Switzerland) • Adrian Hill (University of Oxford, UK) • Heinrich Klech (Vienna School of Clinical Research, Austria) • Alfredo Nicosia (Okairos s.r.l, Italy) • Patricia Wambui Njuguna (Kenya Medical Research Institute (KEMRI), Kenya) • Seth Owusu-Agyei (Kintampo Health Research Center, Kenya) • Sodiomon Sirima (Centre national de recherche de Formation sur le Paludisme (CNRFP), Burkina Faso) • Alfred Tiono (CNRFP, Burkina Faso) • Nicola Katrin Viebig (EVI, Germany)
Site Principal Investigator(s):	Badara Cisse (Senegal) Sodiomon Sirima (Burkina Faso)
Clinical Trial/Study Sponsor:	Oxford University (UK)
Goal:	This project aims to determine whether addition of a Circumsporozoite Protein (CSP) particle in adjuvant will enhance the efficacy of vectored prime-boost vaccines for P. falciparum. The consortium will conduct two CT's that will assess the safety, immunogenicity and efficacy of the CSP particle in adjuvant sporozoite vaccine alone and combined with a vectored liver-stage malaria vaccine in Africa adults and children
Trial/Study title:	Trial 1: A phase I safety and immunogenicity, age de-escalation CT of the malaria combination vaccine candidate in West African adults, children and infants in Senegal, West Africa Trial 2: A phase I / IIb safety, immunogenicity and efficacy CT of the combination vaccine candidate compared to a rabies control vaccine in African adults in Burkina Faso
Primary Objective(s):	Trial 1: To assess the safety of a protein particle in adjuvant sporozoite vaccine alone and combined with a vectored liver-stage malaria vaccine in Africa adults, children and infants Trial 2: To assess the efficacy of a protein particle in adjuvant sporozoite vaccine combined with a vectored liver-stage malaria vaccine in Africa adults
Secondary Objective(s):	Trial 1: To assess the humoral and cellular immune responses induced

	by the administration of a protein particle in adjuvant sporozoite vaccine alone and combined with a vectored liverstage malaria vaccine in Africa adults, children and infants Trial 2: To assess the safety of a protein particle in adjuvant sporozoite vaccine combined with a vectored liver-stage malaria vaccine in Africa adults, children and infants To assess the humoral and cellular immune responses induced by the administration of a protein particle in adjuvant sporozoite vaccine combined with a vectored liver-stage malaria vaccine in Africa adults, children and infants
Clinical Trial/Study site(s):	Trial 1: University Cheikh Anta DIOP de Dakar (UCAD), Senegal Trial 2: Centre national de recherche de Formation sur le Paludisme (CNRFP), Burkina Faso
Collaborating site(s):	• EVI (Gemany) • UCAD (Senegal) • CNRFP (Burkina Faso) • KEMRI (Kenya) • MRC Laboratories (The Gambia) • Kintampo Health Research Center (KHRC, Ghana) • University of Oxford (UK) • Okairos s.r.l (Italy) • Novartis International AG, Vaccines and Diagnostics Division (Italy)
Study design:	Trial 1: Randomised, Open label, single blind Trial 2: Randomised, controlled, double-blind
Number of subjects:	Trial 1: Total sample size - 60; 12 Adults (18-50yrs), 24 children (2-6 yrs), 24 children(5 -17 months) Trial 2: 120 adult volunteers aged 18 - 50 yrs
Product(s):	ChAd63 ME-TRAP, MVA ME-TRAP, R21 + MF59
Manufacturer/Developer:	Oxford University, Novartis
Cofunders:	• Medical Research Council (UK) • Department of Foreign Affairs (Ireland) • Swedish International Development Cooperation Agency (SIDA, Sweden)
Status:	Ongoing
Results and Outcomes:	Recruitment is not yet started. Expected impact of the project and; how the results will inform future clinical trials under the EDCTP remit: If good safety and efficacy is observed in the proposed clinical trials, the consortium plans to take the combination vaccine forward to phase IIb field efficacy trials in 5-17 months old.
Publications:	

4.1.12 P27ACTB

EDCTP Project Coordinator:	Salim Abdulla (Ifakara Health Research and Development Centre, Tanzania)
EDCTP Call Title:	Strategic Primer Grants
EDCTP Project Title:	Safety and Immunogenicity of P27A, a novel candidate blood-stage malaria vaccine, in Malaria Exposed African Adults
EDCTP Project Code:	SP.2011.41304.047
EDCTP Project Start Date:	1 December 2012
EDCTP Project End Date:	31 October 2014
Collaborators:	• Sophie Alix Houard (European Vaccine Initiative (EVI), Germany) • Francois Spertini (Centre Hospitalier Universitaire Vaudois (CHUV), Switzerland)
Site Principal Investigator(s):	• Seif Shekalaghe (Tanzania) • François Spertini (Switzerland)
Clinical Trial/Study Sponsor:	• Swiss Tropical and Public Health Institute (Swiss TPH, Switzerland) • Pharmaceutical Medicine Unit (PMU, Switzerland)
Goal:	The objectives of this present project are: • To demonstrate the safety and immunogenicity of P27A with Alhydrogel or GLA-SE in healthy non-exposed European adults and exposed African adults, and • To conduct an antigen and adjuvant dose finding in African adults. It will be a phase Ia/Ib clinical trial with a rapid assessment of safety in Switzerland as go criterion to proceed with a more detailed investigation of the best antigen and adjuvant (GLA-SE) dose in a population living in endemic areas. The clinical trial proposed follows the new momentum of having African scientists involved early in the clinical development process, with study findings relevant for the populations that should benefit from this malaria vaccine.
Trial/Study title:	Safety and Reactogenicity of novel candidate blood-stage malaria vaccine, P27A with Alhydrogel or GLA-SE as Adjuvant in Healthy Malaria Non-Exposed European and Malaria Exposed African Adults aged 18-45 years: A staggered Phase Ia/Ib, Randomised, Double-blind, Antigen and Adjuvant Dose-finding, Multi-Centre trial.
Primary Objective(s):	To evaluate the safety of P27A with Alhydrogel or GLA-SE as adjuvant, in healthy European adults not previously exposed to the parasite Plasmodium falciparum and in healthy African adults previously exposed to the parasite.
Secondary Objective(s):	1. To assess the humoral response to the vaccine antigen by measuring the level of antigen specific IgG in all volunteers and its ability to recognise the native protein on merozoites in European volunteers 2. To assess the cellular immune response by measuring the T cell proliferation and cytokine production following in vitro stimulation with the vaccine antigen in all volunteers.
Clinical Trial/Study site(s):	Phase 1a: University Hospital, Lausanne, Switzerland Phase 1b : Bagamoyo Research and Training Centre, Bagamoyo,Tanzania
Collaborating site(s):	• Ifakara Health Research and Development Centre (Tanzania) • EVI (Germany) • CHUV (Switzerland)
Study design:	Phase Ia/Ib, randomised, double-blind, antigen and adjuvant

	dose-finding, multicentre trial.
Study population:	ADULTS, N=56
Product(s):	• P27A Malaria vaccine (active ingredient: PFF0165c) • Form: Frozen Synthetic Peptide • Adjuvant: Alhydrogel or GLA-SEP27A doses
Manufacturer/Developer:	• GMP P27A drug substance manufactured by Almac (UK) • GMP drug product manufactured by Nova Laboratories, Ltd (UK) • GMP Alhydrogel (aluminium hydroxide) bulk material manufactured by Brenntag (Denmark) • The final unidose vials prapared by Nova Laboratories (UK) • The GMP Glucopyranosil Lipid Adjuvant-Stable Emulsion (GLA-SE) and • The GMP EM060 stable emulsion (SE) manufactured by Infectious Disease Research Institute (IDRI, USA)
Cofunders:	• Ifakara Research Institute (Tanzania) • EVI (Germany) • German Ministry of Education and Research (BMBF, Germany) • CHUV (Switzerland)
Status:	Ongoing
Results and Outcomes:	
Publications:	

4.1.13 PfSPZ Challenge Study

EDCTP Project Coordinator:	Bernhards Ogutu (Kenya Medical Research Institute (KEMRI), Kenya)
EDCTP Call Title:	Strategic Primer Grants
EDCTP Project Title:	Platform for Controlled Human Malaria Infection (CHMI) studies for development of new malaria vaccines, drugs and diagnostics in Africa
EDCTP Project Code:	SP.2011.41304.062
EDCTP Project Start Date:	15 December 2012
EDCTP Project End Date:	30 November 2014
Collaborators:	• Salim Abdulla (Ifakara Health Research and Development Centre, Tanzania) • Ayola Akim Adegnika (Albert Schweitzer Hospital, Gabon) • Pedro Aide (Manhiça Health Research Center, Mozambique) • Pedro Alonso (Hospital Clinic of Barcelona, Spain) • Stephen Hoffman (Sanaria Inc., USA) • Kevin Marsh (KEMRI, Kenya) • Benjamin Mordmüller (University of Tübingen, Germany) • Seth Owusu-Agyei (Kintampo Health Research Center, Ghana) • Robert Sauerwein (Radboud University Nijmegen, Netherlands) • Susanne Sheehy (University of Oxford, UK) • Sodiomon Sirima (Centre national de recherche de Formation sur le Paludisme (CNRFP), Burkina Faso) • Marcel Tanner (Swiss Tropical Institute, Switzerland) • Mahamadou Thera (University of Bamako, Mali)
Study/Trial 1	
Site Principal Investigator(s):	• Bernhards Ogutu (Kenya) • Elizabeth Juma (Kenya)
Clinical Trial/Study Sponsor:	University of Oxford (UK)
Trial/Study title:	A pilot study to optimise controlled human malaria infections in humans with varying degrees of prior exposure to malaria using *P. falciparum* sporozoites administered by needle and syringe
Goal:	Controlled human malaria infection (CHMI) trials are carried out in a controlled environment; they allow unprecedented detailed evaluation of parasite growth and immunological responses, providing essential information for vaccine and drug development. This is a CHMI study of 28 healthy adults with varying degrees of prior exposure to malaria in Kenya. Assessing parasite growth dynamics post CHMI and examining the relationship between this and lab assays of functional immunity to *P. falciparum*.
Primary Objective(s):	To establish and assess the CHMI model using parenterally administered PfSPZ (PfSPZ Challenge) in individuals with varying degrees of prior exposure to *P. falciparum* infection an African setting.
Secondary Objective(s):	To examine the relationship between natural immunity to *P. falciparum* malaria and laboratory assays of natural immunity.
Clinical Trial/Study site(s):	• Nairobi (Kenya)
Collaborating site(s):	• KEMRI (Kenya) • Strathmore University & Centre for Research in Therapeutic Sciences (CREATES, Kenya) • CNRFP (Burkina Faso) • Albert Schweitzer Hospital (Gabon) • Kintampo Health Research Center (Ghana)

	• University of Bamako (Mali) • Manhiça Health Research Center (Mozambique) • Ifakara Health Research and Development (Tanzania) • University of Tübingen (Germany) • Radboud University Nijmegen (Netherlands) • Hospital Clinic of Barcelona (Spain) • Swiss Tropical Institute (Switzerland) • University of Oxford (UK) • Sanaria Inc. (USA)
Study design:	Open label, non randomised, controlled human malaria infection (CHMI) pilot study. This may be conducted in two or more phases if volunteer availability and/or other logistic considerations make this preferable.
Study population:	ADULTS (aged 18-40 years old) N=28
Product(s):	Aseptic, purified, cryopreserved *P. falciparum* sporozoites (PfSPZ) for challenge (PfSPZ Challenge). Intramuscular (IM) needle injection in both deltoid muscles.
Manufacturer/Developer:	Sanaria Inc.
Cofunders:	• Federal Ministry of Education and Research (BMBF, Germany) • German Centre for Infection Research (DZIF, Germany) • University of Tubingen (Germany) • NACCAP (Netherlands) • Institute of Carlos III (Spain) • Swedish International Development Cooperation Agency (SIDA, Sweden) • Swiss Tropical and Public Health Institute (TPH, Switzerland) • University of Oxford (UK) • Kenya Medical Research Institute (KEMRI, Kenya) • Sanaria Inc (USA)
Trial Registration number(s):	PACTR201211000433272
Status:	Ongoing
Results and Outcomes:	All volunteers have now been enrolled in the study and have received the study product: PfSPZ Challenge (aseptic, cryopreserved, *Plasmodium falciparum* sporozoites), by intramuscular needle injection. Inpatient follow-up is currently ongoing.
Publications:	

5 Career Development/Senior fellowships

5.1 HIV/AIDS Career Development and Senior Fellowships

Table 5-1: HIV/AIDS fellowship projects supported by EDCTP

Project Acronym (Coordinator)	Study classification/ design	Product(s)	Manufacturer/ Developer	Study population	Status
Alabi SF -HIV	Laboratory assay development	In-house viral load assays	In-house (based on Roche HIV version)	none	Completed
Ekouevi SF - HIV	Phase II multicentre open label trial	Truvada (Emtricitabine + Tenofivir), Niverapine and Zudovudine/Azidothymid	Gilead Sciences, Boehringer Ingelheim and Tübingen respectively	60 mother-child pairs per step (10 per site and per step in Abidjan, Côte d'Ivoire, Soweto, South Africa and Phnom Penh in Cambodia	Completed
Serwanga- CDF	Prospective cohort study on protective HIV immunity	none	Not applicable	200 HIV serodiscordant couples with particular interest in the seronegative partners at high risk for HIV-1 infection.	Completed
Sevene - CDF	Prospect cohort safety study	Sulphadoxine-Pyrimithamine + standard regimen (Stavudine, lamuvidine and niverapine)	WHO pre-qualified drugs	The pregnant women from first ante-natal visit to deliverly, and both mother and baby followed until the child is 12 months old	Completed
Njai- SF	Longitudinal study on HIV immunology	none	Not applicable	The proposed study will use the unique Rural Clinical Cohort established in 1990	Completed
Ndembi -SF	Prospective cohort study on determinants of dual infection with HIV strains	none	Not applicable	A rural clinical cohort (RCC) of over 500 individuals (HIV+ and HIV-) established in 1990	Completed
Mwinzi - SF	Prevalence study on IRIS in	standard regimen (Stavudine,	WHO pre-qualified drugs	HIV-schistosome co-infection patients undergoing HAART In western Kenya.	Completed

	schistomiasis on HAART	lamuvidine and niverapine)			
Kiepela - SF	Laboratory analyses of HIV mucosal immunity and KIR:HAL genes	none	Not applicable		Ongoing
Kityo -SF	Prospective cohort study on drug resistance in children	standard regimen (Stavudine, lamuvidine and niverapine)	WHO pre-qualified drugs	360 HIV-infected children under 12 years of age in three JCRC clinics already participating in the established PASER network monitoring HIVDR in adults	Ongoing
Burgers -SF	Laboratory study on the effect of HIV on lung immunity in TB patients	None	Not applicable	70 adult latent TB patients: 35 HIV+ with CD4 counts >400 and 35 HIV- persons	Completed
Mduluza –SF	Prospective cohort study on the evolution of neutrolising antibodies in HIV – C	None	Not applicable	Stored samples of 70 individuals aged between 15 - 55 years old with acute/recent stages of HIV-1C infection followed up to day 440 in Botswana	Completed
Kayondo –SF	Laboratory analyses for ART resistace in treatment naïve patients	Combivir + niverapine or tenofivir	?? prequalified formulations	Stored samples from structured treatment interrupted (STI) and continuous treatment (CT) arms of the DART of Combivir + Nevirapine or Tenofovir combination regimen	Ongoing
Kennedy -SF	Capacity building for HIV/STI prevention trials in a post-conflict Liberia	None	Not applicable	None	Completed
Kinyanda – SF	Prevalence study of mental health among clinical trials participants in HIV/AIDS	None	Not applicable	HIV patients on HAART in Uganda	Ongoing
Ndounga - SF	Establishment of a HIV positive cohort for site preparation	None	Not applicable	HIV infected individuals	Ongoing

	for HIV and malaria clinical trials in the Republic of Congo				
Delany Moretlwe - SF	Prospective cohort study on HPV and genital warts in HIV-1 negative and HIV-1 positive men taking ART in South Africa.	None	Not applicable	Men having sex with men	Ongoing
Nchinda - SF	Laboratory pre-clinical evaluation of dendritic cell antigens and HIV gag protein vaccines	None	Not applicable	In vitro studies (samples from chronically HIV infected patients in Cameroon)	Ongoing
Were - SF	Prospective cohort study on HIV incidence	None	Not applicable	Women in HIV serodiscordant stable relationships and sex workers in Eldoret	Ongoing
Orrell - SF	A randomised controlled Trial	None	Not applicable (treatment monitoring device)	Adherence-failure relationships in a South African antiretroviral delivery site using an electronic adherence device and sparse Pharmacokinetic sampling	Ongoing
Kiwanuka - SF	Randomised trial of mobile phone reminder vs physical contact tracing among HIV high risk persons in fishing communities in Uganda	None	Not applicable	HIV risk individuals in fishing communities around Lake Victoria	Ongoing
Ocama - SF	Prevalence survey of Hep B and vertical transmission	None	Not applicable	Mothers attending the postnatal/ immunization clinic in Gulu hospital	Ongoing

Jallow – SF	Cohort studies of sex workers and discordant couples	None	Not applicable	Study participants from WANETAM and WAPHIR cohorts (The Gambia, Guinea Bissau and Senegal)	Ongoing
Masimirembwa -SF	A phase IV prospective study to evaluate a pharmacogenetic-guided dosing algorithm based on patient CYP2B6 genotype	Efavirenz	DuPont Pharmaceuticals	Adult patients (>18 years) who are starting on an Efavirenz containing HAART regimen due to a reaction with Nevirapine or due to undergoing concurrent treatment for TB	Ongoing

5.1.1 Abraham Alabi

EDCTP Project Coordinator:	Abraham Alabi (Medical Research Council (MRC) Laboratories, The Gambia)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Development and evaluation of high throughput, cheap and reliable assays for monitoring HIV-1 and HIV-2 viral loads in ARV programmes and clinical trials in developing countries
EDCTP Project Code:	TA.2004.40200.001
EDCTP Project Start Date:	1 January 2005
EDCTP Project End Date:	28 September 2008
Collaborators:	• Steve Kaye (MRC Laboratories, The Gambia) • Samuel McConkey (MRC Laboratories, The Gambia)
Site Principal Investigator(s):	• Clayton Onyango (The Gambia) • Modou Camara (The Gambia) • Steve Kaye (The Gambia) • Samuel MacConkey (The Gambia) • Sarah Rowland Jones (The Gambia) • Simon Agwale (Nigeria)
Goal:	To develop robust and affordable in-house virus load assays for quantifying HIV-1 and HIV-2 RNA in the blood of an infected individual; with similar sensitivity, specificity, and reproducibility to currently available commercial HIV viral load assays. A secondary objective is to train scientists in the West Africa sub-region to encourage a wider use of the assay
Collaborating site(s):	Medical Research Council (UK)
Study design:	Laboratory assay development and validation
Product(s):	In-house viral load assay
Manufacturer/Developer:	Roche proto-type
Status:	Completed
Results and Outcomes:	The project produced a locally validated HIV viral load assay. 10 scientists from West Africa and 9 from Eastern Africa were trained in the course. Six publications resulted from the grant.
Publications:	

5.1.2 Didier Ekouevi

EDCTP Project Coordinator:	Didier Ekouevi (Centre Hospitalier Universitaire (CHU) de Treichville, Cote d'Ivoire)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Phase II multicentre open label trial to evaluate the pharmacokinetics and the safety and toxicity of the Tenofovir-Emtricitabine combination in pregnant women and infants in Africa and Asia
EDCTP Project Code:	TA.2004.40200.003
EDCTP Project Start Date:	1 January 2005
EDCTP Project End Date:	30 October 2007
Collaborators:	• Gerard Allou (Centre Hospitalier Universitaire (CHU) de Treichville, Cote d'Ivoire) • Patricia Fassinou (CHU de Treichville, Cote d'Ivoire) • Appolinaire Horo (CHU de Treichville, Cote d'Ivoire) • Hassan Toure (CHU de Treichville, Cote d'Ivoire) • Ida Viho (CHU de Treichville, Cote d'Ivoire)
Site Principal Investigator(s):	• Thérèse N'dri-Yoman (Côte d'ivoire) • Eric Nerrienet (Cambodia) • Leang Sim Kruy (Cambodia) • James Mcintyre (South Africa) • Marie-Laure Chaix (France) • Christine Rouzioux (France) • Jean-Marc Treluyer (France) • Elisabeth Rey (France) • Stéphane Blanche (France) • Elise Arrive (France)
Clinical Trial/Study Sponsor:	French National Research Agency (France)
Trial/Study title:	Phase II multicentre open label trial to evaluate the pharmacokinetics and the safety and toxicity of the Tenofovir-Emtricitabine combination in pregnant women and infants in Africa and Asia
Objective(s):	To assess safety, pharmacokinetics (PK) and resistance profile of Truvada® (tenofovir disporoxyl fumarate [TDF 300 mg] + Emtricitabine [FTC 200 mg]), an alternative ARV regimen for PMTCT in resource-limited settings in HIV-infected pregnant women and their infants
Clinical Trial/Study site(s):	Centre Hospitalier Universitaire (CHU) de Treichville (Cote d'Ivoire)
Study design and population:	Phase II trial; Pregnant women (HIV+, ≥18 years, 28-38 weeks gestation) and their infants N=72
Product:	• Truvada (Emtricitabine + Tenofivir) • Niverapine • Zudovudine/Azidothymid
Manufacturer/Developer:	• Gilead Sciences (USA) • Boehringer Ingelheim (Germany) • University of Tübingen (Germany)
Cofunders:	National Agency for AIDS Research (ANRS, France
Trial Registration number(s):	NCT00334256
Status:	Completed
Results and Outcomes:	This study laid a foundation for collaboration in PMTCT trials between South Africa, Ivory Coast and Cambodia. The study

	showed that emtricitabine (FTC) achieves adequate blood levels in mothers and their neonates. Three publications have come out of the studies.
Publications:	1. The TEmAA ANRS 12109 Study group. Tolerance and viral resistance after single-dose nevirapine with tenofovir and emtricitabine to prevent vertical transmission of HIV-1. *AIDS 2009*, Vol 23 No 7. 825-33. 2. D Hirt, S Urien, DK Ekouévi, E Rey, E Arrivé, S Blanche, C Amani-Bosse, E Nerrienet, G Gray, M Kone, SK Leang, J McIntyre, F Dabis and J-M Tréluyer. Population Pharmacokinetics of Tenofovir in HIV-1-Infected Pregnant Women and Their Neonates (ANRS 12109). *Clinical pharmacology & Therapeutics*. 5 November 2008; 1-5 3. Deborah Hirt, Saik Urien, Elisabeth Rey, Elise Arrive´, Didier K. Ekoue´vi, Patrick Coffie´, Sim Kruy Leang, Sarita Lalsab, Divine Avit, Eric Nerrienet, James McIntyre, Ste´phane Blanche, Francois Dabis, and Jean-Marc Tre´luyer. Population Pharmacokinetics of Emtricitabine in Human Immunodeficiency Virus Type 1-Infected Pregnant Women and Their Neonates. *Antimicrobial agents and chemotherapy*, Mar. 2009, p. 1067–1073

5.1.3 Jenifer Serwanga

EDCTP Project Coordinator:	Jenifer Serwanga (Medical Research Council Programme on AIDS - Uganda Virus Research Institute (MRC/UVRI), Uganda)
EDCTP Project Call:	Career Development Fellowship
EDCTP Project Title:	Pattern of HIV-induced T-cell response influencing viral load course following HIV infection
EDCTP Project Code:	TA.2005.40203.003
EDCTP Project Start Date:	30 October 2006
EDCTP Project End Date:	23 May 2010
Collaborators:	• Jill Gilmour (International AIDS Vaccine Initiative, Netherlands) • Martin Grobusch (University of the Witwatersrand, South Africa) • Pontiano Kaleebu (MRC/UVRI, Uganda) • Andrew McMichael (University of Oxford, UK)
Site Principal Investigator(s):	• Heiner Grosskurth (Uganda) • Pontiano Kaleebu (Uganda) • Pietro Pala (Uganda) • Daniel Bugembe Lule (Uganda) • Andrew McMicheal (UK)
Trial/Study title:	Pattern of HIV-induced T-cell response influencing viral load course following HIV infection
Objective(s):	1. To determine the plasma viral load pVL trajectory from primary infection through viral set point and beyond 2. To evaluate the relationship between HLA class I polymorphisms and pVL trajectory 3. To evaluate the pattern and magnitude of HIV-1 specific CD8 T-cell response longitudinally following infection 4. To sequence the virus at specified intervals following HIV-1 infection to assess viral evolution and escape from HIV specific responses.
Study design:	Prospective cohort study on protective HIV immunity
Number of subjects:	200
Status:	Completed
Results and Outcomes:	The study investigated how T cell responses in the early phase of HIV-1 infection may influence the course of disease. The results showed that different persons have different levels of both conserved (sustained) and temporary responses to HIV infection. Six staff (Daniel Lule, Kenneth Musinguzi, Ekii Obuku, Samuel Okurut, Andrew Ekii and Pietro Pala) were trained in various short courses including good clinical practices.
Publications:	

5.1.4 Esperança Sevene

EDCTP Project Coordinator:	Esparanca Sevene (Eduardo Mondlane University, Mozambique)
EDCTP Project Call:	Career Development Fellowship
EDCTP Project Title:	Intensive safety monitoring of antimalarial and anti-retroviral drugs used during pregnancy in Manhiça
EDCTP Project Code:	TA.2005.40203.007
EDCTP Project Start Date:	23 April 2010
EDCTP Project End Date:	27 February 2010
Collaborators:	• Xavier Carne (Hospital Clinic of Barcelona, Spain) • Catarina David (Manhiça Health Research Center, Mozambique) • Alexander Dodoo (University of Ghana) • Sureia Hassamo (Mozambique) • Lidia Laço (Mozambique) • Sonia Machevo (Mozambique) • Alda Mariano (Eduardo Mondlane University, Mozambique) • Clara Menendez (University of Barcelona, Spain) • Ana Sofia Roberto (Mozambique) • Joaquina do Rosário (Mozambique)
Goal:	To describe potential adverse drug reactions to anti-malarial and anti-retroviral drugs in pregnant women including adverse pregnancy outcomes
Objective(s):	To measure the incidence of these adverse drug reactions and to determine risk factors that may contribute to the development of adverse drug reactions to anti-retroviral and antimalarial drugs in the pregnant women
Study design:	Prospect cohort safety study
Number of subjects:	2041
Product:	Sulphadoxine-Pyrimithamine + standard regimen (Stavudine, lamuvidine and niverapine)
Manufacturer/Developer:	WHO prequalified regimen drugs
Status:	Completed
Results and outcomes:	A total of 2041 pregnant woman were recruited in the study. Of these 1608 delivered at the hospital. After delivery, 1473 and 877 mothers presented their babies for assessment at second and twelfth month respectively. Fifteen pregnant women presented adverse drug reactions to drugs used during pregnancy but all recovered without sequelae. The study team attended four courses on pharmacovigilance and data management during the course of the projects.
Publications:	1. E Sevene, A Bardají, A Mariano, S Machevo, E Ayala, B Sigaúque, P Alonso, X Carné, C Menendez. Drug exposure and pregnancy outcomes in Mozambique. *Paediatr Drugs*. 2012 Feb 1;14(1):43-9. doi: 10.2165/11591270 2. Sevene E, González R, Menéndez C. Current knowledge and challenges of antimalarial drugs for treatment and prevention in pregnancy. *Expert Opin Pharmacother*. 2010 Jun;11(8):1277-93. 3. Julie Cliff; Simon Lewin; Godfrey Woelk; Benedita Fernandes; Alda Mariano; Esperanca Sevene; Karen Daniels; Sheillah Matinhure; Andrew Oxman; John Lavis. Policy development in malaria vector management in Mozambique, South Africa and Zimbabwe. *Health Policy and Planning* 2010; doi: 10.1093/heapol/czq008. 4. Woelk G, Daniels K, Cliff J, Lewin S, Sevene E, Fernandes B, Mariano A, Matinhure S, Oxman AD, Lavis JN, Stålsby Lundborg C. Translating research into policy: Lessons

learned from eclampsia treatment and malaria control in three southern African countries. *Health Research Policy and Systems* 2009, 7:31. doi:10.1186/1478-4505-7-31
5. John J Aponte, David Schellenberg, Andrea Egan, Alasdair Breckenridge, Ilona Carneiro, Julia Critchley, Ina Danquah, Alexander Dodoo, Robin Kobbe, Bertrand Lell, Jürgen May, Zul Premji, Sergi Sanz, Esperanza Sevene, et al. Efficacy and safety of intermittent preventive treatment with sulfadoxine-pyrimethamine for malaria in African infants: a pooled analysis of six randomised, placebo-controlled trials. *The Lancet* September 17, 2009.
6. Karen Daniels, Simon Lewin, Practihc Policy Group (Sevene E, Mariano A). Translating research into maternal health care policy: a qualitative case study of the use of evidence in policies for the treatment of eclampsia and pre-eclampsia in South Africa. *Health Res Policy Syst*. 2008 Dec 17;6:12. doi: 10.1186/1478-4505-6-12.
7. Sevene E, Mariano A, Mehta U, Machai M, Dodoo A, Vilardell D, Patel S, Barnes K, Carné X. Spontaneous Adverse Drug Reaction Reporting in Rural Districts of Mozambique. *Drug Safety.* 2008; 31 (10): 867-876.
8. Bardagí A, Sigaúque B, Bruni L, Romagosa C, Sanz S, Mabunda S, Mandomando I, Aponte J, Sevene E, Alonso PL, Menendez C. Clinical malaria in African pregnant women. *Malar J*. 2008; 7 (27): 1-7.
9. Ward SA, Sevene EJP, Hastings IM, Nosten F, Mcgready R. Antimalarial drugs and pregnancy: safety, pharmacokinetics, and pharmacovigilance. *The Lancet Infect Dis* 2007;7:136-44.

5.1.5 Harr Freeya Njai

EDCTP Project Coordinator:	Harr Freeya Njai (Medical Research Council Programme on AIDS - Uganda Virus Research Institute (MRC/UVRI), Uganda)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Characterisation of neutralizing antibody responses in Chronic clades A and D Human Immunodeficiency Virus Type 1 (HIV-1) infections and the relationship with established markers of disease progression – A longitudinal study in rural Uganda
EDCTP Project Code:	TA.2007.40200.001
EDCTP Project Start Date:	13 August 2008
EDCTP Project End Date:	12 August 2010
Collaborators:	• Sunita Balla (Prince Leopold Institute of Tropical Medicine (ITM), Belgium) • Heiner Grosskurth (MRC/UVRI, Uganda) • Pontiano Kaleebu (MRC/UVRI, Uganda) • Anatoli Kamali (MRC/UVRI, Uganda) • David Montefiori (Duke University, USA)
Site Principal Investigator(s):	• Heiner Grosskurth (Uganda) • Pontiano Kaleebu (Uganda) • Anatoli Kamali (Uganda)
Objective(s):	To identify and assess the prevalence and potency of broadly neutralising antibodies in a cohort of non-B HIV chronically infected individuals in rural Uganda.
Collaborating site(s):	• Helen Donners (Belgium) • David Montefiori (Duke University, USA)
Study design:	Longitudinal study on HIV immunology
Cofunders:	• Duke University Medical Center (Uganda) • ITM (Belgium) • MRC/UVRI (Uganda)
Status:	Completed
Results and Outcomes:	Magnitude of the NAb response against SF162.LS (subtype B) and MW965.26 (subtype C) varied but was relatively potent in most cases (ID50 titers >1,000, range 20->43740). Between 5-10 years of infection, samples neutralized MW965.26 more than SF162 with a median of 6,243 at T2; at infections more than 10 years the same neutralization profile is seen (i.e. MW965 is more neutralized than SF162). In infections between 5-10 years median neutralization property was significantly higher at T1 than at T2 among those aged between 5-10 years, p values 0.0048 (MW965.26) and 0.012 (SF162.LS). One publication has come out of this work.
MSc study:	Topic: PCR and sequencing assays Candidate: Juma Magambo (MRC/UVRI, Uganda)
Publications:	1. HF Njai, K Tomusange, B Sokolik-Wolak, D Montefiori, S Balla, G Vanham, J Levin, D Maher, A Kamali, H Grosskurth, P Pala and P Kaleebu. 2009. Prevalence of neutralizing antibody responses in chronic clades A and D human immunodeficiency virus type 1 (HIV-1) infections. *Retrovirology* 2009, 6(Suppl 3):P39.

5.1.6 Nicaise Ndembi

EDCTP Project Coordinator:	Nicaise Ndembi (Medical Research Council Programme on AIDS - Uganda Virus Research Institute (MRC/UVRI), Uganda)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Frequency and determinants of dual infection with different strains of HIV-1 in low- and high-risk populations in Uganda
EDCTP Project Code:	TA.2007.40200.011
EDCTP Project Start Date:	31 July 2008
EDCTP Project End Date:	30 July 2010
Collaborators:	• Eric Arts (ase Western Reserve University, USA) • Frances Gotch (Imperial College London, UK) • Heiner Grosskurth (MRC/UVRI, Uganda) • Pontiano Kaleebu (MRC/UVRI, Uganda) • Philippe Lemey (Katholieke Universiteit Leuven, Belgium) • Pietro Pala (MRC/UVRI, Uganda) • Deogratius Ssemwanga • Annemie Vandamme (Katholieke Universiteit Leuven, Belgium) • Carolyn Williamson (University of Cape Town, South Africa)
Site Principal Investigator(s):	Pontiano Kaleebu (Uganda)
Primary Objective(s):	To evaluate the frequency and determinants of dual infection with different strains of HIV-1 in low- and high- risk populations in Uganda. This study had four major objectives and 1 minor: • Implement and validate novel sequence analysis methods developed at the Rega Institute (Belgium) for the detection of instances of co-infection and superinfection in longitudinally collected samples • Determine the clinical consequences of dual infection by comparing disease progression (viral loads and CD4+ counts) between those with and without dual infection • Determine the course of virologic recombination that occurs after dual infection • Determine the immunologic correlates of dual infection • Determine the prevalence of HIV-1 drug resistance among recently infected commercial sex workers.
Collaborating site(s):	George Shaw (UK)
Study design:	Prospective cohort study on determinants of dual infection with HIV strains
Number of subjects:	500
Status:	Completed
Results and Outcomes:	Various methodologies have been optimised and used for the detection and confirmation of dual infection. The study was unable to determine the incidence of co-infection and superinfection but was able to show HIV-1 subtype distribution, multiple infections, sexual networks and partnership histories in Commercial Sex Workers in Kampala. The prevalence of transmitted drug resistance among newly infected commercial sex workers was done among 42 women that seroconverted in the high risk population. DNA sequencing work is in progress.
Publications:	1. Ssemwanga D, Lyagoba F, Ndembi N, Mayanja BN, Larke N, Wang S, Baalwa J, Williamson C, Grosskurth H, Kaleebu P. Multiple HIV-1 infections with evidence of recombination in heterosexual partnerships in a low risk Rural Clinical Cohort in Uganda. *Virology*. 2011 Mar 1;411(1):113-31. Epub 2011 Jan 15.

	2. Ndembi N, Hamers RL, Sigaloff KC, Lyagoba F, Magambo B, Nanteza B, Watera C, Kaleebu P, Rinke de Wit TF. Transmitted antiretroviral drug resistance among newly HIV-1 diagnosed young individuals in Kampala. *AIDS*. 2011 Apr 24;25(7):905-10 3. Deogratius Ssemwanga, Nicaise Ndembi, Fred Lyagoba, Justine Bukenya, Janet Seeley, JudithVandepitte, Heiner Grosskurth and Pontiano Kaleebu. HIV-1 subtype distribution, multiple infections, sexual networks and partnership histories in Commercial Sex Workers in Kampala, Uganda. Submitted. 4. Deogratius Ssemwanga, Nicaise Ndembi, Frederick Lyagoba, Brian Magambo, Anne Kapaata, Justine Bukenya, George W. Lubega, Silvia Bertagnolio, Judith Vandepitte, Heiner Grosskurth, Pontiano Kaleebu. Transmitted Antiretroviral Drug Resistance among drug-naïve Commercial Sex Workers with recent infection in Kampala, Uganda. Submitted.

5.1.7 Pauline Mwinzi

EDCTP Project Coordinator:	Pauline Mwinzi (Kenya Medical Research Institute (KEMRI), Kenya)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Immune reconstitution inflammatory syndrome (IRIS) in schistosomiasis patients undergoing HAART
EDCTP Project Code:	TA.2008.40200.007
EDCTP Project Start Date:	24 November 2009
EDCTP Project End Date:	24 November 2011
Collaborators:	• Robert Colebunders (Prince Leopold Institute of Tropical Medicine (ITM), Belgium) • Diana Karanja (KEMRI, Kenya) • Luc Kestens (ITM, Belgium) • Erick Muok (KEMRI, Belgium) • Katja Polman (ITM, Belgium)
Site Principal Investigator(s):	• Diana Karanja (Kenya) • Erick Muok (Kenya)
Objective(s):	To study the Immunopathogenesls, clinical aspects and management of manifestation of IRIS in HIV-schistosome co-infection patients undergoing HAART In western Kenya. Schistosome infections are common in the same areas where HIV prevalence is also high.
Collaborating site(s):	Bob Colebunders (Belgium), Luc Kestens (Belgium), Katja Polman(Belgium) (Belgium)
Study design:	Prevalence study on IRIS in schistomiasis on HAART
Product:	Standard regimen (Stavudine, lamuvidine and niverapine) and anti-schtistosmes
Status:	Completed
Results and Outcomes:	622 HIV-positive patients were followed. In the first year of follow up 12 patients expressed signs and symptoms of IRIS of whom two met the case definition of IRIS. As a requirement for all staff participants on this project, GCP/GCLP training was provided online from the EDCTP-sponsored AMANET online courses.
PhD study	Title: Immunology of Schistosoma associated IRIS Candidate: Eric Muok (Kenya)
MSc studies:	Title: Pathogenesis of Schistosomiasis/HIV Co-Infection: Polymorphisms in IL-23 Receptor in Schistosomiasis Patients Undergoing Highly Active Antiretroviral Therapy (HAART)" Candidate: George Ogola
	Title: Role of vitaminD3 (1-ALPHA, 25-Dihydroxyvitamin D3) in Schistosoma -IRIS Candidate: Elses Simuyu
Publications:	

5.1.8 Photini Kiepela

EDCTP Project Coordinator:	Photini Kiepela (Medical Research Council South Africa (MRC), South Africa)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Training in mucosal immunity and the evaluation of KIR:nHLA genes in HIV-1 clade c infection: key components to HIV vaccine design
EDCTP Project Code:	TA.2008.40200.015
EDCTP Project Start Date:	25 March 2010
EDCTP Project End Date:	31 December 2014
Collaborators:	• S. Ganesh (MRC, South Africa) • Sharika Gappoo (MRC, South Africa) • R. Govinden (MRC, South Africa) • Thumbi Ndungu'U (University of KwaZulu-Natal, South Africa) • Thesla Palanee (MRC, South Africa) • Jo-Ann Passmore (University of Cape Town, South Africa) • Gita Ramjee (MRC, South Africa)
Site Principal Investigator(s):	• S Ganesh (South Africa) • Sharika Gappoo (South Africa) • R Govinden (South Africa) • Thumbi Ndung'U (South Africa) • Thesla Palanee (South Africa)
Objective(s):	To answer questions relating to the role of host HLA and KIR genotype as HLA class I contributes to both the innate and adaptive immune responses
Study design:	Laboratory analyses of HIV mucosal immunity and KIR:HAL genes
Status:	Ongoing
Results and outcomes:	KIR: HLA project protocol was developed and ethics approval obtained and the e-learning workshops have compeleted. Statistical training in Methods in HIV Vaccine Trial Design and Evaluation took place place on 28-30 March 2012.
Publications:	

5.1.9 Cissy Kityo Mutuuluza

EDCTP Project Coordinator:	Cissy Kityo (Joint Clinical Research Center (JCRC), Uganda)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Evaluating antiretroviral drug resistance in HIV infected children in Africa
EDCTP Project Code:	TA.2008.40200.022
EDCTP Project Start Date:	23 November 2009
EDCTP Project End Date:	23 November 2012
Collaborators:	• Diana Gibb (Medical Research Council (MRC), UK) • Joshua Kayiwa (JCRC, Uganda) • Peter Mugyenyi (JCRC, Uganda) • Victor Musiime (JCRC, Uganda) • Lillian Nakatudde (JCRC, Uganda) • Tobias Rinke de Wit (International Centre of Reproductive Health (ICRH), Netherlands)
Site Principal Investigator(s):	• Joshua Kiyiwa (Uganda) • Peter Mugyenyi (Uganda) • Victor Musiime (Uganda) • Lillian Nakatudda (Uganda)
Objective(s):	To determine what proportion of a paediatric cohort prevent HIV drug resistance (HIVDR) as measured by viral load suppression, and what HIVDR mutations and mutational patterns are observed in patients not achieving undetectable viral load.
Clinical Trial/Study site(s):	
Collaborating site(s):	MRC (UK)
Study design:	Prospective cohort study on drug resistance in children
Number of subjects:	360
Product:	Standard regimen (Stavudine, lamuvidine and niverapine)
Manufacturer/Developer:	Prequalified regimens
Status:	Ongoing
Publications:	

5.1.10 Wendy Burgers

EDCTP Project Coordinator:	Wendy Burgers (University of Cape Town, South Africa)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	The effect of HIV co-infection on the immune response to *Mycobacterium tuberculosis* (*M.tb*) in the lung
EDCTP Project Code:	TA.2008.40200.020
EDCTP Project Start Date:	9 October 2009
EDCTP Project End Date:	9 October 2011
Collaborators:	• Willem Hanekom (University of Cape Town, South Africa) • Barbara Kalsdorf (Research Center Borstel, Germany) • Gerhard Walzl (Stellenbosch University, South Africa) • Robert Wilkinson (University of Cape Town, South Africa)
Site Principal Investigator(s):	• Willem Hanekom • Barbara Karlsdof • Gerhard Walzl • Robert Wilkinson
Objective(s):	To examine the effect of HIV co-infection on the immune response to *Mycobacterium tuberculosis*. The proposed research aims to identify aspects of the immune response to *M.tb* which differ in persons latently infected with TB in the presence or absence of HIV co-infection.
Study design:	Laboratory study on the effect of HIV on lung immunity in TB patients
Number of subjects:	70
Status:	Completed
Results and outcomes:	By the end of the project 75% of the intended study volunteers were recruited, all samples stored and all planned analyses done. The project has also been successful in being awarded funds (R90,000 for 1 year) from a local South African source, the NHLS Trust, with the Senior Fellow Wendy Burgers as PI (Principal Investigator). This grant will allow completion of the remaining sample collection and analysis on this project, and perform (limited) additional analyses focusing on innate immune dysfunction, in particular alveolar macrophage function in the lungs, as well as establish links with TB researchers at UKZN and Harvard Medical School, Boston, USA.
PhD study:	Rubina Bunjun
MSc study	Narjis Khatoon Thawer
PostDoc study:	Zekerias Ginbot, Andreia Soares
Publications:	

5.1.11 Takafira Mduluza

EDCTP Project Coordinator:	Takafira Mduluza (University of Zimbabwe)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Evolution of neutralizing antibodies among acute to early HIV Subtype C infected individuals in Botswana: one year longitudinal study.
EDCTP Project Code:	TA.2009.40200.005
EDCTP Project Start Date:	14 May 2010
EDCTP Project End Date:	14 May 2012
Collaborato(s):	• Joseph Makhema (Botswana Harvard Partnership (BHP), Botswana) • Keikantse Matlhagela (BHP, Botswana) • Rosemary Musonda (BHP, Botswana)
Site Principal Investigator(s):	• Joseph Makhema (Botswana) • Keikantse Mathlagela (Botswana) • Sikhulile Moyo • Rosemary Musonda (Botswana) • Vladmir Novitsky
Objective(s):	To characterise the evolution of neutralising antibodies against HIV-1 subtype C gp 120 molecular envelope clones from acute/and early heterosexual acquired HIV-1 subtype C infections in Botswana
Study design:	Prospective cohort study on the evolution of neutrolising antibodies in HIV –C
Number of subjects:	72
Status:	Completed
Results and outcomes:	Using stored samples collected from 72 HIV-infected patients in 2005-2008, 50 plasma samples were analysed. Results so far show that broadly neutralizing antibodies are indeed present during pregnancy and at selected time points during the course of infection in the case of acute and recently infected individuals. Most plasmas have 50% neutralizing capacity, but the majority fail to exhibit 90% neutralisation. There was no strong inhibition of IN93, an HIV-1C strain similar to the predominant subtype C in the region. There is potential of identifying samples that show broad inhibition of various virus strains; with some samples showing high inhibition of subtype B (BR92).
MSc studies:	Candidate: Keabetswe Bedi
	Candidate: Sheron Dzoro
Publications:	

5.1.12 Jonathan Kayondo

EDCTP Project Coordinator:	Jonathan Kayondo (Medical Research Council Programme on AIDS - Uganda Virus Research Institute (MRC/UVRI), Uganda)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Evolution of HIV-1 ARV drug resistance mutations in ART naïve individuals during therapy; threshold frequency levels and linkage context associated with treatment failure in Uganda
EDCTP Project Code:	TA.2009.40200.011
EDCTP Project Start Date:	30 March 2010
EDCTP Project End Date:	31 December 2012
Collaborators:	• Pontiano Kaleebu (MRC/UVRI, Uganda) • Jean Mbisa (Health Protection Agency (HPA), UK) • Chris Parry (MRC/UVRI, Uganda) • Deenan Pillay (University College London/HPA, UK)
Objective(s):	To complement the just commenced Wellcome Trust-funded Uganda Virus Research Institute postdoctoral research, which looks at issues related to Nevirapine induced HIV-1 drug resistance, by including in-depth investigations on the evolution of drug resistance mutations in ART-naïve individuals.
Collaborating site(s):	HPA (UK)
Study design:	Laboratory analyses for ART resistance in treatment naïve patients
Number of subjects:	Unspecified stored samples
Product:	Combivir plus niverapine or tenofivir
Manufacturer/Developer:	Prequalified formulations
Status:	Ongoing
Results and Outcomes:	Single genome sequencing has been established by the Principal Investigator (PI) at the UVRI laboratory. The Institute has also acquired phylogenetic and sequence analysis software packages. Four patients that had persistent viraemia during combivir/nevirapine therapy are being followed in the study.
Publications:	

5.1.13 Stephen Kennedy

EDCTP Project Coordinator:	Steven Kennedy (University of Liberia)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Building Research Infrastructure and Capacity to Implement an HIV/STD Prevention Trial in Post-Conflict Liberia
EDCTP Project Code:	TA.2009.40200.023
EDCTP Project Start Date:	7 May 2010
EDCTP Project End Date:	7 May 2012
Collaborators:	
Objective(s):	To support research infrastructure, training and partnerships to prevent HIV/AIDS in rural Liberia and to implement and evaluate an HIV/AIDS programme for high risk rural youth in post-conflict Liberia.
Study design:	Capacity building for HIV/STI prevention trials in a post-conflict Liberia
Number of subjects:	250
Status:	Completed
Results and Outcomes:	HIV and STI baseline data have been collected in post-conflict Liberia. A total of 118 males and 132 females (n=250) were initially enrolled into the programs. The 3-month follow-up survey was administered to 115 males and 126 females (n=241) in both programs from the four communities, thus constituting an overall retention rate of 96% (i.e. attrition rate 4%). The 9-month follow-up survey was administered to 111 males and 113 female (n=224), constituting an overall retention rate of 90% (i.e. attrition rate 10%), respectively.
Publications:	1. Katharine A. Atwood, Stephen B. Kennedy, Steve Shamblen,Jemee Tegli, Salome Garber, Pearl W. Fahnbulleh, Prince M. Korvah,Moses Kolubah, Comfort Mulbah-Kamara, and Shannon Fulton. Impact of school-based hiv prevention program in post-conflict Liberia. *AIDS Education and Prevention*, 24(1), 68–77, 2012 2. Katharine A. Atwood, Stephen B. Kennedy, Steve Shamblen, Curtis H. Taylor, Monica Quaqua, Ernree M. Bee, Mawen E. Gobeh, Daisajou V. Woods and Barclay Dennis. Reducing sexual risk taking behaviors among adolescents who engage in transactional sex in post-conflict Liberia. *Vulnerable Children and Youth Studies*. Vol. 7, No. 1, March 2012, 55–65

5.1.14 Eugene Kinyanda

EDCTP Project Coordinator:	Eugene Kinyanda (Medical Research Council Programme on AIDS - Uganda Virus Research Institute (MRC/UVRI), Uganda)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Clinical trials in HIV/AIDS in Africa: Should they routinely control for mental health factors?
EDCTP Project Code:	TA.2010.40200.011
EDCTP Project Start Date:	12 April 2011
EDCTP Project End Date:	30 July 2014
Collaborators:	• Heiner Grosskurth (LSHTM, UK/Mwanza Intervention Trials Unit (MITU), Tanzania) • Jonathan Levin (MRC/UVRI Uganda Research Unit on AIDS, Uganda) • Vikram Patel (London School of Hygiene and Tropical Medicine (LSHTM), UK/Sangath Centre Porvorim, India)
Objective(s):	The study aims to answer the following questions: 1. What is the prevalence of mental health problems associated with major depressive disorders (MDD) and maladaptive coping style (MACS) among HIV-infected patients in Uganda, and what is the incidence of MDD in HIV/AIDS? 2. Do mental health problems associated with MDD and MACS significantly impact on HIV disease progression in an Ugandian socio-cultural environment including through non-adherence to ART? 3. What would be the potential impact of MDD and MACS mental health covariates on HIV disease progression on the DART trial results under a range of possible differential treatment effects in the subgroups of patients with and without psychological problems?
Study design:	Prevalence study of mental health among clinical trials participants in HIV/AIDS
Number of subjects:	230
Status:	Ongoing
Results and Outcomes:	So far 230 subjects (Entebbe- 140; Masaka - 90) have been recruited. The rate of major depressive disorder in Masaka site (N= 25) is 4%. An MSc student (Alan Kalungi) has developed the proposal, 'Association between serotonin transporter gene polymorphisms and suicidality in HIV/AIDS in a Ugandan population'. In the MSc project DNA will be extracted in Uganda and the genetic analysis will be done in South Africa. The fellow has developed an extensive network within and outside Uganda.
MSc study	Title: Association between serotonin transporter gene polymorphisms and suicidality in HIV/AIDS in a Ugandan population Candidate: Alan Kalungi (Makerere University, Uganda) Dates:
Publications:	1. Eugene Kinyanda, Susan Hoskins, Juliet Nakku, Saira Nawaz and Vikram Patel. Prevalence and risk factors of major depressive disorder in HIV/AIDS as seen in semi-urban Entebbe district, Uganda. *BMC Psychiatry* 2011, 11:205

5.1.15 Mathieu Ndounga

EDCTP Project Coordinator:	Mathieu Ndounga (Centre d'Etudes sur les Ressources Végétales (CERVE), Congo)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Establishment of a HIV positive cohort for site preparation for HIV and malaria clinical trials in the Republic of Congo
EDCTP Project Code:	TA.2010.40200.011
EDCTP Project Start Date:	29 April 2011
EDCTP Project End Date:	29 April 2013
Collaborators:	• Roth Cecile Laure Mapapa Miakassissa (CERVE, Congo) • Rock Fabien Niama (Laboratoire Nationale de Sante Publique, Congo) • Francine Ntoumi (Organization for the Coordination of Endemic Disease Control in Central (OCEAC), Cameroon) • Mayengue Issamou Pembe (University Marien Ngouabi of Brazzaville, Congo) • Celine Samba Louka (CERVE, Congo)
Goal:	This project aims at developing capacities for the conduct of clinical trials on HIV/AIDS, malaria and tuberculosis in Central Africa as part of CANTAM
Objective(s):	• To investigate the effect of HIV infection on clinical malaria infections • To evaluate the impact of clinical malaria on HIV infection • To develop human capacities in the conduct of clinical research for future HIV clinical trials in Brazzaville
Study design:	Clinical site development
Number of subjects:	101 children aged from 9 months to 10 years
Status:	CLOSED
Results and outcomes:	By end of 2012 a cohort of 101 HIV infected children has been established in Brazzaville. Preliminary results show that all the HIV-infected children did not present with positive blood smear after 4 months of follow up.
PhD study:	Topic: Investigate viral load through the Laboratoire national de santé Publique in Brazzaville Candidate: Laure Ghoma Linguissi (Fondation Congolaise Pour La Recherche Médicale, Congo)
Publications:	

5.1.16 Sinead Delany Moretlwe

EDCTP Project Coordinator:	Sinead Delany Moretlwe (University of the Witwatersrand, South Africa)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	HPV in Men (HIM): Natural history of human papillomavirus (HPV) infection and genital warts in HIV-1 negative men, HIV-1 positive men not yet taking ART, and HIV-1 positive men taking ART in South Africa.
EDCTP Project Code:	TA.2010.40200.034
EDCTP Project Start Date:	8 June 2011
EDCTP Project End Date:	31 March 2014
Collaborators:	• David Lewis (National Institute for Communicable Diseases, South Africa) • Philippe Mayaud (London School of Hygiene and Tropical Medicine (LSHTM), UK)
Goal:	To show the epidemiology of HPV infection in men by HIV status and to provide data to inform mathematical models that predict the impact of HPV vaccination (e.g. using Gardasil) in various African settings, including South Africa.
Objective(s):	**Primary objective** To determine the prevalence of HPV disease (anogenital and oropharyngeal), type distribution of low risk (LR)- and high risk (HR)-HPV DNA, and HPV seroprevalence in men in South Africa over a 12 -18 month period. **Secondary objectives** To determine: 1. The incidence of HPV disease and infection in this cohort over a maximum of 18 months 2. The persistence of HPV disease and infection (presence of HPV DNA) in this cohort followed for a maximum of 18 months 3. Socio-demographic, behavioural and clinical factors associated with HPV infection and disease in this cohort 4. Acceptability of anal swabbing in this population of presumed predominantly heterosexual African young men; and knowledge and acceptability of vaccine and factors associated with vaccine acceptability in this cohort.
Study design:	Cohort study on HPV and genital warts in HIV-1 negative and HIV-1 positive men taking ART in South Africa
Number of subjects:	150
Status:	Ongoing
Results and outcomes:	Clinical trial: by end of 2012 recruitment of HIV negative cohort was completed (150 men recruited and 93% retained at 12 months). Plans for recruiting HIV positive cohort in place; preliminary community engagement activities include presentation to CAB, radio activities and community education events. Capacity building: eight staff have received GCP/GCLP training; one MSc student completed her MSc thesis; one PhD student has joined the study; exchange visits with European collaborators planned for November 2012; 7 staff received HIM-SA protocol training in May 2012.
MSc study:	Candidate: Jo Gibbs (LSHTM, UK) Supervisor: Sinead Delany Moretlwe and Philippe Mayaud
Publications:	

5.1.17 Godwin Nchinda

EDCTP Project Coordinator:	Godwin Nchinda (International Reference Centre Chantal Biya (CIRCB), Cameroon)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Pre-clinical evaluation of dendritic cell targeted consensus B, C, CRFO2_AG and MOSAIC HIV gag protein vaccines in PBMC from chronically infected patients in Central Africa
EDCTP Project Code:	TA.2010.40200.016
EDCTP Project Start Date:	10 March 2011
EDCTP Project End Date:	10 March 2013
Collaborators:	• Vittorio Colizzi, (CIRCB, Cameroon) • Ralph Steinman (The Rockefeller University, USA) • Klaus Uerberla (Ruhr University Bochum, Germany)
Goal:	This project will verify if a consensus B based HIV gagP24 vaccine targeted to dendritic cells would be able to recall *in vitro* similar gag specific T cell responses in PBMCs from people chronically infected with the prevalent strains of HIV-1 in Africa.
Objective(s):	1. To examine if a DC targeted consensus B HIV gag p24 protein vaccine could recall in vitro pre-existing gag specific T cells in PBMCs of subjects chronically infected with unrelated HIV-1 strains prevalent in Africa 2. To compare in terms of magnitude, breadth, and depth T cell responses recalled in vitro in PBMCs of subjects chronically infected with HIV-1 in central Africa by 4 four different DC targeted HIV gag p24 protein vaccines based on CRFO2_AG, C, B and MOSAIC HIV gag sequences, which are designed to address the problems associated with HIV-1 diversity.
Collaborating site(s):	• Rokerfeller University (USA) • Ruhr University (Germany)
Study design:	Laboratory pre-clinical evaluation of dendritic cell antigens and HIV gag protein vaccines
Status:	Closed
Results and outcomes:	The project is contributing to training of 4 PhD students, 2 MSc and 1 nurse. The EDCTP funds have been used to purchase of a number of equipment. The project has established links with University of Yaounde 1, Institut Pasteur Cameroon, Case Western Reserve University and Tromsø Science Park of Norway.
PhD studies	Candidate: Georgia Ambada
	Candidate: Carol Ngaye
	Candidate: Tchaji Colin
	Candidate: Benson Nyachongi
MSc studies	Candidate: Nja Nadesh
	Candidate: Archille Nague
Publications:	

5.1.18 Edwin Were

EDCTP Project Coordinator:	Edwin Were (Moi University, Kenya)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Enhancing HIV prevention trial capacity in Eldoret, Kenya through a baseline HIV incidence study on two HIV prevention priority populations
EDCTP Project Code:	TA.2011.40200.012
EDCTP Project Start Date:	29 February 2012
EDCTP Project End Date:	30 June 2014
Objective(s):	The primary objective is to determine the HIV incidence in women in HIV serodiscordant stable relationships and sex workers in Eldoret, Kenya. The secondary objectives are to: 1. Evaluate the acceptability of a model of service provision strategy offering targeted reproductive health services (including STI treatment and condom uptake) to a cohort of HIV serodiscordant couples and commercial sex workers in Eldoret MTRH catchment area 2. Collaborate with established centres such as South African Research Ethics Training Initiative (SARETI) to develop and teach short courses under the existing MUSOM program in Eldoret on good clinical practice and ethical issues in HIV prevention trials. Furthermore, two Masters level training will be supported in the existing MUSOM program
Collaborating site(s):	Family Health Options Kenya (FHOK), Eldoret, Kenya
Study design:	Prospective cohort study on HIV incidence
Number of subjects:	Cohort of 500 to 700 HIV negative women, with approximately 250 to 350 HIV negative female partners of HIV positive men and same number of HIV negative sex workers.
Status:	Ongoing
Results and Outcomes:	The study opened enrolment in April 2012. 113 HIV-uninfected women were enrolled from discordant couples and 557 HIV-uninfected women from the female sex worker population in Eldoret by December 2012. The project will continue with the follow-up of the participants enrolled into the cohorts study. So far the rate of retention is approximately 96.2% and 84.3% for discordant couples and female sex workers respectively. The project has successfully carried out 8 focus group discussions at the beginning of the study. The data has been transcribed, translated into English and thematic analysis is ongoing. During the first year of the study, the project provided reproductive health services to women from both cohorts. Two graduate students in the Masters of International Research Ethics programme in the Moi University were supported through this study.
MSc study:	Masters in International Research Ethics Course Candidate: Margaret Anyango Gogo (Moi University, Kenya)
	Masters in International Research Ethics Course Candidate: Henry K. Lodea (Moi University, Kenya)
Publications:	

5.1.19 Catherine Orrell

EDCTP Project Coordinator:	Catherine Orrell (University of Cape Town, South Africa)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	A randomised controlled trial to explore the adherence-failure relationships in a South African antiretroviral delivery site using an electronic adherence device and sparse pharmacokinetic sampling (The TAP study)
EDCTP Project Code:	TA.2011.40200.015
EDCTP Project Start Date:	29 February 2012
EDCTP Project End Date:	30 June 2014
Collaborators:	• David Bangsberg (Harvard University, USA) • Karen Cohen (University of Cape Town (UCT), South Africa) • Gary Maartens (UCT, South Africa) • Catherine Orrell, Karen Cohen (UCT) • Robin Wood (UCT, South Africa)
Goal:	1. To determine whether an adherence monitoring device (EAMD) with text message and dosing feedback improves adherence, retention in care and virological outcomes among individuals receiving new antiretroviral therapy (ARM 1: EAMD alone, used as a pill box; ARM 2: EAMD with reminder message for late dosing and feedback on dosing patterns at clinical visits). 2. To determine whether population pharmacokinetic data explain the discordance between adherence and virological response.
Objective(s):	This study will use a locally developed real time adherence monitoring tool to explore and improve adherence in ART-naïve individuals commencing treatment in an established ART cohort. The study will use adherence, virological and pharmacokinetic data to examine adherence failure discordance. The questions to be answered by the study are: 1. Does a real-time electronic adherence monitoring tool with text message feedback improve adherence, retention in care and virological outcomes among ART-naïve individuals receiving first-line therapy? 2. Does population pharmacokinetic data explain discordance between adherence and virological response?
Collaborating site(s):	Harvard University (USA)
Study design:	A randomised controlled trial with two arms, as follows: **Control arm:** Standard of care at ART clinic with use of an electronic adherence monitoring device (EAMD or Wisepill) to monitor adherence only (i.e., without any feedback). **Experimental group:** Control arm with the addition of the use of the EAMD text message service when dosing late, and EAMD dosing feedback at 4-monthly visits.
Study population:	ADULTS and ADOLESCENTS (12-80 years); HIV+, ART-naïve individuals N=230
Trial Registration number(s):	PACTR201311000641402
Status:	Ongoing
Results and outcomes:	Site development was completed in May 2012. Study staff were trained in GCP. By end of March 2013, 308 people had been screened and 216 had been randomised. 95 people completed the week 16 visits and have had samples stored for pharmacokinetic analysis, cytochrome 2B6 genotyping and HIV genotyping (if required). Once all patients complete each visit

	the samples will be batched and sent to the laboratory
Publications:	

5.1.20 Noah Kiwanuka

EDCTP Project Coordinator:	Noah Kiwanuka (Medical Research Council Programme on AIDS - Uganda Virus Research Institute (MRC/UVRI), Uganda)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	A randomised trial to assess retention rates using mobile phones versus contact tracing, andto characterize trends in HIV-1 prevalence and incidence in a potential HIV vaccine efficacy population of fishing communities around Lake Victoria, Uganda
EDCTP Project Code:	TA.2011.40200.035
EDCTP Project Start Date:	13 April 2012
EDCTP Project End Date:	13 August 2014
Collaborators:	• Francis Bajunirwe (MRC/UVRI, Uganda) • Anatoli Kamali (MRC/UVRI, Uganda) • Juliet Mpendo (MRC/UVRI, Uganda)
Trial/Study title:	A randomized trial to assess retention rates using mobile phones versus contact tracing, and characterize trends in HIV-1 prevalence and incidence in a potential HIV vaccine efficacy population of fishing communities around L. Victoria, Uganda
Goal:	The aim of the project is to perform an assessment of the suitability of HIV risk individuals in fishing communities around Lake Victoria for HIV vaccine efficacy trials through characterization of recruitment, retention, willingness to participate (WTP), and trends in HIV prevalence and incidence, and to build statistical and data management capacity for clinical trials research. The research questions are: (1) does mobile phone reminder yield significantly higher retention rate than physical contact tracing among HIV high risk persons in fishing communities in Uganda?; (2) what are the trends in HIV-1 incidence and prevalence among HIV risk individuals in fishing communities around Lake Victoria?; (3) what is the level of determinants of willingness to participate in HIV vaccine efficacy studies among HIV-1 risk individuals in fishing communities around Lake Victoria
Objective(s):	**Primary Objective:** 1. To determine whether retention in the study will be significantly different among persons followed up using mobile telephones (calls and text messages) compared to physical contact tracing. **Secondary Objectives:** 1. To characterize trends in HIV-1 incidence and prevalence among HIV risk individuals in fishing communities around Lake Victoria 2. To determine the level and determinants of willingness to participate in HIV vaccine efficacy studies among HIV-1 risk individuals in fishing communities around Lake Victoria 3. To build clinical trials-specific statistical and data management capacity to provide support and skills to clinical trial investigators, faculty and students.
Clinical Trial/Study site(s):	Lambu and Kasenyi, Uganda
Study design:	A randomised controlled trial with two arms, as follows: **Experimental group:** Participants called or sent SMS reminder prior to every scheduled visit (1, 3, 6, 12, 18 months). **Control group:** Physical contact reminders prior to every

	scheduled visit (1, 3, 6, 12, 18 months).
Study population:	ADULTS and ADOLESCENTS (15-49 years); Individuals at high-risk for HIV infection. N=662
Clinical Trial Registration(s):	PACTR201311000696101
Status:	Ongoing
Results and outcomes:	
Publications:	

5.1.21 Ponsiano Ocama

EDCTP Project Coordinator:	Ponsiano Ocama (Makerere University, Uganda)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Early childhood transmission of viral hepatitis B among HIV and non-HIV infected mothers attending postnatal and immunization clinic at Gulu Hospital, Northern Uganda
EDCTP Project Code:	TA.2011.40200.004
EDCTP Project Start Date:	16 February 2012
EDCTP Project End Date:	30 October 2014
Collaborators:	• Robert Colebunders (Prince Leopold Institute of Tropical Medicine (ITM), Belgium) • Felix Kaducu (Gulu University, Uganda)
Goal:	The primary purpose of this proposed study is to investigate the prevalence and factors that may lead to reduction of transmission of hepatitis B virus (HBV) among babies born in Northern Uganda.
Objective(s):	1. To determine the prevalence of hepatitis B surface antigen (HBsAg) in mothers attending the postnatal/immunization clinic in Gulu regional referral hospital 2. To determine the incidence of HBV infection among babies born to HBsAg-positive and HBsAg negative mothers with or without HIV infection attending postnatal/immunization clinic in Gulu regional referral hospital and aged over 9 months 3. To assess factors associated with early transmission of HBV to babies born to HBsAg-positive and HBsAg-negative mothers attending postnatal/immunization clinic in Gulu regional referral hospital.
Collaborating site(s):	ITM (Belgium)
Study design:	Prevalence survey of Hep B and vertical transmission
Number of subjects:	
Status:	Ongoing
Results and outcomes:	
Publications:	

5.1.22 Sabelle Jallow

EDCTP Project Coordinator:	Sabelle Jallow (Medical Research Council (MRC) Laboratories, The Gambia)
EDCTP Call Title:	Senior Fellowship
EDCTP Project Title:	Functional characteristics of effector and memory NK cellular responses and their comparison with adaptive T cell responses in HIV-vaccinated subjects and risk populations
EDCTP Project Code:	TA.2011.40200.053
EDCTP Project Start Date:	1 December 2012
EDCTP Project End Date:	1 December 2014
Collaborators:	• Anders Fomsgaard (Statens Serum Institut, (SSI), Denmark) • Assan Jaye (MRC Laboratories, The Gambia) • Souleymane Mboup (University Cheikh Anta DIOP de Dakar (UCAD), Senegal) • Eleanor Mary Riley (London School of Hygiene and Tropical Medicine (LSHTM), UK)
Clinical Trial/Study Sponsor:	Medical Research Council, The Gambia
Goal:	To explore the existence of effector and re-call NK responses and their comparative functional characteristics with adaptive responses on the available HIV study platforms developed within the network
Objective(s):	1. To determine if NK cell recall responses are elicited in HIV uninfected infants and infected adults who received HIV vaccine candidates. 2. To determine if NK cell recall responses are present in HIV-exposed but uninfected adults and in HIV sero-discordant couples. If present, we will characterise these responses (both the effector recall NK responses). 3. To determine the relationship between NK cell responses and the frequency and quality of CD4+ and CD8+ T cell responses in at-risk populations
Clinical Trial/Study site(s):	The Gambia, Guinea Bissau and Dakar
Collaborating site(s):	• LSHTM (UK) • SSI (Denmark)
Study design:	Laboratory
Number of subjects:	Objective 1: 24 uninfected infants (vaccinated); 24 sex-matched controls (unvaccinated) Objective 2: 25 HIV-infected adults Objective 3: 20 sero-negative subjects, 20 HIV negative individuals (discordant partners) matched with 20 HIV positive partners (discordant); 30 sero-negative sex workers and 30 age matched HIV positive subjects
Status:	Ongoing
Results and Outcomes:	A preliminary analysis or a pilot study has been performed on some of the samples from the discordant couples cohort in Senegal. This data shows that HIV peptides can activate NK functional responses in HIV-positive individuals; and that HIV exposed but uninfected subjects elicit higher NK functional responses (as measured by higher degranulation and higher interferon –gamma production); and less NK activation (lower CD25) as compared to those who are HIV-infected. These results have been presented nationally, regionally and internationally. In a recent international scientific meeting, the 17th Annual meeting of the International Conference on AIDS

	and STIs in Africa (ICASA), in Cape town, South Africa, the abstract on results from this preliminary study won one of the five best abstract awards; the "Best Young Investigators award for basic science.
Publications:	

5.1.23 Collen Masimirembwa

EDCTP Project Coordinator:	Collen Masimirembwa (African Institute of Biomedical Science & Technology (AIBST), Zimbabwe)
EDCTP Call Title:	Senior Fellowship
EDCTP Project Title:	A prospective study to evaluate a pharmacogenetic-guided dosing algorithm based on patient CYP2B6 genotype compared to the empirical standard dose in the safe and efficacious use of efavirenz in HIV/AIDS patients in Zimbabwe
EDCTP Project Code:	TA.2011.40200.052
EDCTP Project Start Date:	1 November 2012
EDCTP Project End Date:	1 November 2014
Collaborators:	• Florence Chingwena (Harare City Health Department, Zimbabwe) • Prosper Chonzi (Harare City Health Department, Zimbabwe) • Milcah Dhoro (AIBST, Zimbabwe) • Gerard Kadzirange (University of Zimbabwe) • Tafireyi Nemaura (AIBST, Zimbabwe) • Charles Nhachi (University of Zimbabwe) • Roslyn Thelingwani (AIBST, Zimbabwe)
Clinical Trial/Study Sponsor:	AIBST (Zimbabwe)
Goal:	To evaluate the impact of an efavirenz pharmacogenetic-guided dosing algorithm with respect to safety and efficacy and comparing it to the empirical standard dosing of efavirenz
Objective(s):	Primary Objectives: 1. To compare efavirenz exposure levels in patients in whom the initiation dose is based on a pharmacogenetic algorithm with those in patients given the standard dose. 2. To compare HIV viral load suppression and CD4 counts in patients in whom efavirenz dose is based on a pharmacogenetic algorithm with those in patients given the standard dose. 3. To compare the incidences and severity of efavirenz associated adverse drug reactions; liver function, skin hypersensitivity reactions and central nervous system (CNS) effects in patients in whom the efavirenz dose is based on a pharmacogenetic algorithm with those given the standard dose. To validate the CYP2D6 genotyping method for use in the clinical study Secondary Objective: 1. To assess the cost-effectiveness of applying the pharmacogenetics dosing algorithm in the use of efavirenz
Clinical Trial/Study site(s):	• Wilkins Infectious Disease Hospital (Harare) • Chitugwiza Hospital, Opportunistic Infections Unit (Chitugwiza)
Study design:	Prospective randomised controlled trial
Number of subjects:	250
Product(s):	Efavirenz
Manufacturer:	Bristol-Myers Squibb
Trial registration number(s):	Not yet registered
Status:	Ongoing
Results and Outcomes:	1. Completion of validation studies on CYP2B6 genotyping

	method (publication) 2. Successful characterization of a cohort of 400 patients on ART, TB and ART/TB coinfection with respect to adverse drug reactions (publication) 3. Formation of the AiBST Clinical Trial Research Group
PhD study	Title: Determination of drug absorption, distribution, metabolism, excretion and toxicity (ADMET) biomarkers for drug safety and efficacy in the treatment of HIV/AIDS and TB in Zimbabwe Candidate: Milcah Dhoro (University of Zimbabwe) Title: Pharmacometric and Statistical considerations in PK and Pharmacogenetics Studies in Analysis of Clinical Data Sets of African HIV/AIDS and TB populations on Different Treatment Regimens. Candidate: Tafireyi Nemaura Masters student: Title: Molecular epidemiology of HIV-1 subtype C drug resistance mutations in patients on antiretroviral drugs in Zimbabwe. Candidate: Benjamin Chimukangara
Publications:	1. Dhoro M, Nhachi C and C Masimirembwa. Technological and cost comparison of cytochrome P450 2B6 (516G>T) genotyping methods in routine clinical practice. *African Journal of Biotechnology*. 2013.12(19): 2706-2710 (DOI: 10.5897/AJB2013.12043) 2. Nemaura T, Dhoro T, Nhachi C, Kadzirange G, Chonzi C and C Masimirembwa. Evaluation of the Prevalence, Progression and Severity of Common Adverse Reactions (Lipodystrophy, CNS, Peripheral Neuropathy, and Hypersensitivity Reactions) Associated with Anti-Retroviral Therapy (ART) and Anti-Tuberculosis Treatment in Outpatients in Zimbabwe. *AIDS and Clinical Research*. 2013, 4 (4). 3. M. Dhoro, B. Ngara, G. Kadzirange, C. Nhachi, C. Masimirembwa. Genetic variants of drug metabolizing enzymes and drug transporter (ABCB1) as possible biomarkers for adverse drug reactions in an HIV/AIDS cohort in Zimbabwe. Curr HIV Res. 2013 Sep;11(6):481-90.

5.2 Tuberculosis Career Development and Senior fellowships

Table 4-2: Tuberculosis fellowship projects supported by EDCTP

Project Acronym (Coordinator)	Type of studyPhase of trial	Product(s)	Manufacturer / Developer	Study population	Status
Mukhtar - SF	Epidemiology of TB	None	Not applicable	100 villages randomly selected from five geographical regions in eastern Sudan, 100 households from each village resulting in recruitment of about 70,000 individuals	Closed
Hanekom - SF	Prospective cohort analyses	None	Not applicable	5,675 neonates	Closed
Rangaka - CDF	Immunology of TB reconstitution in HIV	None	Not applicable	Over 200 patients with HIV and TB	Closed
Adetifa -CDF	Comparison of immunological and molecular TB diagnostics techniques	None	Not applicable	188 stored samples (73 smear positive, 93 smear negative, 22 progressors)	Completed
Dheda - SF	Immunology of TB Lung innate immunity pathways	None	Not applicable	74 TB patients and health contacts	Completed
Nicol - SF	Point of care genotypic diagnosis of TB and drug resistance	GeneXpert	Cepheid, Sunnyvale, CA, USA	2522 patients	Completed
Nachega -SF	Phase II: Randomised placebo control trial for prevention of TB-IRIS with non-steroidal anti-inflammatory drugs	Meloxicam and omeprazole	Not applicable – generic formulations	TB patients on HAART	Ongoing
Oyakhirome - SF	TB, TB-HIV and MDR prevalence in preparation for future trials	None	Not applicable	General population	Completed
Hatherill -SF	Epidemiology of TB and intestinal helminthes infection	None	Not applicable	800 children in South Africa and Kenya	Ongoing
Worodria -SF	Monitoring treatment outcomes of TB patients on ART	None	Not applicable	230 TB patient on HAART in Kampala	Ongoing
Scriba -SF	Cohort studies on immunological determinants of TB	None	Not applicable	4 to 12 year old pre-adolescent children, at risk of progression to TB	Ongoing
Kouanda -SF	Phase II: PK studies for minimum	Rifabutin;	Not applicable	TB-HIV coinfected patients in	On going

	dosage	Lopinavir/ritonavir	(generic)	Burkina Faso	
Lamorde – SF	Phase IIIb: Evaulation of pharmacokinetic interactions between artemisinin-based therapies and rifampicin-based tuberculosis treatment in African patients	Dihydroartemisinin-Piperaquine/ Rifampicin	Sigma-Tau Pharmaceuticals Tubingen	TB patients (18-65 years) in their last month of Rifampicin treatment (Kampala, Uganda)	Ongoing
Padayatchi – SF	Phase IV study: Evaluation of efficacy and safety of 24 weeks moxifloxacin-containing regimen [isoniazid (H), rifampin (R), pyrazinamide (Z), moxifloxacin (M)] with a 32 weeks control regimen [isoniazid (H), rifampicin(R), pyrazinamide (Z), ethambutol (E)] in TB retreatment.	Moxifloxacin Isoniazid/Rifampicin /Pyrazinamide	Bayer HeathCare Tubingen	Adults with a smear positive pulmonary TB with a past history of TB	Ongoing

5.2.1 Maowia Mukhtar

EDCTP Project Coordinator:	Maowia Mukhtar (University of Khartoum, Sudan)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	The burden of tuberculosis in eastern Sudan: epidemiology and drug resistance patterns of Mycobacterium tuberculosis isolates
EDCTP Project Code:	TA.2004.40200.005
EDCTP Project Start Date:	1 January 2005
EDCTP Project End Date:	30 June 2007
Collaborators:	• Greet Dieltiens Prince Leopold Institute of Tropical Medicine (ITM), Belgium • Nageed Saeed (Federal Ministry of Health, Sudan) • Patrick van der Stuyft (ITM, Belgium)
Goal:	To conduct epidemiological studies to identify suitable sites for future diagnostic, treatment and vaccine trials on tuberculosis in Sudan
Primary Objective(s):	• To study and map the burden of tuberculosis in Eastern Sudan • To undestand the epidemiology of pulmonary TB • To determine the drug resistance pattern of Mycobacterium tuberculosis isolates.
Study design:	Epidemiological survey
Number of subjects:	100 villages randomly selected from five geographical regions in eastern Sudan, 100 households from each village resulting in recruitment of about 70,000 individuals
Status:	Completed
Results and outcomes:	The project has produced epidemiological understanding of TB in Sudan which provides a foundation for future trials in TB
Publications:	

5.2.2 Willem Hanekom

EDCTP Project Coordinator:	Willem Hanekom (University of Cape Town, South Africa)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	The BCG-induced immune correlates of protection against tuberculosis
EDCTP Project Code:	TA.2004.40200.004
EDCTP Project Start Date:	1 January 2005
EDCTP Project End Date:	6 October 2008
Collaborators:	• Adrian Hill (University of Oxford, UK) • Gregory Hussey (University of Cape Town, South Africa) • Gilla Kaplan (New Jersey Medical School, USA)
Goal:	To identify BCG immune correlates of protection against TB in children whose understanding is critical for TB vaccine development
Objective(s):	1. To determine whether the post-vaccination number, function and/or antigenic repertoire of specific conventional CD4+ and CD8+ T cells correlate with protection against TB 2. To determine whether the post-vaccination number and/or function of specific regulatory CD4+ T cells correlate with protection against TB 3. To determine whether the post-vaccination gene expression and cytokine secretion profiles of whole blood, and of PBMC, correlate with protection against TB.
Clinical Trial/Study site(s):	
Collaborating site(s):	• New Jersey Medical School (USA) • University of Oxford (UK)
Study design:	Prospective cohort analyses
Number of subjects:	5662 children
Status:	Completed
Results and outcomes:	There were no differences in plasma levels of interferon-gamma, a cytokine commonly used to measure vaccination outcome, or any other cytokine, between the TB protected and TB non-protected children. However, when combinations of cytokines were evaluated, a model that included fractalkine, interleukin 12p40 and epidermal growth factor, correct discrimination in 82% of "protected" and "unprotected" infants was possible. Combinations of cytokines from plasma from blood incubated for 7 hours without antigen also allowed correct discrimination between the 2 groups. The studies on correlates of protective immunity from BCG have strengthened laboratories at SATVI which has since been awarded several EDCTP grants for TB vaccine studies and trials. The fellowship was a re-entry fellowship to support the return of Willem Hanekom to re-establish his research career in South Africa.
Publications:	1. Mark Hatherill, Tony Hawkridge, Andrew Whitelaw, Michele Tameris, Hassan Mahomed, Sizulu Moyo, Willem Hanekom and Gregory Hussey. Isolation of Non-Tuberculous Mycobacteria in Children Investigated for Pulmonary Tuberculosis. *PLoS ONE*, December 2006;1:e21. 2. Hanekom WA. The immune response to BCG vaccination of newborns. *Ann N Y Acad Sci*. 2005 Dec;1062:69-78. 3. Murray RA, Mansoor N, Harbacheuski R, Soler J, Davids V, Soares A, Hawkridge A, Hussey GD, Maecker H, Kaplan G, Hanekom WA. Bacillus Calmette Guerin vaccination of human newborns induces a specific, functional CD8+ T

cell response. *J Immunol*. 2006 Oct 15;177(8):5647-51.
4. Hanekom WA, Abel B, Scriba TJ. Immunological protection against tuberculosis. *S Afr Med J*. 2007 Oct;97(10 Pt 2):973-7.
5. Hussey G, Hawkridge T, Hanekom W. Childhood tuberculosis: old and new vaccines. *Paediatr Respir Rev*. 2007 Jun;8(2):148-54.
6. Scriba TJ, Kalsdorf B, Abrahams D-A, Isaacs F, Hofmeister J, Black G, Hassan HY, Wilkinson RJ, Walzl G, Gelderbloem SG, Mahomed H, Hussey GD, Hanekom WA. Distinct, specific IL-17 and IL-22-producing CD4+ T cell subsets contribute to the human anti-mycobacterial immune response. *J Immunol*. 2008, 180: 1962-1970.
7. Natalie E.R. Beveridge, Helen A. Fletcher, Jane Hughes, Ansar A. Pathan, Thomas J. Scriba, Angela Minassian, Clare R. Sander, Kathryn T. Whelan, Hazel M. Dockrell, Adrian V.S. Hill, Willem A. Hanekom and Helen McShane. A comparison of IFNy detection methods used in tuberculosis vaccine trials. *Tuberculos*. November 2008;88(6):631-640.
8. M Hatherill, T Hawkridge, H J Zar, A Whitelaw, M Tameris, L Workman, L Geiter, W A Hanekom and G Hussey. Induced sputum or gastric lavage for community-based diagnosis of childhood pulmonary tuberculosis? *Arch. Dis. Child*. 2009;94;195-201; originally published online 1 Oct 2008.
9. Soares AP, Scriba TJ, Joseph S, Harbacheuski R, Murray RA, Gelderbloem SJ, Hawkridge A, Hussey GD, Maecker H, Kaplan G, Hanekom WA. Bacille Calmette Guerin vaccination of human newborns induces T cells with complex cytokine and phenotypic profiles. *J Immunol*. 2008 Mar 1;180(5):3569-77.

5.2.3 Molebogang Rangaka

EDCTP Project Coordinator:	Molebogang Rangaka (University of Cape Town, South Africa)
EDCTP Project Call:	Career Development Fellowship
EDCTP Project Title:	Immunological investigation of the HIV-tuberculosis associated immune reconstitution
EDCTP Project Code:	TA.2005.40203.005
EDCTP Project Start Date:	15 December 2006
EDCTP Project End Date:	31 January 2009
Collaborators:	• Gary Maartens (University of Cape Town, South Africa) • Graeme Ayton Meintjes (University of Cape Town, South Africa) • Katalin Andrea Wilkinson (University of Cape Town, South Africa) • Robert Wilkinson (University of Cape Town, South Africa)
Goal:	To determine the frequency of *M.tb* specific T cells and serum cytokine agonist/antagonist ratios amongst IRIS cases compared to controls. The effect of steroid or placebo therapy on these variables was also studied.
Objective(s):	To understand the immune dysregulation that underlies HIV-Tuberculosis associated immune reconstitution inflammatory syndrome (TB IRIS).
Study design:	Laboratory investigations in a cohort of TB-HIV patients
Number of subjects:	>200 patients with HIV-TB co-infection
Status:	Completed
Results and outcomes:	The study has contributed to the establishment of well characterised cohorts of TB/HIV co-infected individuals in parts of Cape Town. Dr Rangaka competed for and was awarded a Wellcome Trust Training Fellowship at the end of the EDCTP award.
Publications:	1. Meintjes G, Rangaka M.X et al. Novel Relationship between Tuberculosis Immune Reconstitution Inflammatory Syndrome and Antitubercular Drug Resistance. *Clin Infect Dis*. 2009 Mar 1;48(5):667-76. doi: 10.1086/596764 2. Meintjes G, Wilkinson K.A, Rangaka M.X et al. Type 1 Helper T Cells and FoxP3-positive T Cells in HIV–Tuberculosis-associated Immune Reconstitution Inflammatory Syndrome. *Am J Respir Crit Care Med*. 2008 Nov 15;178(10):1083-9. doi: 10.1164/rccm.200806-858OC. Epub 2008 Aug 28 3. Dominique J. Pepper, Suzaan Marais, Gary Maartens, Kevin Rebe, Chelsea Morroni, Molebogeng X. Rangaka, Tolu Oni, Robert J. Wilkinson, and Graeme Meintjes. Neurologic Manifestations of Paradoxical Tuberculosis-Associated Immune Reconstitution Inflammatory Syndrome: A Case Series. *Clinical Infectious Diseases* 2009:48 (1 June) 4. Katalin A. Wilkinson, Ronnett Seldon, Graeme Meintjes1, Molebogeng X. Rangaka, Willem A. Hanekom, Gary Maartens, and Robert J. Wilkinson. Dissection of Regenerating T-Cell Responses against Tuberculosis in HIV-infected Adults Sensitized by Mycobacterium tuberculosis. *American Journal of Respiratory and Critical Care Medicine* Vol 180. pp 674–683, 2009 5. Graeme Meintjes, Robert J Wilkinson, Chelsea Morroni, Dominique J Pepper, Kevin Rebe, Molebogeng X Rangaka, Tolu Oni, Gary Maartens. Randomized placebo-controlled

	trial of prednisone for paradoxical TB-associated immune reconstitution inflammatory syndrome. *AIDS*. 2010 Sep 24;24(15):2381-90. doi: 10.1097 6. Rebecca Tadokera, Graeme Meintjes, Keira H Skolimowska, Katalin A Wilkinson, Kerryn Matthews, Ronnett Seldon, Novel N Chegou, Gary Maartens, Molebogeng Xheedha Rangaka , Kevin Rebe, Gerhard Walzl, Robert J Wilkinson. Hypercytokinaemia accompanies HIV-tuberculosis immune reconstitution inflammatory syndrome. *Eur Respir J*. 2011 May;37(5):1248-59. doi: 10.1183/09031936.00091010. Epub 2010 Sep 3.

5.2.4 Ifedayo Adetifa

EDCTP Project Coordinator:	Ifedayo Adetifa (Medical Research Council (MRC) Laboratories, The Gambia)
EDCTP Project Call:	Career Development Fellowship
EDCTP Project Title:	A double blind, placebo controlled randomized trial of vitamin A supplementation for modulation of Mycobacterium tuberculosis immune responses in children aged 5-14 years with latent Tuberculosis
EDCTP Project Code:	TA.2005.40203.001
EDCTP Project Start Date:	15 March 2007
EDCTP Project End Date:	1 July 2010
Collaborators:	• Richard Adegbola (MRC Laboratories, The Gambia) • Martin Antonio (MRC Laboratories, The Gambia) • Philip Hill (MRC Laboratories, The Gambia)
Objective(s):	To provide additional evidence for the performance of novel diagnostics for latent tuberculosis and TB case detection in adults and children especially those with paucibacillary disease in a TB endemic country; and to identify differences in immune responses may improve our understanding of what constitutes protection against progression to TB in those latently infected
Study design:	Immunological studies in TB immunity
Number of samples:	188 stored samples (73 smear positive, 93 smear negative, 22 progressors)
Product:	
Manufacturer/Developer:	
Status:	Completed
Results and Outcomes:	In a cross sectional study, the ELISPOT test was more sensitive than the QFT-GIT for diagnosing TB disease but both tests performed similarly in the diagnosis of LTBI in TB contacts. In an extension of this study to two newly licensed commercial IGRAs, it was found that both IGRAs and the TST responded in a similar manner to a gradient of exposure to TB. In addition, each IGRA in combination with TST increased sensitivity for diagnosis of LTBI but was also associated with a loss of specificity. Also tested as Hain Sciences Line probe assay, MTBDRplus ® in a 2 step-procedure. On 93 smear negative culture positive samples, the LPA had a sensitivity of 45.2% (42 of 93) and over half of the results were blank. There was no relationship between the results from post decontamination ZN concentration staining and failed LPA results. In assessing gene expression for cytokines protective against TB disease progression IFN-γ was significantly lower in progressors compared to both non-progressors and TB cases ($p=0.0328$ and $p=0.0062$ respectively). For other cytokines-IL-10 and IL-12 similar levels were seen between the groups. IL-18 was significantly higher in progressors compared to non-progressors and confirmed TB cases ($p<0.001$ for both).
Publications:	1. Adetifa IM, Lugos MD, Hammond A, et al. Comparison of two interferon gamma release assays in the diagnosis of Mycobacterium tuberculosis infection and disease in The Gambia. *BMC Infect Dis*. 2007 Oct 25; 7:122. 2. Lugos MD, Adetifa IM, Donkor S, Hill PC, Adegbola RA, Ota MO. Evaluation of the contribution of major T cell subsets to IFN-gamma production in TB infection by ELISPOT. *Immunol Invest*. 2009; 38: 341-9. 3. Adetifa IM, et al. Commercial interferon gamma release assays compared to the tuberculin skin test for diagnosis

	of latent Mycobacterium tuberculosis infection in childhood contacts in the Gambia. *Pediatr Infect Dis J*. 2010; 29:439-43. 4. Adetifa IM, Ota MO, Walther B, et al, Hill PC. Decay kinetics of an interferon gamma release assay with anti-tuberculosis therapy in newly diagnosed tuberculosis cases. *PLoS One*. 2010. Sep 1;5(9). pii: e12502.

5.2.5 Keertan Dheda

EDCTP Project Coordinator:	Keertan Dheda (University of Cape Town, South Africa)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Human lung innate immune pathways regulating the stasis and killing of *M. tuberculosis* in a high burden setting
EDCTP Project Code:	TA.2007.40200.010
EDCTP Project Start Date:	28 July 2008
EDCTP Project End Date:	27 July 2010
Collaborators:	• Gregory Hussey (University of Cape Town, South Africa) • Graham Rook (University College London, UK) • Alimuddin Zumla (University College London, UK)
Objective(s):	1. To compare compartment-specific IFN- antigen-specific responses in TB versus non-TB patients 2. To procure and bank biological material (alveolar lavage fluid and cells) from HIV negative close contacts (of sputum smear positive patients) that have laboratory evidence of LTBI (TST+, IGRA+ i.e. converters) versus those that do not (TST-, IGRA- i.e. non-converters) 3. To compare expression and function of innate markers of protective immunity (pathogen recognition molecules/ receptors, cytokines, humoral factors and cell phenotypes) in converters and non-converters.
Collaborating site(s):	University College London (UK)
Study design:	Immunological studies
Status:	Completed
Results and outcomes:	Rapid diagnosis of TB meningitis by smear microscopy and PCR is problematic and the diagnostic delay can often translate into increased morbidity and mortality due to the poor sensitivity of these assays. The TB-specific quantitative T cell ELISPOT assay, when using CSF mononuclear cells and in conjunction with other rapid confirmatory tests (Gram stain and cryptococcal latex-agglutination) is an accurate and rapid rule-in test for TBM in a TB and HIV endemic setting. The RD-1, but not the purified-protein-derivative, cerebrospinal fluid-lymphocyte IFN-γ ELISPOT response is a useful rapid immunodiagnostic test for TBM. Further studies are continuing from the work described above.
Publications:	1. Patel VB, Singh R, Connolly C, ,Coovadia Y, Peer A, Parag P, Kasprowicz V, Zumla A, Ndung"u T, Dheda K. Cerebrospinal T cell responses aid the diagnosis of tuberculous meningitis in a HIV and TB endemic population. *AJRCCM* 2010 May 4. [Epub ahead of print] PMID: 20442433 2. Patel VB, Bhigjee AI, Paruk HF, Singh R, Meldau R, Connolly C, Ndung'u T, Dheda K. Utility of a novel lipoarabinomannan assay for the diagnosis of tuberculous meningitis in a resource-poor high-HIV prevalence setting. *Cerebrospinal Fluid Research* 2009 November,2;6:13. PMID: 19878608 3. Cashmore TJ , Peter GJ, van Zyl-Smit RN, Semple PL, Maredza A, Meldau R, Zumla A, Nurse B, Dheda K. Feasibility and diagnostic utility of antigen-specific interferon-gamma responses for rapid immunodiagnosis of tuberculosis using induced sputum. *PLoS One*. 2010 Apr 28;5(4):e10389. PMID: 20442850? 4. Dheda K, van Zyl-Smit RN, Sechi LA, Badri M, Meldau R, Meldau S, Symons G, Semple L, Maredza A, Dawson R,

Wainright H, Whitelaw A, Vallie Y, Raubenheimer P, Bateman ED, Zumla A. Utility of quantitative T cell responses versus unstimulated IFN-{gamma} for the diagnosis of pleural tuberculosis. *Respir J*. 2009 Nov;34(5):1118-26. Epub 2009 Apr 22. PMID: 19386693

5. Dheda K, Van-Zyl Smit RN, Sechi LA, Badri M, Meldau R, Symons G, Khalfey H, Carr I, Maredza A, Dawson R, Wainright H, Whitelaw A, Bateman ED, Zumla A. Clinical diagnostic utility of IP-10 and LAM antigen levels for the diagnosis of tuberculous pleural effusions in a high burden setting. *PLoS One*. 2009;4(3):e4689. Epub 2009 Mar 11. PMID: 19277111
6. Dheda K, Smit RZ, Badri M, Pai M. T-cell interferon-gamma release assays for the rapid immunodiagnosis of tuberculosis: clinical utility in high-burden vs. low-burden settings. *Curr Opin Pulm Med*. 2009 May;15(3):188-200. Review. PMID: 19387262
7. Dheda K, van Zyl-Smit RN, Meldau R, Meldau S, Symons G, Khalfey H, Govender N, Rosu V, Sechi LA, Maredza A, Semple PL, Whitelaw A, Wainright H, Badri M, Dawson R, Bateman ED, Zumla A. Quantitative lung T cell responses aid the rapid diagnosis of pulmonary tuberculosis. *Thorax*. 2009 Oct;64(10):847-53. Epub 2009 Jul 9. PMID: 19592392
8. van Zyl-Smit RN, Dheda K, Meldau R. Quantitative Pulmonary T-Cell Responses for the Diagnosis of Active Tuberculosis. *Am J Respir Crit Care Med*. 2010 Feb 1;181(3):289; author reply 289-90. PMID: 20093656
9. van Zyl-Smit RN, Pai M, Peprah K, Meldau R, Kieck J, Juritz J, Badri M, Zumla A, Sechi LA, Bateman ED, Dheda K (senior and corresponding author). Within-subject variability and boosting of T-cell interferon-gamma responses after tuberculin skin testing. *Am J Respir Crit Care Med*. 2009 Jul 1;180(1):49-58. Epub 2009 Apr 2. PMID: 19342414
10. van Zyl-Smit RN, Zwerling A, Dheda K, Pai M. Within-subject variability of interferon-gamma assay results for tuberculosis and boosting effect of tuberculin skin testing: a systematic review. *PLoS One*. 2009 Dec 30;4(12):e8517. Review. PMID: 20041113
11. Dheda K, Schwander SK, Zhu B, Van Zyl-Smit RN, Zhang Y. The immunology of tuberculosis: From bench to bedside. *Respirology*. 2010 Apr;15(3):433-50. PMID: 20415982.

5.2.6 Mark Nicol

EDCTP Project Coordinator:	Mark Nicol (University of Cape Town, South Africa)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	The impact of rapid genotypic detection of multi-drug resistant tuberculosis on treatment outcome in a semi-rural region of South Africa
EDCTP Project Code:	TA.2007.40200.009
EDCTP Project Start Date:	29 August 2008
EDCTP Project End Date:	20 September 2011
Collaborators:	• Willem Hanekom (University of Cape Town, South Africa) • Gregory Hussey (University of Cape Town, South Africa) • Lizette Phillips (Brewelskloof Hospital, South Africa) • Danie Theron (Brewelskloof Hospital, South Africa) • Tommie Victor (Stellenbosch University, South Africa) • Robert Wilkinson (University of Cape Town, South Africa)
Goal:	To assess the impact of a novel rapid molecular diagnostic test for tuberculosis and the presence of rifampicin resistance (Xpert MTB/RIF) on patient and health services outcomes.
Objective(s):	To determine whether the detection of tuberculosis by GeneXpert MTB/Rif testing in place of the routine diagnostic algorithm will lead to a reduction in: number of clinic visits prior to appropriate TB treatment; time to appropriate treatment for TB and reduced morbidity and mortality due to undiagnosed TB; number of TB cultures requested per patient; TB-related clinic workload and TB-related laboratory workload
Clinical Trial/Study site(s):	Blewelskloof Hospital, Khayelitsa, Worcester (South Africa)
Study design:	TB point of care diagnosis
Number of subjects:	1577
Product:	GeneXpert
Manufacturer/Developer:	Cepheid, Sunnyvale (USA)
Status:	Completed
Results and outcomes:	1577 patients with suspected TB were recruited. GeneXpert improves accuracy and shortens duration of diagnosis to treatment. The preliminary results of this study formed a substantial component of a report submitted to the WHO Strategic and Technical Advisory Group for Tuberculosis which in September 2010 issued a recommendation that Xpert MTB/RIF replace smear microscopy as the first line diagnostic test for TB in areas with high prevalence of MDR-TB or HIV. South-North networking in the project was well established working with the Foundation for Innovative New diagnostics (FIND) and TB Clinical Diagnostics Research Consortium of Johns Hopkins University and Boston Medical Centre. Other collaborative projects included development of a novel point-of-care diagnostics for TB with Northwestern University, USA. In the south the project links with EDCTP funded TB-NEAT consortium (PI Keertan Dheda), Wellcome Trust project in Malawi and Zimbabwe.
Publications:	1. Catharina C Boehme, Mark P Nicol, Pamela Nabeta, Joy S Michael, Eduardo Gotuzzo, Rasim Tahirli, Ma Tarcela Gler, Robert Blakemore, William Worodria, Christen Gray, Laurence Huang, Tatiana Caceres, Rafail Mehdiyev, Lawrence Raymond, Andrew Whitelaw, Kalaiselvan Sagadevan, Heather Alexander, Heidi Albert, Frank Cobelens, Helen Cox, David Alland, Mark D Perkins, Feasibility, diagnostic accuracy, and effectiveness of decentralised use of the Xpert MTB/RIF test for diagnosis

	of tuberculosis and multidrug resistance: a multicenter implementation study. *Lancet* 2011 Apr 30; 377(9776):1495-505)

5.2.7 Jean Nachega

EDCTP Project Coordinator:	Jean Nachega (Stellenbosch University, South Africa)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	A Multi-Site Double-Blind Placebo Controlled Randomised Clinical Trial to Prevent Immune Reconstitution Inflammatory Syndrome with Non-Steroid Anti-Inflammatory Drugs
EDCTP Project Code:	TA.2008.40200.021
EDCTP Project Start Date:	9 February 2010
EDCTP Project End Date:	31 December 2014
Collaborators:	• Robert Colebunders (Prince Leopold Institute of Tropical Medicine (ITM), Belgium) • Mzileni Olga Mogiyana (University of Limpopo, South Africa) • Ingrid Wilson (Stellenbosch University, South Africa)
Goal:	To investigate immune-modulation of non-steroidal anti-inflammatory treatment in TB IRIS among HIV infected patients
Objective(s):	1. Evaluate the impact of NSAIDs compared to placebo on preventing TB-IRIS in a TB-HIV infected South African Adults 2. Evaluate the impact of NSAIDs compared to placebo on CD4+ T-cell count recovery following initiation of ART in TB-HIV infected South African Adults 3. Evaluate the impact of NSAIDs compared to placebo on HIV-1 RNA response following initiation of ART in TB-HIV infected South African Adults 4. Evaluate the impact of NSAIDs compared to placebo on adherence of both TB and HIV medication following initiation of ART in TB-HIV infected South African Adults 5. Assess the impact of NSAIDs compared to placebo on quality of life following initiation of ART in TB-HIV infected South African Adults
Collaborating site(s):	ITM (Belgium)
Study design:	Phase II: Randomised placebo control trial for prevention of TB-IRIS with non-steroidal anti-inflammatory drugs on TB patients on HAART
Product:	Meloxicam and omeprazole
Manufacturer/Developer:	Generic formulations
Cofunders:	Stellenbosch University (South Africa)
Status:	Ongoing
Results and outcomes:	Enrolment into the study started in September 2012.
Publications:	

5.2.8 Sunny Oyakhirome

EDCTP Project Coordinator:	Sunny Oyakhirome (Albert Schweitzer Hospital, Gabon)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Career development and strengthening institutional capacity for clinical research in TB at the Faculty of Health Sciences in Brazzaville
EDCTP Project Code:	TA.2009.40200.010
EDCTP Project Start Date:	13 April 2010
EDCTP Project End Date:	13 April 2012
Collaborators:	• Michel Bitemo (CERVE) • Vladimir Malonga (Fondation Congolaise pour al Recherche Médicale (FCRM)/Faculté des sciences de la santé (FSSA), Congo) • Pembe Issamou Mayengue (FCRM/FSSA, Congo) • Mitawa Missontsa (FCRM/FSSA, Congo) • Benjamin Mordmüller (Albert Schweitzer Hospital, Gabon) • Francine Ntoumi (FCRM/FSSA, Congo) • Veronique Penlap Beng (University of Yaounde, Cameroon)
Objective(s):	To determine the prevalence of TB, TB/HIV co-infection and multi drug resistant TB (MDR) infections in the Congolese population and identify groups most at risk for recent TB transmission in urban areas of Brazzaville in the Republic of Congo. A follow up will be set up for evaluating TB transmission in Congo; quantify the problem of recent transmission and characterized circumstances and settings for transmission
Clinical Trial/Study site(s):	
Collaborating site(s):	• University of Yaounde (Cameroon) • Albert Schweitzer Hospital (Gabon)
Study design:	Trial site development
Number of subjects:	
Status:	Completed
Results and outcomes:	Preliminary reports show that the EDCTP grant in Congo supported personnel, maintenance of laboratory equipment with their consumables and reagents. A TB research team formed as the result of the grant included a molecular biologist (Dr Pembe), a biostatistician (Mr Bitemo) and a local physician (Dr Mitawa). In the project period the newly formed team devoted time to the preparation of standards operating procedures necessary for handing TB and TB-HIV samples (from recruitment of patients to data analysis). The TB project has established collaboration with the TB CANTAM site at University Yaounde1 in Cameroon (Contact: Prof Penlap), University of Tübingen (contact: Dr Matthias Frank) and Medical research Unit of Albert Schweitzer Hospital in Lambarene, Gabon (Dr Safi and Dr Lell)
Publications:	

5.2.9 Mark Hatherill

EDCTP Project Coordinator:	Mark Hatherill (University of Cape Town, South Africa)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	The risk of pulmonary tuberculosis associated with intestinal helminth infection among children at two tuberculosis vaccine trial sites in sub-Saharan Africa
EDCTP Project Code:	TA.2009.40200.015
EDCTP Project Start Date:	20 April 2010
EDCTP Project End Date:	30 June 2014
Collaborators:	• Willem Hanekom (University of Cape Town, South Africa) • Gregory Hussey (University of Cape Town, South Africa) • Pauline Mwinzi (Kenya Medical Research Institute (KEMRI), Kenya) • Videlis Nduba (KEMRI, Kenya)
Objective(s):	Primary objectives: 1. To determine whether prevalent infection with intestinal helminths is associated with increased risk of pulmonary tuberculosis disease in children 2. To determine whether maternal infection with intestinal helminths is associated with increased risk of pulmonary tuberculosis disease in children 3. To compare the risk of pulmonary tuberculosis disease associated with prevalent infection with intestinal helminths between the research site in Breede Valley, South Africa, and the research site in Siaya District, Kenya. Secondary specific aims: To determine whether prevalent infection with intestinal helminths is associated with increased risk of LTBI in children 1. To determine whether maternal infection with intestinal helminths is associated with increased risk of LTBI in children.
Collaborating site(s):	KEMRI (Kenya)
Study design:	Epidemiology of TB
Number of subjects:	800 (target) in both Kenya and South Africa
Status:	Ongoing
Results and outcomes:	The first participant was enrolled at the UCT site on 7 March 2011. By the end of 2011 total of 135 infants had been enrolled (42% of the 325 target for Year 1). Health system strengthening has resulted in increased use of anthelmintic treatment in the community, with the result that 198 (32%) of 610 screened infants were excluded for this reason. To achieve the final target of 650 infants enrolled in the study from South Africa a no cost extension has been granted to 31 December 2013.
Publications:	

5.2.10 William Worodria

EDCTP Project Coordinator:	William Worodria (Makerere University, Uganda)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Short- and long-term clinical and immunological outcomes of patients with HIV/TB coinfections on ART
EDCTP Project Code:	TA.2010.40200.007
EDCTP Project Start Date:	11 April 2011
EDCTP Project End Date:	11 April 2014
Collaborators:	• Frank Cobelens (KNCV Tuberculosis Foundation, Netherlands) • Robert Colebunders (Prince Leopold Institute of Tropical Medicine (ITM), Belgium) • Jean Pierre van Geertruyden (ITM, Belgium) • Luc Kestens (ITM, Belgium) • Robert Lukande (Makerere University, Uganda) • Yukari Manabe (Makerere University, Uganda) • Harriet Mayanja-Kizza (Makerere University, Uganda) • Alice Nakiwogga-Mawanga (Infectious Diseases Institute, Uganda)
Clinical Trial/Study Sponsor:	University of Amsterdam (Netherlands)
Objective(s):	To study short-term effects of TB and ART treatment (the incidence, predictors and clinical characteristics of TB-IRIS, side effects of the therapy, causes of early mortality) and long term effects of ART after completing TB treatment (clinical events such as infections, late-onset IRIS, adverse effects of therapy or immunological and virological events such as changes in CD4 counts, CD4 %; viral load, viral resistance). Also to study possible factors influencing these outcomes such as adherence and factors affecting them, TB relapse and mycobacteriological factors, immunological defects and social factors that are associated with a recurrent TB episode and causes of mortality
Collaborating site(s):	• ITM (Belgium) • KNCV Tuberculosis Foundation (Netherlands)
Study design:	Treatment monitoring
Number of subjects:	280 (target)
Product:	Prequalified TB regimens and HAART
Status:	Ongoing
Results and outcomes:	By 30 July 2012 the project had enrolled 79 study participants of which 44 were enrolled in the study. 29 of those enrolled in the study are on both HAART and TB treatment. Patient follow-up is continuing. Due to delayed start of the project and slow recruitment the project has been granted a no cost extension to 2014.
Publications:	

5.2.11 Thomas Scriba

EDCTP Project Coordinator:	Thomas Scriba (University of Cape Town, South Africa)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Inflammatory determinants of risk of tuberculosis disease
EDCTP Project Code:	TA.2011.40200.010
EDCTP Project Start Date:	5 March 2012
EDCTP Project End Date:	5 March 2014
Collaborators:	• Willem Hanekom (University of Cape Town, South Africa) • Martin Ota, (Medical Research Council Laboratories (MRC), The Gambia) • Suzanne Verver (KNCV Tuberculosis Foundation, Netherlands) • Robin Wood (University of Cape Town, South Africa)
Goal:	The hypothesis is that the innate response to *M.tb* in pre-adolescent children, with low risk of progression to TB, is characterised by an appropriate and advantageous inflammatory response and this inflammatory response mediates better control of intracellular bacterial growth, compared with innate responses in adolescents, with high risk of progression, who have excessive inflammatory responses.
Objective(s):	The research questions are: 1. Do children between 4 and 12 years of age (low risk of progression to TB) have less pronounced, or more regulated, inflammatory responses to mycobacteria, compared with adolescents (high risk of progression)? 2. Do innate immune cells of children between 4 and 12 years of age have greater capacity to control intracellular bacterial growth, compared with innate immune cells of adolescents? 3. How do mycobacteria-specific T cells modulate the innate immune responses in these two age groups?
Collaborating site(s):	KNCV (Netherlands)
Study design and population:	Cohort studies; 4 to 12 year-old pre-adolescent children, at risk of progression to TB
Number of subjects:	103
Status:	Ongoing
Results and outcomes:	Participant enrolment started on 14 September 2012 and have enrolled 59 adolescents, aged 18 (36 are M.tb infected and 23 are not M.tb infected) and 44 children aged 8 years (16 are *M.tb* infected and 28 are not M.tb infected).
Publications:	

5.2.12 Seni Kouanda

EDCTP Project Coordinator:	Seni Kouanda (Institut de Recherche en Sciences de la Santé, Burkina Faso)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Rifabutin with lopinavir/ritonavir in patients coinfected with tuberculosis and HIV in Burkina Faso: Pilot study of pharmacokinetics to define the minimum effective dose
EDCTP Project Code:	TA.2011.40200.026
EDCTP Project Start Date:	20 March 2012
EDCTP Project End Date:	20 March 2014
Collaborators:	• Potiandi Serge Diagbouga (Centre Muraz, Burkina Faso) • Regazzi Marrio (University of Pavia, Italy) • Alberto Matteelli (University of Brescia, Italy) • Gautier Ouédraogo (Institut de Recherche en Sciences de la Santé, Burkina Faso)
Objective(s):	1. To assess the pharmacokinetic profile of rifabutin (RFB) and its active metabolite 25-O-desacetyl-rifabutin on the two dosing regimens (RFB 150 mg or 300 mg 3 times a week) in TB-HIV coinfected patients in Burkina Faso, a resources-limited country with high prevalence of tuberculosis and HIV 2. To determine the pharmacokinetics parameters of RFB in combination with Lopinavir/ritonavir in Burkinabe HIV infected patients with tuberculosis, in order, to define optimal doses that will be further tested in a larger phase III trial comparing safety, tolerability and efficacy of RBT and RMP regimens in West Africa.
Collaborating site(s):	University of Brescia (Italy)
Study design and population:	Phase II: Pharmacokinectics for dosing; TB-HIV co-infected patients in Burkina Faso
Number of subjects:	
Product:	Rifabutin; Lopinavir/ritonavir
Manufacturer/Developer:	Generic formulations
Status:	Ongoing
Results and outcomes:	
Publications:	

5.2.13 Mohammed Lamorde

EDCTP Project Coordinator:	Mohammed Lamorde (Makerere University, Uganda)
EDCTP Call Title:	Senior Fellowship
EDCTP Project Title:	Evaluating pharmacokinetic interactions between artemisinin-based therapies and rifampicin-based tuberculosis treatment in African patients
EDCTP Project Code:	TA.2011.40200.047
EDCTP Project Start Date:	1 November 2012
EDCTP Project End Date:	1 November 2014
Collaborators:	• Abdulrazaq Habib (Bayero University, Nigeria) • Saye Khoo (University of Liverpool, UK) • Concepta Merry (University of Dublin, Ireland) • Pauline Byakika-Kibwika (Makerere University, Uganda) • Robert Balikuddembe (Makerere University, Uganda) • Andrew Kambugu (Makerere University, Uganda) • Lydia Nakiyingi (Makerere University, Uganda) • Alphonse Okwera (Makerere University, Uganda) • Joel Tarning (Mahidol University, Thailand)
Clinical Trial/Study Sponsor:	IDI, Makerere University College of Health Sciences, Kampala
Goal:	To investigate drug interactions between antimalarial and anti TB drugs with the overall goal of developing co-treatment strategies for malaria and TB co-infection
Objective(s):	Primary • Group 1: To investigate the single-dose PK of dihydroartemisinin (DHA) and piperaquine following oral administration of dihydroartemisinin-piperaquine to patients receiving rifampicin and to the same patients after completing rifampicin regimen. • Group 2: To investigate the single-dose PK of artesunate, DHA, amodiaquine and DEAQ following oral administration of artesunate-amodiaquine to patients receiving rifampicin and to the same patients after completing rifampicin regimen. • Group 3: To investigate the single-dose PK of artesunate and DHA following intravenous administration of artesunate to patients receiving rifampicin and to the same patients after completing rifampicin regimen. Secondary • To assess the short-term safety of the study drugs during rifampicin intake and after completing rifampicin regimen.
Clinical Trial/Study site(s):	Mulago National Teaching and Referral Hospital, Kampala (Uganda)
Collaborating site(s):	Bayero University Kano (Nigeria)
Study design:	Pharmacokinetic study
Number of subjects:	36
Product(s):	• Dihydroartemisinin-piperaquine (tablets) • Amodiaquine-artesunate (tablets) • Artesunate for injection
Trial registration number(s):	Pan African Clinical Trial Registry (PACTR201302000483287).
Status:	Ongoing
Results and Outcomes:	Primary endpoints:

	• Group 1: Plasma concentrations of DHA and piperaquine during rifampicin treatment and after completing rifampicin intake. • Group 2: Plasma concentrations of artesunate, DHA, amodiaquine and DEAQ during rifampicin treatment and after completing rifampicin regimen • Group 3: Plasma concentrations of artesunate and DHA during rifampicin treatment and after completing rifampicin regimen • Secondary endpoint: Short-term safety of the study drugs during rifampicin intake and after completing rifampicin regimen
Publications:	

5.2.14 Nesri Padayatchi

EDCTP Project Coordinator:	Nesri Padayatchi (University of KwaZulu-Natal, South Africa)
EDCTP Call Title:	Senior Fellowship
EDCTP Project Title:	Improving retreatment success of tuberculosis
EDCTP Project Code:	TA.2011.40200.044
EDCTP Project Start Date:	1 January 2013
EDCTP Project End Date:	31 December 2014
Collaborators:	• Gavin John Churchyard (Aurum Institute for Health Research, South Africa) • Wafaa El-Sadr (Columbia University, USA) Sarah Fortune (Harvard School of Public Health, USA) • Gerald Friedland (Yale University, USA) • William Jacobs (Albert Einstein College of Medicine, USA) • Salim S. Abdool Karim (University of KwaZulu-Natal, South Africa)
Clinical Trial/Study Sponsor:	CAPRISA
Goal:	To define an effective, shortened TB retreatment regimen that aims to improve retreatment TB outcomes and reduce TB treatment interruption and failure
Objective(s):	1. To determine if a moxifloxacin-containing regimen [isoniazid (H), rifampin (R), pyrazinamide (Z), moxifloxacin (M)] of 24 weeks duration is superior to a control regimen [isoniazid (H), rifampicin(R), pyrazinamide(Z), ethambutol(E)] of 32 weeks duration in improving treatment outcomes in patients with recurrent TB Secondary objectives: 1. To compare TB Treatment outcomes in the 2 arms 2. Proportion of patients who are culture negative at 8 weeks 3. Time to first culture negative sputum 4. Safety: Comparison of patients with Grade 3 and 4 adverse events 5. Efficacy: Failure of bacteriological cure and relapse within 1 year of completion of therapy as defines by culture using solid media
Clinical Trial/Study site(s):	CAPRISA eThekwini Clinical Research Site (eCRS), adjoining the largest government outpatient TB facilities, the Prince Cyril Zulu Communicable Disease Centre (PCZCDC)
Study design:	Randomised controlled trial
Number of subjects:	362
Product(s):	Moxifloxacin
Manufacturer/Developer:	Bayer
Cofunders:	CAPRISA
Trial registration number(s):	Pending
Status:	Ongoing
Results and Outcomes:	
PhD study:	Title: Improving Retreatment Success in TB Candidate: Nesri Padayatchi (South Africa)
Other/Sub-studies:	PK study on interaction of Moxifloxacin with Tenofivir
Publications:	

5.3 Malaria Career Development and Senior fellowships

Table 5-3: Malaria fellowship projects supported by EDCTP

Project Acronym (Coordinator)	Study classification /design	Product(s)	Manufacturer / Developer	Study population	Status
Djimde - SF	Phase IV randomised trial Mali	AS/AQ, AS/SP and AR-L	Pre-qualified drugs	780 subjects in which 2463 malaria episodes studied	Completed
Nzila - SF	Laboratory study to investigate the mechanism of piperaquine resistance	DHA-piperaquine and artemether-lumefantrine	Not applicable (used samples from completed clinical trials)	In-vitro cultures of Plasmdium falciparum	Completed
Talisuna - SF	Phase IV: Pharmacovigilance of anti-malarial drugs in Uganda		Not applicable	None (training of health staff and comparison by health facility/region)	Completed
Nebie -SF	Immunological studies on the role of T cells in malaria endemicity	None	Not applicable	219 adults and children in Burkina Faso	Completed
Moukoko -CDF	Malaria virulence markers	None	Not applicable	In vitro assays	Completed
Nwakanma - SF	PCR diagnosis of malaria	None	Not applicable	Out patients with malaria symptoms in Gambia	Completed
Cisse - SF	Phase III: IPT with community participation	Pyrimethamine/Sulphamethopyrazine (Dualkin); DHA and Piperaquine; and	Pre-qualified drugs	1893 children	Completed

		AS and AQ			
Dodoo - SF	In-vitro assessment of malaria antibodies	None	Not applicable	In vitro assays	Completed
Happi - SF	Biomarkers of artemesinin resistance	None	Not applicable	In vitro and in vivo assays	Completed
Phiri - SF	Phase II trial of oral iron therapy for treatment of post-malaria iron-deficiency anaemia in children	Iron and iron isotopes	International Atomic Energy Agency	Children under 3 with malaria	Completed
Achidi - SF	Baseline studies for clinical trials site develpment	None	Not applicable	General population in Cameroon	Completed
Tiono - SF	Phase IV: Cluster randomised trial: Impact of nets, home management and rapid diagnosis on malaria mortality in children			40 clusters of 40 children each and followed for 2 years	Ongoing
Byakika Kibwika - SF	Phase II: Safety, efficacy, PK and interaction with ART of iv artesunate and iv quinine	IV artsunate and (Quinine, ACT (Artemether-Lumefantrine or Dihydroartemisin in-piperaquine)	Gilead (for iv artesunate only). And prequalified for oral ACT (Artemether-Lumefantrine or Dihydroartemisinin-piperaquine) and Quinine	330 adult patients	Ongoing
Kouriba - SF	Immunological cohort studies: Role of monocytes in protection	None	Not applicable	In vitro assays	Ongoing

	against malaria in Mali				
Toure - SF	In-vitro studies: Evaluation of malaria immunity and merozoite vaccine candidates	None	Not applicable	In vitro assays	Ongoing
Ndiaye - SF	Cluster randomised Trial: IPT and home management of malaria in Senegal	None	Not applicable	24 clusters of villages randomised to each intervention	Ongoing
Adegnika -SF	Immunology studies of schisto/malaria co-infection	None	Not applicable	School children residing in two communities in the vicinity of Lambaréné	Ongoing
Obonyo – SF	Phase IV: Clindamycin and quinine for treating uncomplicated falciparum malaria: an open-labelled randomized trial	Clindaquine (Cleocine ®) Quinine Artemether-Lumerfantrine	Pfizer Tubingen Novartis International AG	Children (<5 years)	Ongoing
Beavogui - SF	Baseline study of epidemiological and sociological aspects of malaria in the four natural regions of Guinea	None	Not applicable	Children (6-10 years) in the four natural regions of Guinea	Ongoing

5.3.1 Abdoulaye Djimde

EDCTP Project Coordinator:	Abdoulaye Djimde (Malaria Research & Training Center, Malaria)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Assessment of the Public Health Benefit of artemisinin based combination therapies for uncomplicated malaria treatment in Mali
EDCTP Project Code:	TA.2004.40200.003
EDCTP Project Start Date:	1 January 2005
EDCTP Project End Date:	8 February 2009
Collaborators:	• Demba Dembele (Malaria Research & Training Center, Mali) • Bakary Fofana (Malaria Research & Training Center, Mali) • Bakari Sidibe (Malaria Research & Training Center, Mali) • Sekou Toure (Malaria Research & Training Center, Mali)
Objective(s):	1. To test hypothesis that repeated administration of artesunate/amodiquine (AS/AQ), artesunate pyrimethamine (AS/SP) and coartem (AR-L) for treatment of consecutive episodes of uncomplicated malaria reduces the incidence of uncomplicated malaria and attributable malaria 2. To measure the impact of repeated administration of the drugs on malarial immunity and malaria transmission
Study design:	Phase IV randomised trial
Number of subjects:	780
Product:	AS/AQ, AS/SP and AR-L
Manufacturer/Developer:	Prequalified drugs
Status:	Completed
Results and outcomes:	A total of 780 subjects were included to the study with 260 per treatment arm. Collectively, they experienced 2463 episodes of malaria. Combined therapy of Arsucam or Arsumax reduced malaria incidence more than Coartem. Dr Djimde is the Project Coordinator of the WANECAM project (IP.2007.31060.002)
Publications:	1. Kaddouri H., Djimdé A.A., Dama S., Kodio A., Tekete M., Hubert V., Koné A., Maiga H., Yattara O., Fofana B., Sidibe B., Sangaré C.P.O, Doumbo O.K. and Le Bras J. Baseline in vitro efficacy of ACT component drugs on Plasmodium falciparum clinical isolates of Mali. *Int J Parasitol*. 2008 Jun;38(7):791-8. Epub 2008 Jan 3 2. Djimdé A.A., Fofana B., Sagara I., Sidibe B., Toure S., Dembele D., Dama S., Ouologuem D., Dicko A., and Doumbo O.K. Efficacy, Safety, and Selection of Molecular Markers of Drug Resistance by two ACTs in Mali. *Am. J. Trop. Med. Hyg*., 78(3), 2008, pp. 455–461 3. 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. 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. Malar J. 2009 Feb 26;8:34. 4. Barger B., Maiga H., Traore O.B., Tekete M., Timbine A., Dara A, Traore Z.I., Gantt S., Doumbo O.K. and Djimde A.A. Intermittent preventive treatment using artemisinin-based combination therapy reduces malaria morbidity among school-aged children in Mali. *Trop Med Int Health*. 2009 May 26. PMID: 19497079

5.3.2 Alexis Nzila

EDCTP Project Coordinator:	Alexis Nzila (Kenya Medical Research Institute (KEMRI), Kenya)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Understanding the mechanism of piperaquine PQ) resistance
EDCTP Project Code:	TA.2004.40200.003
EDCTP Project Start Date:	1 January 2005
EDCTP Project End Date:	25 November 2008
Collaborators:	• Xin-zhuan Su (National Institute of Health (NIH), USA) • Steve Ward (University of Liverpool, UK)
Goal:	To understand the mechanisms of PQ-resistance, with the overall goal to identify molecular markers that could be used to predict PQ resistance
Objective(s):	1. Assess the selective pressure of the PQ following the use of ArtekinTM 2. Select PQ resistance in vitro: by continuously culturing of parasites in presence of increasing concentrations of PQ 3. Identify molecular markers associated with piperaquine resistance.
Collaborating site(s):	• NIH (USA) • University of Liverpool (UK)
Study design:	Laboratory based investigations: In-vitro drug resistance studies
Product:	• PQ, Lumofantrine (LM) • Dihydroxyartemisin (DHA)
Status:	Completed
Results and outcomes:	The study collected baseline information on the activity of several antimalarials, PQ, Lumofantrine (LM) and Dihydroxyartemisin (DHA) in *P.falciparum* isolates in Kilifi, Kenya. 10 to 20% of isolates had reduced susceptibility to LM, yet this drug has just been introduced in the country; The use of PQ (as part of the use of Artekin®) selected for isolates with higher IC50s to LM, implying that the use of Artekin® may be associated with reduced Coartem® susceptibility. Wild type pfcrt-76 and pfmdr1-86 are associated with increasef LM IC50s. These genes could contribute to LM-resistance, although it is likely that other genes are also involved. Dr Nzila has been the recipient 2006 Royal Society Pfizer Award and 2009 EDCTP Senior Outstanding Scientist Award. He also successfully mentored Dr Leah Mwai who completed her EDCTP funded PhD in 2011.
Publications:	1. Laura K Certain, Marnie R Briceño, B.A.; Steven M Kiara, Alexis M Nzila, William M Watkins, Carol H Sibley. Limited genetic diversity in pyrimethamine resistant strains of Plasmodium falciparum from Kenya. *J Infect Dis*. 2008. 197(12):1743-51 2. Eunice Nduati, Abdi Diriye, Ommeth Sheila, Leah Mwai, Steven Kiara, Victor Masseno, Gilbert Kokwaro and Alexis Nzila. Effect of folate derivatives on the activity of antifolate drugs used against malaria and cancer. *Parasitology Research* 2008, 102 (6): 1227-1234. 3. Leah Mwai, Edwin Ochong, Abdulrahman Abdi, Stevens Murithi, Steve Ward, Kevin Marsh, Gilbert Kokwaro, Phillip Sassy, Steffen Boormann and Alexis Nzila. Chloroquine resistance before and after its withdrawal in Kenya. *Malar J*. 2009 May 18;8:106. doi: 10.1186/1475-2875-8-106. 4. D.M. Kiboi, B. N. Irungu, B. Langat, S. Wittlin, R. Brun, J.Chollet, O. Abiodun J. K. Nganga, V.C.S. Nyambati, G.

	M. Rukunga, A. Bell and A. Nzila. Plasmodium berghei ANKA: Selection of resistance to piperaquine and lumefantrine in a mouse model. *Exp Parasitol*. 2009 Jul;122(3):196-202. doi: 10.1016/j.exppara.2009.03.010. Epub 2009 Mar 24 5. Philip Sasi, Abdi Abdulrahaman, Leah Mwai, Judith Straimer, Elise Schieck, Anja Rippert, Mahfudh Bashraheil, Amina Salim, Judith Peshu, Ken Awuondo, Brett Lowe, Munir Pirmohamed, Peter Winstanley, Steve Ward, Alexis Nzila, Steffen Borrmann. In vivo and in vitro efficacy of amodiaquine against Plasmodium falciparum in an area of continued use of 4-aminoquinolines in East Africa. *J Infect Dis*. 2009 Jun 1;199(11):1575-82. doi: 10.1086/598862.

5.3.3 Ambrose Talisuna

EDCTP Project Coordinator:	Ambrose Talisuna (Ministry of Health, Uganda)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Safety of artemisinin derivatives-based combination therapy in children with uncomplicated malaria and population-based pharmacovigilance (PV): a capacity strengthening proposal for pharmacovigilance of antimalarial drugs in Africa
EDCTP Project Code:	TA.2005.40200.001
EDCTP Project Start Date:	25 May 2007
EDCTP Project End Date:	1 June 2010
Collaborators:	• Umberto D'Alessandro (Prince Leopold Institute of Tropical Medicine-ITM, Belgium) • Moses Kamya (Makerere University, Uganda) • Fred Wabwire (Makerere University, Uganda)
Site Principal Investigator(s):	Moses Kamya, Makerere University, Uganda; Fred Wabwire-Mangen, Makerere University, Uganda
Objective(s):	The objective was to develop a PV system for monitoring the safety of antimalarial treatment at health facilities and within communities. A mixed model of a large multicentre trial at 12 sites (EDCTP funded) and a population based cohort at 2 Ugandan sentinel sites were used to detect signals and test hypotheses on the causal relationship between treatments and AEs.
Collaborating site(s):	ITM (Belgium)
Study design:	Phase IV (Pharmacovigilance)
Status:	Completed
Results and outcomes:	A total of 973 antimalarial treatments given either individually or in combination were followed-up. The highest prescriptions were for AL (59 %) followed by quinine (25%), SP (7%), AQ (4%), CQ (3 %), AS monotherapy (0.7%) and DHAPQP (0.1%). In total, 443 AEs were documented in the active surveillance. Pregnancy registration was implemented between January and December 2009. A total of 808 pregnant women were followed with 568 completing follow upThe key success factors were firstly the availability of focal personnel to collect and distribute the forms as well as provide feedback on a monthly basis, Secondly, linkage to existing schemes such as the health management information system and sentinel surveillance.
Publications:	

5.3.4 Issa Nebie

EDCTP Project Coordinator:	Issa Nebie (Centre national de recherche de Formation sur le Paludisme (CNRFP), Burkina Faso)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Understanding the mechanisms underlying the difference in susceptibility to malaria in an area of hyperendemic malaria in Burkina Faso: The potential role of regulatory T cells
EDCTP Project Code:	TA.2005.40200.008
EDCTP Project Start Date:	30 October 2006
EDCTP Project End Date:	31 May 2010
Collaborators;	• Diadier Diallo (CNRFP, Burkina Faso) • Amidou Diarra (CNRFP, Burkina Faso) • David Modiano (University of Rome La Sapienza, Italy) • Sodiomon Sirima (CNRFP, Burkina Faso) • Maria Gabriella Torcia (University of Florence, Italy)
Goal:	To contribute to the understanding of the role of T cell in susceptibility/resistance to malaria that might help improving or designing new malaria control tools such as malaria vaccine
Objective(s):	• To compare the proportion of regulatory T cells in population living in malaria endemic areas • To estimate the number of Foxp3 and GITR expressing cells as indicators of functional activities of T-reg in populations living in malaria endemic areas • To estimate the number of cells producing regulatory cytokine (IFN-gamma, IL-10 and TGF-β) in populations living in malaria endemic areas • To strengthen research capacity of CNRFP (Burkina Faso) through equipment of laboratories and training of young scientists in cellular immunology.
Collaborating site(s):	• University of Rome La Sapienza (Italy) • University of Florence (Italy)
Status:	Completed
Results and outcomes:	CD4+CD25+high subpopulations which contain the majority of T-reg cells were predominant in Fulani ethnic group (statistical significance (P=0.045)). The proportion of CD4+ subsets and CD4+CD25+IL10+ among CD25+ subpopulation which produced the Th2 type cytokine IL10 were more prevalent in Mossi ethnic group compared to Fulani ethnic group (P=0.05 and P=0.03 respectively). The proportion of CD127low and Foxp3+ subpopulations were similar in both ethnic groups. In sub-cohort 2, CD4+CD25+high and Cd4+CD25+IL10+ among CD4+IL10+ were predominant in children with severe malaria compare to asymptomatic children and the observed differences were statistically significant (P=0.01 and P<0.001 respectively). Mr Sanou Guillaume Sylvestre (CNRFP PhD student) trained in on flow in the labs of the University of Florence (Italy) and University of Bordeaux II (France). Three workshops were organised to standardise the assays and to analyse the data. Personnel have been also recruited (one lab technician, 5 nurses), two physicians had been appointed for the project and 2 students (1PhD and 1 master) were registered to complete their training.
Publications:	

5.3.5 Emboumbou Moukoko

EDCTP Project Coordinator:	Emboumbou Moukoko (University of Buea, Cameroon)
EDCTP Project Call:	Career Development Fellowship
EDCTP Project Title:	Identification of *Plasmodium falciparum* parasite virulence markers for the evaluation of the impact of malaria control intervention according to the local parasite populations
EDCTP Project Code:	TA.2005.40203.006
EDCTP Project Start Date:	21 November 2006
EDCTP Project End Date:	20 November 2008
Collaborators:	• Eric Akum Achidi (University of Buea, Cameroon) • Ogobara Doumbo (University of Bamako, Mali) • Albert Same Ekobo (University of Yaoundé, Cameroon) • Peter Kremsner (University of Tübingen, Germany) • Christophe Rogier (Research Unit in Parasite Biology and Epidemiology, France)
Goal:	To strengthen previous evidences, to determine more accurately the location of loci associated with pathogenicity, and to identify the *P. falciparum* gene(s) and genotypes that affect(s) the susceptibility to severe malaria (SM).
Objective(s):	To perform the combined epidemiological, clinical and genetic analysis (gene mapping of several loci of *P. falciparum* whole-genome and genotyping human haemoglobin) to identify parasite and human genetic markers associated with higher risk of severe disease (including cerebral malaria, severe malaria related anaemia, convulsion and hyperparasitaemia) compared to uncomplicated malaria (UCM) Secondary objectives: 1. To identify *P. falciparum* gene(s) and genotypes that affect(s) the pathogenicity (i.e. to severe malaria) using a genome wide gene mapping approach 2. To identify and control in the statistical the human genetic factors of malaria susceptibility to SM (i.e. haemoglobin and G6PD abnomalies) 3. To identify parasite genotypes associated with drug resistance.
Collaborating site(s):	• University of Bamako (Mali) • Research Unit in Parasite Biology and Epidemiology (France) • University of Tübingen (Germany)
Number of subjects:	956
Status:	Completed
Results and outcomes:	956 malaria patients were recruited from September 2007 to January 2009. Most of the data concerning the age, the sex, the clinical phenotype, the biological data and the clinical outcome were collected. The verification of the data bases was completed in participating countries of Cameroon, Mali and Gabon.The project enabled the grantee to set up molecular epidemiology expertise in his laboratory and he consequently got a lecturer position at University of Douala in Cameroon.
Publications:	

5.3.6 Davis Nwakanma

EDCTP Project Coordinator:	Davis Nwakanma (Medical Research Council (MRC) Laboratories, The Gambia)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Evaluation and implementation of high throughput PCR-based method for diagnosis and measurement of P. falciparum parasitaemia in clinical trials
EDCTP Project Code:	TA.2005.40200.006
EDCTP Project Start Date:	27 November 2006
EDCTP Project End Date:	27 May 2009
Collaborators:	• David Conway (MRC, The Gambia) • Natalia Escobar-Gomez (MRC, The Gambia) • Michael Walther (MRC, The Gambia)
Goal:	To evaluate a number of different quantitative real-time PCR (qPCR) methods to determine and establish a suitable protocol for routine application in malaria diagnosis and measurement of parasite density
Objective(s):	• To establish the application of qPCR determination of malaria parasitaemia for clinical trials • To evaluate parasite density estimates obtained from qPCR amplification of parasite DNA in blood sample for agreement with blood film slide microscopy • To conduct a cost comparison of qPCR with slide microcopy for the determination of malaria parasitaemia.
Study design:	Point of care diagnostics
Status:	Completed
Results and outcomes:	qPCR detected more infections than microscopy (22% vs 18%) but overall the coefficient of agreement between both methods was very high (κ = 0.86). Parasite density estimates by the two methods were very similar with near-perfect concordance (rho_c = 0.968). At 72h post-treatment it was possible to detected parasites by qPCR in ~20% of patients in whom microscopy failed to detect any infection. Median parasite clearance time was 16h by microscopy and 24h by qPCR. Parasite survival curves estimated by the two methods were significantly different (X2. =34.43; p=<.0001). Eleven PhD and MSc students were trained on short courses in the project. One article was published.
Publications:	1. Nwakanma D, Gomez-Escobar N, Walther M, Crozier S, Dubovsky F, Malkin E, Locke E, Conway D. (2009) Quantitative detection of Plasmodium falciparum DNA in saliva, blood and urine. *J Infect Dis* 199: 1567-1574.

5.3.7 Badara Cisse

EDCTP Project Coordinator:	Badara Cisse (University Cheikh Anta Diop, Senegal)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	A pilot study of the Implementation of Seasonal Intermittent Preventive Treatment with Community Participation in Senegal
EDCTP Project Code:	TA.2005.40200.004
EDCTP Project Start Date:	14 May 2007
EDCTP Project End Date:	8 August 2010
Collaborators:	• Pierre Gazin (Institut de Recherche pour le Développement, Senegal) • Omar Gaye (University of Dakar, Senegal) • Brian Greenwood (London School of Hygiene and Tropical Medicine (LSHTM), UK) • Paul Milligan (LSHTM, UK) • Pape Moussa Thior (Ministry of Health and Medical Prevention, Senegal) • Jean-François Trape (Institut de Recherche pour le Développement, Senegal)
Clinical Trial/Study Sponsor:	University Cheikh Anta Diop (Senegal)
Primary Objective(s):	To compare the effectiveness of Dualkin (cure rate at 28 and 42 days) compared to amodiaquine plus artesunate (e.g. Falcimon*) which is the used ACT for the treatment of uncomplicated Plasmodium falciparum. Falcimon* is a combination of amodiaquine plus artesunate. The secondary objectives of this study were to compare delay to fever and parasitemia clearance and to determine the prevalence of gametocyte carriage at day 14, 28 and 42. Other objectives included to assess the clinical efficacy (delay to fever and parasite clearance and prevalence of gametocytes carriage after treatment).
Collaborating site(s):	• LSHTM (UK) • Institut de Recherche pour le Développement (Senegal)
Study design:	Phase III
Study population:	CHILDREN (2 months - 5 years) N=1833
Product:	Dualkin to amodiaquine plus artesunate
Trial Registration number(s):	NCT00529620
Status:	Completed
Results and outcomes:	This study provided evidence that seasonal IPTc with SP+PQ among children is highly effective and well tolerated. The combination of two long-acting drugs is optimal for malaria prevention and is most effective in the face of an emergence of resistant parasite genotypes. It was also demonstrated that amendments to age-based dosing of SP-Amodiaquine had the potential of increasing dosing accuracy and improve tolerability of the IPTc. Two scientific papers were published. The work has been an important reference for the WHO scientific advisory group. One junior physician, 2 nurses and 45 community volunteers were trained. The grantee also recruited an MSc student in parasitology and he was also a recipient of second Senior Fellowship grant from Malaria Capacity Development Consortium. Two more EDCTP funded projects are now linked to the ground work of this project. These are a Senior Fellowship to Jean Louis Ndiaye and the Malaria Vectored Vaccines Consortium - IP_08_31100_001, which were both

	awarded in 2010.
Publications:	1. Cisse B, Cairns M, Faye E, et al. Randomised Trial of Piperaquine with Sulfadoxine-Pyrimethamine or Dihydroartemisinin for Malaria Intermittent Preventive Treatment in Children. *PloS one.* 2009;4(9):e7164 2. M Cairns, B Cisse, C Sokhna, et al. Amodiaquine dosage and tolerability for intermittent preventive treatment to prevent malaria in children. *Antimicrobial Agents and Chemotherapy*. March 2010, p. 1265-1274, Vol 54, No 3.

5.3.8 Daniel Dodoo

EDCTP Project Coordinator:	Daniel Dodoo (Noguchi Memorial Institute for Medical Research, Ghana)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Assessment of functionality of antibodies that associate with protection from clinical malaria using the in-vitro P.falciparum growth inhibition assay
EDCTP Project Code:	TA.2007.40200.012
EDCTP Project Start Date:	24 July 2008
EDCTP Project End Date:	30 March 2011
Collaborators:	• Klavs Berzins (Stockholm University, Sweden) • Michael Theisen (Statens Serum Institut (SSI), Denmark) • David Cavanagh, Edinburgh • Bright Adu, Ghana • Selorme Adukpo, Ghana • Emimanuel Kakra Dickson, Ghana • Edem Badji, Ghana • Judith Antwi, Ghana • Anna Mills, Ghana
Goal:	To measure GLURP and MSP3 isotype and IgG subclass antibodies by ELISA in relation to susceptibility or protection from clinical malaria; establishment and field validation of the in vitro parasite growth inhibition assays using purified GLURP specific antibodies from selected individuals whose ELISA antibody responses to GLURP associate with protection against or susceptibility to clinical malaria after correcting for potential confounders.
Objective(s):	1. To establish in the field, the *in vitro* parasite growth inhibition assays with or without the presence of monocytes, using microscopy and flowcytometric readouts to assess parasite growth inhibition 2. To assess by ELISA, antibody responses to GLURP and MSP3 in relation to protection against or susceptibility to clinical malaria correcting for potential confounders such as age, socio-economic status, area of residence in study area, duration of residence in study area among others 3. To determine the functionality of purified antibodies in individuals who had malaria and those who did not have malaria during the study period by the *in vitro* parasite growth inhibition assay with or without the presence of monocytes.
Collaborating site(s):	• Stockholm University (Sweden) • SSI (Denmark)
Study design:	Laboratory based immunological and molecular biology investigations: in-vitro assays
Status:	Completed
Results and outcomes:	The acquired Growth Inhibition Assay technique by the project staff has been established at the Immunology laboratory of Noguchi Memorial Institute and used in assessing the functionality of antibodies that correlate with protection from clinical malaria in the ELISA procedure. 8 individuals at the centre have been trained in GIA.
Publications:	

5.3.9 Christian Happi

EDCTP Project Coordinator:	Christian Happi (University of Ibadan, Nigeria)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Validation of New Biomarkers for Monitoring *Plasmodium falciparum* Reduced susceptibility/Tolerance or Resistance to Artemisinin Derivatives and Partner Drugs in Nigeria.
EDCTP Project Code:	TA.2007.40200.016
EDCTP Project Start Date:	13 December 2008
EDCTP Project End Date:	12 December 2010
Goal:	To identify and validate new biomarkers/molecular determinants of parasites response to artemisinin derivatives (ARTs) and partner drugs *in vitro* and *in vivo.*
Objective(s):	1. Evaluate clinical treatment response parameters, *in vitro* and *in vivo* efficacy and drug blood levels of artemether-lumefantrine (AL) and artesunate-amodiaquine (AS-AQ) combinations in patients' infected with *P. falciparum* in Ibadan, Southwest Nigeria 2. Use the PCR, DNA sequencing approaches to identify new biomarkers/ molecular determinants of P. falciparum response to ARTs and Partner drugs *in vitro* and *in vivo*. 3. Validate the role of new biomarkers/molecular determinants of *P. falciparum* response to ARTs and partner drugs by collating SNPs/SNPs patterns in parasite genes with clinical treatment response parameters, patients' treatment outcome, blood drug levels and in vitro quantitative responses (phenotypes).
Study design:	*In vitro* and *in vivo* bio-markers studies
Status:	Completed
Results and Outcomes:	5 major sub-studies were completed and four publications produced from the fellowship. The capacity building programme at grantee's laboratory at the College of Medicine, University of Ibadan in Nigeria has been improved and has been used to train Dr Obaro Michael (a clinician) a former Masters Degree Programme student for his fellowship; Dr Onikepe Folarin a post doctoral Fellow to attend the Genome Epidemiology Meeting in Hinxton, UK and Miss Titilola Okuboyejo a PhD student partly being supported by this project to undergo a 3 months training on quantitative qPCR for gametocyte sex ratio determination.
Publications:	1. Akintunde Sowunmi, Elsie O Adewoye, Grace O Gbotosho, Christian T Happi, Abayomi Sijuade, Onikepe A Folarin, Titilope M Okuboyejo and Obaro S Michael. (2010). Factors contributing to delay in parasite clearance in uncomplicated *falciparum* malaria in children. *Malaria Journal.* 9(1):53 2. Grace O. Gbotosho, Christian Happi, Onikepe Folarin, Ochuko Keyamo, Akintunde Sowunmi, and Ayoade MJ Oduola. (2010). Rapid Detection of Lactate Dehydrogenase and Genotyping of *Plasmodium falciparum* in Saliva of Children with Acute Uncomplicated Malaria. *Am. J. Trop. Med. Hyg*. 83 (3): 496-501 3. Obaro S Michael, Grace O Gbotosho, Onikepe A Folarin, Titilope Okuboyejo, Akintunde Sowunmi, Ayoade MJ Oduola and Christian T Happi. (2010). Early variations in *Plasmodium falciparum* dynamics in Nigerian children after treatment with two artemisinin-based combinations: implications on delayed parasite clearance. *Malaria*

	Journal. 9:335. 4. Daria Van Tyne, Daniel J. Park, Stephen F. Schaffner, Daniel E. Neafsey, Elaine Angelino, Joseph F. Cortese, Kayla G. Barnes, David M. Rosen, Amanda K. Lukens, Rachel F. Daniels, Danny A. Milner, Jr, Charles A. Johnson, Ilya Shlyakhter, Sharon R. Grossman, Justin S. Becker, Daniel Yamins, Elinor K. Karlsson, Daouda Ndiaye, Ousmane Sarr, Souleymane Mboup, Christian Happi, Nicholas A. Furlotte, Eleazar Eskin, Hyun Min Kang, Daniel L. Hartl, Bruce W. Birren, Roger C. Wiegand, Eric S. Lander, Dyann F. Wirth, Sarah K. Volkman, Pardis C. Sabeti. (2011). Identification and Functional Validation of the Novel Antimalarial Resistance Locus PF10_0355 in *Plasmodium falciparum*. *PLoS Genet*. E1001383.doi:10.1371/journal.pgen.1001383.

5.3.10 Kamija Phiri

EDCTP Project Coordinator:	Kamija Phiri (University of Malawi)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	A randomised controlled trial of oral iron therapy for treatment of post-malaria iron-deficiency anaemia in Malawian children com paring immediate post-discharge versus delayed treatment on iron uptake and haematological response
EDCTP Project Code:	TA.2008.40200.016
EDCTP Project Start Date:	29 September 2009
EDCTP Project End Date:	29 September 2011
Collaborators:	• Patrick van Rheenen (University Medical Center Groningen, Netherlands) • Feiko ter Kuile (University of Liverpool, UK) • Sarah White (Malawi-Liverpool-Wellcome Trust Research Programme, Malawi)
Clinical Trial/Study Sponsor:	College of Medicine, University of Malawi
Objective(s):	To determine whether delaying oral iron therapy in post-malaria iron deficiency anaemia for at least two weeks improves iron absorption and reduces the risk of iron-induced intestinal inflammation
Clinical Trial/Study site(s):	
Collaborating site(s):	• University Medical Center Groningen (Netherlands) • University of Liverpool (UK)
Study design:	Phase II trial: Evaluation of different forms of oral iron for treatment of post malaria iron deficiency anaemia
Number of subjects:	CHILDREN (4-24 months) N=245
Product:	Iron tonic/ iron isotopes
Manufacturer/Developer:	International Atomic Energy Agency
Trial Registration number(s):	PACTR2010050002141682
Status:	Completed
Results and Outcomes:	In 2010 protocol changes increased the required the sample size increased from 400 to 600. Due to slow recruitment at original study site (Ndirande Health Centre in Blantyre) the study was moved to another district (Zomba) with a reported higher rate of potential study participants. Between September 2011 and end of February 2012 a total of 148 participants had been recruited bringing the total to 245 study participants (41% of required sample). The fellow had also successfully managed to source funds ($100,000) from Malaria Capacity development Consortium (MCDC) of the London School of Hygiene and Tropical Medicine to establish a Tropical Haematology Research Unit (THRU) in the Haematology Department, College of Medicine. A sub-study investigating iron absorption and incorporation into the blood cells has been planned to be carried out in collaboration with partners at the Swiss Federal Institute of Technology (ETH) Institute of Food in Switzerland (Prof Richard Hurrell and team).
PhD study	Nyanyiwe Mbeye
Publications:	

5.3.11 Eric Achidi

EDCTP Project Coordinator:	Eric Achidi (University of Buea, Cameroon)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Malaria baseline studies towards characterising and establishing a clinical trial site at Mutengene, South West Region of Cameroon
EDCTP Project Code:	TA.2009.40200.008
EDCTP Project Start Date:	22 March 2010
EDCTP Project End Date:	22 March 2012
Collaborators:	• Julius Atashili (University of Buea, Cameroon) • Samuel Wanji • Njua Yafi • Judith Anchang
Objective(s):	The epidemiological study is designed to provide data on baseline malariometric parameters valuable for future intervention studies aimed at validating disease control tools. The specific objectives include conducting a population census of the study area, determining the malaria prevalence rates and density in cross sectional surveys, helminth and malaria co-infection rates and densities, number of episodes per year in cohort longitudinal studies, vectors transmitting parasites, their dynamics and inoculation rates, natural immune responses to malaria parasite exposure and prevalence of some genetic traits that protect against malaria.
Clinical Trial/Study site(s):	Mutengene, Fako Division (Cameroon)
Study design:	Epidemiological studies for clinical trials site develpment
Number of subjects:	15,344
Status:	Completed
Results and Outcomes:	At the end of the project a total of 15,344 individuals had been included and a series of baseline studies were conducted. These included studies household mosquito net ownership, prevalence of fever, prevalence of malaria parasitaemia by season, prevalence of intestinal helminthes by season, prevalence of anaemia, the prevalence of the sickle cell trait (HbAS) in the study group and levels of Plasmodium falciparum specific IgE/IgG2 antibodies in study participants. The project is well integrated within the EDCTP funded central African network of excellence, CANTAM and also received additional funding from the European Virtual Institute for Malaria Research (EVIMalaR). Eight members of the study team received various short term trainings.
PhD study:	Candidate: Njua Clarisse Yafi
Publications:	1. Eric A. Achidi, Tobias O. Apinjoh, Judith K. Anchang-Kimbi,Clarisse N. Yafi, Richard Besingi, Nancy W. Awah and Marita Troye-Blomberg. (2012). Plasmodium falciparum Specific IgE, IgG and Anti-GPI IgG Antibodies in Cameroonian Children with Severe and Uncomplicated Malaria. *International Journal of Tropical Disease and Health*. June 2012. 2(3): 157-172 2. Eric A Achidi, Tobias O Apinjoh, Judith K Anchang-Kimbi, Regina N Mugri, Andre N Ngwai, Clarisse N Yafi. (2012). Severe and uncomplicated falciparum malaria in children from three regions and three ethnic groups in Cameroon: prospective study. *Malar J*. 2012 Jun 24;11:215. 3. Gervais Gouana Tchinda, Julius Atashili, Eric A Achidi, Henri L Kamga, Anna L Njunda, Peter M Ndumbe (2012).

	Impact of malaria on hematological parameters in people living with HIV/AIDS attending the Laquintinie Hospital in Douala, Cameroon. *PLoS One*. 2012;7(7):e40553. doi: 10.1371/journal.pone.0040553. Epub 2012 Jul 10

5.3.12 Alfred Tiono

EDCTP Project Coordinator:	Alfred Tiono (Centre National de Recherche et de Formation sur le Paludisme (CNRFP), Burkina Faso)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Phase IV: A cluster-randomised controlled trial to assess the impact of combined strategies (impregnated bed nets + Home management of malaria oriented by Rapid Diagnosis Test) on severe malaria morbidity in children aged 6 to 59 months in Burkina Faso
EDCTP Project Code:	TA.2009.40200.019
EDCTP Project Start Date:	29 April 2010
EDCTP Project End Date:	28 February 2013
Collaborators:	• Issa Ouedraogo Nebie (CNRFP, Burkina Faso) • Sodiomon Bienvenu Sirima (CNRFP, Burkina Faso) • Alphonse Ouedraogo • Abdoulaye Traore
Objective(s):	To show the additional benefit in terms of reduction of severe malaria morbidity by adding the HMM to bed nets for children aged 6-59 months living in a seasonal malaria transmission area and to estimate the incidence of severe malaria in children aged 6-59 months living under Insecticides impregnated bed nets with access to home based management of malaria strategy in a seasonal malaria transmission area
Clinical Trial/Study site(s):	CNRFP (Burkina Faso)
Study design:	Cluster randomised trial of bed nets and home management
Study population:	CHILDREN (6-59 months) N=6191 (40 clusters)
Status:	Ongoing
Results and outcomes:	At the end of first year of the project the following have been achieved and in accordance with the approved work plan: • Approval of the study by the community and ethics review board • Definition of study clusters • Purchase and distribution of bed nets • Training of staff • Conduct 2 of the planned 4 cross sectional studies The remaining activities include: • Third cross sectional study • Fourth cross sectional study • Data analysis • Publications
Publications:	

5.3.13 Pauline Byakika Kibwika

EDCTP Project Coordinator:	Pauline Byakika Kibwika (Infectious Diseases Institute, Makerere University College Of Health Sciences (Uganda)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Comparison of efficacy, safety and pharmacokinetics of intravenous artesunate and intravenous quinine followed by oral artemisinin combination therapy for severe malaria treatment in Uganda AND evaluation of pharmacokinetic drug interactions of artesunate, quinine, lumefantrine and piperaquine with antiretroviral drugs
EDCTP Project Code:	TA.2009.40200.020
EDCTP Project Start Date:	14 March 2011
EDCTP Project End Date:	30 September 2013
Collaborators:	• Jane Achan (Makerere University, Uganda) • Moses R. Kamya (Makerere University (Uganda) • Elly Katabira (Makerere University, Uganda) • Noah Kiwanuka (Makerere University, Uganda) • Mohammed Lamorde (Makerere University, Uganda) • Harriet Mayanja-Kizza (Makerere University, Uganda) • Concepta Merry (Makerere University, Uganda/Trinity College, Ireland)
Clinical Trial/Study Sponsor:	Institute of Infectious Diseases (Uganda)
Goal:	To evaluate the effectiveness of IV artesunate plus ACT and IV quinine plus ACT as well as to study the pharmacokinetics of artemether-lumefantrine (AL) and dihydroartemisinin-piperaquine (DP) for treatment of severe malaria in adults and children in Tororo district hospital, Uganda.
Objective(s):	1. To compare treatment outcome (measured as risk of recurrent parasitaemia and risk of recurrent symptomatic malaria) following treatment with IV quinine followed by oral ACT (Artemether-Lumefantrine or Dihydroartemisinin-piperaquine) and IV artesunate followed by oral ACT (AL or DP) for treatment of severe malaria in Ugandan patients 2. To compare parasite clearance time following treatment with IV quinine followed by oral ACT (AL or DP) and IV artesunate followed by oral ACT (AL or DP) for treatment of severe malaria in Ugandan patients 3. To investigate the pharmacokinetic parameters of IV quinine, IV artesunate, oral AL and oral DP during severe malaria treatment in Ugandan patients and correlate these with treatment outcome 4. To investigate the pharmacokinetic drug interactions of quinine, artesunate, lumefantrine and piperaquine with the antiretroviral drugs (Nevirapine, Efavirenz, Lopinavir/ritonavir) in Ugandan patients.
Collaborating site(s):	University of Liverpool (UK)
Study design:	PK and drug interaction studies
Number of subjects:	400 (target)
Product:	Quinine, ACT (Artemether-Lumefantrine or Dihydroartemisinin-piperaquine) and IV artesunate
Manufacturer/Developer:	Gilead (for iv artesunate only)
Cofunders:	International Society of Infectious Diseases grants to support laboratory work
Trial Registration number(s):	PACTR201110000321348

Status:	Completed
Results and Outcomes:	By mid-2012 the project had screened 57 patients, recruited 39 and had 1 lost to follow up.
Publications:	

5.3.14 Bourema Kouriba

EDCTP Project Coordinator:	Bourema Kouriba (University of Bamako, Mali)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Role of functionally distinct monocyte subpopulations in protection against clinical Plasmodium falciparum malaria in people living in endemic area of Mali
EDCTP Project Code:	TA.2010.40200.007
EDCTP Project Start Date:	13 May 2011
EDCTP Project End Date:	13 May 2013
Collaborators:	• Charles Aarama (Malaria Research & Training Center, Mali) • Issa Diarra (Malaria Research & Training Center, Mali) • Abdoulaye Kone (Malaria Research & Training Center, Mali) • Amadou Niangaly (Malaria Research & Training Center, Mali) • Mahamadou S. Sissoko (Malaria Research & Training Center, Mali) • Kourane Sissoko (Malaria Research & Training Center, Mali)
Objective(s):	To assess the role of monocytes activation by infected red blood cell in the protection against clinical falciparum malaria in endemic area and determine the frequency of monocytes subpopulations according to the clinical outcome (asymptomatic, mild and severe) of malaria infection
Study design:	Immunological cohort studies
Study population:	CHILDREN (1-15 years old); N=210
Status:	Ongoing
Results and outcomes:	A cohort of 210 children aged 1-15 years was established in May 2011. Three cross-sectional studies will be conducted on this cohort before completion of the project.
Publications:	

5.3.15 Aissatou Toure

EDCTP Project Coordinator:	Aissatou Toure (Pasteur Institute of Dakar, Senegal)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Optimization and standardization of the new functional antibody dependant respiratory burst (ADRB) assay to evaluate anti-malarial immunity in endemic populations and merozoite based vaccine candidates
EDCTP Project Code:	TA.2010.40200.027
EDCTP Project Start Date:	26 April 2011
EDCTP Project End Date:	31 December 2013
Collaborators:	• Sylvie Bay (Institut Pasteur, France) • Shirley Longacre (Institut Pasteur, France) • Adama Tall (Institut Pasteur de Madagascar)
Objective(s):	1. To optimize and standardize a "new" functional assay developed recently in our research unit, the Antibody Dependant Respiratory Burst (ADRB) assay detected by chemiluminescence, which has been correlated with clinical protection against malaria 2. To compare ADRB results with those of other commonly used functional assays such as the growth inhibition assay (GIA) 3. To use the ADRB assay as a tool to evaluate the level of malaria immunity in different endemic populations and to validate merozoite surface antigen vaccine candidates
Study design:	Laboratory based investigations: *in vitro* immunological and molecular biological assays
Status:	Completed
Results and outcomes:	In the first year of the project the team studied mononuclear cells in comparison with polymorphonuclear neutrophils but concluded that using freshly isolated polymorphonuclear neutrophils give better results. Conditions of Ph for optimising the ADRB assay were also studied and the conclusion is that better results are obtained with alkaline Ph. The team finished by studying different strains of *P. falciparum* in the ADRB using the Palo Alto strain of *P. falciparum* as reference in comparison with local adapted *P. falciparum* strain. They observed that the ADRB is significantly higher when the merozoites originated from local *P. falciparum* strains. After comparing optimized ADRB using the data bank and sera collection available in the Pasteur Institute associated with the Dielmo project monitoring the immune status of two endemic Populations the rResults showed again a correlation between high level of ADRB and a lower risk of malaria attack that confirm our previous results.
PostDoc study	Charlotte Joos Ndiaye
Publications:	

5.3.16 Jean Louis Ndiaye

EDCTP Project Coordinator:	Jean Louis Ndiaye (University Cheikh Anta Diop of Dakar, Senegal)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Intermittent preventive treatment in children combined with malaria home management in an area with persisting high malaria prevalence in Senegal
EDCTP Project Code:	TA.2010.40200.032
EDCTP Project Start Date:	11 April 2011
EDCTP Project End Date:	11 April 2013
Collaborators:	• Badara Cisse (University Cheikh Anta DIOP de Dakar (UCAD), Senegal) • Oumar Gaye ((UCAD, Senegal) • Paul Milligan (London School of Hygiene and Tropical Medicine (LSHTM), UK) • Youssoupha Ndiaye (Ministere de la sante et de la prevention medicale, Senegal) • Pape Moussa Thior (Ministere de la sante et de la prevention medicale, Senegal)
Clinical Trial/Study Sponsor:	University Cheik Anta Diop de Dakar (Senegal)
Objective(s):	To determine whether seasonal IPTc with sulfadoxine-pyrimethamine plus amodiaquine provide added benefit in populations with access to prompt effective treatment through home–based management; whether IPTc has previously been shown effective when give for three months in areas with a short transmission season and whether seasonal IPTc is safe and acceptable when given for a longer period in areas with a longer transmission season. To also show the cost-effectiveness of adding seasonal IPTc to home management of malaria (HMM)
Collaborating site(s):	London School of Hygiene and Tropical Medicine (LSHTM, UK)
Study design:	Phase IV: Cluster randomised trial
Study population:	CHILDREN (3 months-10 years) N=4554
Product:	Sulfadoxine-pyrimethamine, Amodiaquine, Artemether-lumefantrine
Trial Registration number(s):	NCT01449045
Status:	Ongoing
Results and outcomes:	Twenty four Community Health Workers and malaria volunteers were trained by the department of Parasitology to do thick and thin blood smear to confirm all malaria cases in the 24 villages involved in that EDCTP research project. Out of 4554 chldren enrolled in the study approximately 2000 children have received IPTc at fifth month (97% of intended sample of intervention group).
MSc studies	Candidate: Dr Mamadou Sarifou
	Candidate: Mr Cheikh Tidiane Ba
Publications:	

5.3.17 Akim Ayola Adegnika

EDCTP Project Coordinator:	Akim Adegnika (Medical Research Unit Albert Schweitzer Hospital, Gabon)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Impact of schistosoma hematobium infection on immunological and clinical aspects of *P. falciparum* malaria in children
EDCTP Project Code:	TA.2011.40200.025
EDCTP Project Start Date:	9 February 2012
EDCTP Project End Date:	9 December 2014
Collaborators:	• Abraham Alabi (Albert Schweitzer Hospital, Gabon) • Maria Yazdanbakhsh (Leiden University, Netherlands)
Objective(s):	This project aims to study the impact of *S. haematobium* infection on *P. falciparum* malaria induced immune response and clinical features in school children residing in two communities in the vicinity of Lambaréné (PK15 and PK17), where the malaria incidence rate is 1.3 person-years. The research questions to be answered by the project are: 1. How are plasmodia-specific pro-inflammatory Th1 and Th17 immune responses affected by coinfection with *S. haematobium*? 2. How does *S. haematobium* infection influence the clinical and parasitological profile of *P.falciparum* malaria?
Collaborating site(s):	Leiden University (Netherlands)
Study design:	Immunology studies of schisto/malaria co-infection
Status:	Ongoing
Results and outcomes:	
Publications:	

5.3.18 Charles Obonyo

EDCTP Project Coordinator:	Charles Obonyo (Kenya Medical Research Institute (KEMRI), Kenya)
EDCTP Call Title:	Senior Fellowship
EDCTP Project Title:	Clindamycin plus quinine for treating uncomplicated *falciparum* malaria: an open-label randomized trial
EDCTP Project Code:	TA.2011.40200.059
EDCTP Project Start Date:	1 November 2012
EDCTP Project End Date:	1 November 2014
Collaborators:	• Charles Obonyo (Kenya Medical Research Institute (KEMRI), Kenya) • Dr Elizabeth Juma (KEMRI, Kenya) • Dr Bernhards Ogutu (KEMRI, Kenya) • Dr John Logedi (MOH, Kenya) • Dr Kevin Omondi (KEMRI, Kenya)
Clinical Trial/Study Sponsor:	KEMRI (Kenya)
Goal:	To evaluate the efficacy and safety of clindamycin plus quinine compared with artemether-lumefantrine among children less than 5 years of age diagnosed with uncomplicated *falciparum* malaria in western Kenya
Primary Objective(s):	1. To measure the clinical and parasitological efficacy of Clindamycin plus quinine and Artemether-Lumefantrine (current recommended regimen) among patients between 6-59 months of age suffering from uncomplicated P falciparum malaria, by determining the proportion of patients with Early Treatment Failures (ETF), Late Clinical Failures (LCF), Late Parasitological Failures (LPF), or with Adequate Clinical and Parasitological Response (ACPR) during a 28 day follow-up period.
Secondary Objective(s):	1. To differentiate recrudescence from new infections through Polymerase Chain Reaction (PCR) analysis 2. To determine fever and parasite clearance rates 3. To determine gametocyte carriage rates 4. To determine the change in mean haemoglobin by day 28 5. To determine the frequency of molecular markers for drug resistance.
Clinical Trial/Study site(s):	Homa Bay District Hospital, Western Kenya
Collaborating site(s):	Ahero District Hospital
Study design:	Phase IV open-label randomized trial
Number of subjects:	384 children
Product(s):	Clindamycin quinine Control product: Oral Artemether-lumefantrine (Novartis)
Manufacturer/Developer:	Pfizer
Trial registration number(s):	PACTR20129000419241
Status:	Ongoing
Results and Outcomes:	A study team of twelve (12) members have been recruited and trained on the study protocol.
Publications:	

5.3.19 Abdoul Habib Beavogui

EDCTP Project Coordinator:	Abdoul Habib Beavogui (Centre National de Formation et de Recherche en Santé Rurale (CNFRSR) Jean SENECAL de Mafèrinyah, Guinea)
EDCTP Call Title:	Senior Fellowship
EDCTP Project Title:	Baseline Study of Epidemiological and Sociological aspects of Malaria in the four Natural Regions of Guinea
EDCTP Project Code:	TA.2011.40200.062
EDCTP Project Start Date:	1 November 2012
EDCTP Project End Date:	1 November 2014
Collaborators:	• Alexandre Delamou (Centre National de Formation et de Recherche en Santé Rurale (CNFRSR) Jean SENECAL de Mafèrinyah, Guinea) • Mohamed Diaby (University of General Lansana Conte, Guinea) • Abdoulaye Djimde (Malaria Research & Training Center, Mali) • Abdoulaye Doumbouyah (Centre National de Formation et de Recherche en Santé Rurale (CNFRSR) Jean SENECAL de Mafèrinyah, Guinea) • Issaka Sagara (University of Bamako, Mali)
Clinical Trial/Study Sponsor:	Ministry of Public Health and Hygiene (Guinea)
Goal:	The aim of this study is to characterize at the national level malaria epidemiological patterns and malaria indicators in children aged between 6 months and 10 years, depending on the season for two consecutive years.
Primary Objective(s):	1. Estimate malaria infection prevalence and disease prevalence in children aged between 6 months and 10 2. years in Guinea in dry and raining seasons 3. Evaluate haemoglobin levels in children aged between 6 months and 10 years in Guinea 4. Measure the genotype of the main resistance genes namely Pfcrt (*P. falciparum* chloroquine resistance 5. transport), pfmdr1 *(P. falciparum* multidrug resistance 1); pfatp6 6. Determine impregnated or treated mosquito nets use in Guinea 7. Assess knowledge, attitudes and practices of mothers and legal parents of children aged between 6 months 8. 10 years towards malaria in the first year of study and during the high malaria transmission season 9. Estimate entomological parameters of malaria transmission for two consecutive years and seasons withinthe four natural regions of Guinea.
Clinical Trial/Study site(s):	The study will be conducted in the four (4) natural regions of Guinea: Lower Guinea, Middle Guinea, Upper Guinea and Forest Guinea
Study design:	Observational, cross-sectional survey
Study population:	400 children aged 6 months to 10 years and their mothers/legal guardians
Status:	Ongoing
Results and Outcomes:	
PhD study:	Title: Malaria Epidemiology in Republic of Guinea Candidate: Dr Sidikiba SIDIBE
MSc study:	Title: Msc in Biostatistics Candidate: Dr Alexandre Delamou
Publications:	

6 PhD and MSc scholarships

Table 6-1: Stand-alone (individual) PhD and MSc scholarships in HIV/AIDS, tuberculosis and malaria supported by EDCTP. Other PhD and MSc grants are included under their respective integrated/clinical trial projects

Project Acronym (Coordinator)	Disease area	Project details	Study population	Status of project
Jobe - MSc	HIV	Master of Science in Reproductive and Sexual Health Research	TBD	Closed
Oyakhirome - MSc		Public Health	Not applicable	Completed with a Diploma
Sikateyo - PhD	HIV	Informed consent process in HIV trials in Zambia	Participants in an HIV vaccine trial in Lusaka	Completed
Yindom - PhD	HIV	Immunogenetics for HIV vaccine design	600 unrelated adults in Gambia	Closed
Yimer - PhD	TB	TB drug and ART interaction and metabolism	758 ART naïve TB, TB-HIV and HIV infected individuals	Completed
Mthiyane - PhD	TB	Interferon gamma responses in TB-HIV coinfected individuals	TB-HIV infected patients	Completed
Mwai - PhD	Malaria	Lumefantrine resistance	250 in vitro culture isolates	Closed
Ramatoulie - PhD	Malaria	Pharmcogenetics of chlorproguanil in adults and children	Malaria patients in Gambia	Closed
Arama - PhD	Malaria	Immungenetic factors in malaria prevention	77 patients in Mali	Completed

6.1 Alasan Jobe

EDCTP Project Coordinator:	Alasan Jobe (National Malaria Control Program, Department of State for Health and Social Welfare, The Gambia)
EDCTP Call Title:	MSc Studentship
EDCTP Project Title:	Masters in Reproductive and Sexual Health Research
EDCTP Project Code:	TA.2005.40205.001
EDCTP Project Start Date:	10 August 2006
EDCTP Project End Date:	30 October 2007
Supervisor(s):	
Goal:	
Objective(s):	
Status:	Completed
Results and Outcomes:	
Site Principal Investigator(s):	Malang Fofana (The Gambia)
Collaborators:	Joanne Cooper (UK)
Publications:	

6.2 Sunny Oyakhirome

EDCTP Project Coordinator:	Sunny Oyakhirome (Medical Research Unit, Albert Schweitzer Hospital, Gabon)
EDCTP Call Title:	MSc Studentship
EDCTP Project Title:	MSc in Public Health
EDCTP Project Code:	TA.2005.40205.002
EDCTP Project Start Date:	27 June 2006
EDCTP Project End Date:	27 June 2007
Institution:	London School of Hygiene and Tropical Medicine (LSHTM, UK), Distance learning in MSc in public health
Supervisor(s):	• Saadou Issifou (Medical Research Unit, Albert Schweitzer Hospital, Gabon) • Peter Kremsner (University of Tübingen, Germany) • Bertrand Lell (Medical Research Unit, Albert Schweitzer Hospital, Gabon)
Goal:	Candidate aim: Improvement in the health of populations, communities and particular groups within them (eg children), through the evaluation of practical, effective interventions against major public health diseases: Malaria, Tuberculosis; AIDS. With emphasis on evidence based methods of analysis of treatment and care; investigation, development and critical evaluation of conceptual models.
Objectives:	To provide a sound ability to apply knowledge of the core disciplines; statistics, epidemiology, health economics, and social research, to real health problems. In addition, graduates should be able to: 1. Demonstrate knowledge and understanding of the principle theories, methods and interventions used in health promotion 2. Demonstrate knowledge and understanding of the development of health promotion internationally and its evolution as a multidisciplinary field 3. Assess the appropriate use of population-wide versus targeted health promotion interventions 4. Consider how to develop health promotion policy and practice that is relevant to varying public health issues in diverse contexts 5. Show competence in critically evaluating and communicating research evidence 6. Apply the knowledge and analytical skills they have gained to inform health promotion policy-making, programme planning, implementation and evaluation, and research design.
Status:	Completed
Results and Outcomes:	
Publications:	

6.3 Bornwell Sikateyo

EDCTP Project Coordinator:	Bornwell Sikateyo (Central Board of Health, Zambia)
EDCTP Call Title:	PhD Studentship
EDCTP Project Title:	Understanding participants' consent undertaken by in an Entero-Toxigenic vaccines trial in Misisi Township in Lusaka, Zambia
EDCTP Project Code:	TA.2005.40204.026
EDCTP Project Start Date:	1 November 2006
EDCTP Project End Date:	30 March 2011
Supervisor(s):	• Roger Beech (University of Keele, UK) • Nancy E. Kass (Johns Hopkins Bloomberg School of Public Health, USA) • Douglas Wassenaar (University of KwaZulu-Natal, South Africa)
Objectives:	The specific objectives of this PhD project were: (a) To describe the interactions between research staff and participants in which "consent" is negotiated and maintained, (b) to explore participants' social and economic characteristics, everyday life and situations as these impact the "consent process" and (c) to assess how negotiations of participant consent evolve and change over the course of the trial in view of the complex procedures.
Status:	Completed
Results and Outcomes:	This study found that study participants in a vaccine trial in Missi in Zambia enrolled to gain access to the resources necessary for survival. These included improved health care and cash incentives.
Publications:	

6.4 Louis Marie Yindom

EDCTP Project Coordinator:	Louis Marie Yindom (Medical Research Council (MRC) Laboratories, The Gambia)
EDCTP Call Title:	PhD Studentship
EDCTP Project Title:	The role of Human leukocyte antigen (HLA) and killer immunoglobulin-like receptor (KIR) in HIV-2 infection: a key component to HIV vaccine design and its evaluation in Africa
EDCTP Project Code:	TA.2005.40204.013
EDCTP Project Start Date:	1 August 2006
EDCTP Project End Date:	31 August 2009
Supervisor(s):	• Assan Jaye (MRC Laboratories, The Gambia) • Sarah Rowland-Jones (MRC Laboratories, The Gambia) • Giorgio Sirugo (MRC Laboratories, The Gambia)
Goal:	To comprehensively characterise the distribution of HLA class I molecules in populations in the Gambia and Guinea-Bissau and to look at immunogenetic associations, focusing on HLA and KIR genotypes, with clinical outcome in HIV-2 infection which is largely confined to West Africa and provides a valuable model of attenuated HIV disease
Objectives:	The major objectives of this project are to: 1. Determine the distribution of HLA class I and KIR genes among HIV-2 cases and healthy individuals in Caio (Guinea-Bissau) and Fajara (Gambia) 2. Study the association of individual HLA-A, HLA-B, HLA-C, and KIR genes with susceptibility or resistance to HIV-2 infection The secondary objectives are to: 1. Determine the epistatic effect between HLA and KIR gene variants in HIV-2 disease outcome using indicators of disease 2. Progression such as CD4+ T cell count and plasma viral load (PVL) 3. Develop sequence specific techniques for subsequent detection of KIR and HLA alleles from genomic DNA
Status:	Completed
Results and outcomes:	The study showed that HLA-KIR compound genotypes did not affect risk of HIV-2 acquisition in Gambia.
Publications:	

6.5 Getnet Yimer

EDCTP Project Coordinator:	Getnet Yimer (Department of Pharmacology, Medical Faculty, Addis Ababa University, Ethiopia)
EDCTP Call Title:	PhD Studentship
EDCTP Project Title:	Anti tuberculosis-anti retroviral drugs induced Hepatotoxicity and interaction of these drugs at the level of CYP 450 metabolism
EDCTP Project Code:	TA.2005.40204.005
EDCTP Project Start Date:	2 August 2006
EDCTP Project End Date:	2 December 2010
Goal:	To evaluate the prevalence, severity, and outcome of hepatotoxicity associated with intake of anti TB and/or ARV drugs when taken concomitantly and when taken alone; and to determine the pharmacokinetic drug-drug interaction between anti TB and ARV at the level of drug metabolism and thereby assess the distribution of CYP 3A4, 3A5, 2C9/19, 2B6, and NAT2.
Objectives:	To assess and compare the prevalence, severity and prognosis of anti-TB and ARV drugs induced hepatotoxicity and evaluate the drug-drug interaction at the level of CYP 450 among Ethiopian patients. Specific objectives 1. To determine the prevalence of DIH in HIV positive TB patients taking anti-TB alone 2. To determine the prevalence of DIH in HIV positive TB patients taking anti-TB and ART 3. To see the distribution of CYP 3A4, 3A5, 2C9/19, 2B6 polymorphism in our study participants 4. To see the effect of CYP 3A4, 3A5, 2C9/19, 2B6 polymorphism on the development of DIH 5. To assess the drugdrug interaction between the anti-TB and ARV drugs 6. To assess the severity as well as outcome of DIH in our study participants.
Status:	Completed
Results and outcomes:	The study is reported to have shown that drug induced liver injury (DILI) is common among Ethiopian TB-HIV patients who have a slow acetylation status related to CYP2B6 516TT genotype. This is particularly relevant to patients on efavirenz based regimen. Through these findings close follow up and regular monitoring of plasma efavirenz concentration and liver enzymes during early therapy particularly in patients with, and those with elevated serum amino-transferases, lower haemoglobin, platelet count and albumin at baseline is recommended for early management of efavirenz-based HAART induced liver injury.
Publications:	

6.6 Thuli Mthiyane

EDCTP Project Coordinator:	Thuli Mthiyane (Medical Research Council, South Africa
EDCTP Call Title:	PhD Studentship
EDCTP Project Title:	Safety tolerability and monitoring of combined anti-tuberculosis and antiretroviral therapy (Reconstitution of TB antigen specific IFN-γ responses in TB-HIV co-infected participants)
EDCTP Project Code:	TA.2005.40204.025
EDCTP Project Start Date:	10 November 2006
EDCTP Project End Date:	31 October 2011
Supervisor(s)	• Graham Rook (University College London, UK) • A. W. Sturm (Nelson R Mandela School of Medicine University of KwaZulu Natal, South Africa) • A. Zumla (University College London, UK)
Goal:	To evaluate contribution of anti-TB and ART to hepatotoxicity through tests for NAT2 and Cytochrome P450 and to assess quality of life of patients on these drugs
Objectives:	1. To determine if there is a difference in the experience of 2. adverse events (AEs) and serious adverse events (SAEs) 3. hepatotoxicity grade 1-4 4. immune Reconstitution Syndrome in TB/HIV co-infected patients receiving TB treatment and HAART concomitantly and TB/HIV co-infected patients receiving TB treatment then commencing HAART 5. To determine if patients starting ARVs early during TB treatment have a better HRQOL than patients starting ARVs after completion of TB treatment in TB/HIV co-infected patients 6. To determine polymorphisms in cytochrome P450 and N-acetyltransferase and their relationship to hepatotoxicity 7. and efavirenz bioavailability in participants receiving anti-TB treatment and HAART 8. To determine the kinetics of mycobacterial cellular immune responses in patients treated with HAART and tuberculosis drugs using an INF-γ release assay.
Status:	Completed
Results and outcomes:	The first PhD project was entitled "Reconstitution of TB antigen specific IFN-γ responses in TB-HIV co-infected participants". The hypothesis was that IRIS may be facilitated by the absence of regulatory T-cell (Treg) activity preventing the development of pathogen specific memory T cells. The plan was to measure T-cell responses to immunological profile change during treatment and assess adverse events associated with levels of CD4, IFN-γ and viral load. This was changed mid-way to study "Safety tolerability and monitoring of combined anti-tuberculosis and antiretroviral therapy". The justification for the change has been given. The second study aimed to assess treatment responses to combined TB and HIV therapy in co-infected patients recruited in a WHO funded study called "Bioavialability of fixed dose formulation Rifafour coantaining isoniazid, rifampicin, pyrazinamide and ethambutol". The data to be assessed was in terms of adverse events, interferon gamma release assays in respsonse to treatment, quality of life and genetic polymorphisms affecting drug pharmacokinetics. The achievements in the projects are: Registration of PhD moved from University of Kwa Zulu Natal to University of Cape Town under Professor Keertan Dheda;

	recruitment of 89 study participants and completed 24 months follow up
Publications:	

6.7 Leah Mwai

EDCTP Project Coordinator:	Leah Mwai (Kenya Medical Research Institute (KEMRI)/Wellcome Trust Research Program, Kenya)
EDCTP Call Title:	PhD Studentship
EDCTP Project Title:	Understanding the mechanism of resistance to lumefantrine by *Plasmodium falciparum*
EDCTP Project Code:	TA.2005.40204.011
EDCTP Project Start Date:	18 July 2006
EDCTP Project End Date:	1 October 2010
Supervisor(s):	• Alexis Nzila (KEMRI)/Wellcome Trust Research Program, Kenya) • Steve Ward (Liverpool School of Tropical Medicine and Hygiene (LSHTM), UK)
Objectives:	To clarify the mechanisms of LM/PQ/DEAQ resistance, and to identify molecular markers that could be used to predict LM-ATM, DHA-PQ and AQ efficacy
Status:	Completed
Results and outcomes:	This study which was studentship under Dr Alexis Nzila's supervision showed mechanisms of emerging resistance to three artemesinin combination therapies against malaria and the molecular markers linked to the resistance patterns
Publications:	1. Mwai L, Kiara SM, Abdirahman A, Pole L, Rippert A, Diriye A, Bull P, Marsh K, Borrmann S, Nzila A. *In vitro* activities of piperaquine, lumefantrine and dihydroartemisisn in Kenyan *Plasmodium falciparum* isolates and polymorphisms in Pfcrt and pfmdr1, *Antimicrob Agents Chemother*. 2009 Dec;53(12):5069-73. Epub 2009 Sep 21 2. Mwai L, Ochong E, Abdirahman A, Kiara SM, Ward S, Kokwaro G, Sasi P, Marsh K, Borrmann S, Mackinnon M, Nzila A. Chloroquine resistance before and after its withdrawal in Kenya, Malar J. 2009 May 18;8:106 3. Nzila A, Mwai L. In vitro selection Plasmodium falciparum drug-resistant parasite lines. *J Antimicrob Chemother*. 2009 Dec 18 4. Sasi P, Abdulrahaman A, Mwai L, Muriithi S, Straimer J, Schieck E, Rippert A, Bashraheil M, Salim A, Peshu J, Awuondo K, Lowe B, Pirmohamed M, Winstanley P, Ward S, Nzila A, Borrmann S. In vivo and in vitro efficacy of amodiaquine against *Plasmodium falciparum* in an area of contimued use of 4- aminoquinolines in Africa. *J Infect Dis*. 2009 Jun 1;199(11):1575-82 5. Gilbert Kokwaro, Leah Mwai and Alexis Nzila. Artemether-lumefantrine in the treatment of uncomplicated *falciparum* malaria. *Expert Opin Pharmacother*. 2007 Jan;8(1):75-94 6. Mwai L, Diriye A, Masseno V, Muriithi S, Feltwell T, et al. (2012) Genome Wide Adaptations of *Plasmodium falciparum* in Response to Lumefantrine Selective Drug Pressure. *PLoS ONE* 7(2): e31623. doi:10.1371/journal.pone.0031623

6.8 Janha Ramatouli

EDCTP Project Coordinator:	Janha Ramatouli (Medical Research Council (MRC) Laboratories, The Gambia)
EDCTP Call Title:	PhD Studentship
EDCTP Project Title:	Investigating the effects of inactive CYP2C19 alleles on chlorproguanil pharmacokinetics in adults and in children with mild malaria following Lapdap® treatment
EDCTP Project Code:	TA.2005.40204.018
EDCTP Project Start Date:	23 August 2006
EDCTP Project End Date:	1 March 2010
Supervisor(s):	• Munir Pirrmohamed (University of Liverpool, UK) • Robert Walton (MRC Laboratories, The Gambia) • Fatoumatta Sisay-Joof (MRC Laboratories, The Gambia)
Goal:	To investigate whether CYP2C9 and its genetic polymorphs participate in the biotransformation of the antimalarial biguanides
Objectives:	This project aims to: 1. Survey the range of genetic variation present in CYP2C19, an enzyme important in activating antimalarial drugs 2. Identify and biochemically characterise new genetic variants of this enzyme 3. Determine whether existing and newly defined variants affect response to therapy in large randomised controlled clinical trial.
Status:	Completed
Results and outcomes:	This project has described the frequency of the gain-of-function polymorphism and the loss-of-function polymorphism that influence variable pharmacokinetics of chlorcycloguanil in Gambian adults. The conclusion is that genetic variations in CYP2C9 and CYP2C19 influence chlorcycloguanil pharmacokinetics and may lead to the accumulation of toxic dapsone. These factors need to be taken into consideration in future clinical trials involving antimalarial biguanides/dapsone to avoid the adverse events of haemolytic anaemia that could be severe and therefore improve on the success of the trials.
Publications:	

6.9 Charles Arama

EDCTP Project Coordinator:	Charles Arama (Malaria Research & Training Center, Mali)
EDCTP Call Title:	PhD Studentship
EDCTP Project Title:	Host immunogenetic factors involved in the susceptibility to malaria in sympatric ethnic groups (Dogon and Fulani) in Mali
EDCTP Project Code:	TA.2005.40204.003
EDCTP Project Start Date:	10 August 2006
EDCTP Project End Date:	10 December 2010
Supervisor(s):	• Amagana DOLO (Malaria Research & Training Center, Mali) • Ogobara K. Doumbo (Malaria Research & Training Center, Mali) • Troye-Blomberg, Marita (Stockholm University, Sweden)
Objectives:	To investigate whether antigen presenting cells (APCs) obtained from Fulani and Dogon children exhibited differences in terms of activation status and toll-like receptor (TLR) responses during malaria infection
Status:	Completed
Results and outcomes:	The study results showed that Plasmodium falciparum infection impairs the phenotype of blood dendritic cells and alters toll-like receptor responses (TLR) of peripheral blood mononuclear cells (PBMC) from Dogon children. On the other hand, specific dendritic cells subsets are activated in the Fulani children and their PBMC respond normally to TLR stimuli. In particular, malaria infection induces differential innate IFN-γ release in the two ethnic groups
Publications:	

7 Member States Initiated projects

Table 7-1: Member states initiated projects in HIV/AIDS, tuberculosis, and malaria capacity building and networking projects supported by EDCTP. Details of individual projects can be found in the sections on HIV/AIDS, tuberculosis, capacity building and networking projects.

Project Acronym (Coordinator)	Phase of trial	Product(s)	Manufacturer / Developer	Study population	Status
Fomsgaard MSI-HIV vaccine (Fomsgaard)	I	HIV vaccine peptide and CAF01 adjuvant	SSI	Untreated healthy individuals with chronic HIV-1 N=23	Completed
Strub-Wourgaft - Malaria Treatment (Strub Wourgaft)	IV	Artesunate Mefloquine (ASMQ) Artemether – Lumefantrine (Coartem®)	Cardinal Systems	Young children who are particularly at risk of malaria. N=940	Ongoing
FATI (Hoelscher)	IIa	Fozivudine	Chiracon	Adults (male and female), ≥ 18 years of age, HIV-1 positive, ATR naïve, n = 75 participants both in Mbeya, Tanzania and Abidjan, Côte d'Ivoire sites.	Ongoing
TBTEA (Kaufmann)	n/a	n/a	n/a	n/a	Ongoing
WANETAM PLUS (Jaye)	n/a	n/a	n/a	n/a	Ongoing
quinACT (Van Geertruyden)	III	Artemether-lumefantrine combination (Coartem®) ; Artesunate-Amodiaquine combination (Co-arsucam®) ; Quinine (Quinimax®)/Sanofi-Aventis + Clindamycin (Dalacin®)	Novartis, Sanofi-Aventis, Pfizer	1800 children per site (Democratic Republic of Congo and Uganda) between 6 and 59 months with non-severe malaria	Ongoing
Kreidenweiss	n/a	n/a	n/a	n/a	Ongoing
XACT (Dheda)	n/a	Urine LAM lateral flow strip test (Determine TB®) GeneXpert	Inverness Medical Professional Diagnostics Cepheid, Sunnyvale, California USA	Adults (≥18 years old) HIV positive and negative N = 400 per site	Ongoing

Project Acronym (Coordinator)	Capacity Building Goal	Study population	Status of project
Fomsgaard MSI-HIV vaccine (Fomsgaard)	• To sustain healthy and HIV-I infected cohorts in the Republic of Guinea-Bissau (RGB) in preparation for HIV AIDS vaccine trials. • To transfer sustainable HIV AIDS clinical-trial capacity, technology, infrastructure, knowledge and expertise from four countries (Denmark, the UK, The Gambia and Senegal) to the Republic of Guinea-Bissau. • To compare the safety and immunogenicity of an Iipid-adjuvanted, CTL-epitope based HIV vaccine in two distinct populations, one living in Denmark and the other one living in Guinea-Bissau.	n/a	Completed
Magesa MSI-Malaria Capacity Building (Magesa)	• To build capacity for research management • To build capacity for laboratory support of clinical trials. Hospital through the construction of a research laboratory • To improve networking and to create a scientific forum for Tanzanian and European Researchers • To improve capacity of junior staff to participate in clinical research	n/a	Ongoing
FATI (Hoelscher)	• The design and conduct of an EMA compliant phase II clinical trial with 4 different doses of Fozivudine in comparison with the standard AZT containing regimen. • A rational for selecting the appropriate doses to be carried forward in more advanced clinical development • The continuation of ongoing upgrades of clinical and research infrastructure as well as equipment and laboratory infrastructure will allow future expansion of the HIV related monitoring lab facilities in Mbeya, Kumasi and Abidjan • Promote direct interaction between the five African study sites and European partner institutions to facilitate sharing of expertise and intellectual resources needed for implementation and successful completion of HIV drug trials.	Adults (male and female), ≥ 18 years of age, HIV-1 positive, ATR naïve, n = 75 participants both in Mbeya, Tanzania and Abidjan, Côte d'Ivoire sites.	Ongoing
TBTEA (Kaufmann)	• Through sharing and exchanging of scientific, technological, clinical and infrastructural know-how and practical experiences between all involved European and African partners on the following clinical interactions, SSI-AHRI (H1/IC31), UOXF-SATVI and UOXF-LEDANTEC (MVA85A), and MPIIB-SUN (VPM1002). This will stimulated in a joint workshop (networking work package) and short term training of technical and laboratory staff with specific emphasis on novel and existing clinical assays. • Through early and timely exchange of know-how and technology transfer between UNIZAR (MTBVAC) and INSERM (HBHA) with prospective African	n/a	Completed

	partners, to prepare and build (specific) capacity for future clinical trials on MTBVAC and HBHA. This will be stimulated through short term training and exchange visits of post doc fellows to the clinical sites. • Through continuous north-north, north-south and south-south exchange and transfer of knowledge and technologies by Post docs, Students and PhDs on current, and novel or improved assays for clinical evaluation of immune responses towards all these vaccines, specifically regarding multi-parameter FACS based assays, HBHA-IGRA, and Mycobacterial Growth Inhibition Assays (MGIAs).		
WANETAM PLUS (Jaye)	• Establishment of links with the newly formed BE-supported TB network and the West African Platform for HIV Intervention Research • Involvement of new partners for TB and malaria • A practical GCP course co-developed by Dr. Halidou Tinto at the Clinical Research Unit Malaria in Nanoro (Burkina Faso) and Prof. Umberto d'Alessandro, with the support of the Clinical Trials Unit (Raffaella Ravinetto) at ITM • A course in biomedical engineering at the MRC Gambia • A course in laboratory management at the MRC Gambia • English language training at the MRC Gambia • Four Masters/ short course equivalents at the ITM in Antwerp • Hands-on TB training on second line drug resistance testing in Antwerp • Hands-on training on P. falciparum genotyping related to clinical trials in Antwerp in year 1, followed by transfer of this training to The Gambia • Two scholarships per year for WANETAM plus members to attend the annual Diplome Universitaire laboratory science course organized by Prof. Mboup in Dakar • A network meeting with workshop on "clinical research in Africa with specific attention to ethical issues" • Strengthening of the WANETAM website	n/a	Ongoing
quinACT (Van Geertruyden)	• To determine the safety and efficacy of 2 ACTs (ASAQ and AL) vs quinine when administered to children under five with recurrent P. falciparum infection and to collect explanatory variables for treatment failure (PCRcorrected) and for recurrent parasitaemia. • To develop disease-endemic country (DEC) research capacity through training and professional development of scientists, building of infrastructure and transfer of technology. • To coordinate research efforts on treatment and prevention tools of malaria in children and, by doing so, finalise a common research agenda and promote the rational use of available resources.	1800 children per site, between 6 and 59 months with non-severe malaria.	Ongoing

Kreidenweiss	• To develop an assay for detection of multiple parasitic infections during pregnancy including potentially cryptic placental *Plasmodium falciparum*. This is based on the joint expertise of the German and the French research projects where the Germans bring in the microbead platform for simultaneous parasite detection and the French their competence in pregnancy-associated malaria. • The investigators intend to do this work in frame of capacity building activities of African scientists to enable African institutions performing high-level research which is competitive amongst the international malaria research community. • Amongst the 3 collaborators the activities will harmonize research procedures and techniques and ensure further effective collaborations in the development of cutting edge diagnostic technologies for controlling malaria.	n/a	Ongoing
XACT (Dheda)	• XACT has 3 main streams of capacity development. These are: (i) the training of students through sponsorhip of studies and the research activity that forms part of their projects, (ii) the development of infrastructure for support future research, and (iii) the training of personnel through courses. The proposed project will be conducted in the community as a mobile health unit. However, symptomatic persons will be taken to the local clinic where considerable site infrastructure has already been developed through the TB-Susgent (EU FP7-funded), TB-Neat (EDCTP-funded), and TESA (EDCTP-funded) projects. The designated clinics in Harare and Cape Town have already been extended and upgraded, have had Gene Xpert machines installed, infection control measures and other facilities have been established in order to undertake the clinical trials, including communication infrastructure, etc. Thus, there is considerable interaction between the different studies and the foundations and infrastructure setup through the EDCTP-funded and EU FP7-funded projects are now being utilised here to create a multiplier effect.	400 per site (N = 1200)	Ongoing

7.1 Fomsgaard AFO-18

EDCTP Project Coordinator:	Anders Fomsgaard (Statens Serum Institut, (SSI), Denmark)
EDCTP Call Title:	Call for the support of member states initiated projects within the scope of EDCTP activity areas
EDCTP Project Title:	A joint initiative to sustain HIV vaccine trials and research capacity in the Republic of Guinea-Bissau, West Africa
EDCTP Project Code:	MS.09.10800.001
EDCTP Project Start Date:	27 July 2010
EDCTP Project End Date:	26 July 2012
Collaborating partners:	• Peter Aaby (Bandim Health Project, Guinea-Bissau) • David Da Silva Te (Hospital Nacional Simao Mendes, Guinea-Bissau) • Vibeke Fonsholt (SSI, Denmark) • Victor Gomes (Bandim Health Project, Guinea-Bissau) • Tomas Hanke (University of Oxford, UK) • Assan Jaye (Medical Research Council (MRC) Laboratories, The Gambia) • Skov Sanne Jensen (SSI, Denmark) • Kristoffer Jarlov Jensen (SSI, Denmark) • Zacarias José da Silva (National Public Health Laboratory NPHL, Guinea-Bissau) • Gitte Kronborg (Hvidovre University Hospital, Denmark) • Souleymane Mboup (University Cheikh Anta DIOP de Dakar (UCAD), Senegal) • Candida Medina Rodrigues (ospital Nacional Simao Mendes, Guinea-Bissau) • Amabelia Rodrigues (SSI, Denmark)
Clinical Trial	
Site Principal Investigator(s):	David de Silva Te (National HIV secretariat, Ministry of Health, Guinea Bissau) Anders Fomsgaard (Statens Serum Institutet)
Clinical Trial/Study Sponsor:	Statens Serum Institut (Denmark)
Trial/Study title:	HIV-1 Peptide immunisational individuals in West Africa to prevent disease (AFO-18)
Goal:	Evaluate the safety and tolerability of the vaccine and the immunological and anti-retroviral response in vaccinated individuals
Primary Objective(s):	Evaluate the safety and tolerability of the vaccine
Secondary Objective(s):	Determine whether vaccine with the selected epitope antigens can induce a measurable specific immune response to the patient's HIV-1 when used during chronic HIV-1 infection and to evaluate the clinical effect measured as induction of new T-cell immune response, lowering of viral load, and increase in the CD4 cell count.
Third Objective	Evaluate the feasibility of conducting an HIV immunisation study in a poorly resourced African setting
Clinical Trial/Study site(s):	• Projecto de Saúde de Bandim (Guinea-Bissau) • Clinica Tratamento Antiretrovirais, Hospital Nacional Simão Mendes (Guinea-Bissau) • Laboratório Nacional de Saúde Pública (LNSP, Guinea-Bissau)
Collaborating site(s):	• Simão Mendes Hospital Céu e Terra (Guinnea-Bissau) • Laboratoire de Bacteriologie Virologie, Université Cheikh Anta DIOP (Senegal) • Immunology Section, Viral Diseases Programme, MRC Fajara

	Laboratories (The Gambia) • Department of Virology, SSI (Denmark)
Study design:	Single-Blinded, placebo-controlled phase I trial
Product(s):	cationic liposome-adjuvanted CAF01 HIV-1 peptide vaccine (AFO-18)
Manufacturer/Developer:	SSI (Denmark)
Cofunders	• Danish International Development Agency, Denmark (DANIDA) • Medical Research Council UK, UK (MRC UK)
Trial Registration number(s):	• PACTR 201110000274327 • NCT 01009762 • NCT 01141205 (DK study)
Status:	Completed
Results and Outcomes:	Following vaccine testing on similar HIV positive individuals first in Copenhagen (approved and followed by Danish Medicine Association, Ethical committee, etc), the study started in Guinea-Bissau in August 2010. Recruitment in RGB was completed with a total of 23 patients (18 vaccinees and 5 placebos).Trial was completed in September 2011 and follow up in December 2011. There were two drop-outs and one non-vaccine-related serious adverse event in the vaccine treatment arm. In the placebo treatment arm there was one dropout and one non-vaccine-related serious adverse event. Thus a total of 18 participants completed the six-month follow-up (15 vaccinees as planned and 3 placebos). Immunization with peptides in the new adjuvant CAF01 induced T-cell responses to epitopes previously undetected in 6/14 vaccinated individuals. The immunizations were safe and well tolerated albeit with no significant changes in HIV-1 viral load or CD4 T-cell counts.
Capacity Building	
Site Principal Investigator(s):	Amabelia Rodrigues (Denmark) Christoph Janitzek (Denmark)
Clinical Trial/Study Sponsor:	SSI (Denmark)
Goal:	• To transfer sustainable HIV/ AIDS clinical -trial capacity, technology, infrastructure, knowledge and expertise from four countries (Denmark, the UK, The Gambia and Senegal) to the Republic of Guinea-Bissau. • To sustain healthy and HIV-1 infected cohorts in the Republic of Guinea-Bissau in preparation for HIV/AIDS vaccine trials
Primary Objective(s):	Introduce and maintain haematology and clinical chemistry and viral and immunology techniques
Secondary Objective(s):	Train key personnel in English and GCP
Clinical Trial/Study site(s):	• Projecto de Saúde de Bandim (Guinea-Bissau) • Clinica Tratamento Antiretrovirais, Hospital Nacional Simão Mendes (Guinea-Bissau) • Laboratório Nacional de Saúde Pública (LNSP, Guinea-Bissau)
Collaborating site(s):	• The John Radcliffe MRC Human Immunology Unit, University of Oxford (UK) • Projecto de Saúde de Bandim (Guinea-Bissau) • Clinica Tratamento Antiretrovirais, Hospital Nacional Simão Mendes (Guinea-Bissau) • Laboratório Nacional de Saúde Pública (LNSP, Guinea-Bissau) • Laboratoire de Bacteriologie Virologie, Université Cheikh Anta DIOP (Senegal) • Immunology Section, Viral Diseases Programme, MRC

	Laboratories (The Gambia) • Department of Virology, SSI (Denmark)
Total number of subjects (cohort/epidemiological/ other studies):	Cohort: app 300 HIV-1 positive healthy individuals
Cofunders	• Danish International Development Agency (DANIDA, Denmark) • Medical Research Council UK, UK (MRC UK)
MSc studies:	Title: MSc Biology - Biotechnology HIV-1 subtypes in Republic of Guinea Bissau Candidate: Sanne Skov Jensen (University of Copenhagen, Denmark) Completed: 2011 - June 2011
	Title: LSHTM long-distance course MSc Clinical Trials under Candidate: Delfim Vicente Mendes (Hospital Rauol Follereau, Guinnea-Bissau) Completed: 2010 - June 2012
Results and Outcomes:	The capacity building efforts that have come to fruition through the project's "learning-by-doing" approach have been substantial. Primarily achieving the objective of providing courses in GCP and Research Ethics in three languages, English-language training, enrolment of a local Medical Doctor to a MSc online course and building a molecular biology and serology platform in Bissau in preparation for future clinical trials in the region. The project has also introduced and sustained new laboratory techniques (molecular virology and testing of patients for CD4 counts, viral-load, haematology/clinical chemistry parameters. In terms of networking, the project enabled the setting up and definition of a new African network involving The Gambia and Senegal via WAPHIR for continued support of the capacity building programme initiated through this EDCTP grant. Lastly, the project used innovative methods such as documentaries and TV interviews to communicate research and public health projects in the region.
Publications:	1. Fomsgaard A, Karlsson I, Gram G, Schou C, Tang S, Bang P, Kromann I, Andersen P, Andreasen LV. Development and preclinical safety evaluation of a new therapeutic HIV-1 vaccine based on 18 T-cell minimal epitope peptides applying a novel cationic adjuvant CAF01. *Vaccine*. 2011 Sep 16;29(40):7067-74. Epub 2011 Jul 19 2. Karlsson I, Kløverpris H, Jensen KJ, Stryhn A, Buus S, Karlsson A, Vinner L, Goulder P, Fomsgaard A. Identification of Conserved Subdominant HIV Type 1 CD8(+) T Cell Epitopes Restricted Within Common HLA Supertypes for Therapeutic HIV Type 1 Vaccines. *AIDS Res Hum Retroviruses*. 2012 Nov;28(11):1434-43. doi: 10.1089/AID.2012.0081. Epub 2012 Aug 14. 3. Karlsson I, Brandt L, Vinner L, Kromann I, Andreasen LV, Andersen P, Gerstoft J, Kronborg G, Fomsgaard A. Adjuvanted HLA-supertype restricted subdominant peptides induce new T-cell immunity during untreated HIV-1-infection. *Clin Immunol*. 2013 Feb;146(2):120-30. doi: 10.1016/j.clim.2012.12.005. Epub 2012 Dec 21. 4. Gómez Román VR, Skov Jensen S, Leo-Hansen C, Jarlov Jensen K, Janitzek CM, Medina Rodrigues C, Jespersen S,

	Katzenstein TL, da Silva Té D, Fomsgaard A. Assessing HIV-1 patient recruitability in Guinea-Bissau: African versus North-American haematology and biochemistry reference intervals. *Clin Vaccine Immunol*. 2012 Aug;19(8):1322-5. Epub 2012 Jun 6 5. Jensen KJ, Gómez Román VR, Jensen SS, Leo-Hansen C, Karlsson I, Katzenstein TL, Rodrigues CM, Jespersen S, Janitzek CM, Té Dda S, Hayes P, Fomsgaard A. Clade A HIV-1 Gag-specific T cell responses are frequent but do not correlate with lower viral loads in a cohort of treatment-naïve HIV-infected individuals living in Guinea-Bissau. *Clin Vaccine Immunol*. 2012 Dec;19(12):1999-2001. doi: 10.1128/CVI.00399-12. Epub 2012 Oct 17.

7.2 Magesa MSI-Malaria Capacity Building

EDCTP Project Coordinator:	Stephen Magesa (National Institute for Medical Research (NIMR), Tanzania)
EDCTP Call Title:	Call for the support of member states initiated projects within the scope of EDCTP activity areas
EDCTP Project Title:	Capacity and network strengthening measures within the framework of malaria research in Tanzania by the Joint Malaria Programme (JMP)
EDCTP Project Code:	MS.09.10800.002
EDCTP Project Start Date:	29 July 2010
EDCTP Project End Date:	28 January 2014
Collaborating partners:	• Adrian Luty (Radboud University Nijmegen, Netherlands) • Raimos Olomi (Kilimanjaro Christian Medical Centre (KCMC), Tanzania) • Hugh Reyburn (KCMC, Tanzania) • Thor Theander (University of Copenhagen, Denmark)
Capacity Building	
Site Principal Investigator(s):	Stephen Magesa (Tanzania)
Goal:	1. To build capacity for research management. The JMP Secretariat will be strengthened through provision of salary support for the JMP Manager and an Assistant, upgrading of office furniture and equipment and transport costs to support training and supervision visits to research project sites. The primary outcomes will be the integration of high quality accounts packages, establishing regular internal audit and standardising a high quality human resource management system through JMP. 2. To build capacity for laboratory support of clinical trials. To strengthen the infrastructure for clinical trials at Teule Hospital through the refubrishment of a research laboratory. The facility will meet the exacting demands of GCLP and external quality assurance to international standards. 3. To improve networking and to create a scientific forum for Tanzanian and European Researchers. To hold an annual scientific meeting for JMP projects to report results to important stakeholders including the National Malaria Control Programme, the Ministry of Health and health service providers. In addition there will be meetings specifically directed to new proposals from young Tanzanian scientists and a one-week proposal writing workshop will be linked at the end of the scientific meeting. 4. To improve capacity of junior staff to participate in clinical research through provision of regular short courses on GCP, good laboratory practice, clinical research ethics, biosafety with certification for qualifying staff in order to improve the quality of research. In addition short courses will be run on research administration and financial management.
Collaborating site(s):	• LSHTM (UK) • University of Copenhagen m(Denmark) • NIMR (Tanzania) • Kilimanjaro Christian Medial College (KCMC, Tanzania) • Radboud University of Nijmegen (Netherlands)
Cofunders	• DANIDA (Denmark)

	• ACT Consortium (UK) (funding via Bill and Melina Gates Foundation) • LSHTM (UK) • FEAST Imperial College London (UK) • NACCAP (Netherlands)
Status:	Ongoing
Results and Outcomes:	The project has improved their ties with the National Ethical Review Board and other regulatory authorities. They participated in the malaria symposium session at the 26th NIMR Annual Joint Scientific Conference held in April 2012 in Arusha, Tanzania as well as the Sixth EDCTP Forum held in Addis Ababa, Ethiopia. In terms of training, two courses on GCP were conducted in January and May 2012 and 68 participants were trained. The 11th JMP annual workshop was successfully held in November 2011. The project has launched the programme website under www.jmp.or.tz to further local and global networking. The necessary office space and infrastructure upgrades have been made at the JMP Secretariat in addition to the grant providing for the personnel costs. Ward refurbishment and upgrade of data management tools at the Teule site were completed in October 2011. As part of laboratory refurbishment and upgrade we procured humidifier and humidistat, microscopes and centrifuge machines, desktops and related accessories and office furniture.

7.3 Strub-Wourgaft - Malaria Treatment

EDCTP Project Coordinator:	Nathalie Strub-Wourgaft (Drugs for Neglected Diseases Initiative (DNDi), Switzerland)
EDCTP Call Title:	Call for the support of member states initiated projects within the scope of EDCTP activity areas
EDCTP Project Title:	Assessment of the fixed-dose combination of Artesunate Mefloquine (ASMQ) as an alternative antimalarial treatment for children in Africa
EDCTP Project Code:	MS.09.10800.004
EDCTP Project Start Date:	16 August 2010
EDCTP Project End Date:	30 April 2014
Collaborating parties:	• Gwenaelle Carn (DNDi, Switzerland) • Ylana Chalem (Cardinal Systems, France) • Laurent Decosterd (Centre Hospitalier Universitaire Vaudois (CHUV), Switzerland) • Zakayo Mrango (National Institute for Medical Research (NIMR), Tanzania) • Michel Vaillant (Centre de Recherche Public de la Santé, Luzembourg) • Laurence Vielfaure (DNDi, Switzerland)
Clinical Trial	
Site Principal Investigator(s):	• Zakayo Mrango (NIMR, Tanzania) • Ali Mtoro (IHI, Tanzania) • John Lusingu (NIMR, Tanzania) • Bernhards OGUTU (KEMRI, Kenya) • Sodiomon Sirima (CNRFP, Burkina Faso)
Clinical Trial/Study Sponsor:	DNDi (Switzerland)
Trial/Study title:	Efficacy, Safety and Population-Pharmacokinetics of Artesunate-Mefloquine combination for the Treatment of Uncomplicated Falciparum Malaria in African children versus Artemether-Lumefantrine
Goal:	To compare the efficacy and safety of the fixed-dose combination of ASMQ with AM-LM in children under the age of five with uncomplicated falciparum malaria in Africa.
Primary Objective(s):	To evaluate efficacy of Artesunate-Mefloquine fixed-dose by determining the proportion of patients achieving a negative parasitaemia without recrudescence by 63 days.
Secondary Objective(s):	1. To measure the parasite reduction ratio on Day 1, 2 and 3 2. To compare the proportion of patients with parasitaemia on Day 2 and 3 3. To compare the proportion of patients with fever on Day 2 and 3 4. To compare the gametocyte carriage at Day 2 and 3, and Day 28, 42 and 63 5. To evaluate cure rate at 28 and 42 days 6. To evaluate the population-pharmacokinetics of Artesunate-Mefloquine in under-5 children 7. To evaluate the incidence and severity of adverse events 8. To evaluate the incidence of Serious Adverse Events and adverse events leading to treatment discontinuation 9. To analyze the discrepancy of time course and vomiting frequency
Clinical Trial/Study site(s):	• Kilosa District Hospital, National Institute for Medical Research (NIMR, Tanzania) • NIMR in Korogwe, Tanzania Ikakara Health Institute (IHI) in

	Bagamoyo (Tanzania) • Ahero District Hospital Kisumu (KEMRI, Kenya) • Balonghin and Banfora District Hospitals (CNRFP, Burkina Faso)
Collaborating site(s):	• National Institute for Medical Research (Tanzania) • Kenya Medical Research Institute (Kenya) • Centre National de Recherche et de Formation sur le Paludisme (Burkina Faso) • CHUV Lausanne (Switzerland) • Cardinal Systems (France) • Centre de Recherche Public – Santé (Luxembourg)
Study design:	Phase IV randomised, controlled, multicentre efficacy and safety study
Total number of subjects:	CHILDREN (≤5 years) children with uncomplicated falciparum malaria N=940
Product(s):	• Artesunate Mefloquine (ASMQ) • Artemether – Lumefantrine (Coartem®)
Manufacturer/Developer:	Farmanguhinos (Brazil) and Cipla (India)
Cofunders	• United Kingdom Department for International Development (DFID) • Netherlands Ministry of Foreign Affairs (DGIS) • ARPE Foundation (Switzerland) • French Development Agency (AFD) for the extension period
Status:	Ongoing
Results and Outcomes:	The trial has completed recruitment of 945 subjects as of 26 June 2013. Burkina Faso : 390 patients Kenya: 347 patients Tanzania :208 patients There were 21 SAE reported during the period: – 7 severe malaria – 6 pneumonia – 3 severe anaemia – 3 malaria – 1 tonsilitis – 1 burns Last monitoring visits were performed in July 2013 in Burkina Faso and August 2013 in Tanzania and Kenya. Database lock expected in Q1 2014.
Trial Registration number(s):	PACTR 201202000278282 ISRCTN 17472707

7.4 FATI

EDCTP Project Coordinator:	Michael Hoelscher (Ludwig-Maximilians Universitat Munchen, Germany)
EDCTP Call Title:	Call for the support of member states initiated projects within the scope of EDCTP activity areas
EDCTP Project Title:	FATI-1: A prospective, multicenter Phase 2a trial to confirm a sustained virological suppression defined as HIV-RNA <50 copies/ml of 4 different doses of Fozivudine in context to a standard Zidovudine based antiretroviral therapy regimens after 24 weeks of treatment in ART naïve, non subtype B HIV-1 infected individuals from Tanzania and Ivory Coast
EDCTP Project Code:	MS.2010.10800.001
EDCTP Project Start Date:	6 October 2011
EDCTP Project End Date:	30 November 2014
Collaborating partners:	• Xavier Anglaret (INSERM, Unité 897, France) • Chales Nde Awasom (Bamenda Provincial Hospital, Cameroon) • Brigite Bazin (ANRS, France) • Ulrich Braun (Ludwig-Maximilians Universitat Munchen, Germany) • Gerd Burchard (Bernhard-Nocht-Institut for Tropical Medicine, Germany) • Christine Danel (Programme PACCI (Site ANRS Abidjan), Côte d'Ivoire) • Serge Paul Eholie (Service de maladies infectieuses et tropicales du centre hospitalier universitaire de Treichville (SMIT), Côte d'Ivoire) • Torsten Feldt (Bernhard-Nocht-Institut for Tropical Medicine, Germany) • Martin Fischer (Klinikum of the Ludwigs-Maximilians-University München, Germany) • Pierre-Marie Girard (University Hospital Saint-Antoine, France) • Sonja Henne (Ludwig-Maximilians Universitat Munchen, Germany) • Arne Kroidl (Klinikum der Universität München/NIMR-MMRP, Germany/Tanzania) • Jan van Lunzen (University Medical Center Hamburg-Eppendorf, Germany) • Leonard Maboko (NIMR-MMRP, Tanzania) • Betty Norman (Komfo Anokye Teaching Hospital, Ghana) • Papa Salif Sow (University of Dakar, Senegal) • Friedrich Adolf Herbert Otto Von Massow (Institute for Life Sciences and Environment (i-LSE) GmbH, Germany) • Alexander Zoufaly (Bernhard-Nocht-Institute for Tropical Medicine at the Bamenda Provincial Hospital, Cameroon) • Ralf Zuhse (Chiracon GmbH, Germany) • Juergen Reinhardt (United Nations Industrial Development Organisation, Austria) • Palu Dhanani (Universal Corporation Ltd.(UCL), Kenya) • Yan Ho Choo (Stada Vietnam, Vietnam)
Clinical Trial	**FATI-1**
Site Principal Investigator(s):	• Arne Kroidl (Tanzania) • Serge Eholie (Côte d'Ivoire)
Clinical Trial/Study Sponsor:	Clinic Study Centre, Klinikum of the University of Munich
Trial/Study title:	FATI-1: A prospective, multicenter Phase 2a trial to confirm a

	sustained virological suppression defined as HIV-RNA <50 copies/ml of 4 different doses of Fozivudine in context to a standard Zidovudine based antiretroviral therapy regimens after 24 weeks of treatment in ART naïve, non subtype B HIV-1 infected individuals from Tanzania and Ivory Coast
Goal:	The overarching goal of this evaluation is to help optimize the effectiveness of the antiretroviral treatment programs by identifying variables and characteristics that have the greatest impact on reducing treatment failure as defined by viral suppression.
Primary Objective(s):	To confirm a sustained virological suppression (HIV RNA <50 copies/ml) after 24 weeks of treatment between three different doses of Fozivudine (FZD) based antiretroviral 1st line treatment regimen in context to a standard Zidovudine (ZDV) based treatment regimen in non subtype B HIV-1 infected individuals from Africa.
Secondary Objective(s):	1. HIV-RNA log10 reduction of HIV-RNA at 2, 4 and 8 weeks of treatment between different arms 2. Virological response (HIV RNA <50 copies/ml) at 8 and 12 weeks of treatment between different arms 3. Virological response (HIV RNA <400 copies/ml) at 8, 12 and 24 weeks of treatment between different arms 4. Immunologic response: variation in CD4 lymphocytes between different arms 5. Drug toxicity, particularly anaemia, neutropenia and gastrointestinal adverse events 6. Resistance pattern for in patients with virological failure 7. Clinical trial capacity building of African study sites within the FATI network 8. Establishment of a Fozivudine Drug developing consortium (NET) including members of pharmaceutical manufacturers in Asia, Africa and Europe. 9. Development and piloting of a capacity development monitoring and evaluation framework
Clinical Trial/Study site(s):	The NIMR-Mbeya Medical Research Programme (MMRP) supporting the Mbeya Referral Hospital (MRH) (Tanzania) SMIT (Service de Maladies Infectieuses et Tropicales) in collaboration with the PACCI Program Abidjan (Côte d'Ivoire)
Collaborating site(s):	• INSERM, Unité 897 (France) • Ministry of Health through the Komfo Anokye Teaching Hospital (Ghana) • Bernhard-Nocht-Institut for Tropical Medicine (Germany) • Bamenda Provincial Hospital (Cameroon) • University Medical Center Hamburg-Eppendorf (Germany) • University of Dakar (Senegal) • University Hospital Saint-Antoine –and Institut de Médecine et d'Epidémiologie Appliquée (IMEA) (France) • French National Agency for Research on AIDS and Viral Hepatitis (ANRS) (France) • Chiracon GmbH (Germany) • Institute for Life Sciences and Environment (i-LSE) GmbH (Germany)
Study design:	Open-label, multicenter, prospective, randomised Phase IIa proof of concept and dose evaluating study. Arm A (N=30): FZD 600mg BD + 150mg 3TC BD + 600mg EFV OD Arm B (N=30): FZD 800mg OD + 300mg 3TC OD + 600mg EFV OD

	Arm C (N=30): FZD 1200mg OD + 300mg 3TC OD + 600mg EFV OD Arm D (N=30): AZT 300mg/3TC 150 mg BD + 600mg EFV OD *OD: Once daily *BD: Twice daily
Number of subjects:	A total of 120 ART naive HIV-1 infected individuals with the indication to start antiretroviral treatment according to WHO and country guidelines will be enrolled. Each of the two study sites will enrol 60 participants (15 participants per arm). A minimum of 30% female or male participants will be requested per site.
Product(s):	• Fozivudine (FZD) • Lamivudine (3TC) • Efavirenz (EFV) • Zidovudine (AZT)
Manufacturer/Developer:	FZD (Chiracon) and for the rest, they are available through national HIV programmes.
Cofunders:	• Federal Ministry of Education and Research (Germany) • National Agency for AIDS research/ANRS (France) • Chiracon GmbH (Germany) • Heidelberg Pharma AG (Germany) • University of München (Germany) • Deutsche Gesellschaft für Technische Zusammenarbeit (GTZ) (Germany)
Trial Registration number	PACTR201205000384379 NCT01714414
Status:	Ongoing
Results and Outcomes:	
Publications:	

7.5 TBTEA

EDCTP Project Coordinator:	Stefan Kaufmann (Max Planck Society, Germany)
EDCTP Call Title:	Call for the support of member states initiated projects within the scope of EDCTP activity areas
EDCTP Project Title:	Collaboration and integration of Tuberculosis Vaccine Trials in Europe and Africa
EDCTP Project Code:	MS.2010.1800.002
EDCTP Project Start Date:	2 September 2011
EDCTP Project End Date:	31 December2013
Collaborating partners:	• Abraham Aseffa (Armauer Hansen Research Institute, Ethiopia) • Mark Doherty (SSI, Denmark) • Leander Grode (Vakzine Projekt Management, Germany) • Willem Hanekom (University of Cape Town/Tuberculosis Vaccine Initiative, South Africa) • Andrew Kambuga (The Infectious Diseases Institute at Makerere University, Uganda) • Camille Locht (Institut Pasteur de Lille, Inserm, France) • Yukari Manabe (Makerere University, Uganda) • Markos Abebe (AHRI, Ethiopia) • Carlos Martin (University of Zaragoza, Spain) • Helen McShane (University of Oxford, UK) • Souleymane Mboup (CHU Le Dantec, Senegal) • Gilles Riveau (Espoir Pour La Santé, Senegal) • Søren Tetens Hoff (Statens Serum Institute, Denmark) • Jelle Thole (Tuberculosis Vaccine Initiative, The Netherlands) • Gerhard Walzl (Stellenbosch University, South Africa)
Study 1	Capacity Building/Networking
Site Principal Investigator(s):	Stefan Kaufmann (Germany)
Trial/Study title:	Collaboration and integration of Tuberculosis Vaccine Trials in Europe and Africa
Goal:	To build a sustainable platform where knowledge and know-how on clinical trials of ongoing and future clinical TB vaccine evaluations in Europe and Africa can be exchanged, where joint activities can be explored and coordinated, where clinical trials capacity will be improved, broadened, integrated, and where overlap and unnecessary duplication of work will be prevented by the creation of synergies.
Primary Objective(s):	1. Through sharing and exchanging of scientific, technological, clinical and infrastructural know-how and practical experiences between all involved European and African partners on the following clinical interactions, SSI-AHRI (H1/IC31), UOXF-SATVI and UOXF-LEDANTEC (MVA85A), and MPIIB-SUN (VPM1002). This will stimulated in a joint workshop (networking work package) and short term training of technical and laboratory staff with specific emphasis on novel and existing clinical assays 2. Through early and timely exchange of know-how and technology transfer between UNIZAR (MTBVAC) and INSERM (HBHA) with prospective African partners, to prepare and build (specific) capacity for future clinical trials on MTBVAC and HBHA. This will be stimulated through short term training and exchange visits of post doc fellows to the clinical sites 3. Through continuous north-north, north-south and south-south exchange and transfer of knowledge and

	technologies by Post docs, Students and PhDs on current, and novel or improved assays for clinical evaluation of immune responses towards all these vaccines, specifically regarding multi-parameter FACS based assays, HBHA-IGRA, and Mycobacterial Growth Inhibition Assays (MGIAs).
Collaborating site(s):	• Tuberculosis Vaccine Initiative (Netherlands) • University of Oxford (UK) • Statens Serum Institute (Denmark) • Universidad de Zaragoza (Spain) • Inserm U1019 (France) • AHRI (Ethiopia) • SATVI (South Africa) • Stellenbosch University (South Africa) • Infectious Diseases Institute (Uganda) • Espoir Pour La Santé (Senegal) • Hospitalier CHU Le Dantec (Senegal)
Cofunders:	• Federal Ministry of Education and Research (BMBF, Germany) • BMGF (USA) • EU FP7 programme (Belgium) • SSI (Denmark) • Wellcome Trust (UK) • AERAS (USA) • Innocash Programme (Spain) • Ministry of economy, finances and industry (France)
Status:	Ongoing
Results and Outcomes:	
Post-doc studies:	Title: Characterization of innate and memory phenotypes to TB and hormone modulations in apparently healthy children and adolescents across age Candidate: Liya Wassie Dubale (AHRI, Ethiopia)
	Title: Global transcriptome analyses of peripheral blood leukocytes from vaccinees to determine immunologic responses to vaccination Candidate: Pedro Moura Alves and Natalie Nieuwenhuizen (Max Planck Society of the Advancement of Science, Germany)
	Title: Evaluation of the robustness and sensitivity of mycobacterial growth inhibition assays to measure mycobacterial immunity, and use of this and other assays to evaluate MVA85A induced immunity in field trials Candidate: Iman Satti (University of Oxford, UK)
	Title: Evaluation of the robustness and sensitivity of mycobacterial growth inhibition assays to measure mycobacterial immunity, and use of this and other assays to evaluate MVA85A induced immunity in field trials Candidate: Benjamin Kagina (University of Oxford, UK)
	Title: Search for immunological correlates of protection for MTBVAC Candidate: Juan Ignacio Aguiló (University of Zaragoza, Spain)
Publications:	1. Maertzdorf J, Weiner III J, Kaufmann SHE. Enabling biomarkers for tuberculosis control. *Int. J. Tuberc. Lung Dis*. 2012; 16(9):1140–1148 2. Kaufmann SHE. Tuberculosis vaccine development: strength lies in tenacity. *Trends Immunol*. 2012, 33(7): 373-379

7.6 WANETAM plus

EDCTP Project Coordinator:	Assan Jaye (Medical Research Council (MRC) Laboratories, The Gambia)
EDCTP Call Title:	Call for the support of member states initiated projects within the scope of EDCTP activity areas
EDCTP Project Title:	Towards strengthening of the West African Node of Excellence for TB, AIDS and malaria: WANETAM plus
EDCTP Project Code:	MS.2010.18000.003
EDCTP Project Start Date:	27 October 2011
EDCTP Project End Date:	31 August 2014
Collaborating partners:	• Dissou Affolabi (Centre National Hospitalier de Pneumo-Phtisiologie, Benin) • Umberto D'Alessandro (Institute of Tropical Medicine, Belgium) • Bouke de Jong (Institute of Tropical Medicine, Belgium) • Bassirou Diarra (SEREFO, University of Bamako, Mali) • Luc Kestens (Institute of Tropical Medicine, Belgium) • Souleymane Mboup (University Cheikh Anta DIOP de Dakar (UCAD), Senegal) • Martin Manzi (MRC, The Gambia) • Alain Nahum (Centre de Recherche Entomologique de Cotonou (CREC), Benin) • Raffaella Ravinetto (Institute of Tropical Medicine, Belgium) • Halidou Tinto (Centre Muraz, Burkina Faso)
Study/Trial 1	**Capacity Building**
Site Principal Investigator(s):	Assan Jaye (The Gambia)
Trial/Study title:	Towards strengthening of the West African Node of Excellence for TB, AIDS and malaria: WANETAM plus
Goal:	To strengthen the existing WANETAM network with new network initiatives on HIV, TB, and malaria recently developed in the region
Primary Objective(s):	1. Capacity building and technology transfer to prepare West African institutions for the successful leadership and conduct of clinical trials 2. Creation of a network for regional scientific collaborations
Secondary Objective(s):	1. Establishment of links with the newly formed Belgium-supported TB network and the West African Platform for HIV Intervention Research 2. Involvement of new partners for TB and malaria 3. A practical GCP course co-developed by Dr. Halidou Tinto at the Clinical Research Unit Malaria in Nanoro (Burkina Faso) and Prof. Umberto d"Alessandro, with the support of the Clinical Trials Unit (Raffaella Ravinetto) at ITM 4. A course in biomedical engineering at the MRC Gambia 5. A course in laboratory management at the MRC Gambia 6. English language training at the MRC Gambia 7. Four Masters/ short course equivalents at the ITM in Antwerp 8. Hands-on TB training on second line drug resistance testing in Antwerp 9. Hands-on training on P. falciparum genotyping related to clinical trials in Antwerp in year 1, followed by transfer of this training to The Gambia 10. Two scholarships per year for WANETAM plus members to attend the annual Diplome Universitaire laboratory science

	course organized by Prof. Mboup in Dakar 11. A network meeting with workshop on "clinical research in Africa with specific attention to ethical issues 12. Strengthening of the WANETAM website
Cofunders:	• FOD Buitenlandse Zaken (Belgium) • Institut of Tropical Medicine (Belgium) • MRC (UK)
Status:	Ongoing
Results and Outcomes:	
MSc study:	Title: Master Public Health – Including 8-week Short Course Health Policy, Health Systems Management, Disease Control Candidate: TBD (Institut of Tropical Medicine Antwerp, Belgium) Supervisor: Marleen Boelaert, Umberto D'Alessandro and Marie Laga (Institut of Tropical Medicine)
Publications:	

7.7 QuinACT

EDCTP Project Coordinator:	Jean-Pierre Van Geertruyden (University of Antwerp, Belgium)
EDCTP Call Title:	Call for the support of member states initiated projects within the scope of EDCTP activity areas
EDCTP Project Title:	The impact of retreatment with an artemisinin-based combination on malaria incidence and its potential selection of resistant strains
EDCTP Project Code:	MS.2010.18000.004
EDCTP Project Start Date:	29 September 2011
EDCTP Project End Date:	28 February 2014
Collaborating partners:	• Robert Colebunders (Prince Leopold Institute of Tropical Medicine, Belgium) • Umberto D'Alessandro (Prince Leopold Institute of Tropical Medicine, Belgium) • Martin Grobusch (University of Amsterdam, The Netherlands) • Pascal Lutumba (University of Kinshasa, Democratic Republic of Congo) • Raffaella Ravinetto (Institute of Tropical Medicine, Belgium) • Hypolite Muhindo (University of Kinshasa, Democratic Republic of Congo) • Carolyn Nabasumba (Mbarara University of Science and Technology, Uganda) • Halidou Tinto (Centre Muraz, Burkina Faso) • Andrew Kambugu (Infectious Diseases Institute, University Makarere, Uganda) • Ambrose Talisuna (Regional Scientific Director, East Africa • World Wide Antimalarial Resistance Network (WWARN), Uganda)
Clinical Trial	
Site Principal Investigator(s):	• Carolyne Nabasumba (Uganda) • Hypolyte Muhindo (RD Congo)
Clinical Trial/Study Sponsor:	University of Antwerp (Belgium)
Trial/Study title:	The impact of retreatment with an artemisinin-based combination on malaria incidence and its potential selection of resistant strains
Goal:	To identify if first line ACT can be safely and efficaciously used to retreat children with recurrent malaria occurring beyond 14 days after initial treatment and consequently preserve quinine for severe malaria treatment.
Primary Objective(s):	1. To determine the safety and efficacy of 2 ACTs (ASAQ and AL) vs quinine when administered to children under five with recurrent *P. falciparum* infection and to collect explanatory variables for treatment failure (PCR corrected) and for recurrent parasitaemia 2. To develop disease-endemic country (DEC) research capacity through training and professional development of scientists, building of infrastructure and transfer of technology 3. To coordinate research efforts on treatment and prevention tools of malaria in children and, by doing so, finalise a common research agenda and promote the rational use of available resources.
Clinical Trial/Study site(s):	• Lisungi Health Center (Democratic Republic of Congo) • Makerere University (Uganda)

Collaborating site(s):	• Institut de recherche en science de la santé (IRSS/DRO) / Centre Muraz (Burkina Faso) • Prince Leopold Institute of Tropical Medicine (Belgium) • Stichting AMC CPCD Foundation (Uganda) • Academic Medical Centre at the University of Amsterdam (Netherlands)
Study design:	Two-centre, non inferiority, phase III, randomised, open label, 3-arm trial
Number of subjects:	3600; 1800 children (between 12 and 59 months inclusive) per site
Product(s):	• Quinine • Artemether-lumefantrine (AL) • Amodiaquine artesunate (ASAQ)
Manufacturer/Developer:	All products used in this trial are available through national programmes
Cofunders:	• University of Amsterdam (Netherlands) • Research Foundation Flanders- FWO (Belgium)
Trial Registration number	NCT01374581
Status:	Ongoing
Results and Outcomes:	
PhD studies:	Title: The impact of retreatment with an artemisinin-based combination on malaria incidence and its potential selection of resistant strains? Candidate: Hypolite Muhindo (University of Kinshasa, Democratic Republic of Congo) Dates: September 2011-June 2013
	Title: Antimalarial treatment in the Greater Mbarara district, Uganda: efficacy, use and access Candidate: Carolyn Nabasumba (Epicentre Mbarara Research Base, Mbarara University, Uganda)
Publications:	

7.8 Kreidenweiss

EDCTP Project Coordinator:	Dr Andrea Kreidenweiss (University of Tübingen, Germany)
EDCTP Call Title:	Support for Member States Initiated (MSI) Projects within the scope of EDCTP activity areas
EDCTP Project Title:	Enhancing research capacities through the joint development of a multiplex flow cytometric bead assay for polyparasite detection in pregnant African women
EDCTP Project Code:	MS.2011.10800.001
EDCTP Project Start Date:	1 October 2012
EDCTP Project End Date:	31 May 2014
Collaborating partners:	• Adrian Luty (Institut de Recherche pour le Développement (IRD), France) • Marguerite Massinga Loembé (Medical Research Unit (MRU), Gabon)
Goal:	The overall aim of this German/French/Gabonese MSI project is to develop a novel diagnostic tool that allows for the simultaneous identification of multiple parasitic infections present in a single individual using a single smallvolume sample of plasma including the particular emphasis of detecting malaria in pregnant African women.
Primary Objective(s):	To develop an assay for detection of multiple parasitic infections during pregnancy including potentially cryptic placental Plasmodium falciparum. This MSIP is based on the joint expertise of the German and the French research projects where the Germans bring in the microbead platform for simultaneous parasite detection and the French their competence in pregnancy-associated malaria. Therefore, VAR2CSA will be evaluated for its potential as a biomarker for P. falciparum infection detected in a patient blood sample.
Clinical Trial/Study site(s):	Medical Research Unit (Gabon)
Collaborating site(s):	• University of Tübingen (Germany) • Institut de Recherche pour le Développement (France)
Status:	Ongoing
Results and Outcomes:	Pending
PhD studies:	Title: Implementation of a multiplex flow cytometric bead assay for polyparasite detection in African pregnant women Candidate: Anthony Ajua (Medical Reseach Unit, Gabon) Dates: 1 March 2013 – TBD
Postdoc studies:	Peter Soboslay (Medical Reseach Unit, Gabon)
Publications:	Pending

7.9 XACT (Dheda)

EDCTP Project Coordinator:	Professor Keertan Dheda (University of Cape Town, South Africa)
EDCTP Call Title:	Support for Member States Initiated (MSI) Projects within the scope of EDCTP activity areas
EDCTP Project Title:	The utility of intensified case finding combined with a package of novel TB diagnostics using a mobile clinic in Africa- a randomized controlled trial (XACT)
EDCTP Project Code:	MS.2011.10800.003
EDCTP Project Start Date:	1 November 2012
EDCTP Project End Date:	31 December 2014
Collaborating partners:	• Lynn Zijenah (University of Zimbabwe Collesge of Health Sciences, Zimbabwe) • Leonardo Sechi (University of Sassari, Italy) • Bram van Ginneken (Radboud University, The Netherlands)
Clinical Trial	The XACT study
Site Principal Investigator(s):	• Keertan Dheda (South Africa) • Lynn Zijenah (Zimbabwe)
Clinical Trial/Study Sponsor:	University of Cape Town
Trial/Study title:	The utility of intensified case finding combined with a package of novel TB diagnostics using a mobile clinic in Africa- a randomized controlled trial (XACT)
Goal:	The use of point-of-care diagnostic tools (system screening, HIV and urine LAM strip testing, and GeneXpert MTB/RIF) will be compared to standard methods (system screening, lab-based sputum smear microscopy and culture) for intensive case to determine which arm will significantly increase the proportion of TB cases initiating and completing TB treatment. Thus, we seek to determine what package of novel point-of-care diagnostics technologies can add to active case finding.
Primary Objective(s):	The proportion of culture-positive TB cases initiating TB treatment in each study arm
Clinical Trial/Study site(s):	• Langa and Gugulethu communities (South Africa) • Mabvuku district, Zimbabwe
Collaborating site(s):	
Study design:	Randomised controlled trial
Number of subjects:	800 (400 per site)
Product(s):	GeneXpert
Manufacturer/Developer:	Cepheid (USA)
Cofunders:	• Radboud University (Netherlands) • Istituto Superiore di Sanità Dipartimento del Farmaco (Italy) • University of Cape Town (South Africa) • University of Zimbabwe (Zimbabwe) • Alere Diagnostics (South Africa) • DST (South Africa)
Trial Registration number	NCT01990274
Status:	Ongoing
Results and Outcomes:	Pending
PhD studies:	
Publications:	

8 Joint Call by Member States (JCMS)

Table 8-1: JCMS 2010 call for 'Evaluating the Impact of Clinical Trials in Africa' supported by EDCTP

Project Acronym (Coordinator)	Health Systems Disease Area	Trials under study	Trial Sites	Status
Munguambe	Malaria/TB	• A phase IIb proof-of-concept efficacy trial of the RTS,S/AS candidate malaria vaccine in children 1 to 4 years in Mozambique, and in infants in Tanzania • A trial of the RTS, S/AS candidate malaria vaccine in newborns in Mozambique and Tanzania • A phase III efficacy trial of the RTS,S malaria vaccine candidate in children aged 5 to 17 months, and infants aged 6 to 12 weeks in Gabon, Tanzania, and Mozambique • Trial to evaluate alternative antimalarial drugs to sulfadoxine-pyrimethamine (SP) for intermittent preventive treatment in pregnancy (IPTp) in the context of insecticide treated nets in Gabon, Tanzania, and Mozambique (EDCTP funded) • Intermittent preventive treatment of malaria in infants (IPTi) with SP in Gabon, Tanzania, and Mozambique • A phase II trial of GMZ2.4 malaria vaccine candidate in children 1-5 years in Gabon • In vivo trial of combination therapy for treatment of malaria in Tanzania • Phase II assessment of TB therapy in Tanzania (EDCTP funded)	1. Mozambique - Manhiça study area, which includes the Manhiça District Hospital and 5 health centres (Maragra, Ilha Josina, Taninga, Malavele, and Palmeira). 2. Tanzania - Bagamoyo and Kisarawe Districts. Bagamoyo District - Bagamoyo District Hospital. 3. Gabon - Ogooué et Lacs District - the Albert Schweitzer District Hospital, the Lambarene Regional District Hospital, the Fougamou Regional Rural Hospital, the Makouke Health care centre and 10 dispensaries.	Ongoing
Pare Toe	Malaria	• Burkina Faso and Zambia: PREGACT (Donor: EDCTP. Status: ongoing) • Multicentre trial "Safe and efficacious artemisinin-based combination treatments for African pregnant women with malaria" (PREGACT, NCT00852423) • Burkina Faso Malactres trial (Funder FP7. Status:	1. Burkina Faso – Nanoro: Institut de Recherche en Science de la Santé (IRSS) and Centre Médical avec Antenne chirugicale (CMA). Bobo Dioulasso: IRSS/Centre Muraz and Dafra district hospital.	Ongoing

		completed at the end of 2010) "In vivo and in vitro efficacy of the recommended first line antimalarial treatments (artemetherlumefantrine and amodiaquine-artesunate) in children with uncomplicated malaria in Burkina Faso" (Malactres, NCT00808951) is carried out in Bobo Dioulasso (Burkina Faso). • Ghana, Study 13-Rectal Artesunate. (Funder WHO/TDR and EU. Status: ended). • Multi-center double-blind randomisedcontrolled trial that evaluated the effect of rectal artesunate on child mortality in the Kassena-Nankana district of northern Ghana.	2. Zambia – Nchelenge district 3. Ghana - Kassena-Nankana district: Navrongo Health Research Center.	
Asante	Malaria	Ghana and Kenya : • Kintampo and Kilifi Malaria Vaccine Trial – phase II efficacy, safety and immunogenicity trial of GSK's RTS,S malaria vaccine with the aim of integrating into routine immunization for infants. • Phase I Safety and immunogenicity of heterologous prime-boost with the candidate malaria vaccines AdCh63 ME-TRAP and MVA ME-TRAP in healthy adults in a malaria endemic area • the phase IIb and malaria drug trials that preceded the RTS,S vaccine Burkina Faso: • Since 2003, CNRFP has conducted three phase I trials among children 12-24 months old and adults 18-40 years respectively. Also as part of an EDCTP funded integrated Project • IP_08_31100 (MVVC) CNRFP will implement a Phase IIb clinical trial entitled "Integrating capacity building and networking in the design and conduct of Phase I and II clinical trials of viral vectored candidate malaria vaccines in East and West African children and infants". This multi-site Phase II trial also involves KEMRI-Kilifi, Kenya. This clinical trial will commence in 2011 and will end in 2013	1. Ghana – Kintampo: Kintampo Health Research Centre 2. Kenya – Kilifi: KEMRI Kilifi 3. Burkina Faso – Ouagadougou: Centre Nacional du Recherche et de formation sur le Paludisme (CNFRP)	Ongoing

8.1 Munguambe

EDCTP Project Coordinator:	Khatia Munguambe (Manhiça Health Research Center, Mozambique)
EDCTP Call Title:	JCMS Evaluating the Impact of Clinical Trials in Africa
EDCTP Project Title:	Evaluating the impact of clinical trials on health services delivered to women and children in three countries (Mozambique, Gabon and Tanzania) of sub-Saharan Africa
EDCTP Project Code:	JC.2010.10300.005
EDCTP Project Start Date:	30 December 2011
EDCTP Project End Date:	29 December 2013
Collaborators:	• Salim Abdulla (Ifakara Health Research and Development Centre, Tanzania) • Selidji Todagbe Agnandji (Albert Schweitzer Hospital, Gabon) • John Aponte (Hospital Clinic of Barcelona, Spain) • Caterina Guinovart (Hospital Clinic of Barcelona, Spain) • Bertrand Lell (Albert Schweitzer Hospital, Gabon) • Elisa Sicuri (Centre de Recerca en Salut Internacional de Barcelona (CRESIB), Spain)
Site Principal Investigator(s):	• Khatia Munguambe (Mozambique) • Salim Abdulla (Tanzania) • Selidji Agnandji (Gabon)
Trial/Study title:	Evaluating the impact of clinical trials on health services delivered to women and children in three countries (Mozambique, Gabon and Tanzania) of sub-Saharan Africa
Goal:	This study aims to understand the influence of clinical trials targeting women and children on healthcare delivered to these population groups in clinical trial sites in 3 sub-Saharan African countries: Mozambique, Tanzania and Gabon
Primary Objective(s):	1. The qualitative indicators will be evaluated through data generated by focus group discussions with community members, and case studies of the above listed clinical trials 2. The quantitative assessment will be done through a community based household survey and a health facility survey.
Clinical Trial/Study site(s):	• Manhiça study area, which includes the Manhiça District Hospital and 5 health centres (Maragra, Ilha Josina, Taninga, Malavele, and Palmeira) where clinical trials are being or have been conducted. The control cluster will include the rest of the district, not covered by DSS, with Xinavane Rural Hospital and 4 other health centres (Munguine, Maluana, Calanga, and 3 de Fevereiro). • Bagamoyo (74 Km North of Dar-es-salaam) and Kisarawe (40 Km South-west of Dar-es-salaam) Districts. The intervention cluster will be Bagamoyo District - Bagamoyo District Hospital. The control cluster will be Kisarawe district, with Kisarawe District hospital and its surrounding dispensaries, where there is no research infrastructure and no ongoing clinical trials. • Lambarené study population: Ogooué et Lacs (250 km from Libreville) and Mouila (580 Km from Libreville). The intervention cluster will be Ogooué et Lacs District - the Albert Schweitzer District Hospital, the Lambarene Regional District Hospital, the Fougamou Regional Rural Hospital, the Makouke Health care centre and 10 dispensaries, all previously and/or currently involved in clinical trials. The

	control cluster will be Mouila District with a population of 15,000.
Collaborating site(s):	• Institute of Tropical Medicine, University of Tuebingen (Germany) • Hospital Clinic of Barcelona CRESIB (Spain)
Study design:	Cross-sectional cluster survey comparing intervention and control groups
Number of subjects:	There will be a total of 6 clusters: one intervention and one control cluster per site.
Cofunders:	NACCAP (Netherlands) ISCIII (Spain) University of Teubingen (Germany)
Status:	Ongoing
Results and Outcomes:	Quantitative and qualitative studies have both started at all sites.

8.2 Pare Toe

EDCTP Project Coordinator:	Léa Pare Toé (Centre Muraz, Burkina Faso)
EDCTP Call Title:	JCMS Evaluating the Impact of Clinical Trials in Africa
EDCTP Project Title:	Impact of clinical trials on the health behaviours of the communities and the quality of the health services in West and South Africa (Burkina Faso, Ghana and Zambia)
EDCTP Project Code:	JC.2010.10300.008
EDCTP Project Start Date:	4 October 2011
EDCTP Project End Date:	3 August 2013
Collaborators:	• James Akazili Ghana (Navrongo Health Research Centre, Ghana) • Frank Baiden (Kintampo Health Research Center, Ghana) • Victor Chalwe (Tropical Diseases Research Centre, Zambia) • Umberto D'Alessandro (Prince Leopold Institute of Tropical Medicine (ITM), Belgium) • K. Maxime Drabo (Centre Muraz, Burkina Faso) • Derrick Elemu (University of Zambia (UNZA), Zambia) • Abraham Hodgson (Navrongo Health Research Centre, Ghana) • Koen (Peeters ITM, Belgium) • Rafaella Ravinetto (ITM, Belgium) • Nancy Soko (Tropical Diseases Research Centre, Zambia) • Halidou Tinto (Centre Muraz, Burkina Faso)
Site Principal Investigator(s):	• Lea Pare Toe (Burkina Faso) • Victor Chalwe (Zambia) • Abraham Hodgson (Ghana)
Trial/Study title:	Impact of clinical trials on the health behaviours of the communities and the quality of the health services in West and South Africa (Burkina Faso, Ghana and Zambia)
Goal:	Carry out a comprehensive evaluation of the impact of public health oriented clinical trials on local communities and the corresponding health system. To achieve this, the project will address the following research questions: Does the implementation of clinical trials have an impact on access to care and health facility utilization, i.e. frequency of attendance, early attendance or delay, increased/decreased trust, etc? In case of positive changes, can these be maintained over time and beyond the presence of the research team? If negative or no changes, is there anything that could be done to improve the situation? What is the impact on health staff and health services in terms of: quality of care for all patients; skills and motivation of the health staff; other possible factors of change. Is there any indirect benefit (development of trade, employment or local infrastructure) related to the implementation of the trials, and if yes, can these be maintained?
Primary Objective(s):	• To analyse the impact of clinical trials on the quality of care and the community's health behaviour • To describe the skills and motivation of the health staff in the context of clinical trial implementation versus the context of no clinical trial • To describe the quality of care for all patients in the context of clinical trial implementation versus the context of no clinical trial • To analyse patients' and communities' perception of the various benefits and constraints of participation in clinical trials (e.g., free care, loss of time, reimbursements, home visit by health workers, risks of participating)

	• To analyse changes in the patterns of individual/family care seeking (medical, traditional, consultation of various health providers, etc.) during and after a clinical trial.
Clinical Trial/Study site(s):	• Institut de Recherche en Science de la Santé (IRSS) and Centre Médical avec Antenne, Nanoro (Burkina Fasp) chirugicale (CMA). Bobo Dioulasso: IRSS/Centre Muraz and Dafra district hospital • Tropical Diseases Research Centre Ndola and University of Zambia, Lusaka, Nchelenge district (Zambia) • Kintampo Health Research Center and Navrongo Health Research Center, Kassena-Nankana district (Ghana).
Collaborating site(s):	Institute of Tropical medicine Prince Leopold (Belgium)
Study design:	Quantative and qualitative data analysis
Cofunders:	NACCAP (Netherlands) SIDA (Sweden)
Status:	Ongoing
Results and Outcomes:	All qualitative surveys were completed with in total 141 interviews realised in Ghana, 221 in Zambia and 333 in Burkina Faso. The quantitative surveys are ongoing in all three countries.

8.3 Asante

EDCTP Project Coordinator:	Kwaku Poku Asante (Kintampo Health Research Center, Ghana)
EDCTP Call Title:	JCMS Evaluating the Impact of Clinical Trials in Africa
EDCTP Project Title:	An evaluation of the impact of malaria clinical trials on the delivery of health care, particularly for women and children, in sub-Saharan Africa
EDCTP Project Code:	JC.2010.10300.009
EDCTP Project Start Date:	27 October 2011
EDCTP Project End Date:	26 April 2013
Collaborators:	• Traore Abdoulaye (Centre national de recherche de Formation sur le Paludisme (CNRFP), Burkina Faso) • Bright Akpalu (Kintampo Health Research Center, Ghana) • Konate Amadou Tidiana (CNRFP, Burkina Faso) • Yaro Jean-Baptiste Bibié (CNRFP, Burkina Faso) • Daniel Chandramohan (London School of Hygiene and Tropical Medicine (LSHTM), UK) • Roma Chilengi (African Malaria Network Trust, Tanzania) • Lawrence Gyabaa Febir (Kintampo Health Research Center, Ghana) • Egeruan Babatunde Imoukhuede (European Vaccine Initiative (EVI), Germany) • Caroline Jones (Kenya Medical Research Institute (KEMRI), Kenya) • Malick Lankoandé (CNRFP, Burkina Faso) • Deborah Mogaka (KEMRI, Kenya) • Sassy Molyneux (KEMRI, Kenya) • Issa Ouedraogo Nebie (CNRFP, Burkina Faso) • Seth Owusu-Agyei (Kintampo Health Research Center, Ghana) • Benjamin Sombie (CNRFP, Burkina Faso) • Charlotte Tawiah-Agyemang (Kintampo Health Research Center, Ghana) • Alfred Tiono (CNRFP, Burkina Faso) • Jayne Webster (LSHTM, UK)
Site Principal Investigator(s):	• KP Asante (Ghana) • Roma Chilengi (Kenya) • Amadou Tidiana (Burkina Faso) • Alfred Tiono (Burkina Faso)
Trial/Study title:	An evaluation of the impact of malaria clinical trials on the delivery of health care, particularly for women and children, in sub-Saharan Africa.
Goal:	The study is designed to assess the impact of clinical trials on the communities and facilities where they are conducted, with emphasis on the impact on women and children.
Primary Objective(s):	The proposed research seeks to address the following principal questions: 1. What is the range of inputs (infrastructural and human resource capacity) that malaria clinical trials bring to trial centres in SSA? 2. What are the expectations and perceptions among health providers, community members, public health service providers, and policy makers of the impacts of clinical trials especially on health services provided for women and children; and specifically with regard to: 1) delivery of routine health care 2) quality of care 3) policy change? 3. What are the key factors that limit or enhance positive and negatives impacts associated with trials (e.g. local and international regulations, type of trial, type of

	implementing institution, level of embeddedness in health systems, nature of the local health system, community engagement strategy, perceptions of the key stakeholders etc)? 4. What are the ways in which clinical trials in SSA are embedded within health facilities and wider health systems and the perceptions of key stakeholders such as health service providers, researchers and policy makers on the different approaches taken? 5. Do the range of inputs, perceptions of community and key health stakeholders, and impacts of clinical trials in SSA change over the life of the trial and in post-trial contexts, and why?
Clinical Trial/Study site(s):	• Kintampo Health Research Centre (Ghana) • KEMRI – Kilifi (Kenya) • Centre National de Recherche et de Formation sur le Paludisme, Ouagadougou (Burkina Faso)
Collaborating site(s):	• London School of Hygiene and Tropical Medicine (UK) • KEMRI-Wellcome Trust Research Programme (UK) • European Vaccine Initiative (Germany)
Study design:	Quantative and qualitative data analysis
Cofunders:	• NACCAP (Netherlands) • SIDA (Sweden) • MRC (UK)
Status:	Ongoing
Results and Outcomes:	Qualitative data collection has started and ongoing in Kintampo; data collection is pending in CNRFP and KEMRI Kilifi.
Publications:	

9 Ethics (IRB and NEC)

Table 9-1: Summary table of ethics projects (Institutional Review Boards (IRBs) and National Ethics Committees (NECs))

Project Acronym (Coordinator)	Type of Project (NEC or IRB)	Project Goal	Hosting Institution	Status
JANKO-VSCR-ETHICS	Support for courses on ethics	Capacity Building	Vienna School of Clinical Research	Completed
ASEFFA-PABIN-ETHICS	Support for courses on ethics	Capacity Building	Armauer Hansen Research Institute (AHRI)	Terminated
SPRUMONT-TRREE1-ETHICS	Support for courses on ethics	Capacity Building	University of Neuchâtel	Completed
MATSIEGUI-GABON-ETHICS	NEC	Capacity Building	Ministry of Public Health, Republic of Gabon	Completed
TINDANA-NAVRONGO-ETHICS	IRB	Capacity Building	Navrongo Health Research Centre, Ghana Health Service	Completed
BENGO-MALAWI-ETHICS	NEC, IRB	Capacity Building	College of Medicine, University of Malawi	Completed
BENGO (NDEBELE)-MALAWI-ETHICS	NEC, IRB	Capacity Building	College of Medicine, University of Malawi	Completed
FALUSI-IBADAN-ETHICS	IRB	Capacity Building	University of Ibadan	Completed
MANAFA-NIMR-ETHICS	IRB	Capacity Building	Nigerian Institute of Medical Research (NIMR)	Completed
MOODLEY-ERECCA-ETHICS	Support for courses on ethics	Capacity Building	University of Stellenbosch	Completed
KILAMA-AMANET1-ETHICS	Support for courses on ethics	Capacity Building	African Malaria Network Trust (AMANET)	Completed
SEWANKAMBO-MAKERERE-ETHICS	IRB	Capacity Building	Makerere University College of Health Sciences (MUCHS)	Completed
HOLM-CARDIFF-ETHICS	Support for courses on ethics	Capacity Building	Cardiff University	Completed
MUNYATI-MUSESENGWA-ETHICS	NEC, IRB	Capacity Building	Medical Research Council of Zimbabwe (MRCZ)	Completed
HOUNGNIHIN-	NEC	Capacity Building	Ministry of Health (Benin)	Completed

BENIN-ETHICS				
PETROS-ETBIN1-ETHICS	IRB	Capacity Building	Addis Ababa University	Completed
ADEBAMOWO-WABT-ETHICS	NEC	Capacity Building	West African Bioethics Training Program (WAB), University of Ibadan	Completed
WANE (KAYITENKORE)-RWANDA-ETHICS	NEC	Capacity Building	Rwanda National Ethics Committee, Ministry of Health	Completed
CHANGALUCHA-NIMR-ETHICS	IRB	Capacity Building	National Institute for Medical Research (NIMR)	Completed
CHILENGI (KILAMA)-AMANET2-ETHICS	Support for courses on ethics	Capacity Building	Africa Malaria Network Trust (AMANET)	Completed
MASSAGA (MASHALLA)-TANHER-ETHICS	NEC	Capacity Building	Tanzania Health Research Forum, National Institute for Medical Research	Completed
ONAPA-UNCST-ETHICS	NEC	Capacity Building	Uganda National Council for Science and Technology (UNCST)	Completed
MASON-BRTI-ETHICS	IRB	Capacity Building	Biomedical Research and Training Institute (BRTI)	Completed
KHULUMANI (KASULE)-BOTSWANA-ETHICS	NEC, IRB	Capacity Building	Health Research Unit, Ministry of Health Botswana	Completed
MUPENDA-CIBAF-MZADI-ETHICS	IRB	Capacity Building	Centre Interdisciplinaire de Bioéthique pour l'Afrique Francophone (CIBAF)	Completed
OKITOLONDA-CIBAF-PALABRE-ETHICS	NEC	Capacity Building	Centre Interdisciplinaire de Bioethique pour l'Afrique Francophone (CIBAF), Kinshasa School of Public Health	Completed
BOATENG-NMIMR-ETHICS	NEC, IRB	Capacity Building	Noguchi Memorial Institute for Medical Research, College of Health Sciences, University of Ghana	Completed
WASUNNA-KEMRI-ETHICS	IRB	Capacity Building	Kenya Medical Research Institute (KEMRI)	Completed
FUMANE-MOZAMBIQUE-ETHICS	NEC, IRB	Capacity Building	Ministry of Health, National Health Institute, Comité Nacional de Bioética para Saúde (CNBS)	Completed
UKPONG-NHVMS-ETHICS	Support for courses on ethics	Capacity Building	New HIV Vaccine and Microbicide Advocacy Society (NHVMAS)	Completed
SARR-CNRS-ETHICS	NEC	Capacity Building	Senegal National Health Research Council (Conseil National pour la Recherche en Sante -CNRS)	Completed

WASSENAAR-SARECCER-ETHICS	Support for courses on ethics	Capacity Building	University of KwaZulu-Natal	Completed
IJSSELMUIDEN-MARCI-ETHICS	Coordination function	Capacity Building	Council on Health Research for Development (COHRED)	Completed
MBIDDE-UVRI-ETHICS	IRB	Capacity Building	Uganda Virus Research Institute (UVRI)	Completed
SPRUMONT-TREEE2-ETHICS	Support for courses on ethics	Capacity Building	Institute of Health Law, University of Neuchâtel	Completed
MATSIEGUI-CAEN-ETHICS	NEC	Capacity Building	Comité National d'Éthique pour la Recherche du Gabon	Ongoing
KOLLIE-LIBERIA-ETHICS	IRB	Capacity Building	University of Liberia-Pacific Institute for Research and Evaluation Africa Center (PIRE)	Completed
RULISA-KUTH-ETHICS	IRB	Capacity Building	Kigali University Teaching Hospital (KUTH)	Completed
MUGYENYI-JCRC-ETHICS	IRB	Capacity Building	Joint Clinical Research Centre (JCRC)	Completed
GAIE (NDEBELE)-BOTSWANA-ETHICS	IRB	Capacity Building	University of Botswana	Completed
KAPTUE-CNEC-ETHICS	NEC	Capacity Building	Cameroon National Ethics Committee (CNEC)	Completed
WOLDEAMANUEL (PETROS)-ETBIN2-ETHICS	NEC, IRB	Capacity Building	Ethiopian Bioethics Initiative (ETBIN), Addis Ababa University	Completed
YEVOO-GHANA-ETHICS	IRB	Capacity Building	Dodowa Health Research Centre (DHRC)	Completed
BHATT-KENYA-ETHICS	NEC	Capacity Building	University of Nairobi	Completed
BUKUSI-KENYA-ETHICS	IRB	Capacity Building	Kenya Medical Research Institute (KEMRI)	Ongoing
OTIENO-KENYA-ETHICS	IRB	Capacity Building	Centre for Research and Technology Development (RESTECH)	Completed
MANDA-MALAWI-ETHICS	IRB	Capacity Building	College of Medicine, University of Malawi	Completed
OTUONYE-NIMR-ETHICS	IRB	Capacity Building	Nigerian Institute of Medical Research (NIMR)	Completed
OYEDEJI-NIMR-ETHICS	IRB	Capacity Building	Nigerian Institute of Medical Research (NIMR)	Completed
KRUGER-SAREN-	Coordination	Capacity Building	University of Stellenbosch	Ongoing

ETHICS	function			
MSAMBICHAKA-TANZANIA-ETHICS	IRB	Capacity Building	Ifakara Health Institute	Completed
TEMU-LZIRB-ETHICS	IRB	Capacity Building	National Institute for Medical Research (NIMR)	Completed
BIRUNGI-TASO-ETHICS	IRB	Capacity Building	The AIDS Support Organization (TASO)	Completed
ZIMBA-ZIMBABWE-ETHICS	IRB	Capacity Building	Harare City Health Department	Completed
OUEDRAOGO-BURKINA FASO-ETHICS	IRB	Capacity Building	Centre Muraz Research Institute	Ongoing
TANGWA-CAMBIN-ETHICS	Coordination function	Capacity Building	Cameroon Bioethics Initiative (CAMBIN)	Ongoing
OSEI-ATWENEBOANA-CSIR-ETHICS	IRB	Capacity Building	Council for Scientific and Industrial Research (CSIR)	Ongoing
DAMASCENO-MOZAMBIQUE-ETHICS	IRB	Capacity Building	Eduardo Mondlane University and Maputo Central Hospital	Completed
NTSIBA-CERSSA-ETHICS	IRB	Capacity Building	Comité d'Ethique de la Recherche en Sciences de la Santé (CERSSA) [Congolese Ethics Committee]	Ongoing
NOOR-AAPH-ETHICS	IRB	Capacity Building	Africa Academy for Public Health (AAPH)	Ongoing
OKULLO-MAKERERE-ETHICS	IRB	Capacity Building	Makerere University College of Health Sciences (MakCHS)	Ongoing
OLUPOT-OLUPOT-MRHIRC-ETHICS	IRB	Capacity Building	Mbale Regional Hospital Institutional Review Committee (MRHIRC)	Completed
NKANDU-ZAMBIA-ETHICS	IRB	Capacity Building	University of Zambia (UNZA)	Completed
MUTENHERWA-BRTI-ETHICS	IRB	Capacity Building	Biomedical Research and Training Institute (BRTI)	Completed
OLOO-CREATES-ETHICS	IRB	Capacity Building	Strathmore University, Centre for Research in Therapeutic Sciences (CREATES)	Ongoing
EKOUEVI-TOGO-ETHICS	NEC	Capacity Building	Département d'Epidémiologie et de santé Publique, Faculté Mixte de Médecine et de Pharmacie, Université de Lomé (Togo)	Ongoing
KANGWENDE-ZIMBABWE-ETHICS	IRB	Capacity Building	Africa University	Ongoing
MBAE-ECSA-ETHICS	IRB	Capacity Building	East, Central and Southern Africa – Health Community	Ongoing

MOMBO-NGOMA-MRU-ETHICS	IRB	Capacity Building	Medical Research Unit – Institutional Review Board (MRU-IRB), Albert Schweitzer Hospital	Ongoing
NYIKA-ZIMFRI-ETHICS	Coordination function	Capacity Building	Public Health Projects in Africa (PHPAfrica)	Ongoing
OKOYE-AGCPN-ETHICS	Support for courses on ethics	Capacity Building	Association for Good Clinical Practice in Nigeria (AGCPN)	Completed
SOW-CNERS-ETHICS	NEC	Capacity Building	Guinean National Ethic Committee for Health Research (CNERS)	Ongoing
ATASHILI-BUEA-ETHICS	IRB	Capacity Building	University of Buea	Ongoing
TOUKO (PEYOU NDI)-OCEAC-ETHICS	IRB, NEC	Capacity Building	OCEAC: Organisation de Coordination pour la lute contre les Endémies en Afrique Centrale (Organization for the Coordination of Endemic Disease Control in Central Africa)	Ongoing
IJSSELMUIDEN-MARCII-ETHICS	Coordination function	Capacity Building	Council on Health Research for Development (COHRED)	Ongoing

9.1.1 Janko-VSCR–Ethics

EDCTP Project Coordinator:	Christa Janko (Vienna School of Clinical Research, Austria)
EDCTP Call Title:	Support for Courses and Seminars on Ethics
EDCTP Project Title:	Training on Ethical Aspects of Clinical Research for Members of African National Ethics Committees and for African physicians and investigators
EDCTP Project Code:	CB.2005.41300.008
EDCTP Project Start Date:	1 December 2006
EDCTP Project End Date:	30 November 2008
Collaborators:	• Michel Anoumou Missinou (Gabon)
Type of Project:	Support for courses on ethics
Goal:	The aim of the training on ethical aspects in clinical research is to help African clinical researchers as well as African National Ethics Committee (NEC) members to understand the basic principles and internationally acknowledged standards, guidelines and regulations of ethics in clinical research.
Objectives:	• Develop an understanding of the principles and basic considerations of ethics in clinical research • Appreciate the roles and the responsibilities of ethics committees as defined by current guidelines and regulations • Understand the unique aspects associated with vulnerable patient populations and specific therapeutic areas • Understand the legal, administrative and organisational aspects associated with ethics in clinical research.
Cofunders:	• Austrian Federal Ministry of Science (Austria) • INDEPTH Network (Ghana)
Status:	Completed
Results and Outcomes:	1. Training (resources developed (e.g. manuals) and human capacity developed) 2. Trained eight participants in the "Train the Trainer" course and 18 participants in the "Ethical Aspects of Clinical Research" course. 3. Networking/collaborations developed 4. Medical Research Unit, Albert Schweitzer Hospital Lambarene (MRU) 5. University of Health Sciences (USS), Libreville 6. National Centre for Medical Research (CIRMF), Franceville

9.1.2 Aseffa-PABIN–Ethics

EDCTP Project Coordinator:	Abraham Aseffa (Armauer Hansen Research Institute (AHRI), Ethiopia)
EDCTP Call Title:	Support of an African Coordinating Office for Ethics
EDCTP Project Title:	Establishing an African Coordinating Office for Ethics (PABIN – Pan African Bioethics Initiative)
EDCTP Project Code:	CB.2005.41301.001
EDCTP Project Start Date:	15 December 2006
EDCTP Project End Date:	23 September 2008
Collaborators:	• Getachew Aderaye Desta (Ethiopia) • Tsehaynesh Messele (Ethiopia) • Zerihun Tadesse (Ethiopia) • Yemane Teklai (Ethiopia) • Wenceslaus Kilama (Tanzania) • Pierre Effa (Cameroon) • Juntra Karbwang (WHO / TDR) • Francis Crawley (Belgium) • Josef Glasa (Slovakia) • Christa Janko (Austria) • Reider Lie (Norway) • Gunnar Bjune (Norway) • Emilio Modini (Italy) • Christian Herve (France)
Type of Project:	Support for courses on ethics
Goal:	This project intended to strengthen the work of the Pan-African Bioethics Initiative (PABIN) and its Secretariat in promoting the establishment/strengthening of national bioethics initiatives and ethical review committees (ERCs) in Africa.
Objectives:	The main aim of the project was to build capacity in health research ethics in Africa in order to contribute to meeting major African public health needs through strategic research initiatives. The project was to develop research ethics capacity that promotes national capacity for carrying out clinical trials with the support of European and international partners. Specifically, the project was to contribute to creating, as needed, national ethics committees, local ethical review committees, and national systems for ensuring high quality and efficiency in the ethical review of clinical trials and health research generally.
Status:	Completed
Results and Outcomes:	Project was stopped based on EDCTP strategic advisory board (Partnership Board) recommendation in May 2008. The following was achieved: 1. Infrastructure / Capacity Development – One computer, one photocopy machine and one colour printer were purchased. A part-time coordinator and assistant were employed. 2. Training (resources developed (e.g. manuals) and human capacity developed) – The PABIN Executive Committee meeting was held (18-19 January 2007; 9 participants). PABIN was registered in Lusaka, Zambia. The PABIN Secretariat organised training on SIDCER Recognition Program for the national ethical committee of Ethiopia, the AHRI/ALERT Ethics Committee and the Addis Ababa University Medical Faculty Ethics Committee on Human Subject Protection and Standard Operating Procedures (20-24 November

	2006). The follow-up on this is continuing with assistance to the committees in finalising their SOPs and implementation. PABIN secretariat conducted training on research ethics (human subject protection and SOP development) and GCP ethics committee members and researchers in Zanzibar (4-9 February 2008; 16 participants). PABIN Secretariat sponsored six month hands on training in ethics review for three participants at Western Institutional Review Board (WIRB) in Olympia, USA, with financial support from WHO/TDR and WIRB. The PABIN secretariat collaborated with AHRI and Norwegian partners to launch FRONTER, an internet-based ethics training of medical professionals (residents) at Addis Ababa University. The training was launched at a workshop in Addis Ababa (27-28 February 2008). The modules were jointly developed by AAU and the University of Oslo. The training involves a period of face-to-face contact/discussions in addition to online interaction with trainers. 3. Networking/Collaborations Developed – African Malaria Network Trust (AMANET)

9.1.3 Sprumont–TRREE-1-Ethics

EDCTP Project Coordinator:	Dominique Sprumont (Health Law Institute, Switzerland)
EDCTP Call Title:	Support for Courses and Seminars on Ethics
EDCTP Project Title:	Training and Resources in Research Ethics Evaluation for Africa (TRREE for Africa)
EDCTP Project Code:	CB.2005.41300.004
EDCTP Project Start Date:	1 November 2006
EDCTP Project End Date:	1 November 2008
Collaborators:	• Clement Adebamowo (Nigeria) • Charles Becker (Senegal) • Marie-Charlotte Bouësseau (Switzerland) • Ogobara Doumbo (Mali) • Marie Hirtle (Canada) • Wen Kilama (Tanzania) • Dirk Lanzerath (Germany) • Peter Ndumbe (Cameroon) • Marcel Tanner (Switzerland) • Douglas Wassenaar (South Africa) • John Williams (France)
Type of Project:	Support for courses on ethics
Goal:	The aim of TRREE for Africa is to develop a training programme and capacity building resources in research ethics for all those involved in clinical trials in Africa (e.g. researchers, ethics committees, institutions, research participants and regulators).
Objectives:	1. Increase knowledge as well as practical skills of those involved in the management and conduct of ethics evaluation and research partnerships 2. Create a participatory process that will nourish lasting partnerships with and amongst African as well as other low and middle income partners 3. Create a resource that will facilitate the dissemination of knowledge. Overall, this will strengthen the research ethics evaluation capacities in African and other participating countries.
Cofunders:	• Swiss National Science Foundation (Switzerland) • KFPE – Commission for Research Partnership (Switzerland) • Swiss Academy of Science (SCNAT) (Switzerland) • Swiss Academy of Medical Sciences (SAMS) (Switzerland) • Health Law Institute(Switzerland) • Canadian Institute for Health Research (Canada)
Status:	Completed
Results and Outcomes:	1. Infrastructure / Capacity Development – The three African collaborators received a laptop and the necessary office supplies. 2. Training (resources developed (e.g. manuals) and human capacity developed) – The online training programme was developed (www.trree.org), including national modules for: Mali, Cameroon, Tanzania and Switzerland – All collaborators received personal coaching and two completed three month internships. – Networking/collaborations developed – AMANET (Tanzania) – MRTC (Mali) – University of Yaoundé (Cameroon) – Institute of Health Law, University of Neuchâtel (Switzerland)

	– SARETI (South Africa) – West African Bioethics (Nigeria)
Publications:	1. Ateudjieu Jérome, Baume Cédric, Joyce Ikingura, Marie Hirtle, Alassane Niaré and Dominique Sprumont, Training Needs Assessment in Research Ethics Evaluation Among Research Ethics Committees Members in Three African Countries: Cameroon, Mali And Tanzania. *Developing World Bioethics*, 2009 on-line, Vol. 10 (2) August 2010, Pages: 88–98 2. Dominique Sprumont, Formation de base en éthique de la recherche: retour aux sources avec le projet TRREE. *Bioethica Forum* (2009) Vol. 2, n° 2, pp. 79-81

9.1.4 Matsiegui-Gabon-Ethics

EDCTP Project Coordinator:	Pierre-Blaise Matsiegui (Ministry of Public Health, Gabon)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Establishment and support of a National Ethics Committee in Gabon
EDCTP Project Code:	CB.2005.41302.012
EDCTP Project Start Date:	30 July 2007
EDCTP Project End Date:	30 January 2010
Collaborators:	• Dominique Collin (Gabon) • Saadou Issifou (Gabon) • Christa Janko (Austria) • Dominique Sprumont (Switzerland) • Eduard Ngou Milama (Gabon) • Appolinaire Essono (Gabon) • Constant Roger Aynangoye (Gabon) • Rufin Dikoumba (Gabon) • Peter Kremsner (Germany) • Fidèle Pierre Nze-Nguema (Gabon) • Marie Charlotte Bouësseau (Switzerland) • Paul Bekale (Gabon) • Aissatou Toure (Senegal)
Type of Project:	National Ethics Committee
Goal:	The main goal of this project is the establishment of a NEC based on the following activities: 1. Establishment of an administrative structure (office and personnel) for the adequate functioning of an NEC 2. Establishment of procedures for the functioning of the NEC and for guidance of the review process.
Objectives:	1. Development and implementation of standard operational procedures for protocol review and follow-up of research 2. activities and internal structure and functioning 3. Proposition of laws and legal regulations and guidelines for the control of biomedical research in Gabon 4. Ensuring sustainability by looking for new financing possibilities 5. Organising workshops on ethical issues in Gabon 6. Awareness campaign on ethical problems through information, education, and communication for researchers, health workers, communities and the whole country 7. Creation of a documentation centre 8. Networking with other ethics committees in Central Africa and in Africa.
Status:	Completed
Results and Outcomes:	1. Infrastructure / Capacity Development – A computer and printer were purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed) – Establishment of a Gabonese NEC – Establishment of an administrative structure – Establishment of procedures, including implementation of SOPs – Training of NEC members - 64 participants received training on ethics – A webpage has been designed: www.cner-gabon.org/cner/

	3. Networking/collaborations developed – Medical Research Unit (MRU), Albert Schweitzer Hospital in Lambarene – Vienna School of Clinical Research – Université desSciences de la Santé (USS) – Ministry of Science and Research and Ministry of Finance (Gabon) – AMANET (African Malaria Network Trust) – WHO – Facultes de Droit des Universités Fribourg etde Neuchatel – Institut Pasteur – UNESCO – The Ethics Committee of the University of Tübingen – The Joseph and Rose Kennedy Institute of Ethics, Georgetown University

9.1.5 Tindana-Navrongo-Ethics

EDCTP Project Coordinator:	Paulina Tindana (Ghana Health Service, Ghana)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	A proposal for strengthening the capacity of six Research Ethics Committees in Ghana
EDCTP Project Code:	CB.2005.41302.004
EDCTP Project Start Date:	21 June 2006
EDCTP Project End Date:	14 November 2007
Collaborators:	• Okyere Boateng (Ghana) • Abraham Hodgson (Ghana)
Type of Project:	Institutional Review Board
Goal:	The aim of this project was to strengthen the capacity of administrators and members of the six ethics review committees in Ghana.
Objectives:	This project was an intervention phase of an initial survey of research ethics committees (RECs) in Ghana, which was conducted in 2005. The initial survey identified logistics and training as the major challenges facing ethics review committees in the country. Therefore, this project sought to support all the six ethics committees in Ghana to overcome these challenges through the provision of office equipment, local training in research ethics for REC administrators, specifically on the operations of RECs and a national conference to create awareness on the role of ethics review in health research and to foster a relationship between all the RECs in Ghana.
Status:	Completed
Results and Outcomes:	1. Infrastructure / Capacity Development – Six desktop computers, six printers, six filing cabinets and six UPS (universal power systems) were purchased for each of the six RECs that received support via this project 2. Training (resources developed (e.g. manuals) and human capacity developed) – The administrators of six RECs received training on developing SOPs and protocol submission forms. A three-day national conference on "Ethics in Human Research in Ghana" was held (5-7 February 2007). 3. Networking/collaborations developed – African Malaria Network Trust (AMANET) – Pan African Bioethics Initiative (PABIN)

9.1.6 Bengo-Malawi-Ethics

EDCTP Project Coordinator:	Joseph Mfutso-Bengo (University of Malawi)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening the National Health Sciences Research Committee (NHSRC) and College of Medicine Ethics Committee (COMREC)
EDCTP Project Code:	CB.2005.41302.011
EDCTP Project Start Date:	20 October 2006
EDCTP Project End Date:	19 October 2007
Collaborators:	• Mike Kachedwa (Malawi) • Willard Kazembe (Malawi) • Lie Reidar (Norway) • Rosemary Musesengwa (Zimbabwe) • Paul Ndebele (Malawi)
Type of Project:	National Ethics Committee/Institutional Review Board
Goal:	The main goal of the project was to strengthen the two ethics committees in Malawi, namely the College of Medicine Ethics Committee (COMREC) and the National Health Sciences Research Committee (NHSRC) so as to enhance their roles in research oversight, ethical review and clinical trial monitoring as well as to ensure their independence, competence and transparency. This programme has contributed directly towards improving the quality of research conducted in Malawi. The programme has ultimately improved the trust of the research community by the general public. The strengthening of national capacity for ethical review ensures that only research that addresses national health priorities is conducted in Malawi, thereby directly supporting the health system by supporting evidence based decision making. The trial monitoring component has resulted in the improvement of clinical data generated from Malawi and has also resulted in further safeguarding the rights and welfare of research participants. Ultimately the programme has improved the relevance of clinical trials to Malawi and its population.
Objectives:	1. To strengthen the capacities of NHSRC and COMREC in ethical review and clinical trials monitoring 2. To adequately equip the ethics committee offices so that they can be able to perform all their tasks without limitations
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – Four laptops and a motor vehicle were purchased for the committee Secretariat offices 2. Training (resources developed (e.g. manuals) and human capacity developed) – A four day workshop was held during which members of the two ethics committees developed standard operating procedures for the two ethics committees. The standard operating procedures covered various issues including ethical review and clinical trials monitoring so as to ensure that the two committees are using internationally acceptable standard operating procedures 3. Networking/collaborations developed – Pan African Bioethics Initiative (PABIN)
Publications:	1. Mfutso-Bengo, J. (2008). Report on the workshop "Enhancing Clinical Trial Oversight in Malawi". *Malawi Medical Journal (MMJ),* 20 (2), 63–64

	2. Mfutso-Bengo, J., Masiye, F., & Muula, A. (2008). Ethical challenges in conducting research in humanitarian crisis situations. *Malawi Medical Journal (MMJ),* 20 (2), 46–49.

9.1.7 Bengo -Malawi-Ethics

EDCTP Project Coordinator:	Joseph Mfutso-Bengo (University of Malawi)
EDCTP Call Title:	Support for Courses and Seminars on Ethics
EDCTP Project Title:	Building and strengthening national capacities in ethical review and clinical trials monitoring in Malawi
EDCTP Project Code:	CB.2005.41300.007
EDCTP Project Start Date:	20 October 2006
EDCTP Project End Date:	30 April 2010
Collaborators:	• Mike Kachedwa (Malawi) • Willard Kazembe (Malawi) • Lie Reidar (Norway) • Rosemary Musesengwa (Zimbabwe) • Paul Ndebele (Malawi)
Type of Project:	National Ethics Review Committee/Institutional Review Board
Goal:	This project aimed at building and strengthening the capacities of the College of Medicine Research and Ethics Committee (COMREC) and the National Health Sciences Research Committee (NHSRC) in ethical review and clinical trial monitoring. The two bodies are the only ethics committees in Malawi.
Objectives:	The main objective of the project was to build and strengthen the capacities of the College of Medicine Research and Ethics Committee (COMREC) and the National Health Sciences Research Committee (NHSRC) in ethical review and clinical trial monitoring. The programme targeted ethics committee members, clinical trial monitors, researchers and officials from the Ministry of Health and Population, National Commission for Science and Technology (NCST) as well as all constituent colleges of University of Malawi. The main objective was achieved through the following steps: Strengthening national capacity for ethical review in Malawi Intermediate steps: • Training workshops in research ethics, Good Clinical Practice (GCP) and ethical review were conducted in all regions and an annual national conference was held during the project's duration. Introduction and strengthening of clinical trial monitoring in Malawi Intermediate steps: • Two clinical trial monitors were employed for the two committees (one for each) • Training of clinical trial monitors in clinical trial inspection. • GCP and ethics training workshops • Clinical inspectors/monitors training courses were developed and conducted • Development of SOPs for inspection activities of approved studies.
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – An overhead projector as well as consumables and supplies for the COMREC Secretariat were purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed) – Three annual national conferences were held. During the conferences, members of COMREC, NHSRC and PMPB were trained in research ethics, GCP and ethical review. Two regional training workshops for members of NHSRC,

	COMREC and PMPB as well as researchers in research ethics and GCP were conducted. Two clinical trial inspectors were hired in 2008 and have been inspecting studies approved by COMREC and NHSRC. The clinical trial inspectors have acquired the skills and expertise in clinical trial monitoring, audits and inspections as well as GCP and research ethics. In conjunction with Kendle South Africa and the College of Medicine Research Support Centre, training courses for clinical trial inspectors for COMREC, NHSRC and PMPB were conducted in Malawi, Zimbabwe and South Africa. Standard Operating Procedures (SOPs) have been developed for COMREC, NHSRC and PMPB. Material transfer agreement documents were finalised and are in use by COMREC, NHSRC and PMPB. The review process of clinical trials between the two ethics committees (NHSRC and COMREC) and the regulatory authority (PMPB) has been harmonised. Members of Medical Rights Watch received funding and training. 3. Networking/collaborations developed – Pan African Bioethics Initiative (PABIN) – Southern African Research Ethics Training Initiative (SARETI) – Partnership for Enhancing Human Research Protection in Africa (PEHRP AFRICA) – African Malaria Network Trust (AMANET)
Publications:	1. Mfutso-Bengo, J. (2008). Report on the workshop "Enhancing Clinical Trial Oversight in Malawi". Malawi *Medical Journal (MMJ*), 20 (2), 63–64 2. Mfutso-Bengo, J. (2008). Report on the workshop "Enhancing Clinical Trial Oversight in Malawi". Malawi *Medical Journal (MMJ),* 20 (2), 63–64 3. Ndebele, P., Mfutso-Bengo, J., & Mduluza, T. (2008). Compensating clinical trial participants from limited resource settings in internationally sponsored clinical trials: A proposal. *Malawi Medical Journal (MMJ),* 20 (2), 42–45.

9.1.8 Falusi-Ibadan-Ethics

EDCTP Project Coordinator:	Adeyinka Falusi (University of Ibadan, Nigeria)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening the Capacity of Research Ethics Committees in Africa
EDCTP Project Code:	CB.2005.41302.008
EDCTP Project Start Date:	22 November 2006
EDCTP Project End Date:	21 November 2008
Collaborators:	• Marie-Charlotte Bouësseau (Switzerland) • Prince Eleh (Nigeria) • Paul Ndebele (Malawi) • W. Ogala (Nigeria) • Paulina Tindana (Ghana) • John Williams (France)
Type of Project:	Institutional Review Board
Goal:	The goal of this project was to provide technical, administrative and material support to the three research ethics committees (RECs) for effective and efficient capacity building for research oversight to their institutions and possibly others in their localities.
Objectives:	1. Document the existing infrastructure, manpower capacity and operational details of the selected RECs to appropriately assess their needs 2. Develop an intervention package of a training programme and provision of a seed grant to improve capacity building and infrastructural facilities to the three sites 3. Monitor and evaluate the outcomes of the intervention package 4. Empower the core group trained to become trainers in their localities 5. Stimulate the development of ethics guidelines with the incorporation of African concepts.
Status:	Completed
Results and Outcomes:	1. Infrastructure/Capacity Development – Desktop computer, printer, UPS, power surge arrestor, scanner and photocopier were provided to each of the three RECs 2. Training (resources developed (e.g. manuals) and human capacity developed) – A four-day training workshop was held (13-16 February 2007) on ethics. Participants from each REC included the Chair, secretary and three other members. The host institution's IRB, Oyo State Ministry of Health Ethics Committee and Nigerian Bioethics Initiative (NIBIN) representatives also participated actively with a total of 255 participants at the opening ceremony and 40 participants at the training sessions. RECs developed Operational Guidelines 3. Networking/collaborations developed – World Health Organization (WHO) – World Medical Association (WMA)

9.1.9 Manafa-NIMR-Ethics

EDCTP Project Coordinator:	Ogenna Manafa (Nigerian Institute of Medical Research, Nigeria)
EDCTP Call Title:	Support for Courses and Seminars on Ethics
EDCTP Project Title:	Capacity strengthening of Nigerian researchers and ethics committee members on ethics
EDCTP Project Code:	CB.2005.41300.006
EDCTP Project Start Date:	20 October 2006
EDCTP Project End Date:	19 October 2008
Collaborators:	• Carel Ijsselmuiden (Switzerland) • Juntra Karbwang (Switzerland) • Abolarinwa Timothy Olusola (Nigeria) • Kolawole Solomon Oyedeji (Nigeria) • Douglas Wassenaar (South Africa)
Type of Project:	Institutional Review Board
Goal:	The goal was to establish a Health Research Ethics Training Centre at the Nigerian Institute of Medical Research (NIMR) with the objective of building institutional and individual capacity in ethics by training researchers, investigators and members of the ethics committee in the country and establishing an ethics committee in other major institutes and universities that conduct biomedical research.
Objectives:	1. Organise ethics workshops and seminars for researchers and ethics committee members both at national and institutional level 2. Train five to 10 resource people who will serve as the centre's trainers together with the participants 3. Organise and conduct Standard Operating Procedure (SOP) workshops for research ethics committee members and also assist ethics committees in developing SOPs for the proper conduct of their ethics committee 4. Survey established ethics committees to ensure that they meet adequate standards 5. Provide a platform for collaboration between Nigeria, African and other northern institutes and promote discussion on contemporary issues and dilemmas of health research ethics in the African context.
Status:	Completed
Results and Outcomes:	1. Training (resources developed (e.g. manuals) and human capacity developed) – A five day training workshop on Human Subject Protection (11-13 June 2007) and Standard Operating Procedures (SOPs) (14-16 June 2007) writing for investigators and members of RECs/IRBs took place. These workshops were attended by 45 participants. A second five day workshop (21-25 April 2008) was held for investigators and members of RECs/IRBs in northern Nigeria–34 participants attended. An evaluation of three ethics committees took place. A survey visit to some of the ethics committees trained during the June and April workshops was held between October and November 2008. – Networking/collaborations developed – TDR/WHO which houses the Scientific Initiative for Developing Capacity in Ethical Review (SIDCER) – West African Bioethics Initiative – Nigerian Institute of Medical Research (NIMR)

9.1.10 Moodley-ERECCA-Ethics

EDCTP Project Coordinator:	Keymanthri Moodley (University of Stellenbosch, South Africa)
EDCTP Call Title:	Support for Courses and Seminars on Ethics
EDCTP Project Title:	Enhancing Research Ethics Capacity and Compliance in Africa (ERECCA)
EDCTP Project Code:	CB.2005.41300.003
EDCTP Project Start Date:	18 August 2006
EDCTP Project End Date:	30 November 2008
Collaborators:	• Johan Hattingh (South Africa) • Lyn Horn (South Africa) • Landon Myer (South Africa) • Jimmy Volmink (South Africa)
Type of Project:	Support for courses on ethics
Goal:	The ERECCA project focuses on capacity development in two niche areas in the African context – Good Clinical Practice (GCP) and Research Ethics Review. GCP training has become a compulsory requirement for researchers in South Africa and in other parts of Africa. Most researchers have some form of basic GCP training, but have a need to update this training on a regular basis (either annually or every two to three years).
Objectives:	Intermediate objectives: • To extend refresher GCP courses to a wider audience via WEB CT • To develop new capacity for ethics review. Final objectives: • To improve compliance with national and international standards of ethical review • To expedite the ethics review process via improved training • To strengthen expertise in the ethical conduct of clinical trials in South Africa.
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – A computer was purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed) – Online GCP refresher course was developed – all 12 modules have been developed – 94 delegates have completed the ERECCA programme. REC Seminar was presented to 52 delegates. 3. Networking/collaborations developed – University of Ibadan, Nigeria – University of Zambia – Pan African Bioethics Initiative (PABIN) – Medicines Control Council (MCC) – University of Cape Town (UCT)

9.1.11 Kilama-AMANET-1-Ethics

EDCTP Project Coordinator:	Wenceslaus Kilama (African Malaria Network Trust (AMANET), Tanzania)
EDCTP Call Title:	Support for Courses and Seminars on Ethics
EDCTP Project Title:	Creating web-based research training courses in biomedical research ethics for Africans
EDCTP Project Code:	CB.2005.41300.002
EDCTP Project Start Date:	1 June 2006
EDCTP Project End Date:	13 June 2007
Collaborators:	• Chilengi, Roma (Tanzania) • Francis Crawley (Belgium) • Joyce Ikingura (Tanzania) • Juntra Karbwang (Switzerland) • Souleman Mboup (Senegal) • Joseph Mfutso Bengo (Malawi) • Alwyn Mwinga (Zambia) • Paul Ndebele (Malawi) • Edphose Nfuka (Tanzania) • Godfrey Tangwa (Cameroon)
Type of Project:	Support for courses on ethics
Goal:	This project will develop a web-based training course on basic biomedical research ethics whose curriculum will be developed through a tailormade approach for the African situation.
Objectives:	The objective of this project is to provide training in biomedical research ethics in Africa through creation of a web-based system of offering formal training to Africans using validated course materials. To achieve this, a training faculty of known health research experts in Africa and Europe has been constituted. They will be responsible for development of the course curriculum and facilitate during the pilot workshop. A "user-friendly" training programme will be developed by a select faculty of experienced health research trainers and will be refined by a sample of the target trainees at a workshop. The courses will offer lecture type and other resource materials on several modules. A pass will be mandatory to proceed from one module to the next, and one has to complete a minimum set of modules to be successful.
Status:	Completed
Results and Outcomes:	1. Training (resources developed (e.g. manuals) and human capacity developed) – Ten modules were developed. By closing date of the project 629 people were reported to have undergone on-line training. A 'call for training workshop' was held and 25 participants were trained.
Publications:	1. Chilengi, R., Nyika, A., Tangwa, G. B., Noor, R. A., Ramadhani, S. W., Bosomprah, S., & Kilama, W. L. (2013). Role of e-learning in teaching health research ethics and Good Clinical Practice in Africa and beyond. Cambridge Quarterly of Healthcare Ethics, 22, 110-119.

9.1.12 Sewankambo-Makerere-Ethics

EDCTP Project Coordinator:	Nelson Sewankambo (Makerere University, Uganda)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Supporting research through enhancement of the IRB processes at Makerere Medical School
EDCTP Project Code:	CB.2005.41302.010
EDCTP Project Start Date:	12 October 2006
EDCTP Project End Date:	11 October 2009
Collaborators:	• Patrick Cras (Belgium) • Elly Katabira (Uganda) • Steven Kiwuwa (Uganda) • Paul Kutyabami l (Uganda)
Type of Project:	Institutional Review Board
Goal:	The goal was to train faculty staff in ethical processes; establish a tracking system for research activities; strengthen the infrastructure of the Institutional Review Board (IRB) secretariat and its staffing; establish a financing mechanism to ensure sustainability of IRB activities; institute support mechanisms for ethics committee member retention; and carry out operational research on IRB and related ethical processes.
Objectives:	1. Establish a tracking system for research activities at the Faculty of Medicine. IRB standard forms continue to be in use. Through the support of a grant from the African Malaria Network Trust (AMANET), the institution obtained and installed heavily subsidised ProIRB software that is now fully operational. In this software, a database containing information of all projects approved at the institution is stored and continuously updated 2. Establish a system of financial sustainability through institution of IRB review charges. Revenue was collected from new applications for ethical approval 3. Improve the human resource capacity of the IRB Secretariat. Part-time data entry staff were hired to assist the IRB office to capture, as much as possible, all the information from the records that existed prior to acquisition of the database software 4. Improve the infrastructure of the IRB secretariat. All the necessary equipment was fully procured and because of this operations have continued to be efficient 5. Compensate IRB members in carrying out IRB activities. Time compensation allowances for committee members have continued to be paid and this has provided motivation and commitment. These funds are drawn from the resources obtained through charging of IRB fees 6. Train a pool of Faculty of Medicine staff in ethical review processes.
Cofunders:	African Malaria Network Trust (AMANET)
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – Part-time data entrants were hired to assist with data capturing. A laptop, LCD projector, office furniture, chairs, cabins and a printer were purchased 2. Training (resources developed (e.g. manuals) and human capacity developed) – The institution obtained and installed heavily subsidised ProIRB software, which is now fully operational. In this

	software, a database containing information of all projects approved at the institution is stored and continuously updated. Forty ethics committee members attended a health research ethics workshop (15-17 June 2009) as well as a National Ethics Committee Conference (15-17 July 2009) hosted by the Uganda National Council for Science and Technology (UNCST) 3. Networking/collaborations developed – University of Antwerp Ethics Committee – Africa Malaria Network Trust (AMANET)

9.1.13 Holm-Cardiff-Ethics

EDCTP Project Coordinator:	Søren Holm (Cardiff University, UK)
EDCTP Call Title:	Support for Courses and Seminars on Ethics
EDCTP Project Title:	Developing a distance learning research ethics course for East Africa
EDCTP Project Code:	CB.2005.41300.005
EDCTP Project Start Date:	30 October 2006
EDCTP Project End Date:	15 October 2008
Collaborators:	• Heta Gylling (Finland) • Azaveli Lwaitama (Tanzania) • Jan Helge Solbakk (Norway)
Type of Project:	Support for courses on ethics
Goal:	The overall aim of the project is to develop, pilot and finalise a distance learning course in biomedical research ethics that will provide participants from Eastern Africa with the necessary knowledge and skills to act responsibly in their roles as principal investigators, members or chairs of research ethics committees and editors of scientific journals.
Objectives:	A modular course will be developed that can be delivered either as a paper-based course with e-mail support or as a fully web-based course using the Blackboard system (Blackboard is the e-learning system used by the University of Dar Es Salaam and by Cardiff University). The development will consist of the following steps: 1. Drafting of a ten module course covering the main research ethics issues relevant in the region 2. Seminar in Tanzania with key stakeholders from the East African region followed by finalisation of draft 3. Pilot of draft course including evaluation and revision. 4. Running of final course including evaluation 5. The final result will be a course that the University of Dar Es Salaam can continue to run after the project has ended. The European partners agree to provide academic input to the updating of the course for three years after the end of the project.
Status:	Completed
Results and Outcomes:	1. Training (resources developed (e.g. manuals) and human capacity developed) – Online training course developed but had poor sustainability. 2. Networking/collaborations developed – University of Dar Es Salaam – University of Helsinki – University of Oslo

9.1.14 Munyati-Musesengwa-Ethics

EDCTP Project Coordinator:	Shungu Munyati and Rosemary Musesengwa (Medical Research Council (MRC), Zimbabwe)
EDCTP Call Title:	Support for Courses and Seminars on Ethics
EDCTP Project Title:	Building national capacity for research oversight in Zimbabwe
EDCTP Project Code:	CB.2005.41300.001
EDCTP Project Start Date:	11 June 2006
EDCTP Project End Date:	1 March 2010
Collaborators:	• Rutendo Kuwana (Zimbabwe) • Lie Reider (Noway) • Shungu Munyati (Zimbabwe) • Paul Ndebele (Malawi) • Priscilla Nyambayo (Zimbabwe)
Type of Project:	National Ethics Committee, Institutional Review Board
Goal:	The main goal was to strengthen national capacities in health research ethics, ethical review and clinical trial monitoring, so as to create an enabling environment for the ethical conduct of research in Zimbabwe and to ensure that trials meet international ethical and Good Clinical Practice standards.
Objectives:	1. Strengthening national and institutional ethical review processes and ethics review capacity in Zimbabwe 2. Strengthening of clinical trial monitoring in Zimbabwe.
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – Motor vehicle, laptops, colour printer, LCD projector and digital camera were purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed) – Training on ethics (10-12 April 2006; 10 July 2007; 14 November 2008; 7-8 April 2009; 23-24 April 2009; 11-12 June 2009; 16-18 November 2009) and GCP workshops (5-7 December 2006; 25-26 January 2007; 8-9 March 2007; 28-31 March 2007; 12-13 April 2007; 28-29 June 2007) took place. The National Ethics Committee received training on research ethics (16 February 2006). In total, 762 researchers, students, IRB and CAB members were trained. Eight clinical trial inspectors were trained. 3. Networking/collaborations developed – Medicines Control Authority of Zimbabwe (MCAZ) – Biomedical Research and Training Institute (BRTI) – African Malaria Network Trust (AMANET) – World Health Organization (WHO) – College of Medicine, Malawi

9.1.15 Houngnihin-Benin-Ethics

EDCTP Project Coordinator:	Roch A. Houngnihin (Ministere de la Sante Publique, Benin)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Support project for the establishment and strengthening of the Benin National Ethics Committee
EDCTP Project Code:	CB.2007.41302.012
EDCTP Project Start Date:	22 October 2008
EDCTP Project End Date:	21 October 2010
Collaborators:	• Jules Affodji (Benin) • Ferdinand Guedou (Benin) • Dorothée Kinde Gazard (Benin) • Raouf A. Osséni (Benin) • Eric Pliya (Benin)
Type of Project:	National Ethics Committee
Goal:	This project aimed to contribute to reinforce the capacities of the National Ethics Committee (NEC) in Benin.
Objectives:	This project contributed to the setting up and the reinforcement of the capacities of the National Ethics Committee (NEC). For this objective, many workshops and meetings were organised within the technical recipients, actors and members of the NEC to define a conceptual framework for a homogeneous proposal, in the light of international strategic plans, in order to retain the strategic objectives, the fields of services provisions, essential activities, mechanisms of coordination and monitoring and evaluation. The project coordination will profit by assistance from the WHO local office, EDCTP and international consultants. A plan of transfer of competencies was elaborated and carried out.
Cofunders:	Pfizer
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – Equipment and computers for the Secretariat were purchased 2. Training (resources developed (e.g. manuals) and human capacity developed) – The law on the creation of a National Ethics Committee was revised and adopted by the Parliament. All of the members of the National Ethics Committee were trained on ethics in Benin (Cotonou) (10-12 August 2010; 40 participants). Training on research ethics ("Conducting research responsibly") took place in Kenya (Nairobi) (3-5 October 2010; four participants). Forty five researchers were trained on the role of an ethics committee (for its good knowledge and its perception in Benin). Information leaflets were developed and a website: www.ethique-sante.org 3. Networking/collaborations developed – National institutions: National Ethics Committee, Faculty of Health Sciences, WHO (Benin), Regional Institute of Public Health, Clinapharm/PharmaClin Society, Faculty of Law, Faculty of Human Sciences – Steve Biko Centre for Bioethics - University of Witwatersrand (South Africa)

9.1.16 Petros-ETBIN-1-Ethics

EDCTP Project Coordinator:	Beyene Petros (University of Addis Ababa, Ethiopia)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening the ethics of health research in Ethiopia
EDCTP Project Code:	CB.2007.41302.017
EDCTP Project Start Date:	29 August 2008
EDCTP Project End Date:	30 April 2010
Collaborators:	• Abraham Aseffa (Ethiopia) • Fisseha Hailemeskel (Ethiopia)
Type of Project:	Institutional Review Board
Goal:	Research departments in the five newly established universities did not have the capacity to establish their own institutional review committees. Therefore, assisting these institutions to form their own Institutional Review Boards (IRBs) and strengthening the existing IRBs in the established institutions falls within the remit of the Ethiopian Bioethics Initiative (ETBIN). Mandate is also given to research and higher learning institutions and health bureaus of regional states to provide ethical clearance to projects that do not require national approval (i.e. small grant projects supported by ESTC or local institutes). The aim was to establish and strengthen Health Research Ethics Committees in Ethiopia.
Objectives:	1. Establishing Institutional Review Boards (IRBs) in five newly established universities 2. Strengthening three existing IRBs 3. Popularising health research ethics in the country.
Cofunders:	Armauer Hansen Research Institute (AHRI, Ethiopia)
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – Eleven printers, 12 computers, one photocopier and one scanner were purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed) – A Human Participant Protection, GCP and SOP Bioethics Training Workshop took place (27-31 July 2009; 6-10 February 2010; 41 participants). Training on health research ethics was provided to five new IRB members (27-31 July 2009). A second training session on ethics for IRB members from universities and research institutions that have existing IRBs took place (6-10 February 2010) for 35 participants. A 35-page popularisation manuscript on Human Participant Protection and Good Clinical Practice (GCP) was prepared in Amharic (Ethiopian official language). 3. Networking/collaborations developed – Bioethics Unit, School of Medicine, Addis Ababa University (AAU) – Pan African Bioethics Initiative (PABIN)

9.1.17 Adebamowo-WABT-Ethics

EDCTP Project Coordinator:	Clement Adebamowo (West African Bioethics Training Program, Nigeria)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening the National Health Research Ethics Committee of Nigeria (NHREC)
EDCTP Project Code:	CB.2007.41302.001
EDCTP Project Start Date:	29 August 2008
EDCTP Project End Date:	28 August 2010
Collaborators:	• Yakubu Aminu (Nigeria) • Yemisi Ajibose (Nigeria)
Type of Project:	National Ethics Commiteee
Goal:	The objective of this work was to provide training for members of theNational Health Research Ethics Committee of Nigeria in order to strengthen the committee in carrying out its mandate as defined by the National Code for Health Research Ethics, Nigeria government laws and regulations.
Objectives:	1. Provide training in health research ethics for those members of the NHREC who have not had specific training in health research ethics 2. Increase the capacity of the NHREC members to review research protocols and contribute to policy formulation in health research ethics for Nigeria.
Cofunders:	West African Bioethics Training Program (Nigeria)
Status:	Completed
Results and Outcomes:	1. Training (resources developed (e.g. manuals) and human capacity developed) – Thirteen participants received training in a course on "Informed Consent and Management of an Ethics Committee" (April 2009). In June 2010, 10 members from the National Health Research Ethics Committee (NHREC) received materials (e.g. books) and training towards a diploma in research ethics at the West African Bioethics Training Programme (WABTP) based at the University of Ibadan. 2. Networking/collaborations developed – Federal Ministry of Health of Nigeria

9.1.18 Wane -Rwanda-Ethics

EDCTP Project Coordinator:	Justin Wane (Rwanda National Ethics Committee, Rwanda)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening of the Rwanda National Ethics Committee
EDCTP Project Code:	CB.2007.41302.013
EDCTP Project Start Date:	15 September 2008
EDCTP Project End Date:	14 September 2011
Collaborators:	• Dariya Mukamusoni (Rwanda) • Emmanuel Nkeramihigo (Rwanda)
Type of Project:	National Ethics Committee
Goal:	The Rwanda National Ethics Committee (RNEC) was created in 2002 by the Minister of Health. It is currently composed of 10 members: a chairperson, a vice-chair, a secretary, a treasurer and seven other members. It is gender balanced and has laypersons representing the community. The committee meets on a monthly basis and has drafted Standard Operating Procedures (SOPs). An administrator was recruited with the responsibility of running the office on a day-to-day basis. The Ministry of Health allocated an office to the committee and provided basic infrastructure in the form of an old computer and printer as well as desks and shelves. The lack of appropriate infrastructure, expertise and resources are major constraints. The project intended to strengthen the process of review of the ethics of research related to healthcare by improving the infrastructure available to the functioning of the RNEC and improve the committee's expertise by providing continuous training.
Objectives:	The plan is to strengthen the National Ethics Committee by: 1. Training in human subject's protection course 2. Completion of SOPs 3. Training in SOPs 4. Improvement of the infrastructure, internet and telephone connectivity 5. Acquisition of shelves and metal lockable cabinets for archiving documents 6. Providing a stable salary to the administrator 7. Publish guidance documents, such as RNECs SOPs National Guidelines on the Ethics of Health Related Research in Rwanda 8. Setting up a website providing access to guidance documents and important links 9. Meeting to discuss with research community, national workshop to explain procedures, e.g. SOPs, forms 10. Propose National Guidelines for Ethical Review 11. Organise training of local IRBs and teaching of ethics in health training institutions 12. Networking activities with dissemination of information.
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – The following items were purchased: one computer, one printer, one refrigerator, one office utensil cabinet, shelves, one coffee table, five chairs and three lockable cupboards for archiving documents. Infrastructure has been improved, namely internet and telephone connectivity. The office and meeting room were painted. A website was developed (www.rnec.moh.gov.rw). The

	grant provided capacity to cover staff salaries including one for a short-term administrator when the administrator attended training abroad 2. Training (resources developed (e.g. manuals) and human capacity developed) – SOPs for the RNEC were developed. A training course in Human Subjects Protection was conducted (12-14 July 2010) – 21 participants were trained. Local IRBs were trained and local IRBs were established. This grant allowed institutional capacity strengthening for the RNEC where five board members and the administrator attended different training sessions/conference abroad. The project facilitated site visits to monitor implementation of approved protocols 3. Networking/collaborations developed – African Vaccine Regulatory Forum (AVAREF) – Africa Malaria Network Trust (AMANET) – International Partnership for Microbicides (IPM) – International AIDS Vaccine Initiative (IAVI) – Mapping African Research Ethics and Drug Regulatory Capacity (MARC) – Centers for Disease Control (CDC) – Public Responsibilty in Medicine and Research (PRIM&R) – FWA – Western Institution Review Board in Olympia (United States of America)

9.1.19 Changalucha-NIMR-Ethics

EDCTP Project Coordinator:	John M. Changalucha (National Institute for Medical Research (NIMR), Tanzania)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Establishment of Ethics Review Board (ERB) in Mwanza, Tanzania and collaboration between local and national IRBs
EDCTP Project Code:	CB.2007.41302.018
EDCTP Project Start Date:	29 August 2008
EDCTP Project End Date:	28 February 2010
Collaborators:	• Zaba Basia (United Kingdom) • Joyce Ikingura (Tanzania) • Saidi Kapiga (Tanzania)
Type of Project:	Institutional Review Board
Goal:	The establishment of a well-functioning local Institutional Review Board (IRB) with members trained in Tanzania; clear terms of reference; a Secretariat to support its operations; developed SOPs and guidelines on conducting ethical health review; a forum for local IRBs and strengthened collaboration between local IRBs and the National Ethics Committee.
Objectives:	The main objective of this project was to establish a local IRB to serve institutions conducting medical research in the Lake Victoria and Western zones of Tanzania; and to strengthen collaboration between the local IRBs in major Tanzanian health research institutions and the National Ethics Committee. A steering committee was formed to guide the establishment of a local ethics review board (ERB) in Mwanza, Tanzania. Members of the ERB were trained in research ethics.
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – Equipment including two computers, one laser printer, three filing cabinets and one photocopier machine were purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed) – A steering committee was formed to establish the IRB, SOPs were developed and a secretariat was formed. A two day training workshop for 16 participants was conducted in order to orient IRB members on Health Research Ethics (HRE), their duties and responsibilities (5-6 March 2009). The first National Workshop of Health Research Ethics Review Committees and Regulatory Authorities was held in order to share experiences between all active IRBs in Tanzania (21 March 2009; 21 participants). 3. Networking/collaborations developed – Bugando Medical Centre – African Medical and Research Foundation (AMREF) – Sekou Toure Hospital – Tanzania Essential Strategies Against AIDS (TANESA)

9.1.20 Chilengi (Kilama)-AMANET-2-Ethics

EDCTP Project Coordinator:	Roma Chilengi (Wenceslaus Kilama) (African Malaria Network Trust, Tanzania)
EDCTP Call Title:	Support for Courses and Seminars on Ethics
EDCTP Project Title:	Continuation and expansion of the web based learning platform to more courses
EDCTP Project Code:	CB.2007.41300.001
EDCTP Project Start Date:	25 February 2008
EDCTP Project End Date:	24 February 2009
Collaborators:	• Joyce Ikingura (Tanzania) • Joseph Mfutso-Bengo (Malawi) • Paul Ndebele (Malawi) • Edephonse Nfuka (Tanzania) • Godfrey Tangwa (Cameroon) • Paulina Tindana (Ghana) • Aceme Nyika (Tanzania) • Ramadhani Noor Abdalla (Tanzania) • Saad Ramadhani (Tanzania) • William Mwatu (Kenya) • Djouaka Rousseau (Benin)
Type of Project:	Support for courses on ethics
Goal:	This one year project was funded to carry forward work from the previous grant that supported creation of a web based Health Research Ethics (HRE) course at the African Malaria Network Trust (AMANET).
Objectives:	The project supported continuation of the basic HRE course; creation of a French version of the basic HRE course, an Advanced HRE course; and a Good Clinical Practices (GCP) course. The other key expected outcomes of this new effort include the following: 1. Improved delivery of the web based course with new features 2. Increased francophone Africa participation on the basic course 3. Further training for individuals interested in higher understanding of research ethics 4. Using the web learning to deliver GCP training.
Cofunders:	African Malaria Network Trust (AMANET, Tanzania)
Status:	Completed
Results and Outcomes:	1. Training (resources developed (e.g. manuals) and human capacity developed) – A new platform licence was procured. The basic HRE course was successfully translated into French. The web-based GCP course was released. Advanced HRE course was designed.
Publications:	1. Chilengi, R., Nyika, A., Tangwa, G. B., Noor, R. A., Ramadhani, S. W., Bosomprah, S., & Kilama, W. L. (2013). Role of e-learning in teaching health research ethics and Good Clinical Practice in Africa and beyond. Cambridge Quarterly of Healthcare Ethics, 22, 110-119.

9.1.21 Massaga -TANHER-Ethics

EDCTP Project Coordinator:	Julius J. Massaga (National Institute for Medical Research (NIMR), Tanzania)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening ethical standards and practices in the protection of participants in health research in Tanzania
EDCTP Project Code:	CB.2007.41302.005
EDCTP Project Start Date:	16 September 2008
EDCTP Project End Date:	15 March 2010
Collaborators:	• Andrew Kitua (Tanzania) • Mwele Malecela (Tanzania) • Leonard Mboera (Tanzania)
Type of Project:	National Ethics Committee
Goal:	The Tanzania Health Research Forum (TANHER-Forum) was established in 1999 as a body corporate of partner institutions in health research in Tanzania. The project planned to strengthen ethical conduct of health research in Tanzania.
Objectives:	The aim of the project was to strengthen ethical conduct of health research in Tanzania through the following activities: 1. Review the National Guidelines for Health Research in Tanzania developed in 2001 in order to take into account recent developments in health research including molecular biology, genomics and research on emerging diseases and clinical trials 2. Build capacity of the TANHER-Forum for improved efficiency and effectiveness by strengthening the office management through procurement of office furniture and modern office equipment (computer, network printer, photocopy machine, scanner with advanced document feeder), for facilitating storage and retrieval of information 3. Develop national guidelines for insurance and compensation of research participants involved in clinical trials 4. Organise a stakeholders meeting to disseminate the revised guidelines, SOPs and guidelines on insurance and compensation of clinical trials research participants.
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – Office furniture (two tables and two office chairs), cabinets (two units), desktop computers (two units), laptop (one unit), printer (one unit), photocopier (one unit), scanner with advanced document feeder (one unit) and UPS (two units) were purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed) – Stakeholder's workshop (10 September 2008); stakeholder's meeting to discuss insurance of clinical trials participants in Tanzania (08 June 2010; 29 participants); workshop to develop proposal on reduction of maternal and new-born mortality in Tanzania (August 2010); and a symposium on research ethics in clinical studies in sub-Saharan Africa (05-07 April 2011) were held. The National Guidelines on ethics for health research in Tanzania (2nd version, 2009) was revised. Standard Operating Procedures for the National Ethics Review Committee in Tanzania

	(www.nimr.or.tz/ethical_guidelines.html) were developed. Guidelines on Insurance of Clinical Trial Participants were developed.

9.1.22 Onapa-UNCST-Ethics

EDCTP Project Coordinator:	Maxwell Otim Onapa (Uganda National Council for Science and Technology, Uganda)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening the national scientific and ethical review system and process in Uganda
EDCTP Project Code:	CB.2007.41302.007
EDCTP Project Start Date:	5 September 2008
EDCTP Project End Date:	4 September 2011
Collaborators:	• Julius Ecuru (Uganda) • Leah Nawegulo (Uganda) • Jane Nabuto (Uganda) • Winfred Badanga (Uganda)
Type of Project:	National Ethics COmmittee
Goal:	The goal of this project is to strengthen the National Scientific and Ethical Review System and process in Uganda through improving the efficiency, effectiveness and coordination of the national system for scientific and ethical review of research protocols.
Objectives:	1. To ensure that a minimum standard is applied for post-approval monitoring of research 2. To develop the accreditation standards for all institutional review/ethics committees (IRCs) based on the existing national and international human subject's protection guidelines 3. To develop standard operating procedures (SOPs) for the National AIDS/HIV Research committee (NARC) in Uganda 4. To establish a network of IRC chairpersons for an improved coordination of the ethical review system in Uganda 5. To organise and launch the First Annual Research Ethics Conference. 6. To improve the infrastructure for the NARC and Health Sciences Committee.
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – The following equipment was purchased: one desktop computer and accessories, two laptops, one LCD projector, one scanner, one printer, one paper shredder, two office tables and two office chairs. 2. Training (resources developed (e.g. manuals) and human capacity developed). – Foundational Research Ethics Training course was launched at the first ANREC. Organised and hosted the Annual Research Ethics Conference (ANREC) (15-17 July 2009; 14-16 July 2010 and 13-15 July 2011). SOPs for the National HIV/AIDS Research Committee (NARC), a committee of the Uganda National Council for Science and Technology, were developed and approved. Educational materials in research ethics were developed (training manual). A network of IRC Chairpersons in Uganda was established. 3. Networking/collaborations developed – Uganda Virus Research Institute (UVRI) – Makerere University – Gulu University

	– Lacor Hospital – Mbarara University of Science and Technology – Mbale Regional Hospital – Vector Control Division, Ministry of Health – Mildmay Uganda – The AIDS Support Organization (TASO) – Joint Clinical Research Centre (JCRC) – Mengo Hospital

9.1.23 Mason-BRTI-Ethics

EDCTP Project Coordinator:	Peter Mason (Biomedical Research and Training Institute (BRTI), Zimbabwe)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Establishing an Ethics Research Unit
EDCTP Project Code:	CB.2007.41302.008
EDCTP Project Start Date:	24 July 2008
EDCTP Project End Date:	30 September 2009
Collaborators:	• Jens Mielke (Zimbabwe)
Type of Project:	Institutional Review Board
Goal:	The conduct of ethical review of human subject's research in Zimbabwe is constrained by the limited facilities and human resources available to conduct an efficient review process. Improved training and information dissemination are needed to imrove this situation.
Objectives:	1. Provide administrative support to the BRTI-IRB 2. Provide a forum for discussion on ethical review problems in Zimbabwe 3. Produce a booklet with relevant case studies to use in training IRB and ERC members and researchers in Zimbabwe 4. Improve information dissemination through an online newsletter that discusses ethical issues in research.
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – A fully fledged and standalone unit was established within the BRTI. Wireless connectivity to the internet, computers, printers and office furniture were purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed) – Publication of an ethics handbook and ARENA newsletter. Workshop on 'ethical issues in health research in Africa' (23 March 2009; 43 participants) and an ethics training course (24-27 March 2009; 21 participants) were held.

9.1.24 Khulumani -Botswana-Ethics

EDCTP Project Coordinator:	Pilate Khulumani (Ministry of Health, Botswana)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening of the Botswana IRB, and establishment of Health Institutions and Health Districts Ethics Committees
EDCTP Project Code:	CB.2008.41302.012
EDCTP Project Start Date:	23 February 2010
EDCTP Project End Date:	22 February 2013
Collaborators:	• David Guwatudde (Uganda) • Keymanthri Moodley (South Africa) • Paul Ndebele (United States of America)
Type of Project:	National Ethics Committee, Institutional Review Board
Goal:	The goal of this project was to strengthen the capacity of Botswana's National Research Ethics Committee (BNREC) through training its members in general ethics principles, structure of good clinical practice and new developments in biomedical research associated with ethical review of clinical trials in order to empower members with the knowledge and skills necessary to carry out their mandate. The project was also meant to assist in training BNREC members to audit and monitor clinical trials at all stages and to develop a well documented system. Community Advisory Boards (CABs) were set up as part of this project to sensitise communities in Botswana about health research, especially clinical trials conducted in their communities. This project aimed to target the multinational organisations that conduct clinical trials in Botswana e.g. The Botswana Harvard Partnership, The Botswana-USA (BOTUSA) collaboration, Baylor Children's Centre of Excellence that deals with antiretroviral treatment in children, The University of Pennsylvania, The University of John Hopkins, The University Research, CIET, University of Botswana and many other research organisations that are based in Botswana. A strong IRB will assist in reducing delays encountered in clearing clinical trial proposals submitted by the above organisations. In addition, strengthening the IRB will build human resource capacity and improve research ethics standards.
Status:	Completed
Objectives:	1. Strengthen the Botswana National Research Ethics Committee (NREC) and establish Institutional Review Boards (IRBs) 2. Sensitise and increase awareness in communities on the values of clinical trials and the ethical conduct of relevant research in their communities as well as the obligation of investigators to protect the rights, safety and welfare of research participants and communities 3. Establish IRBs in all health training institutions and districts in Botswana 4. Train ethics committee members in the ethical and scientific review of research proposals as well as auditing and monitoring of approved studies, especially clinical trials 5. Develop review guidelines, Standard Operational Procedures (SOPs) and Clinical Trial Guidelines 6. Improve office infrastructure through purchasing

	equipment and stationery.
Results and Outcomes:	7. Infrastructure/capacity development - One laptop, one heavy duty photocopier, one camera, one printer, four filing cabinets and one shredder were purchased. 8. Training (resources developed (e.g. manuals) and human capacity developed) - Two seminars on research ethics were held in collaboration with the University of Pennsylvania and University of Botswana (16-17 September 2010; 22 participants) and (8-9 December 2010; 22 participants). Clinical trials training took place (8-9 June 2010; 27 participants). Three Community Advisory Board workshops took place (23-24 September 2010; 21 participants); (23-24 February 2010; 22 participants) and (28 March 2011; 24 participants). Three workshops for NREC members and one audit training took place (12-13 December 2011; 14 participants). CABs were established in three districts. A CAB workshop took place (9 November 2011; 18 participants). Five out of seven Institutes of Health Sciences have established their own ethics committee. Review guidelines and SOPs were developed. Members from Serowe Institute of Health Sciences (28-29 November 2011; 30 participants), Sekgoma Memorial Hospital, Kanye Seventh Day Adventist School of Nursing (22-23 November 2011; 29 participants) and Serowe College of Education received training. Application forms, consent forms and a review checklist were developed for students' research. Two IRBs received training: Letsholathebe Memorial Hospital (21-22 February 2012; 17 participants) and Nyangabwe Referral Hospital. Three members from the secretariat and one IRB member visited South Africa on a bench marking exercise (13–17 March 2012). One member of staff from the Health Research and Development Division completed a two week short course on ethics at Stellenbosch University (11-22 February 2013). Training of Deborah Retief Memorial Hospital-School of Nursing IRB on ethics in health research was conducted in Mochudi (25-26 June 2012; 22 participants). Two CABs were established and trained in Kanye (Southern District) (13-14 September 2012; 20 participants) and Serowe (Central District) (18-19 September 2012; 13 participants). Members from the IRB and BNREC (Botswana National Research Ethics Committee) completed the online Collaborative Institutional Training Initiative (CITI) programme. 9. Networking/collaborations developed – University of Pennsylvania – University of Botswana – University of Stellenbosch – Botswana Harvard Partnership – Harvard School of Public Health – Boehringer-Ingelhiem – Makerere University – Baylor College of Medicine – Mapping African Research Ethics and Drug Regulatory Capacity (MARC) – Council for Scientific and Industrial Research (CSIR)

	(South Africa) – University of Limpopo-MEDUNSA Campus (South Africa) – Human Science Research Council (HSRC) (South Africa) – National Health Research Ethics Council (NHREC) (South Africa)
Publications:	1. Barchi, F. H., Kasimatis-Singleton, M., Kasule, M., Khulumani, P., & Merz, J. F. (2013). Building research capacity in Botswana: A randomized trial comparing training methodologies in the Botswana ethics training initiative. *BMC Medical Education*, 13:14. http://www.biomedcentral.com/1472-6920/13/14

9.1.25 Mupenda-CIBAF-Mzadi-Ethics

EDCTP Project Coordinator:	Bavon Mupenda (Centre Interdisciplinaire de Bioéthique pour L'Afrique Francophone (CIBAF), Democratic Republic of Congo)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	The Mzadi project: Strengthening research ethics capacity in the Republic of Congo-Brazzaville and the Democratic Republic of Congo
EDCTP Project Code:	CB.2008.41302.014
EDCTP Project Start Date:	18 December 2009
EDCTP Project End Date:	17 December 2010
Collaborators:	• Stephane Leyens (Belgium) • Jean-Vivien Mombouli (Congo Brazzaville) • Félicien Munday (Democratic Republic of Congo) • Stuart Rennie (United States)
Type of Project:	Institutional Review Board
Goal:	The primary aim of this project was to strengthen the capacity of the ethics committee at Marien Ngouabi University, enabling the latter to conduct high quality ethical review of submitted scientific protocols.
Objectives:	1. Establish sustainable, mutually supportive relationships between the research ethics committees of Marien Ngouabi University (Brazzaville, Republic of Congo) and the Kinshasa School of Public Health (Kinshasa, Democratic Republic of Congo) 2. Increase the capacity of ethics committee members at both institutions to contribute to policy formation regarding research ethics in their respective countries 3. Enhance the culture of research ethics at both institutions through south-to-south educational activities among key stakeholders in the health research enterprise.
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – Desks and tables (four in total), one laptop and one inkjet printer were purchased. 2. 2. Training (resources developed (e.g. manuals) and human capacity developed) – SOPs were finalised, national guidelines were developed and a researcher's brochure were developed. A webpage on the existing website was created to assist researchers with the ethical review process. A two day guideline development workshop was held. Four research ethics seminars and workshops at both Brazzaville and Kinshasa, which targeted different populations, were conducted. Research ethics invited seminars involved a restricted group (15 participants and three technical assistants) of experienced researchers, clinicians, nurses and university administrators involved in biomedical research. 3. Networking/collaborations developed – Marien Ngouabi University – Kinshasa School of Public Health – University of North Carolina–Chapel Hill – University of Namur (Belgium)

9.1.26 Okitolonda-CIBAF-Palabre-Ethics

EDCTP Project Coordinator:	Emile Okitolonda Wemakoy (Centre Interdisciplinaire de Bioéthique pour L'Afrique Francophone (CIBAF), Democratic Republic of Congo)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	The Palabre project: Developing national research ethics guidelines for the Democratic Republic of Congo
EDCTP Project Code:	CB.2008.41302.025
EDCTP Project Start Date:	16 February 2010
EDCTP Project End Date:	15 February 2011
Collaborators:	• Guillaume Louis Kiyombo (Democratic Republic of Congo) • Mampunza Ma Miezi (Democratic Republic of Congo) • Stuart Rennie (United States)
Type of Project:	National Ethics Commitee
Goal:	This project aimed at strengthening the capacity of the National Health Ethics Council (NHEC) and developing national ethics guidelines.
Objectives:	1. Strengthening the capacity of the National Health Ethics Council. Activities in support of this aim included: – Formation of an ethics working group, including the Centre Interdisciplinaire de Bioéthique pour l'Afrique Francophone (CIBAF) members and members of the National Health Ethics Council – Training members from the National Health Ethics Council who have not had formal research ethics education, including extensive review of other national research ethics guidelines – Drafting of Standard Operating Procedures (SOPs) for the Council, and finalising its constitution and mandate. 2. Developing national ethics guidelines for biomedical and public health research. Activities in support of this aim include: – Drafting of national guidelines for medical and public health research in the Democratic Republic of Congo – Holding public panel discussions regarding the national ethics guidelines, and incorporating feedback into the final version – Dissemination of guidelines on the Democratic Republic of Congo – Ministry of Health website and publishing summaries of the guidelines in the national press.
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – Two laptops, four desks/ tables and one printer were purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed) – SOPs were developed. National guidelines for medical and public health research in the Democratic Republic of the Congo were drafted. Members of the National Health Ethics Council received training (11 participants). A National Research Ethics Guidance workshop was organised inviting participants from the following groups and institutions: members of research ethics committees; local stakeholders in the health research enterprise (representatives from the Ministry of Health, members of the National AIDS and TB Control Boards,

	principal investigators of local research projects, hospital and clinic directors, local health-related NGOs, local human rights organisations, pharmaceutical company representatives); interested members from the general public, including participants from the 11 provinces that compose the DRC. 3. Networking/collaborations developed – Human African Trypanosomiasis Platform

9.1.27 Boateng-NMIMR-Ethics

EDCTP Project Coordinator:	Okyere Boateng (University of Ghana)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Establishment of National Research Ethics Committee and strengthening of newly established IRBs and RECs in Ghana
EDCTP Project Code:	CB.2008.41302.016
EDCTP Project Start Date:	18 December 2009
EDCTP Project End Date:	31 March 2011
Collaborators:	• Isaac Adams (Ghana) • John Gyapong (Ghana) • Paulina Tindana (Ghana) • Abraham Hodgson (Ghana)
Type of Project:	National Ethics Committee, Institutional Review Board
Goal:	The project was put forward to address some ethical concerns related to the general research ethics environment in the country. Research proposals intending to use human subjects as participants have to undergo ethical review to address issues concerning the protection and welfare of the research participants. As such it is necessary to ensure that reviewers have the requisite skills and knowledge to help in the review of proposals.
Objectives:	1. Enhance the quality of the scientific and ethical review of proposals/protocols involving human subject/participants by ethical review committees through capacity building 2. Develop National Ethical Guidelines in the conduct of research involving human subjects 3. Establish a database for Institutional Review Boards (IRB)/Research Ethics Committees (RECs) in the country 4. Promote networking and sharing of ideas among IRB/REC and researchers 5. Resource IRBs/RECs that were not covered by the earlier grant from EDCTP by providing them with office equipment.
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – Four computers, four printers, four cabinets and five shredders were purchased. The target institutions for the supply of equipment were: – The University of Ghana Medical School (UGMS) Ethics and Protocol Review Committee – The Centre for Scientific Research into Plant Medicine (CSRPM) Institutional Review Board – The University of Development Studies (UDS) Institutional Review Board – The Secretariat, National Health Research Ethics Board – Noguchi Memorial Institute for Medical Research 2. Training (resources developed (e.g. manuals) and human capacity developed) – A two day Health Research Ethics seminar was held (17-18 November 2010; 36 participants) for researchers, IRB members and lecturers. The training and mentoring of IRB administrators from the eight IRBs took place throughout the programme/period. A two day National Research Ethics Review Conference for Stakeholders was held on 08 and 09 March 2011. National Research Ethics Guidelines drafted. New IRBs have received training and

	guidelines in developing their SOPs. In the process, already established IRBs reviewed their SOPs. Establishment of a Secretariat to work towards establishment of the National Health Research Ethics Board. Improved databases for the IRBs 3. Networking/collaborations developed – African Malaria Network Trust (AMANET) – Kenya Medical Research Institute (KEMRI) – Networking among the local IRBs

9.1.28 Wasunna-KEMRI-Ethics

EDCTP Project Coordinator:	Christine Wasunna (Kenya Medical Research Institute (KEMRI), Kenya)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening capacity for ethics review and monitoring of approved projects at the Kenya Medical Research Institute
EDCTP Project Code:	CB.2008.41302.024
EDCTP Project Start Date:	18 December 2009
EDCTP Project End Date:	31 May 2012
Collaborators:	• Juma Rashid (Kenya) • Jayesh Pandit (Kenya)
Type of Project:	Institutional Review Board
Goal:	The project aims to build capacity for ethics review and monitoring of Kenya Medical Research Institute's (KEMRI)-approved studies and strengthen research oversight through partnership with the Pharmacy and Poisons Boards' Expert Committee on Clinical Trials (PPB ECCT). The proposed activities are considered critical in enhancing adoption of internationally accepted ethics review standards at KEMRI and to heighten monitoring of new and existing drugs for spontaneous adverse drug reaction. The goal of the project is to strengthen research ethics capacity and provide a framework auditing research approved by the KEMRI ERC and PPB ECCT. The KEMRI ERC currently serves as the national ethics review board. They propose, within one year, to train members at KEMRI/National Ethics Review Committee (KEMRI NERC) and PPB ECCT, in Good Clinical Practices (GCP) and research monitoring through KEMRI's Centre for Clinical Research (CCR). The core activities in year two include establishing a research audit package and initiating a joint electronic clinical trials database between the two institutions.
Objectives:	1. Improve the ethical review process at KEMRI through: – Training KEMRI ERC members in international health research ethics – Facilitating health research ethics workshops for researchers at KEMRI and PPB twice a year 2. Develop a system for auditing research approved for implementation by the KEMRI ERC in order to provide important research safeguards by: – Facilitating three clinical research monitoring and GCP workshops (three workshops) for site auditors (senior research officers selected from three KEMRI Research Centres in Nairobi, Kisumu and Kilifi); KEMRI ERC and PPB ECCT members – Developing an auditing checklist for project initiation, interim project evaluation and project completion 3. Promote high standards of clinical research oversight through partnership with the Pharmacy and Poisons Board of Kenya by: – Launching a database on all clinical trials in Kenya – Promoting pharmacovigilance through adverse drug reaction reporting within the study sites.
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development - KEMRI ethics review committee received one laptop, one projector and one desktop computer. Pharmacy and

	Poison's Board received: one multipurpose unit comprising a printer, photocopier and scanner; and one desktop computer. 2. Training (resources developed (e.g. manuals) and human capacity developed) - One KEMRI staff member completed a BSc degree in Computer Information Systems at Kenya Methodist University. An electronic submission and review system for clinical trials applications has been developed and implemented at the Pharmacy and Poisons Board (PPB) (www.ctr.pharmacyboardkenya.org). The adverse drug reporting (ADR) system has been reinforced and two tools (Suspected Adverse Drug Reaction Reporting Form and Form for Reporting Poor Quality Medicinal Products) have been developed and promulgated nationally. A Standard Operating Procedure for Routine Monitoring Visits was developed. The following training took place: – Refresher Good Clinical Practice (GCP) and Good Clinical Laboratory Practice (GCLP) (59 participants; 5 July 2010) – Clinical research monitoring (module one) (21 participants; 12-16 July 2010) – Clinical research monitoring (module one: back to basics) (14 participants; 22-26 November 2010) – Clinical research monitoring (module two) (12 participants; 21-25 February 2011) – Clinical research monitoring (modules three and four) (20 participants; 14-17 February 2012 and 20-23 February 2012) – Good Clinical Practice (GCP) and Good Clinical Laboratory Practice (GCLP) (32 participants; 16-18 November 2010) – GCP and essentials of informed consent (18 participants; 28-30 November 2011) – Ethical issues in social science and behavioural studies (17 participants; 30 August 2010) – Genetic and genomic research and data sharing (8 participants; 18 February 2011). 3. Networking/collaborations developed – Pharmacy and Poison's Board (PPB) – Aga Khan University Teaching Hospital – University of Nairobi – Kenyatta National Hospital – Centres for International Programs-Kenya (ICAP-Kenya) – Centre for Research in Therapeutic Sciences (CREATES), Strathmore University, Kenya – National Council for Science and Technology (Kenya) – Consortium for National Health Research (CNHR)

9.1.29 Fumane-Mozambique-Ethics

EDCTP Project Coordinator:	João Manuel de Carvalho Fumane (Ministry of Health/National Institute of Health, Mozambique)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Consolidation of a National Ethic Committees Network in Mozambique by promoting training collaboration with African and European networks
EDCTP Project Code:	CB.2008.41302.019
EDCTP Project Start Date:	16 February 2010
EDCTP Project End Date:	15 February 2012
Collaborators:	• Xavier Carne (Spain) • Raquel Hernandez (Spain) • Nuria Sanz (Spain)
Type of Project:	National Ethics Committee, Institutional Review Board
Goal:	The Mozambican National Ethic Committee, called CNBS (Comité Nacional de Bioéticapara Saúde), was created in 2002. The CNBS coordinated the proposed activities, which consisted of the establishment of a national networking of ethic committees in Mozambique and on strengthening the collaboration with a similar institution in Europe.
Objectives:	To accomplish the goal of the project, training was addressed to members of the existing ethic committees in Mozambique (CNBS and Institutional) and to researchers, other health professionals, health authorities and students from the medical school. The expected outcome of the project was to increase the ethical judgment of ethic committees' members in the view that the Mozambican population should benefit from the relevant research that takes place in their country. On a first step of the training process, the CNBS and IEC members received African Malaria Network Trust (AMANET) and European Clinical Research Infrastructures Network (ECRIN)/Vienna School of Clinical Research (VSCR) training and exchanged capacity building expertise with ECRIN. And on a second step, already trained CNBS and IEC members trained researchers, health professionals, health authorities and medical school students. The second objective was to create a network of Mozambican Institutional Ethics Committees (IECs).
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – One computer, one photocopy machine and two cupboards were purchased. A CNBS protocol database was developed and all protocols were uploaded. 2. Training (resources developed (e.g. manuals) and human capacity developed) – Training on "Ethics committees and clinical trials performed in developing countries" took place in Maputo (29-31 March 2010; 30 participants) – Training on "Regulation for the Institutional Ethics Committees (IEC)" was conducted (24-26 August 2010; 25 participants) – Site visit to ECRIN (European Clinical Research Infrastructures Network: www.ecrin.org), Barcelona, took place (20-24 September 2010) by three members of the CNBS – Training was carried out by the Vienna School for Clinical Research (VSCR) on 22-24 November 2010 in Vienna.

	The topic of the course was "Ethical aspects of clinical research". One member of the CNBS attended the training – Training on "Institutional Review Boards" was conducted in Maputo (25-27 July 2011; 19 participants) – Training on "The use of biological samples" took place in Maputo (19 December 2011; 20 participants) – Training on "The Institutional Review Board in University of Lurio" took place (22-23 April 2012; 17 participants) – In order to standardise procedures for accrediting local institutional ethics committees (IEC), the CNBS has developed rules for IECs. 3. Networking/collaborations developed – Hospital Clinic de Barcelona (Spain) – European Clinical Research Infrastructures Network (ECRIN) – Vienna School for Clinical Research (VSCR) – African Malaria Network Trust (AMANET) – IRB of Catholic University – IRB of National Institute of Health – IRB of Manhiça Health Research Centre – IRB of University of Lurio – IRB of Institute for Health Science

9.1.30 Ukpong-NHVMS-Ethics

EDCTP Project Coordinator:	Morenike Oluwatoyin Folayan Ukpong (New HIV Vaccine and Microbicide Advocacy Society (NHVMAS), Nigeria)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Building capacity of laypersons on IRBs to review research protocols and provide constructive feedback
EDCTP Project Code:	CB.2008.41302.013
EDCTP Project Start Date:	18 January 2010
EDCTP Project End Date:	17 January 2011
Collaborators:	• Bayo Adejumo (Nigeria) • Olayide Akanni (Nigeria) • O Dada (Nigeria) • Bode-Law Faleyimu (Nigeria)
Type of Project:	Support for courses on ethics
Goal:	This project was a proposed follow up to an earlier pilot project with grant support from SIDACTION, France. This project was part of a well thought out systematic capacity building effort for members of IRB institutions in Nigeria. NHVMAS piloted a novel programme to build the capacity of laypersons on IRBs in Nigeria. This was the first ever effort in the country. The initiative was applauded by the National Ethics Board and the Institutional Review Boards from where the trainees came. Laypersons are a subset of community persons who are research gatekeepers for the community. In Nigeria all ethics committees are expected to have at least one layperson on the committee. They are expected not only to address the rights of research participants, but also to address the peculiar needs of their communities. While the role of community oversight is specific to the layperson, for many the capacity to play this role is defective as many are not trained to engage with the research process. This project was specifically designed to address this gap.
Objectives:	1. Provide 20 lay members of the Health Research Ethics Committees in Nigeria with state of the art training on ethical considerations in HIV/AIDS related research over eight months 2. Familiarise 20 lay members of Ethics Committees in Nigeria with the operational guidelines for conducting ethical research in Nigeria over a period of eight months 3. Familiarise 20 lay members of Ethics Committees in Nigeria with the specific issues and principles of design and implementation of HIV prevention and treatment research 4. Enhance the skills of 20 lay Ethics Committee members on reviewing research protocols and providing constructive feedback to those applying for ethical clearance over a period of eight months.
Status:	Completed
Results and Outcomes:	1. Training (resources developed (e.g. manuals) and human capacity developed) – Training manual was developed, printed and distributed. Workshop on how to review a research protocol and provide constructive feedback was conducted – 33 participants were trained. 2. Networking/collaborations developed – National Health Research Ethics Committee – National Bioethics Society of Nigeria

Publications:	3. Folayan, M. O., Adaranijo, A., Durueke, F., Ajuwon, A., Adejumo, A., Ezechi, O., Oyedeji, K., & Akanni, O. Impact of three years training on operations capacities of research ethics committees in Nigeria. *Developing World Bioethics*. 2012 Sep 24. doi: 10.1111/j.1471-8847.2012.00340.x

9.1.31 Sarr-CNRS-Ethics

EDCTP Project Coordinator:	Samba Cor Sarr (Conseil National pour la Recherche en Sante-(CNRS), Senegal)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Programme for strengthening National Research Ethic Committee of Senegal (CNRS) and promoting ethics awareness in Senegal and in West Africa
EDCTP Project Code:	CB.2008.41302.026
EDCTP Project Start Date:	2 December 2009
EDCTP Project End Date:	1 December 2011
Collaborators:	• Charles Becker (Senegal) • Aïssatou Toure (Senegal)
Type of Project:	National Ethics Committee
Goal:	The expected outcomes of this project were the optimisation of the functioning and progressive strengthening of human resources for all the processes of ethic review and follow up of research protocols.
Objectives:	1. The broad objective of the project was to develop the capacity of members of the CNRS for providing competent review of research projects, monitoring the implementation of the projects, and serve as trained trainers. Specific objectives: 2. Improve the human resources of the CNRS Secretariat 3. Improve the infrastructure of the CNRS Secretariat 4. Train the different stakeholders in research ethics: ethic committee 5. members and researchers 6. Improve the review process of health research proposals 7. Establish a tracking system for research proposals 8. Create a website for adequate information for all the stakeholders, awareness and discussion on ethics issues.
Cofunders:	• United Nations Children's Fund (UNICEF) • Council on Health Research for Development (COHRED)
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – Two computers, one laptop, two printers and one video projector were purchased. Literature on ethics and law was purchased for the library. A website was created: http://www.der.sn/ A database was created in order to facilitate the access to information about the protocols examined by the CNERS. 2. Training (resources developed (e.g. manuals) and human capacity developed) – Seventeen participants attended the training and discussion on the SOPs; 21 participants attended the workshop on health research management; and 40 participants attended the workshop on the sharing of health research results. Workshops for conception and validation of working documents as well as writing draft of legal texts on ethics of health research were held. Meetings to review protocols and support experts were held. Five visits to oversee on-going projects in the field were done. The working group produced and harmonised the SOPs. 3. Networking/collaborations developed – Training and Resources in Research Ethics Evaluation for

	Africa (TRREE) – Council on Health Research for Development (COHRED) – The New Partnership for Africa's Development (NEPAD) – West African Health Organisation (WAHO)

9.1.32 Wassenaar-SARECCER-Ethics

EDCTP Project Coordinator:	Douglas Wassenaar (University of KwaZulu-Natal, South Africa)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening African Research Ethics Committees' capacity for ethical review of HIV prevention research
EDCTP Project Code:	CB.2008.41302.002
EDCTP Project Start Date:	16 November 2009
EDCTP Project End Date:	15 November 2012
Collaborators:	• Mariana Kruger (South Africa) • Catherine Slack (South Africa)
Type of Project:	Support for courses on ethics
Goal:	The Ethics, Law and Human Rights Centre of the WHO/UNAIDS African AIDS Vaccine Programme sponsored by EDCTP funded five African REC members per year to attend two existing and well established SARETI intensive training modules developed and hosted by the South African Research Ethics Training Initiative (SARETI) at the University of KwaZulu-Natal, South Africa. The module content includes institutionalising ethical review of health research and ethical issues in HIV preventative research. The SARETI modules have been taught since 2002 and are run by experts in the topic areas. Each module is formally examined by way of written assignment and formally evaluated by attendees.
Objectives:	The overall objective of the training programme is to strengthen African RECs functioning and capacity to review HIV prevention research. The training programme aims to provide African REC members with advanced theoretical and practical knowledge in the ethical review of complex protocols like HIV prevention trials, and to help institutionalise research ethics review in their home institution.
Status:	Completed
Results and Outcomes:	1. Training (resources developed (e.g. manuals) and human capacity developed) – In 2010, five participants (from Tanzania, Botswana, Liberia, Egypt and Nigeria) completed Module one ('institutionalising ethical review of health research': 6–10 September 2010) and Module two ('ethical issues in HIV preventative research': 13–17 September 2010). In 2011, five African REC members (from Ethiopia, Ghana, Kenya, Nigeria and Zimbabwe) were selected to attend two SARETI modules on 'institutionalising ethical review of health research' (12–16 September 2011) and 'ethical issues in HIV preventative research' (5–9 September 2011). In 2012, five African REC members (from Kenya, Mauritius, Senegal and Tanzania) were selected to attend two SARETI modules on 'institutionalising ethical review of health research' (10-14 September 2012) and 'ethical issues in HIV preventative research' (17-21 September 2012). 2. Networking/collaborations developed – South African National Health Research Ethics Council – Human Sciences Research Council Research Ethics Committee – University of Stellenbosch – Training and Resources in Research Ethics Evaluation for Africa (TRREE)

	– Mapping African Research Ethics and Drug Regulatory Capacity (MARC) – NIH/Fogarty's Medical Education Partnership Initiative (MEPI)
Publications:	1. Kombe, F., Anunobi, E. N., Tshifugula, N. P., Wassenaar, D., Njadingwe, D., Mwalukore, S., Chinyama, J., Randrianasolo, B., Akindeh, P., Dlamini, P. S., Ramiandrisoa, F. N., & Ranaivo, N. (2013). Promoting research integrity in Africa: An African voice of concern on research misconduct and the way forward. *Developing World Bioethics*, 1471-8731.

9.1.33 IJsselmuiden-MARC-Ethics

EDCTP Project Coordinator:	Carel IJsselmuiden (Council on Health Research for Development (COHRED), Switzerland)
EDCTP Call Title:	Support for Courses and Seminars on Ethics
EDCTP Project Title:	Mapping of ethics review and trial regulatory capacity in sub-Sahara Africa
EDCTP Project Code:	CB.2008.41303.001
EDCTP Project Start Date:	19 December 2008
EDCTP Project End Date:	30 June 2012
Collaborators:	Douglas Wassenaar (South Africa)
Type of Project:	Coordination function
Goal:	The MARC (Mapping African Research Ethics and Drug Regulatory Capacity) project aims to develop a map of the capacity to ethically review health research in all African countries where EDTCP operates.
Objectives:	The core deliverables of this project are: 1. A continuously updated ('self-updating'), systematic map of African health research ethics review committees (HRECs) and clinical trial related regulatory activities that are linked to general health research system information of the countries where the ethics committees are located, and is integrated into a global map of health research systems and, where possible, linked with other web-based resources in health research ethics 2. Comprehensive regular reporting on health research ethics activities (capacity programmes and regulatory situation) in sub-Saharan Africa 3. Networking of African regional ethics training initiatives and active HRECs through Health Research Web (HRWeb) and developing the content and display of HREC information in ways that suit the key audiences best 4. Developing sustainability and capacity, in specific: 5. Agreement on criteria for research ethics committee registration on HRWeb 6. Support from donors and research sponsors to demand review by registered research ethics committees 7. Mechanisms for 'self-funding', additional donors in place 8. Beginnings of a pan African accreditation mechanism
Cofunders:	• NIH/Fogarty International Center (United States) • Pfizer (United States)
Status:	Completed
Results and Outcomes:	**Mapping** • One hundred and sixty-six (166) HRECs were identified to be operating across Africa – with great variability in skills, membership and efficiency. The mapped information consists of (1) basic contact information; (2) capacity information which provides detailed quantitative insight into the functions, capacity, resources and needs of the respective HRECs; and (3) HREC support documents • The ethics pages of HRWeb are developed with various analysable functionalities • MARC has an independent website: www.researchethicsweb.org • MARC's platform has found rapid uptake in Latin America and the Caribbean though a collaboration with the Pan American Health Organisation (PAHO). 1008 RECs have been mapped from Latin America (data also available at:

www.researchethicsweb.org). The latter has extensively increased the MARC web strategic users, with an average of 1716 visits recorded in the past three months.

Networking
MARC has launched a research ethics social network platform accessible at www.researchethicsweb.org. The platform is intended to:

- Promote connection and interaction between trainees and staff from HRECs/IRBs in their home countries, also to encourage formation of local activity groups to find solutions to difficult and diverse research ethics questions through blogs, question/answer lists and online discussion forums
- Provide 'closed/private' forums, which enable HRECs to undertake joint review of multi-centre trials. This special feature contributes to the empowerment of less capacitated HRECs. It provides accelerated access to HREC members, ethics trainees and other resource persons active in research ethics and drug regulation
- The success of this initiative will add a new dimension to African research ethics training and capacity building initiatives. It may expand to create a virtual network of trained individuals – a pan African research ethics discussion platform.

Mapping of Medicines Regulatory Authorities (MRAs) commenced in June 2011. To date HRWeb has been adapted to include MRAs information, 16 countries (MRAs) have been mapped, and 54 African countries have been verified as having MRAs.

Meetings

- In September 2011 (26-28), MARC hosted a very successful first ever African Conference for Administrators of Research Ethics Committees (AAREC) in Botswana
- AAREC sought to facilitate a comprehensive understanding of the essential roles, establish a collaborative approach to strengthen and improve the capacity and competence of African research ethics committee administrators, hence, the theme 'striving for quality and efficiency of ethical review of health research in Africa'. A publication based on the proceedings of the AAREC meeting is in the advanced stage of preparation.

Information Management System

- MARC's and COHRED's support to research ethics review capacity in Africa includes the adaptation of the web-based platform that is global to a cloud-based software package for project management for research ethics committees. The package was launched during Forum 2012 in Cape Town under the title of 'RHInnO Ethics' (www.rhinno.net). It is expected that this will revolutionise the efficiency and impact of research ethics review in Africa and beyond
- The overall objective of the RHinnO platform is to provide governments, ethics committees, medicines regulatory authorities, research institutions and networks with a low cost, secure, fully web-based solution for managing and tracking research applications throughout the entire life-cycle of the research project
- RHinnO will provide quick, reliable and 'real-time' data,

	tables and graphs that can be used to monitor, evaluate and communicate. The MARC / HRWeb Initiative was positively noted and acknowledged in the landmark December 2011 report of the US Presidential Commission for the Study of Bioethics Issues, titled "Moral science - Protecting participants in Human Subjects Research". The report was commissioned by President Obama at the end of 2010 and was released in December 2011. (see: http://bioethics.gov/cms/sites/default/files/Moral%20Science%20-%20Final.pdf).
Publications:	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.

9.1.34 Mbidde-UVRI-Ethics

EDCTP Project Coordinator:	Edward Katongole Mbidde (Medical Research Council Programme on AIDS - Uganda Virus Research Institute (MRC/UVRI), Uganda)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening the capacity of the Uganda Virus Research Institute Science and Ethics Committee (SEC) and preparing it for WHO recognition
EDCTP Project Code:	CB.2008.41302.018
EDCTP Project Start Date:	7 February 2010
EDCTP Project End Date:	6 February 2012
Collaborators:	• Tom Lutalo (Uganda) • Robert Ssekubugu (Uganda)
Type of Project:	Imstitutional Review Board
Goal:	There was an urgent need to strengthen the current UVRI (Uganda Virus Research Institute) secretariat by designing and operationalising guidelines and Standard Operating Procedures specific to the type of research work from the partners and core departments. There was also an urgent need to put together guidelines for running the secretariat.
Objectives:	The main objective of the project was to strengthen the review capacity and process of the UVRI Science and Ethics Committee. This required continuing training of the current and potential future members, the scientific staff from the collaborating programs and core UVRI departments. The funds were used to train trainers who would continue with the training process. The funds were also used to strengthen the UVRI Secretariat so that it guides the scientific staff at the Institute on how to write and submit proposals. The process of preparing for the WHO recognition survey was also shared with the other IRBs in the country so that the review process in the country is strengthened. The following is a break-down of the process: • Equipped the science and ethics office with necessary office tools • Prepared the Standard Operating Procedures (SOPs) and regulations for the Science and Ethics Committee • Disseminated SOPs and regulations to the partner programmes • Conducted research site visits to ensure compliance, offered support supervision and continuous training • Facilitated science and ethics review meetings. • Established an IRB forum in the country and liaised with PABIN to strengthen the review process.
Cofunders:	Uganda Virus Research Institute (UVRI)
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity Development – One desktop computer, one printer, one office table, one UPS, two chairs, one scanner and five constructed filing cabinets were purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed) – SOPs were developed. A team of seven surveyors were trained. With support from this grant, the Strategic Initiative for Developing Capacity in Ethical Review (SIDCER) recognition core team trained the local surveyors on recognition/accreditation survey

	techniques. Monitoring visits by SEC members were conducted at six study sites and eight sites were visited for protocol monitoring. A workshop was held on research ethics (2-3 December 2010; 11 participants). 3. Networking/collaborations developed – Medical Research Council-Uganda (MRC) – Rakai Health Sciences Program (RHSP) – Centre for Disease Control-Uganda (CDC) – International AIDS Vaccine Initiative (IAVI) – Uganda National Council for Science and Technology (UNCST) – Joint Clinical Research Centre IRB – Mbarara University IRB – Makerere School of Public Health IRB – Mildmay Uganda

9.1.35 SPRUMONT-TRREE-2-Ethics

EDCTP Project Coordinator:	Dominique Sprumont (Health Law Institute, Switzerland)
EDCTP Call Title:	Support for Courses and Seminars on Ethics
EDCTP Project Title:	Training and Resources in Research Ethics Evaluation for Africa (TRREE for Africa): Extending to Senegal, Nigeria and Mozambique and strengthening the existing Network
EDCTP Project Code:	CB.2009.41302.005
EDCTP Project Start Date:	29 March 2010
EDCTP Project End Date:	28 March 2011
Collaborators:	• Clement Adebamowo (Nigeria) • Samba Cor Sarr (Senegal) • Aïssatou Toure (Senegal) • Eusebio Macete (Mozambique) • Peter M. Ndumbe (Cameroon) • Ogobara Doumbo (Mali) • Wenceslaus Kilama (Tanzania) • Marie Hirtle (Canada) • John R. Williams (Canada) • Marcel Tanner (Switzerland) • Dirk Lanzerath (Germany) • Marie Charlotte Bouësseau (Switzerland) • Douglas Wassenaar (South Africa) • Charles Becker (Senegal) • Dirce Guilhem (Brazil)
Type of Project:	Support for courses on ethics
Goal:	To grow after the initial phase, both in terms of content and countries involved with the programme.
Objectives:	The supported activities have firstly enabled the expansion of TRREE to new countries, namely Senegal, Nigeria and Mozambique, who will benefit from its online training programme and e-resources. Secondly, the online training programme has been made available in Portuguese in addition to the French, English and German versions that have already been developed. This will significantly increase the number of persons who will have direct access to the programme and facilitate further extension and networking in Africa. Thirdly, this new development provides the present TRREE partners with resources to update and upgrade their programmes, thereby offering sustained support to their national and local Research Ethics Committees and strengthening much needed collaboration on research ethics at national and local levels.
Cofunders:	• Swiss National Science Foundation • Institute of Health Law, University of Neuchâtel
Results and Outcomes:	1. Training (resources developed (e.g. manuals) and human capacity developed) – The online training programme (www.trree.org) was extended with four new national modules: – Senegal – Nigeria – Mozambique – Germany – There is also an additional module on informed consent. The programme has been translated into Portuguese. 2. Networking/collaborations developed – African Malaria Network Trust (AMANET) – Comité d'Ethique National de la Recherche en santé (CNRS) (Senegal)

	– European Network of Research Ethics Committees (EURECNET) – Institute of Health Law, University of Neuchâtel (Switzerland) – Manhiça Health Research Center (Mozambique) – Malaria Research & Training Center (MRTC) (Mali) – South African Research Ethics Training Initiative (SARETI) – University of Yaoundé (Cameroon) – West African Bioethics (Nigeria)
Publications:	1. Ateudjieu J., Williams, J., Hirtle, M., Baume, C., Ikingura, J., Niaré, A., & Sprumont, D. (2009). Training needs assessment in research ethics evaluation among research ethics committee members in three African countries: Cameroon, Mali And Tanzania. *Developing World Bioethics*, 10 (2), 88–98. 2. Sprumont, D. (2009). Formation de base en éthique de la recherche: Retour aux sources avec le projet TRREE. *Bioethica Forum*, 2 (2), 79-81.

9.1.36 Matsiegui-CAEN-Ethics

EDCTP Project Coordinator:	Pierre-Blaise Matsiegui (Comité National d'Éthique pour la Recherche du Gabon, Gabon)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening of the National Ethics Committee in Gabon and creation of a Central African Ethics Committee Network (CAEN)
EDCTP Project Code:	CB.2009.41302.001
EDCTP Project Start Date:	17 May 2010
EDCTP Project End Date:	16 August 2013
Collaborators:	• Sophie Bipolo (Gabon) • Adèle Sambo (Gabon) • Jean Baptiste Moussavou Kombila (Gabon) • Jaqueline Obone Mba (Gabon) • Saadou Issifou (Gabon) • Jean Paul Akue (Gabon) • Christiane Mbili (Gabon) • Véronique Niangui (Gabon) • Dafna Feinholz (France)
Type of Project:	National Ethics Committee
Goal:	A Gabonese National Ethics Committee (NEC) was established with a previous EDCTP grant. Today, the NEC is fully in charge of ethical issues related to research in Gabon (including review of study protocols) and is legally accepted by the Gabonese government. Nevertheless, further selective investment is needed to ensure the sustainability of the Gabonese NEC.
Objectives:	This project is meant to strengthen the Gabonese NEC in a sustainable way by: 1. Investing in infrastructure 2. Providing taylor-made training 3. Raising public awareness in Gabon on ethical issues in (clinical) research as well as the role and responsibilities of the NEC 4. Networking with other African NECs, especially in Central Africa for Creating a Central African Ethics Committee Network (CAEN). The overall expected outcome is a well-established Gabonese NEC working according to international standards and being accepted by and embedded in Gabonese society.
Cofunders:	• Ministry of Public Health (Gabon) • Ministry of Research and Science (Gabon) • Vienna School of Clinical Research (VSCR) (Austria)
Status:	Ongoing
Results and Outcomes:	1. Infrastructure/capacity development – Five computers, two printers, an office table and a UPS power saver were purchased. Regarding IT infrastructure, a server as well as the internet connection (parabolic reflector) has been installed in Fougamou. A second office (for receiving study protocols) has been established in Libreville. The maintenance and upgrade of the NEC's website took place: www.cner-gabon.org/cner 2. Training (resources developed (e.g. manuals) and human capacity developed) – Members of the NEC as well as representatives of the Ministry of Public Health and the Presidency of the Republic of Gabon attended a CANTAM/AMANET

	workshop on health research ethics (for Ethics Review Committees and National Regulatory Authorities) in Yaoundé, Cameroon (27 September-1 October 2010) – Two NEC members assisted with the AVAREF (WHO) meeting in September 2010 in Nairobi allowing them to exchange knowledge on vaccines and regulations with their African colleagues – In February 2011 a one-day workshop on legal aspects (writing/implementing/revising and amending laws) was held in Fougamou – From 25 to 27 May 2011 a three-day long event ('scientific days') was organised in Libreville. The first day contained an intensive training on ethics in general and ethical aspects of clinical research. More than 60 participants attended the ethics training day. The second day took place at the national broadcasting agency (RTG) and was organised as a panel discussion. The third day took place at the two main universities of the country: Université de Sciences de la Santé and Université Omar Bongo aiming at developing an ethics curriculum for both universities. An ethics curriculum will be implemented at the Université de Sciences de la Santé. The curriculum will be mandatory for students of the following subjects: medicine, philosophy, biology and law – Training of ethics committee members and regulatory authorities' representatives, offered by UNESCO via the EDCTP project on 'assistance of bioethics communities', held in Libreville (23 to 27 July 2012; 20 participants) – Internal training of the NEC's members by the President of the NEC on the human genome research question in Gabon and in Africa (6 to 7 April 2012; 13 participants) – Scientific seminar of the Moyen-Ogouée at the Albert Schweitzer Hospital (5 May 2012; 24 participants). 3. Networking/collaborations developed **National institutions:** – Ministry of Public Health – Ministry of Research and Science – Université des Sciences de la Santé (Libreville) – Université Omar Bongo (Libreville) – Medical Research Unit, Albert Schweitzer Hospital Lambaréné – International Centre of Medical Research of Franceville – Comité d'Ethique Régional Indépendant de Lambaréné – L'Union **International institutions:** – United Nations Educational, Scientific and Cultural Organization (UNESCO) – World Health Organization (WHO) – Ethics Committee of the Chantal Biya International Reference Centre for Research on HIV/AIDS Prevention and Management (CIRCB) (Cameroon) – Comitéd'Ethique de la Recherche en Sciences de la Santé (CERSSA) (Republic of Congo) – Comitéd'Éthique National de Burkina Faso (Burkina Faso) – Ethics Committee, Medical University Vienna (Austria) – Comité International de Bioéthique (France) – Faculty of Law, University of Fribourg and Neuchâtel (Switzerland)

	– Vienna School of Clinical Research (VSCR) (Austria) – National Ethics Committee of Cote d'Ivoire – Ethics Committee of Health in Benin

9.1.37 KOLLIE-Liberia-Ethics

EDCTP Project Coordinator:	James Kollie (University of Liberia)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening the capacity of UL-PIRE IRB (University of Liberia Pacific Institute for Research and Evaluation Institutional Review Board)
EDCTP Project Code:	CB.2009.41302.020
EDCTP Project Start Date:	13 April 2010
EDCTP Project End Date:	12 April 2012
Collaborators:	• Cecelia Morris (Liberia) • Robert Draper (Liberia) • Ellen George-Williams (Liberia) • Jemee Tegli (Liberia)
Type of Project:	Institutional Review Board
Goal:	The University of Liberia (UL) Institutional Review Board (IRB) was established in 2005 through a collaborative agreement between the Pacific Institute for Research and Evaluation (PIRE), based in the United States, and UL for the purpose of protecting human subjects and maintaining the conduct of scientific research in ethical standards in post-conflict, resource-constrained Liberia. This project was designed to address potential IRB-related challenges in post-conflict, resource-constrained settings like Liberia. UL-PIRE IRB is the only IRB presently operating in the country.
Objectives:	1. Increase and build the capacity of the UL-IRB 2. Introduce the UL deans, coordinators, researchers to human research ethics 3. Appraise the ethical knowledge of the UL graduate and professional programmes.
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – Two laptop computers, one desktop computer, one digital camera, one desk, two chairs and an overhead projector were purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed) – Two-day training workshop (16-17 September 2010; 50 participants) on ethics in research involving human subjects was held. 3. Networking/collaborations developed – African Malaria Network Trust (AMANET)

9.1.38 Rulisa-KUTH-Ethics

EDCTP Project Coordinator:	Stephen Rulisa (University Central Hospital of Kigali, Rwanda)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Establishment and training of an Institutional Review Board (IRB) at the Kigali University Teaching Hospital (KUTH) to strengthen the ethical review capacities in Rwanda
EDCTP Project Code:	CB.2009.41302.008
EDCTP Project Start Date:	4 May 2010
EDCTP Project End Date:	3 November 2011
Collaborators:	• Heinrich Klech (Austria) • Christiane Druml (Austria) • Pierre-Blaise Matsiegui (Gabon)
Type of Project:	Institutional Review Board
Goal:	The current ethical review system in Rwanda consists of one single National Ethics Committee (NEC) that reviews all protocols carried out in the country. In order to cope with the increasing demand, the decision has been made to change the current system and establish Institutional Review Boards (IRBs) across the country to share the workload. However, there are limited resources, which hinder a rapid realisation of this plan. The EDCTP grant therefore provided an important impetus to speed up the re-organisation of the Rwandan ethical review system.
Objectives:	The Kigali University Teaching Hospital (KUTH) was chosen to be the first Rwandan research institution where an IRB will be established. INTERACT was in charge of organising a training course on ethics and for providing access to an online course on Good Clinical Practice (GCP). The training course was combined with a train-the-trainer where candidates were instructed in training skills so that they can put together and conduct their own training sessions. Additionally, this project aimed to analyse the current Rwandan legislation, to identify necessary changes or additions and to develop a strategy to be recommended to the Competent Authority. To ensure the success of the project, an administrative office with an employee experienced in clinical research, research ethics, capacity building and with organisational skills will be responsible for six month (part-time) administrative support and coordination of the IRB (one meeting per month) and the knowledge exchange between European and African ethics committees.
Cofunders:	University Central Hospital of Kigali
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – One computer, one photocopy machine, one fax machine and one lockable cupboard were purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed) – Ethics committee members were trained on research methods (5–9 September 2011; 10 participants) and GCP training was held (15-16 September 2011; 20 participants) – Training on Human Subjects for the 3 IRBs (Centre Hospitalier Universitaire De Kigali [CHUK], Centre Hospitalier Universitaire de Butare [CHUB] and Kigali Health Institute [KHI]) were held (11-13 January 2012; 17 participants).

	3. Networking/collaborations developed – Centre Hospitalier Universitaire de Butare (CHUB) – Kigali Health Institute (KHI)

9.1.39 Mugyenyi-JCRC-Ethics

EDCTP Project Coordinator:	Peter Mugyenyi (Joint Clinical Research Centre (JCRC), Uganda)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening of the ethical review capacity of the Joint Clinical Research Centre (JCRC) IRB and collaborating IRBs in north and western Uganda
EDCTP Project Code:	CB.2009.41302.011
EDCTP Project Start Date:	17 May 2010
EDCTP Project End Date:	16 May 2012
Collaborators:	• Cissy Kityo (Uganda) • Jesse Kagimba (Uganda) • Jasper Ogwal Okeng (Uganda) • Ferrie Nangobi (Uganda)
Type of Project:	Institutional Review Board
Goal:	To enhance the capacity of the JCRC-IRB to oversee bioethical issues in human research.
Objectives:	1. Improving policies and Standard Operating Procedures (SOPs) for pre- and post-approval of research 2. Mentorship of Gulu University IRB Members 3. Facilitating and supporting education in biomedical research ethics related to research reviews. JCRC proposes to conduct an annual five day training course on Bioethics and Good Clinical Practice targeting JCRC-IRB members, networking IRBs in the country as well as researchers and other health scientists 4. IRB database. Develop a modern database where IRB members and researchers can get information on the JCRC-IRB activities and actions, on-going studies, status of submitted proposals, IRB members' names and contact details, SOPs and Terms of Reference. Networking of IRBs. JCRC-IRB Secretariat will host meetings and videoconference discussions of IRB members from collaborating and other IRBs in the country to discuss ethical issues/challenges, make recommendations on necessary policy changes and review progress of the project activities.
Cofunders:	Clinical Operationals and Health Services Research (COHRE) Training Program based at Joint Clinical Research Centre (Uganda)
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – A LCD projector, one laptop computer, one desktop computer (and accessories), one printer, one desk, one shredder, one filing cabinet and three chairs were purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed) – Two Good Clinical Practice (GCP) and Research Ethics (RE) training sessions were conducted in the first year. The first workshop targeted IRB members and researchers from within Kampala, Gulu and Mbarara IRBs (1-4 November 2010; 40 participants) – The second GCP and RE training was held in Gulu in northern Uganda, targeting IRB members and researchers (2-5 May 2011; 25 participants). At the end of the two workshops, participants received a joint GCP

	and RE certificate – A 'training of trainers (TOT)' workshop as a follow-up to the GCP and RE was held (23-24 March 2011; 25 participants). In the second year, three training workshops were conducted – A 'Good Clinical Practice and research ethics and onsite support training' for Gulu University IRB members took place (9 February 2012; 30 participants) – A two day training on 'Good Clinical Practice and research ethics training' took place (7-8 May 2012; 40 participants). Participants were drawn from EDCTP partner institutions and other IRB members from institutions within Kampala – A three day 'training of trainers' workshop took place (9-11 May 2012; 40 participants). Participants were purposively selected personnel that had been previously trained in GCP and research ethics and these included IRB members from JCRC, Gulu University and Mbarara University as well as other collaborating IRC members. SOPs for the JCRC-IRB were developed and are being used by other collaborating IRBs while they develop their own. 3. Networking/collaborations developed – Center for Social Science Research (CeSSRA), United States – Uganda National Council for Science and Technology (UNCST) – Strategic Initiative for Development of Capacity in Ethical Review (SIDCER) – Gulu University – Mbarara University of Science and Technology (MUST) – Mukono University – Mildmay Uganda – Uganda Virus Research Institute (UVRI) – Makerere University – The Aids Support Organization (TASO) – Nsambya Hospital IRB – Ndejje University – Infectious Disease Institute Uganda – Makerere University John Hopkins Collaboration (MUJHU Research Collaboration)

9.1.40 Gaie -Botswana-Ethics

EDCTP Project Coordinator:	Joseph Balatedi Radinkudikae Gaie (University of Botswana, Botswana)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening of the University of Botswana IRB and establishment of the UB Research Integrity Office
EDCTP Project Code:	CB.2010.41302.020
EDCTP Project Start Date:	21 March 2011
EDCTP Project End Date:	20 September 2013
Collaborators:	• Mike Kachedwa (Malawi) • Mary Kasule (Botswana) • Isaac Mazonde (Botswana) • Rosemary Musesengwa (Zimbabwe)
Type of Project:	Institutional Review Board
Goal:	The project aimed to ensure that studies conducted by the University of Botswana (UB) staff and students conform to internationally accepted standards. In addition, the project ensured that the UB Institutional Review Board (IRB) plays a more central role in coordinating human research and is in a better position to respond to both national and international challenges in research oversight.
Objectives:	The main objective was to strengthen UB's IRB so as to enhance its capacity in research oversight, ethical review and monitoring of research conducted by UB staff, students and affiliates. The project ultimately contributed towards the independence, competence and transparency of the UB IRB. To address this objective, the project included five components: 1. Enhancing the ethical review and monitoring of studies conducted by UB staff, students and affiliates 2. Streamlining the clearance of research and the issuing of research permits by government ministries 3. Setting up the IRB Office, including hiring an IRB assistant and purchasing relevant equipment necessary for the smooth functioning of the IRB Office 4. Developing Standard Operating Procedures for the IRB 5. Sensitising UB staff, students and affiliates in research ethics and integrity through various ways.
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – The IRB office was set up and the following equipment was purchased: one desktop computer, one printer, one laptop, one shredder and one hard drive. The post of IRB administrator was created and the position filled. 2. Training (resources developed (e.g. manuals) and human capacity developed) – SOPs and guidelines on human research were developed during the IRB Workshop (21-22 October 2011; 16 participants) – Seminar on 'fundamentals of research ethics' was held for graduate students (28 October 2011; 11 participants) – Seminar on 'informed consent in research with humans' was held for UB staff (13 September 2011; 12 participants) – Two IRB members attended a workshop in South

	Africa (4-5 August 2011) on 'fundamentals of research ethics' organised by the Tshwane University of Technology and SARIMA – Two IRB members attended the African Administrators Research Ethics Conference in Botswana (26-27 September 2011) – The University of Botswana in collaboration with the Department of Research, Science and Technology hosted a workshop on research oversight (17 September 2012; 30 participants) – Research ethics training for staff and students took place in Maun (12-13 August 2013; 31 participants) – An induction workshop for new IRB members took place (5-6 September 2013; 17 participants) – Two IRB members attended SARETI modules: a) Module on 'ethical issues in HIV preventative research' (17-21 September 2012) b) Module on 'institutionalising ethical review of health research' (10-14 September 2012). 3. Networking/collaborations developed – National Health Research Development Committee – Mapping African Research Ethics and Drug Regulatory Capacity (MARC)

9.1.41 Kaptue-Cameroon-Ethics

EDCTP Project Coordinator:	Lazare Kaptue (Cameroon National Ethics Committee (CNEC), Cameroon)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening the Cameroon National Ethics Review Committee
EDCTP Project Code:	CB.2010.41302.008
EDCTP Project Start Date:	11 April 2011
EDCTP Project End Date:	10 April 2013
Collaborators:	• Jérôme Ateudjieu (Cameroon) • Ogobara Doumbo (Mali) • Sylvie Hansel-Esteller (France) • Marceline Djuidje Ngounoue (Cameroon) • Dominique Sprumont (Switzerland) • Jonas Tchakoa (Cameroon) • Timoléon Tchuinkam (Cameroon)
Type of Project:	National Ethics Committee
Goal:	EDCTP support to the CNEC (Cameroon National Ethics Review Committee) is used to achieve CNEC's priorities expecting to sustainably improve its transparency, independency, and effectiveness during protocols evaluation and to promote the development of cooperation and communication between the CNEC local and regional committees. In addition, it will help strengthen through the CNEC collaboration with local partners, other African National Research Ethics Committees and with international partners like the TRREE for Africa project, The Volkswagen Foundation; north–south and south-south network of ethical review to contribute in ensuring the highest competence in biomedical research.
Objectives:	This project supported the CNEC in strengthening its capacity in reviewing research protocols by: 1. Updating Standard Operating Procedures (SOPs) for protocol review and monitoring, and contribute to the harmonisation of SOPs of other ethics committees in Cameroon 2. Ensuring on-going training of its members in protocol evaluation, site visits monitoring and follow-up of protocols implementation 3. Improving access to infrastructure for its activities 4. Improving the condition of protocols and informed consent evaluation and follow-up 5. Organising training at the university level 6. Organising workshop for investigators.
Cofunders:	• Cameroon National Ethics Committee for Human Health Research (Cameroon)
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – One laptop, one desktop, one photocopier, one printer, one video projector, one projection screen, one camera, one table, twelve chairs, a filling cabinet and a desk were purchased. Internet installation material was acquired. Internet connection is now permanent for the office and mobile/USB connection is also available for full-time staff. A website for the Cameroon National Research Ethics Committee for Human Health has been developed: www.cameroon-ethics.cm Training (resources developed (e.g. manuals) and human

	capacity developed) 2. Training (resources developed (e.g. manuals) and human capacity developed) – Training sessions on health research ethics took place: o 1 June 2011: Banganté (49 participants) o 28 July 2011: Yaoundé (52 participants) o 31 August – 1 September 2011: Workshop for investigators - Yaoundé (65 participants) o 27 January 2012: University of Dschanq (51 participants) o 7 February 2012: Douala (17 participants) o 8 February 2012: University of Buea (35 participants) o 1 December 2012: Cameroon National Research Ethics Committee for Human Health (12 participants) o 7 May 2013: University of Bamenda (82 participants). o Workshop on 'harmonisation of SOPs' for Research Ethics Committees (RECs) took place in Yaoundé (27-29 June 2012; 25 participants). SOPs were drafted and adopted by four ethics committees in Cameroon (Ethics Committee of Université des Montagnes; Faculty of Health Sciences IRB of the University of Buea; Cameroon Baptist Convention IRB; and Biotechnology Centre IRB). More than 300 protocols were reviewed in 2011. From January to September 2012, about 250 protocols were reviewed. More than 97% of research protocols implemented in Cameroon are reviewed by the CNEC. Members completed online TRREE courses. Thirty research protocols in the implementation stage have been monitored around the country. 3. Networking/collaborations developed – Training Resources in Research Ethics Evaluation (TRREE) – Chaire de droit de la santé, University of Neuchatel, Switzerland – Comité de Protection des personnes, Montpellier, France – University of Yaoundé I – University of Dschang – University of Buea – University des Montagnes – University of Bamenda – Ministry of Public Health – Ministry of Scientific Research and Innovation
Publications:	1. Fokunang CN, Tembe-Fokunang EA, DjuidjeNgounoue M, Chi PC, Ateudjieu J, Awah Pascal, Magne G, Ndje NM, Abena AMT, Sprumont D, KaptueLazare. 2013. Contribution of Biomedical Research Ethics in Public Health Advances. Current Topics in Public Health, Intech Open science/open minds; May 2013. Chapter 26: 625-659. 2. Fokunang CN, Tembe-Fokunang EA, Awah P, DjuidjeNgounoue M, Chi PC, Ateudjieu J, Langsi R, KaptueLazare, Abena OMT. 2013. The Role of Ethics in Public Health Clinical Research. Current Topics in Public Health, Intech Open science/open minds; May 2013. Chapter 27: 660-683.

9.1.42 Woldeamanuel -ETBIN-2-Ethics

EDCTP Project Coordinator:	Yimtubezinash Woldeamanuel
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Establishing and strengthening health research ethics committees in Ethiopia
EDCTP Project Code:	CB.2010.41302.014
EDCTP Project Start Date:	20 April 2011
EDCTP Project End Date:	19 October 2013
Collaborators:	• Abraham Aseffa (Ethiopia) • Fisseha Haile Meskal (Ethiopia)
Type of Project:	National Ethics Committee, Institutional Review Board
Goal:	This project is a continuation of the Ethiopian Bioethics Initiative (ETBIN's) EDCTP supported project towards establishing and strengthening IRBs in Ethiopia.
Objectives:	1. Assist with the formation of new IRBs and build their capacity, including helping establish IRBs in the seven new universities identified, training members of the new IRBs, and providing material support to the new IRBs 2. Monitor and provide professional support to the IRBs that were formed through the previous EDCTP supported ETBIN project as well as train new members appointed/elected to existing IRBs 3. Translate the ethics booklet written in Amharic (with EDCTP support) into at least two more Ethiopian languages, thus contributing to much broader awareness creation 4. Strengthen the ETBIN office (office space, equipment and reference materials) to enable it not only to manage projects, but also develop and sustain an effective network of IRCs 5. Organise ETBIN's General Assembly to enhance its organisational capacity 6. Provide administrative support to organising PABIN's General Assembly.
Cofunders:	Armauer Hansen Research Institute (AHRI)
Status:	Ongoing
Results and Outcomes:	1. Training (resources developed (e.g. manuals) and human capacity developed) – The process of assisting the formation of new IRBs started with a needs assessment and awareness creation visits to five newly established universities followed by a five day bioethics training (Human Subject Protection, GCP, SOP development; 5-9 September 2011; 40 participants) workshop for the newly formed IRB members from the universities. The training is based on a standard curriculum, recognised by SIDCER/WHO. The following are the beneficiary institutions: • Adama University • Jijiga University • Wollo University • Nekemt University • Debre Birhan University – Strengthening existing IRBs: one newly appointed member, who has no basic training in bioethics, from each of the institutions with an already existing IRB was also included in the five day training workshop that was

	given to the IRB members of the new universities. The following institutions benefitted from this training: Gondar University; Aklilu Lemma Institute of Pathobiology, AAU; Wollega University; Armauer Hansen Research Institute (AHRI/ALERT); Arbaminch University; Mekele University; Haramaya University; Bahir Dar University; Hawassa University; and National Ethics Committee. – A 35-page Health Research Popularization Booklet, which was prepared in Amharic (national language) with funding through the previous EDCTP project to ETBIN, has been translated into two other major languages in Ethiopia (Tigrigna and Afan Oromo) and is ready for publication. 2. Networking/collaborations developed – Adama University – Jijiga University – Wollo University – Nekemt University – Debre Birhan University

9.1.43 Yevoo-Ghana-Ethics

EDCTP Project Coordinator:	Lucy Yevoo (Dodowa Health Research Centre, Ghana)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Establishment and strengthening the activities of the Dodowa Health Research Centre's Institutional Review Board
EDCTP Project Code:	CB.2010.41302.015
EDCTP Project Start Date:	11 April 2011
EDCTP Project End Date:	10 April 2013
Collaborators:	• Sheila Addei (Ghana) • Okyere Boateng (Ghana) • Margaret Gyapong (Ghana) • John Gyapong (Ghana) • Raymond Aborigo (Ghana)
Type of Project:	Institutional Review Board
Goal:	The Dodowa Health Research Centre (DHRC) is one of the three research institutions within the Ministry of Health (MOH) and the Ghana Health Service (GHS) mandated to conduct research that contributes to the improvement of the health status of the people of Ghana. Currently, the centre does not have a permanent Institutional Review Board (IRB).This project aimed to establish and strengthen the activities of an IRB for the DHRC.
Objectives:	1. Establish an Ethical Review Board for the Dodowa Health Research Centre 2. Develop Standard Operating Procedures (SOPs) for the IRB 3. Promote networking and sharing of ideas among IRB members and researchers to ensure high standards 4. Train ethics review board members 5. Catalogue protocols 6. Educate community members about their ethics rights in research activities 7. Establish institutional structures and communication strategies for the IRB 8. Set up field monitoring processes by committee members for on-going research.
Cofunders:	• Dodowa Health Research Centre (DHRC) (Ghana)
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development - One desktop computer and accessories, one lap top, one paper shredder, one photocopier, one printer, one projector, one UPS stabiliser, one cabinet, two desks, four chairs and one scanner were purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed) – Terms of reference, SOPs and operational guidelines for the IRB were developed. A schedule for IRB meetings has been published (the Board meets bimonthly). The following training took place: – Historical development of ethics and the aims, objective and importance of an IRB (28 June 2011; 14 participants) o Informed consent and reviewing a protocol (13 September 2011; 17 participants) o Refresher training for board members (15 August 2012; 13 participants) o Training for new board members (10 April 2013; 7

	participants) ○ Both IRB coordinators received short term training in the field of 'health ethics human subject research' from the Noguchi Memorial Institute of Medical Research. 3. Networking/collaborations developed – Noguchi Memorial Institute of Medical Research (NMIMR) – Research and Development Division, Ghana Health Service (RDD) – Georgetown University – Copenhagen Sustainable Sanitation (SUSA) Project – Institute of Infectious Diseases of Poverty – Centre for Disease Control and the School of Public Health, School of Allied Sciences, University of Ghana

9.1.44 Bhatt-Kenya-Ethics

EDCTP Project Coordinator:	Kirana Bhatt (University of Nairobi, Kenya)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening of National Ethics Research Committees, networking and capacity building in Kenya
EDCTP Project Code:	CB.2010.41302.024
EDCTP Project Start Date:	15 April 2011
EDCTP Project End Date:	14 April 2012
Collaborators:	• Anastasia Guantai (Kenya) • Christine Kigondu (Kenya) • Micah Oyaro (Kenya) • Simon Lang'at (Kenya)
Type of Project:	National Ethics Committee
Goal:	This project aimed at improving the efficiency and expansion of Ethical Research Committees (ERC) in Kenya.
Objectives:	An inventory of all ethics review committees was taken. It also expanded its functional capacity through purchase of new office equipment (computers, printers, projectors and photocopiers), training of ERC members on bioethics, networking with local and external ERCs (north to south, south to south) to enhance ethical review processes in single and multi-clinical projects in Africa where the burden of infections is high. To improve the efficiency and functional capacity, a well-structured questionnaire was designed to take inventory of various ethics committees in Kenya, their location, facilities and composition of its members. The study also identified the gaps and challenges. It is anticipated that the turnaround time for ethical review process will reduce by half, 100% composition of all ERCs in Kenya will be known, more than 90% of all ERCs represented in the project will receive all the necessary Standard Operating Procedures (SOPs), including the other relevant information. In addition, a long-term sustainability plan was established through joint collaborations to ensure continuous updating of ethical review research activities through the websites and monitoring of the various ERCs activities under the National Council of Science and Technology, which is the governing body of all research in Kenya.
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – One laptop, three desktop computers, one LCD projector, one photocopier, two printers and one scanner were purchased. The website was upgraded and a database for capturing data relating to research activities was created. 2. Training (resources developed (e.g. manuals) and human capacity developed) – A three-day workshop on "Ethics and research" took place (15-18 January 2012; 58 participants) – A second follow-up workshop was held to review progress and assess the immediate benefits of the ethics workshop (18 May 2012; 36 participants). An inventory of all ethics review committees in Kenya was undertaken in collaboration with the National Council for Science and Technology (NCST). A needs assessment was carried out countrywide to identify the existing ERCs and institutions in the process of establishing their own ERCs in Kenya in

	consultation with the NCST. A draft strategic plan was formulated through this grant, which was used as the key resource document by the University of Nairobi and Kenyatta National Hospital in the formulation of the final version of the strategic plan. A database was created and data entry is ongoing. 3. Networking/collaborations developed – Gertrude's Children's Hospital – Kenyatta University – Jomo Kenyatta University of Agriculture and Technology – Coast Provincial General Hospital – AMREF – ICIPE – Pwani University – Mombasa Polytechnic University College – Great Lakes University of Kisumu – Moi University – University of Eastern Africa – Baraton – Catholic University of East Africa – ThePresbyterian University of East Africa – Kakamega Provincial General Hospital – New Nyanza Provincial General Hospital – MasindeMuliro University of Science and Technology – Maseno University – Kijabe Hospital – Chuka University College – Kenya Methodist University – Nairobi Hospital – NationalCouncil for Science and Technology (NCST) – Kenya Medical Research Institute (KEMRI) – Aga Khan University Hospital

9.1.45 Bukusi-Kenya-Ethics

EDCTP Project Coordinator:	Elizabeth Bukusi (Kenya Medical Research Institute (KEMRI), Kenya)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	ADILI – The KEMRI Bioethics Centre
EDCTP Project Code:	CB.2010.41302.016
EDCTP Project Start Date:	21 March 2011
EDCTP Project End Date:	20 March 2014
Collaborators:	• Caroline Kithinji (Kenya) • Gerald Mkoji (Kenya) • Sammy Njenga (Kenya) • Christine Wasunna (Kenya)
Type of Project:	Institutional Review Board
Goal:	This project seeks to set up the ADILI Bioethics Centre at Kenya Medical Research Institute (KEMRI) to build capacity in ethics training for both members of the ethics review committees and for investigators at the institute.
Objectives:	The aim is to establish an independent bioethics unit at KEMRI and ensure that it is appropriately staffed, trained, resourced, and entrenched within KEMRI's structures to oversee the ethical review process at the institute. To achieve this, consensus will first be built and a proposal developed (board paper) to submit to the KEMRI board of management seeking to establish the bioethics unit. Upon receiving the board's approval, training of the current Institutional Review Board (IRB) members will be initiated and a new review structure will be piloted consisting of multiple committees, which when fully established will form a fully-fledged multi-committee model in which several committees will work simultaneously to review protocols. Reviewers will be trained to conduct specialised review of highly complex protocols. To expedite and improve efficiency, an electronic review system for submission of protocols will be set up. The independent unit will provide bioethics training to scientists within KEMRI, including the graduate students, and it will establish review guidelines for the committees.
Cofunders:	• US National Institute of Health through the University of California San Francisco • US National Institute of Health through the University of Cape Town
Status:	Ongoing
Results and Outcomes:	1. Infrastructure/capacity development - Six computers, two laptops, two LCD projectors, two printers, two scanners and a server were purchased. The purchase of computers and server have aided in the development of the online protocol management and tracking system (http://www.kemri.org/ssc/). 2. Training (resources developed (e.g. manuals) and human capacity developed) - A one-day training for ethics review committee members took place (19 December 2011; 18 participants). The training included presentations on handling protocol deviation and violation. Three ethics review committee members attended a short course on bioethics (20-24 February 2012). Staff received training via online programmes, namely AMANET and the Collaborative Institutional Training Initiative (CITI). New forms for

	submission and review of protocols were developed. The task force and ERC secretariat members jointly conducted centre-level informed consent training sessions for Centre Scientific committee members at all of the 11 KEMRI centres. 3. Networking/collaborations developed – Uganda National Council for Science and Technology (UNCST) – University of Nairobi/Kenyatta National Hospital (UoN/KNH) Ethics Research Committee – National Council of Science and Technology (Kenya)

9.1.46 Otieno-Kenya-Ethics

EDCTP Project Coordinator:	Wellington Otieno (Centre for Research and Technology Development (RESTECH), Kenya)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Establishment of Institutional Research and Ethics Committee (IREC) in Western Kenya
EDCTP Project Code:	CB.2010.41302.025
EDCTP Project Start Date:	3 March 2011
EDCTP Project End Date:	2 June 2013
Collaborators:	• Erick Nyambedha (Kenya) • Wilson Odero (Kenya) • Collins Otieno (Kenya) • Job Jondiko (Kenya)
Type of Project:	Institutional Review Board
Goal:	The Centre for Research and Technology Development (RESTECH) was established in 2007 and is located in Kisumu City in Nyanza Province, Western Kenya. Currently, research institutions and universities in Western Kenya do not have an ethics review committee. Ethical approval of all research proposals developed by staff and postgraduate students at universities and research organisations in Western Kenya can only seek ethics approval from one of the three local IRBs (Kenyatta National Hospital/University of Nairobi Research and Ethics Committee (KNH-ERC), Kenya Medical Research Institute Institutional Review Board (KEMRI IRB), and Moi University Institutional Research and Ethics Committee (IREC)). Researchers from Western Kenya institutions often obtain ethical approval from KNH-ERC or KEMRI-IRB, yet given the close geographical proximity of RESTECH to the research sites, it would be more appropriate to receive approval and ethical oversight from the proposed IREC to be based at RESTECH in Kisumu to serve the local needs of the researchers.
Objectives:	1. Increase awareness and appreciation for the ethical approval process and oversight in the conduct of research, as well as the uptake of ethical review services among university academic staff, National Research Institute, NGOs and students 2. Establish a functional Institutional Research and Ethics Committee (IREC) at the RESTECH Centre, with the capacity to review biomedical and social science research proposals and provide ongoing ethical oversight to studies conducted by or in collaboration with the universities and the National Research Institutes within the region 3. Design strategies to ensure technical and financial sustainability of the Institutional Research Ethics Committee for Western Kenya (WK-IREC).
Cofunders:	• Maseno University (Kenya) • Centre for Research and Technology Development (RESTECH) (Kenya)
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development - Two computers, two printers, two book shelves and two working tables were purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed) - A website for the REC was set up (www.restechkenya.org

	(for capacity building documents); www.maseno.ac.ke (for project proposal ethical clearance)). A Local Area Network (LAN) has been developed linking the researchers and project staff at RESTECH and Maseno University. Several members of staff from Maseno University, RESTECH, other universities as well as national research institutes in Western Kenya were given short-term training (2011 to 2013) on principles and practices on Institutional Research Ethics Committee operations. Strengthening WK-IREC and its collaborating institutions in research ethics culture by developing REC Terms of Reference (TOR), Policies and Procedures (PPs), and Standard Operating Procedures (SOPs) to guide all functions and the judicious appraisal of protocols submitted by students and scientists in collaborating institutions took place. The following documents have been developed: - Ethics Review Committee guidelines for Standard Operating Procedures (SOPs) - Application form for ethics review - Ethics review evaluation form - Information sheet/consent form. - The following training took place: - Using renewable energies to support fishing communities around Lake Victoria: The role of research and ethical consideration (5-8 March 2012; 12 participants) - Research ethics training for postgraduate students (9-10 August 2012; 26 participants) - Workshop on ethical review committees (20-21 May 2013; 25 participants) - 4. Health research ethics training workshop (27-28 May 2013; 18 participants). 3. Networking/collaborations developed - University of Boston School of Public Health - International Centre of Insect Physiology and Ecology (ICIPE) - South African Research and Ethics Committee (SAREC) - London School of Hygiene and Tropical Medicine (LSHTM) - African Malaria Network Trust (AMANET) - Kenya Medical Research Institute (KEMRI) - Kenyatta National Hospital and Moi University Referral Hospital

9.1.47 Manda-Malawi-Ethics

EDCTP Project Coordinator:	Lucinda Manda-Taylor (University of Malawi, Malawi)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Enhancing community understanding and participation in human subjects protection in Malawi
EDCTP Project Code:	CB.2010.41302.012
EDCTP Project Start Date:	31 March 2011
EDCTP Project End Date:	30 March 2013
Collaborators:	• Tamara Chipasula (Malawi) • Linda Kalialani-Phiri (Malawi) • Joseph Mfutso-Bengo (Malawi) • Victor Mwapasa (Malawi)
Type of Project:	Institutional Review Board
Goal:	The aim of this project was to build the capacity of local researchers and research participants.
Objectives:	1. Enhancing understanding of the research community in Malawi, which includes researchers within and out of the College, faculty and students, on human subject's protection in research. This will improve human subject's protection compliance from proposal development through to implementation, and therefore also strengthen Good Clinical Practice and regulatory compliance in clinical research 2. Enhancing knowledge and understanding of communities (research participants) on matters of human subject's protection. This will have several positive benefits to research, including improving the informed consent process, improved protection of research participants and possibly improved study recruitment and compliance 3. Firstly, the aim is to develop and/or adapt a course on human subject protection that will be offered to the research community in Malawi. Secondly, the aim is to develop/adapt human subject's protection course for research participants in and around villages near clinical research sites and establish and train Community Advisory Boards (CABs) at sites where CABs are absent. These objectives contribute to the overall function of and will be guided by COMREC (College of Medicine's Research and Ethics Committee) and informed by local and international research ethics and regulatory guidelines.
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – One laptop was purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed) - A three day course in human subjects protection took place (6-8 June 2011; 25 participants) - A three day course in human subjects protection and CABs took place in Mpemba (11-13 July 2011; 36 participants). Thereafter, a CAB was established in the community that was linked to a clinical trial site taking place at the health centre in the area - A three day course in human subjects protection and CABs took place in Madziabango (21-24 September 2011; 29 participants). Thereafter, a CAB was established in the community that was linked to a

	clinical trial site taking place at the health centre in the area - A three day course in human subjects protection and CABs took place in Thyolo (26-28 January 2012; 40 participants). Thereafter, a CAB was established in the community that was linked to a clinical trial site taking place at the health centre in the area - A three day course in human subjects protection was offered (23-25 May 2012; 43 participants) in Zomba. A CAB was established after the training - A three day course in human subjects protection was conducted (9-11 October 2012; 32 participants) in the Ndirande Health Centre - A follow-up meeting for CAB members in Mpemba and Madziabango took place in December 2012. The primary aim was to touch base with the CABs that had been established in August and October 2011 to get feedback on their successes and challenges - A three day course in human subjects protection was conducted (16-18 January 2013; 43 participants) in the Zomba Central Hospital catchment area. This is the second CAB established in Zomba by the project because the consensus was that one CAB was not sufficient for this big catchment area - A follow-up meeting with the CAB in Thyolo was held on 15 February 2013 (38 participants) - A follow-up meeting with the CAB in Ndirande was held on 5 March 2013 (29 participants) - A follow-up meeting with the CAB in Zomba was held on 8 March 2013 (40 participants). - In total, six CABs (Mpemba, Madziabango, Ndirande, Thyolo, Zomba 1 and 2) were established (228 participants trained). The project trained 40 research staff on human subjects protection. All community engagement training activities were preceded by a sensitisation workshop where community leaders and local health surveillance officers were invited and informed about the objectives of the training. 3. Networking/collaborations developed – National Commission for Science and Technology (Malawi) – Pharmacy, Medicines and Poisons Board (PMPB) (Malawi) – Medical Research Council of Zimbabwe (MRCZ)
Publications:	1. Manda-Taylor, L. (2013). Establishing community advisory boards for clinical trial research in Malawi: Engendering ethical conduct in research. *Malawi Medical Journal*, 25:4.

9.1.48 Otuonye-NIMR-Ethics

EDCTP Project Coordinator:	Ngozi Otuonye (Nigerian Institute of Medical Research, Nigeria)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Establishment of RECs and capacity building of human resources and infrastructure in Nigeria
EDCTP Project Code:	CB.2010.41302.027
EDCTP Project Start Date:	11 April 2011
EDCTP Project End Date:	10 October 2012
Collaborators:	• Nwaokorie Franka (Nigeria) • Dominique Sprumont (Switzerland) • Tinto Halidou (Burkina Faso)
Type of Project:	Institutional Review Board
Goal:	This project improved the capacity of health personnel (doctors, nurses, medical laboratory scientists, pharmacists, clergies, lawyers, community representatives and research scientists) to effectively conduct ethically sound research that is of international standard. HRECs were established at Mainland Hospital Yaba (MHY) and Ambrose Ali University (AAU). Their infrastructure was strengthened to improve the administrative capacity and efficiency of the HRECs.
Objectives:	This project established competent, operational and independent HRECs that will protect the wellbeing of participants, especially highly vulnerable groups. In addition, the infrastructural capacity was strengthened to improve the HREC administrators' capacity. This enables them to understand the operations of a research ethics committee and how to adequately review research protocols and monitor research. The newly elected HREC members from the two institutions (AAU and MHY) were mentored by NIMR IRB in collaboration with NHREC and NHVMAS. This was to facilitate the conduct of ethical research in practice at their various sites.
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – The HREC offices at MHY and AAU were equipped with the following: two air conditioners, two tables, six chairs, two photocopiers, two printers, two scanners, two computers, two fridges, two filing cabinets, two UPS and two fans. A one year internet subscription was purchased for MHY and AAU. 2. Training (resources developed (e.g. manuals) and human capacity developed) – Research ethics training modules were prepared and endorsed by the NHREC. Health personnel and researchers received training on ethics (GCP, research ethics guidelines, research monitoring, informed consent): MHY (28 June-1 July 2011; 69 participants) and AAU (18-21 October 2011; 42 participants). HREC members were appointed in line with the NHREC guidelines. The NHREC inaugurated the elected HREC members from MHY (11 member committee) and AAU (15 member committee). Mentorship training on operationalising IRB and research monitoring (14-16 August 2012; 27 participants from MHY, AAU and NIMR IRB). The mentorship programme covered organisation/administration of the IRB secretariat, procedures/conduct of IRB meetings, and monitoring of

	research programmes. Participants were registered to conduct online training in research ethics through the following programmes: TRREE and AMANET. 3. Networking/collaborations developed – New HIV Vaccine and Microbide Advocacy Society (NHVMAS) – Nigerian Institute of Medical Research IRB (NIMR IRB) – African Malaria Network Trust (AMANET) – Training and Resources in Research Ethics Evaluation for Africa (TRREE) – West African Bioethics Training Programme (WAB) – University of Neuchâtel – Centre Muraz (Burkina Faso)

9.1.49 Oyedeji-NIMR-Ethics

EDCTP Project Coordinator:	Kolawole Oyedeji (Nigerian Institute of Medical Research, Nigeria)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Capacity building and support for three ethics review committees in North Central and South Western geopolitical zones of Nigeria
EDCTP Project Code:	CB.2010.41302.022
EDCTP Project Start Date:	11 April 2011
EDCTP Project End Date:	28 February 2013
Collaborators:	• Timothy Abolarinwa (Nigeria) • David Johnson (Nigeria) • Oliver Ezechi (Nigeria) • Morenike Ukpong (Nigeria)
Type of Project:	Institutional Review Board
Goal:	This project aimed to provide some basic support and training for three ethics review committees in two geopolitical zones in Nigeria, namely North Central and South Western: University of Ilorin Teaching Hospital (UITH), Ilorin; Ladoke Akintola University of Technology Teaching Hospital (LAUTECHTH); and Oshogbo and Olabisi Onabanjo University Teaching Hospital (OOUTH), Shagamu.
Objectives:	1. Organise a training workshop for ethics review committee members of the University of Ilorin Teaching Hospital, Ladoke Akintola University Teaching Hospital and Olabisi Onabanjo University Teaching Hospitals on protocol review and providing constructive feedback, research monitoring and the use of PRO-IRB software 2. Support institutional capacity building for these three ethics review committees through the purchase and installation of basic computer hardware and software. This will enable each ethics review committee to ensure improved Secretariat performance through proper record keeping and access to continuing education training and re-training of the ethics review committee members 3. Provide a platform for networking, collaboration and promote discussion on contemporary issues and dilemmas of health research ethics among these ethics review committees and other local and national ethics committees through communication via internet based fora.
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – Three printers, three UPS, three desktop computers, three modems, one laptop and one projector were purchased. The three ethics committees therefore received full computer systems and internet connectivity. 2. Training (resources developed (e.g. manuals) and human capacity developed) - The Nigerian Institute of Medical Research (NIMR) organised a five day training session for members of the three ethics committees (UITH: 18-22 July 2011, 30 participants; LAUTECHTH: 5-9 September 2011, 27 participants; OOUTH: 1-5 December 2011, 40 participants) on how to review a protocol and provide constructive feedback. The programme also provided

	training on the use of PRO-IRB computer software for record keeping and documentation of the protocol review process in the respective ethics committees. The training was accredited by the NHREC with accreditation number: NHREC training certificate No. NHREC/TR/15/07/2011 according to the National Code on Health Research Ethics (NCHRE) in the country. Websites were developed for all three research ethics committees (UITH, OOUTH, and LAUTECHTH) (www.uitherc.org, www.ooutherc.org, www.lautecherc.org). 3. Networking/collaborations developed – South African Research Ethics Training Initiative (SARETI) – West African Bioethics Training Programme (WABTP) – National Health Research Ethics Committee (NHREC) – New HIV Vaccine and Microbicide Advocacy Society (NHVMAS)

9.1.50 Kruger-SAREN-Ethics

EDCTP Project Coordinator:	Mariana Kruger (Stellenbosch University, South Africa)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Network of Southern Africa Research Ethics Committee (REC) Chairpersons and development of a review textbook for African REC members (SAREN – South African Research Ethics Network)
EDCTP Project Code:	CB.2010.41302.010
EDCTP Project Start Date:	21 March 2011
EDCTP Project End Date:	20 December 2013
Collaborators:	• Phil Hans-Jörg Ehni (Germany) • Lyn Horn (South Africa) • Urban Wiesing (Germany)
Type of Project:	Coordination function
Goal:	This project will enable the chairs of ethics review committees as well as other leaders in the field of research ethics in Africa to identify and explore the current issues in ethics review. The exploration of these concepts will be used as the basis for an African textbook of ethics review to assist African ethics review members in their important task of protecting research participants.
Objectives:	The first objective of this project is to establish a network of Chairpersons of sub-Saharan Research Ethics Committees. The starting point of this network will be to host a two or three day face to face meeting of Chairpersons of sub-Saharan and Southern Africa and other REC members in order to identify and discuss common problems and challenges. The second purpose of this meeting will be to initiate and identify a steering committee that will plan and write a detailed review textbook for African IRBs similar in part to the Institutional Review Board: Member Handbook by Robert J. Amdur and Elizabeth A. Bankert (Jones & Bartlette Publishers), now in its third edition and used extensively by IRB members in the USA and Canada. The second phase of the project, after the 'Forum of Chairpersons' meeting, will be the writing of the textbook and the development of a sustainable online REC discussion forum and blog.
Status:	Ongoing
Results and Outcomes:	1. Training (resources developed (e.g. manuals) and human capacity developed) – A workshop for African REC Chairs, members and administrators to discuss health care research issues in Africa and to plan for the textbook was held (12–13 August 2011). 2. Networking/collaborations developed – Mapping African Research Ethics and Drug Regulatory Capacity (MARC) – University of Ghana – Cameroon National Ethics Committee – Kenya Medical Research Institute (KEMRI) – Medical Research Council Zimbabwe (MRCZ) – St John's University (Tanzania) – Biomedical Research and Training Institute (BRTI) – Walter Sisulu University – CERMES – Medical Research Institute (Egypt) – University of Liberia

	– Ministry of Defence (Nigeria) – University of Zimbabwe

9.1.51 Msambichaka-Tanzania-Ethics

EDCTP Project Coordinator:	Beverly Msambichaka (Ifakara Health Institute (IHI), Tanzania)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Customisation and strengthening of the IHI-IRB capacity to regulate health research ethics
EDCTP Project Code:	CB.2010.41302.026
EDCTP Project Start Date:	3 March 2011
EDCTP Project End Date:	2 March 2013
Collaborators:	• Abdallah Mkopi (Tanzania) • Mwifadhi Mrisho (Tanzania) • Saumu Ahmed (Tanzania)
Type of Project:	Institutional Review Board
Goal:	The IHI–IRB (Ifakara Health Institute Institutional Review Board) seeked to establish a training unit in health research ethics serving Tanzanian institutions and others in Africa.
Objectives:	1. Customise the IHI-IRB office This objective addresses the challenge of document storage to match the increasing volume of printed material. It also addresses the issue of having the facilities to accommodate a dedicated person (part-time) to take on the role of establishing and maintaining an up to date IRB database and archive. These are considered to be important challenges, taking into consideration that the IRB is expected to adhere and comply to all ethical requirements and at the same time be eligible for auditing at any time by local and international ethical authorities. 2. Establish a well-managed database and archiving system for IHI-IRB This objective assumes the responsibility of ensuring that the IRB secures a suitable candidate to take up the role of managing IRB data following a short training. It is expected, from this objective, that the IHI-IRB will be able to produce a quarterly report on general IRB performance as well as overall performance of the project. 3. Support personnel cost and IRB members allowance This objective addresses the problem of low review allowances for IRB members and responsibility allowances for members of the Secretariat. In this project the project coordinators and data manager's salaries will receive responsibility allowances. It is expected that IRB members' attendance of review meetings will continue to be maintained at not less than 70%. The responsibility allowance is a contribution towards time spent in implementing the project. 4. Promote HRE awareness among clinical trial communities This objective targets the clinical trial communities. Through public awareness activities, these communities will be able to get a better understanding of the importance of clinical trials and their valuable contribution in participation as well as the importance of HRE, the informed consent process, their rights and responsibilities. Through discussions in the seminar, we may deduce how best to enhance our IRB. 5. Facilitate effective clinical trial oversight visits The aim is to be able to develop a platform for effective clinical trial oversight visits with a proper format for review

	of clinical trials that can be replicated elsewhere in similar settings. 6. Build capacity of IRB members and IHI staff on HRE The aim is to strengthen IRB members' capacity to identify relevant issues of ethical concern during review. The purpose of inviting different participants is to propagate the know-how, but at the same time to develop a common direction or approach between the NEC and IRBs in reviewing documents. From this training, NECs and IRBs should be able to develop their own protocol review guides, which in future could be harmonised across ethical bodies and thereby reduce duplication of efforts. Investigators will be trained on the informed consent process and Good Clinical Practice, while field workers will be strengthened on field HRE application skills.
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – One desk, one office chair and one desk top computer were purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed) - An assistant data and archiving manager was recruited and successfully completed a two-year diploma on record management. An electronic IRB records management system was developed. Three oversight visits have been conducted on two TB clinical trials (1 December 2011) and one malaria transmission intensity study in Bagamoyo (26-27 November 2012). A training guide on basic health research ethics for field workers has been developed with training content. The brochure on 'rights and responsibilities' of participants was distributed to clinical trial participants and field workers during training on 28 February 2013, and 27 and 28 May 2013. The following training sessions for IRB members and investigators took place: - Experimental designs and how it impacts on health research ethics (10 June 2011; 12 participants) - Informed consent process (23–24 August 2011; 18 participants) - Good Clinical Practice: A step further for investigators (25–26 August 2011; 18 participants) - Awareness seminar on health research ethics for clinical trial participants of malaria vaccines (25 February 2013; 12 participants) - Basics of health research ethics training for field supervisors (27 May 2013; 18 participants) - Basics of health research ethics training for field workers (28 May 2013; 20 participants). 3. Networking/collaborations developed – African Malaria Network Trust (AMANET) – Clinical Research Africa (CRA)

9.1.52 Temu-LZIRB-Ethics

EDCTP Project Coordinator:	Mansuet Temu (National Institute for Medical Research (NIMR), Tanzania)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening the capacity of the Lake Zone Institutional Review Board (LZIRB)
EDCTP Project Code:	CB.2010.41302.006
EDCTP Project Start Date:	20 April 2011
EDCTP Project End Date:	19 April 2013
Collaborators:	• John M. Changalucha (Tanzania) • Joyce K. Ikingura (Tanzania) • Joseph R. Mwanga (Tanzania) • Mark Urassa (Tanzania)
Type of Project:	Institutional Review Board
Goal:	This project aimed to strengthen the capacity of LZIRB, which was established by funds from EDCTP in 2008. Being a new organ there are many activities that need to be supported in order to make the IRB strong and independent according to the laid down guidelines. Among the activities that need financial support include training (local and international) of its members and secretariat, purchasing of equipment, furniture and supplies, top up allowance to the members of the secretariat and attendance at an ethics meeting in the country.
Objectives:	Due to limited resources in developing countries and considering the rise in the number of health researchers due to various reasons, it is justifiable to apply for funds to strengthen the capacity the local IRBs. The objectives of the project are to strengthen the LZIRB through further training of the members, train a group of protocol reviewers, train one resource person within the country, attach a secretary from within the Institute and refurbish the secretariat office. Through these activities there will be an assurance that the IRB can work properly in the protection of rights and welfare of study participants. The specific objectives were to: 1. Provide additional health research ethics training to the members of the LZIRB 2. Train and mentor a group of protocol reviewers, especially in clinical trials protocols 3. Train a resource person within the country 4. Attach a secretary and recorder from within the institute to support operations of the LZIRB office 5. Refurbish and furnish the secretariat office The intermediate steps included: 1. Identification of a trainer who will offer continued training to the members and a group of protocol reviewers 2. Identify a person with an interest in research ethics who will be trained within the country as a resource person in research ethics 3. Identify a secretary within the institute 4. Procure furniture and other items for the secretariat office.
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development - Two laptops, two desktop computers, one overhead projector, one scanner, one printer, two air conditioner split units, three tables, six chairs, three

	power stabilisers, one laminating machine, one spiral binding machine, one network switch, one paper cutter machine, one slide presentation pointer and two wireless modems were purchased. The Secretariat office was painted and minor repairs were carried out. PROIRB software was purchased and installed. 2. Training (resources developed (e.g. manuals) and human capacity developed) - The workshop on 'health research ethics' took place (28-30 November 2011; 16 participants). Training for protocol reviewers (facilitated by the NatHREC) took place (27-28 February 2013; 39 participants). Standard Operating Procedures were reviewed. . Monitoring visits took place and also meetings with other active local IRBs. 3. Networking/collaborations developed – African Malaria Network Trust (AMANET) – National Health Research Ethics Committee (Tanzania) – Southern African Research Ethics Network (SAREN)

9.1.53 Birungi-TASO-Ethics

EDCTP Project Coordinator:	Josephine Birungi (The AIDS Support Organization (TASO), Uganda)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening of TASO (The AIDS Support Organization) Institutional Review Board for HIV/AIDS research in Uganda
EDCTP Project Code:	CB.2010.41302.013
EDCTP Project Start Date:	11 April 2011
EDCTP Project End Date:	10 April 2013
Collaborators:	• Shabbar Jaffar (United Kingdom) • Concepta Merry (Ireland) • Edward Mills (Canada)
Type of Project:	Institutional Review Board
Goal:	The goal of this project was to strengthen The AIDS Support Organization (TASO) Institutional Review Board (IRB) and support operational and community-based clinical HIV/AIDS research within and outside TASO.
Objectives:	1. Developing clear procedures for identifying and recruiting members of the TASO IRB 2. Reviewing and further developing TASO IRB Standard Operating Procedures (SOPs) 3. Developing a curriculum for training members of the TASO IRB and other IRBs 4. Documenting and disseminating relevant lessons learned about the establishment and strengthening of IRBs in Uganda at national and international conferences/meetings.
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development - One desktop computer, one laptop, one desk, one office cabinet, one scanner and one notice board were purchased. The IRB now has a furnished office with 24 hour internet services. 2. Training (resources developed (e.g. manuals) and human capacity developed) - SOPs were developed. Six planning meetings for IRB members were held. Standardised and objective tools for the review of research protocols have been developed as well as guidelines for monitoring research sites. A monitoring tool was designed and rolled out in two field monitoring visits. A tabled document for research proposals received and reviewed was created. These documents are being used by the IRB members to execute the functions of the IRB. A five day workshop in research ethics took place (16-20 May 2011; 19 participants). A two day orientation for IRB members was held (1-2 March 2012; 17 participants). Ethics training took place on (5-7 June 2012; 19 participants) and (19-20 April 2013; 68 participants). A human subject protection and compliance monitoring course (19-20 April 2013; 76 participants) took place. Nine IRB members completed the NIH online ethics course on 'protection of human subjects'. Twenty six TASO members of staff attended the Fifth Annual National Research Ethics conference organised by UNCST TASO IRC was

	accredited by the Uganda National Council for Science and Technology (UNCST) (IRC number UG-IRC-010). 3. Networking/collaborations developed – Uganda National Council for Science and Technology (UNCST) – Joint Clinical Research Centre (JCRC) – Population Council – University of Washington

9.1.54 Zimba-Zimbabwe-Ethics

EDCTP Project Coordinator:	Moses Zimba (Harare City Health Department, Zimbabwe)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Establishment of an Institutional Review Board for health facilities in City of Harare
EDCTP Project Code:	CB.2010.41302.004
EDCTP Project Start Date:	15 March 2011
EDCTP Project End Date:	14 March 2012
Collaborators:	• Richard Chigerwe (Zimbabwe) • Clemence Duri (Zimbabwe) • Stanley Mungofa (Zimbabwe)
Type of Project:	Institutional Review Board
Goal:	Harare City Health Department has the mandate to review each and every research proposal accompanying applications, but the capacity to review the proposals and monitor clinical trials was limited due to inadequate knowledge and trained manpower. The goal was to establish an Institutional Review Board (IRB) for health facilities in the City of Harare.
Objectives:	The objective of this project was to establish an IRB for health facilities in the City of Harare through training 33 health workers, including doctors, nurses, pharmacists, laboratory scientists and the clergy. At the end of the project, five of the trained health workers became members of the central IRB and the other 28 became members of extension IRBs in four districts to assist the central IRB with the general monitoring of compliance by researchers in the respective health facilities as they perform their normal duties and will be drawn to fill vacancies arising in the IRB due to resignations and natural causes. Non-compliance with research ethics during project implementation is a major challenge. Researchers have the tendency to abandon the approved procedure of handling research participants, hence the need for closer monitoring. The project sought to improve the conduct of health research and ensure that proposed disease intervention clinical trials are conducted using internationally accepted standards. The project also aimed to help set up offices, procure equipment, establish a Secretariat and strengthen the capacity of the proposed IRB to review proposals with a clear understanding of study designs and implementation.
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – An office for the IRB was refurbished including replacement and painting of ceiling, painting of walls, door and window frames, and installation of a security screen. The office was furnished and equipped with two desk top computers, two laptop computers, one desk, five office chairs and one filing cabinet. 2. Training (resources developed (e.g. manuals) and human capacity developed) – The training manuals for the course on "Health research ethics and Good Clinical Practice" were developed and training conducted by the Medical Research Council of Zimbabwe (MRCZ). The Medicines Control Authority of Zimbabwe (MCAZ) produced the manuals and conducted the training on "Clinical trial regulation and monitoring". The University of Zimbabwe conducted a course on

	research methodology. Three training sessions took place: – Health Research Ethics and Good Clinical Practice (04-06 May 2011; 33 participants) – Clinical Trials Regulations and Monitoring (30 June 2011; 33 participants) – Research Methodology (04-05 October 2011; 33 participants). 3. Networking/collaborations developed – Medical Research Council of Zimbabwe (MRCZ) – Medicines Control Authority of Zimbabwe (MCAZ) – University of Zimbabwe – Southern African Research Ethics Network (SAREN)

9.1.55 Ouedraogo-Burkina Faso-Ethics

EDCTP Project Coordinator:	Abdoulaye Ouedraogo (Centre Muraz, Burkina Faso)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Capacity building programme for Centre Muraz IRB of Bobo-Dioulasso, Burkina Faso
EDCTP Project Code:	CB.2011.41302.019
EDCTP Project Start Date:	6 March 2012
EDCTP Project End Date:	5 March 2014
Collaborators:	• Dezemon Zingue (Burkina Faso) • B. N. Hervé Kpoda (Burkina Faso)
Type of Project:	Institutional Review Board
Goal:	The activities aim to provide Centre Muraz with a skilled and functioning IRB.
Objectives:	To achieve this goal, the capacity strengthening programme includes the following objectives: 1. Developing guidelines and SOPs for the ethics committee 2. Training the ethics committee members on health research ethics and the protocol review process 3. Training investigators and their collaborators on health research ethics and the responsible conduct of research 4. Conducting high quality field supervision and auditing of health research projects 5. Improving the committee secretariat 6. Promoting human rights and safety protection of health research participants in Africa through networking.
Status:	Ongoing
Results and Outcomes:	1. Infrastructure/capacity development – The following equipment was purchased: one desktop, one laptop, one modem, one printer, one portable hard drive, 15 chairs and four tables. 2. Training (resources developed (e.g. manuals) and human 3. Networking/collaborations developed – Mapping African Research Ethics and Drug Regulatory Capacity (MARC)

9.1.56 Tangwa-CAMBIN-Ethics

EDCTP Project Coordinator:	Godfrey Tangwa (Cameroon Bioethics Initiative (CAMBIN), Cameroon)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Documenting facilities and needs of ethics committees and implementing a training intervention to strengthen ethical review capacity in Central Africa
EDCTP Project Code:	CB.2011.41302.021
EDCTP Project Start Date:	10 February 2012
EDCTP Project End Date:	9 December 2013
Collaborators:	• Sylvie Kwedi (Cameroon) • Aceme Nyika (Tanzania) • Azza Saleh Radwan (Egypt)
Type of Project:	Coordinating function
Goal:	In this project, the intention is to go one step back and examine the functioning of existing ethical review committees (ERCs) and Institutional Review Boards (IRBs) through data collected from a survey. This analysis will then provide evidence to build an intervention package for targeted training that will address the needs identified from the results of the survey.
Objectives:	The objectives of this project are to: 1. Adapt the SIDCER survey to fit programme needs 2. Administer the survey to identified ERCs and IRBs 3. Analyse the results of the survey 4. Customise the training intervention package 5. Provide short-term, self-directed training 6. Conduct two training workshops 7. Establish an online discussion forum (i.e. yahoo groups) to enhance knowledge exchange and networking 8. Recruit a permanent staff member 9. Purchase equipment to enable the proper functioning of the CAMBIN secretariat 10. Purchase software (ProIRB Plus Inc) to facilitate the activities of the CAMBIN Ethics Review and Consultancy Committee (ERCC) 11. Train members of the secretariat to use the software 12. Develop SOPs for the CAMBIN ERCC.
Status:	Ongoing
Results and Outcomes:	1. Infrastructure/capacity development – One laptop, one desk and two chairs were purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed) – A training package specific for the training needs of each of the RECs identified in the project is being customised. Draft SOPs for the CAMBIN ERCC is now available and is being tested for validation. An online discussion forum (i.e. yahoo groups) to enhance knowledge exchange and networking is being established – A *google* group on health research ethics in central Africa has been created and RECs/IRBs in Central Africa are now part of this forum. 3. Networking/collaborations Developed – Egyptian Network of Research Ethics Committees (ENREC) – Capacity for Leadership Excellence and Research (CLEAR, Inc) – Fondation Congolaise pour la Recherche Médicale

	(FCRM) – Public Health Projects (PHP) Africa (Zimbabwe) – Cameroon Baptist Health Board (IRB) – Training and Resources in Research Ethics Evaluation (TRREE)
Pulications:	1. Ouwe-Missi-Oukem-Boyer, O., Nchangwi, S. M., Ntoumi, F., Nyika, A., & Tangwa, G. B. (2013). Capacity building in health research ethics in Central Africa: Key players, current situation and recommendations. *Bioethica Forum*, 6 (1), 4-11. 2. Tangwa, G. B. (2014). Cameroon. In H. A. M. J. ten have & B. Gordijn (Eds.), *Handbook of global bioethics*, (pp. 941-958). Springer Science.

9.1.57 Osei-Atweneboana-CSIR-Ethics

EDCTP Project Coordinator:	Mike Yaw Osei-Atweneboana (Council for Scientific and Industrial Research (CSIR), Ghana)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening of Institutional Review Board of Council for Scientific and Industrial Research and capacity building on ethical review in Ghana
EDCTP Project Code:	CB.2011.41302.013
EDCTP Project Start Date:	16 February 2012
EDCTP Project End Date:	15 December 2013
Collaborators:	• Pamela Emefa Selormey (Ghana) • Okyere Boateng (Ghana)
Type of Project:	Institutional Review Board
Goal:	The goal of this project is to strengthen the Institutional Review Board (IRB) of the Council for Scientific and Industrial Research (CSIR) and contribute towards the strengthening of the National Ethics Committee.
Objectives:	This project is expected to equip and strengthen the IRB of CSIR and Ghana as a whole. It is envisaged that the CSIR-IRB will be more effective and efficient in its operations and contribute directly towards improving the quality of health research in Ghana. The specific objectives of the project are: 1. To strengthen the technical component of the CSIR-IRB 2. Train IRB Board members in Ethical Review processes 3. Awareness creation on human research ethics in all 13 CSIR institutes 4. Train research scientists in CSIR and other institutions on research ethics involving human subjects 5. Strengthen the infrastructure of CSIR-IRB secretariat 6. Facilitate the strengthening of the National Ethics Committee 7. Train the CSIR-IRB administrative assistant on research ethics. The following activities will be carried out: 1. Organise training workshops for the IRB members 2. Strengthen the IRB of the CSIR 3. Strengthen the infrastructure of the secretariat of the CSIR-IRB 4. Train CSIR research scientists and scientists from other Ghanaian institutions on ethical processes 5. Institute supporting mechanisms for the retention of members of the ethics board 6. Make the CSIR IRB independent in order to avoid potential conflicts of interest and to safeguard the integrity of the IRB 7. Establish a tracking system for research ethics 8. Supervise and monitor research on human subjects.
Status:	Ongoing
Results and Outcomes:	1. Infrastructure/capacity Development – The following equipment was purchased: one photocopy machine, one shredder, one laptop, and one printer. 2. Training (resources developed (e.g. manuals) and human capacity developed) – Standard Operating Procedures (SOPs) for the CSIR-IRB were developed. The CSIR-IRB administrative

	assistant will complete a Master's degree in health research ethics. Research scientists and technical staff in the 13 CSIR institutes were sensitised on research ethics (approximately 352 scientists and technical staff) (between 7 May 2012 and11 June 2012). They were educated on the need for ethical clearance on research involving the use of human subjects to ensure that the welfare and safety of research participants are protected. The IRB co-ordinator, administrative assistant and resource persons travelled to the 13 CSIR institutes located in the various parts of the country to organise awareness creation seminars on research ethics. The details of the participants are as follows: CSIR-Water Research Institute (WRI), 40 participants; CSIR-Food Research Institute (FRI), 32 participants; CSIR-Institute of Scientific and Technological Information (INSTI), 24 participants; CSIR-Savannah Agriculture Research Institute (SARI), 32 participants; CSIR-Animal Research Institute (ARI), 22 participants; CSIR-Science and Technology Policy Research Institute (STEPRI), 9 participants; CSIR-Soil Research Institute (SRI), 32 participants; CSIR-Forestry Research Institute of Ghana (FORIG), 58 participants, CSIR-Oil Palm Research Institute (OPRI) 29 participants; CSIR-Plant Genetic Resource Research Institute (PGRRI), 22 participants; and CSIR-Crop Research Institute (CRI), 52 participants. Training on 'effective reviewing of protocols' was organised for IRB members (9 participants; 11 July 2012). Workshop for the southern sector on 'strengthening of institutional review boards and capacity building of scientists on research ethics' (60 participants; 22 January 2013) took place. Workshop for the northern sector on 'strengthening of institutional review boards and capacity building of scientists on research ethics' (52 participants; 16 October 2012) took place. The administrative assistant of the CSIR-IRB completed a two week short course on effective writing and communication skills. 3. Networking/collaborations developed – Noguchi Memorial Institute for Medical Research (NMIMR) – Ghana Health Service

9.1.58 Damasceno-Mozambique-Ethics

EDCTP Project Coordinator:	Albertino Damasceno (Eduardo Mondlane University and Maputo Central Hospital, Mozambique)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Establishing a local Institutional Ethical Committee/IRB at Universidade Eduardo Mondlane Faculty of Medicine and Maputo Central Hospital in Maputo, Mozambique
EDCTP Project Code:	CB.2011.41302.015
EDCTP Project Start Date:	23 March 2012
EDCTP Project End Date:	22 September 2013
Collaborators:	• Moshin Sidat (Mozambique) • João Fumane (Mozambique) • Domingos Dias Diogo (Mozambique)
Type of Project:	Institutional Review Board
Goal:	This project seeked to establish an ethics committee to help expand clinical research in Maputo and throughout Mozambique. This new research consortium represents the first decentralised Ethical Committee/IRB in Mozambique.
Objectives:	The aim of this project was to initiate and then strengthen the capacity of this ethics committee (Comité Maputo de Bioética para Saúde - Projeto CMBS). Activities in support of this aim included: 1. Formation of an ethics working group, including CMBS members and members of the National Health Ethics Committee (NHEC) 2. Training of members of the NHEC who have not had formal ethics education, including extensive review of other national research ethics guidelines 3. Drafting of Standard Operating Procedures (SOPs) for CMBS and finalising its constitution and mandate 4. Serve as a decentralised paradigm organisation for developing local institutional ethics guidelines for biomedical and public health research. Research guidelines that are responsive to the different kinds of health research as well as to the challenges of ethically conducting research among diverse population groups in resource-poor settings will be developed 5. Drafting of local institutional guidelines for medical and public health research in Mozambique 6. Holding public panel discussions regarding the CMBS ethics guidelines and incorporating feedback into a final version 7. Dissemination of guidelines on the Mozambican Ministry of Health website.
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – The following equipment was purchased: one laptop, one photocopy machine and three lockable metal filing cabinets. 2. Training (resources developed (e.g. manuals) and human capacity developed) - The ethics committee was recognised by the NEC on 29 November 2012. The following training took place: research ethics training for new ethics committee members (11 participants; 26-27 February 2013); workshop on 'reinforcing capacity in the ethical review of research' (9 participants; 14 May 2013); and research ethics training (7 participants; 31 May

	2013). 3. Networking/collaborations developed – Medical School of Oporto (Portugal)

9.1.59 Ntsiba-CERSSA-Ethics

EDCTP Project Coordinator:	Honoré Ntsiba (Comité d'Ethique de la Recherche en Sciences de la Santé (CERSSA), Republic of Congo)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Enhancement of awareness and implementation of ethics principles for research involving humans in the Republic of Congo
EDCTP Project Code:	CB.2011.41302.006
EDCTP Project Start Date:	31 January 2012
EDCTP Project End Date:	30 December 2013
Collaborators:	• Edouard Makosso (Republic of Congo) • Jean-Vivien Mombouli (Republic of Congo) • Mathieu Ndounga (Republic of Congo)
Type of Project:	Institutional Review Board
Goal:	The goal of this project is to improve the quality of the implementation of ethics principles in research involving humans in scientific activities carried out in the Republic of Congo or involving scientists and institutions from that country.
Objectives:	The following activities will be carried out: 1. Build management capacity to facilitate work and improve yield (including infrastructure development) 2. Enhance skills and knowledge in the evaluation of research protocols 3. Reinforce quality assurance procedures and practices 4. Provide scientists and students with resources to acquire knowledge and skills 5. Enhance awareness of regulatory officials in health sciences research, political leadership and civil society leaders.
Status:	Ongoing
Results and Outcomes:	1. Infrastructure/capacity development – Infrastructure rehabilitation, including security and meeting/teaching room, has taken place. Work was done to floors by adding tiles, doors, steel doors and windows for security, repair of the toilets and painting of all the rooms. A street sign for directions was erected and a plate was positioned above the office suite entrance. Rehabilitation of building: o Security work (doors, steel doors, locks) o Toilet and sewage rehabilitation o Painting o Electrical wiring and lighting o Outside direction board o One entrance panel indicating office suite of CERSSA o Air condition repair o Office furniture: teaching/meeting room (tables, chairs, white retractable project screen, clock); President's office (one office L-shaped desk with three chairs, one placard); secretary's office (one office L-shaped desk with three chairs, two placards, one refrigerator, one coffee machine and one boiler); and archive room (four placards, two office desks, six chairs). – Office equipment including two desktop computers, three lap tops, two scanners, three printers, three voltage regulators, three UPS backup power suppliers (extenders and multiple plug devices), four standalone

	fans, three lap top bags, four USB hubs, Wifi modem (for internet access covering the entire office), one external drive and two antivirus software licenses were purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed) – CERSSA has acquired a substantial information technology platform thereby facilitating access to online training programmes as well as resources from other ethics review boards across Africa and around the world. Members have completed CITI (one participant) and TRREE (four participants) online programmes. SOPs have been adopted. – Training in ethics has been initiated at the Faculty of Health Sciences in the form of lectures. Training materials are in development for the specific training of scientists and students. These sessions will be based on preliminary lectures followed by self-conducted training using TRREE to gain a certificate. As a spin-off of the increased awareness and implementation activities, the Fondation Congolaise pour la Recherche Médicale (FCRM) has created its own IRB. 3. Networking/collaborations developed – Fondation Congolaise pour la Recherche Médicale (FCRM)

9.1.60 Noor-AAPH-Ethics

EDCTP Project Coordinator:	Ramadhani Abdallah Noor (Africa Academy for Public Health (AAPH), Tanzania)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Establishing a functional independent Institutional Review Board (IRB) for trials conducted by Africa Academy of Public Health (AAPH), Tanzania
EDCTP Project Code:	CB.2011.41302.023
EDCTP Project Start Date:	17 February 2012
EDCTP Project End Date:	16 August 2013
Collaborators:	• Guerino Chalamilla (Tanzania) • Joyce Ikingura (Tanzania) • Beverly Msambichaka (Tanzania)
Type of Project:	Institutional Review Board
Goal:	This project proposes establishment of a functional and sustainable Ethics Committee (EC) for the Africa Academy of Public Health (AAPH), a research organisation registered and based in Tanzania.
Objectives:	This 12 month project will involve activities aimed at setting up a functional office for the EC; have on board a full-time administrator for the EC; official establishment of the committee with the appropriate members appointed; as well as SOPs developed and adopted for all key EC operations. This project will also work on the development and piloting of what would ultimately be freely available, user friendly software for the EC administrative records and documentation management. The main expected outcome is to have a functional and compliant EC undertaking ethical review at the institutional level, where great needs exist in ensuring that all on-going and upcoming clinical trials are sufficiently reviewed and optimal oversight is available for these studies to be ethical and the populations involved adequately protected.
Status:	Ongoing
Results and Outcomes:	1. Infrastructure/capacity development – The following equipment was purchased for the AAPH EC: two office tables, two lockable cabinets, one safe, one desktop computer, one UPS, one lap top, one photocopier and one projector. Accounting software, Quick Book license, has been obtained to support the accounting and financial needs of the AAPH ethics committee 2. Training (resources developed (e.g. manuals) and human capacity developed) – A domain for the website has been obtained and secured with high security features. The contents for the website are currently being developed with IT assistance. Potential AAPH ethics committee members and members from local IRBs completed the 'health research ethics and practice: maximising protections, minimising obstacles' training (27 participants; 27-29 February 2012). The development of the online database is in progress. Draft SOPs have been developed. 3. Networking/collaborations developed – National Institute for Medical Research (NIMR) – Tanzania Food and Drug Authority (TFDA) – Ifakara Health Institute (IHI)

	– Muhimbili University – Muhimbili University College of Health Sciences (MUHAS) – Office of Human Research Administration and Compliance at the Harvard School of Public Health (ORARC) – United Nations Interregional and Justice Research Institute (UNICRI) (Italy) – Central African Network on Tuberculosis, HIV/AIDS and Malaria (CANTAM)

9.1.61 Okullo-Makerere-Ethics

EDCTP Project Coordinator:	Isaac Okullo (Makerere University, Uganda)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Establishing and strengthening the Institutional Review Board at the School of Health Sciences, College of Health Sciences, Makerere University
EDCTP Project Code:	CB.2011.41302.010
EDCTP Project Start Date:	22 February 2012
EDCTP Project End Date:	21 February 2014
Collaborators:	• Maria De Rosa (Italy) • Freddy Eric Kitutu (Uganda) • Paul Kutyabami (Uganda) • Charles Rwenyonyi (Uganda) • Nelson K. Sewankambo (Uganda)
Type of Project:	Institutional Review Board
Goal:	To empower the School of Health Sciences IRB to critically review, approve and monitor biomedical and behavioural research involving humans in order to protect their rights and welfare.
Objectives:	The School of Health Sciences proposes to establish an Institutional Review Board (IRB); complete the accreditation process of its IRB with the Uganda National Council of Science and Technology (UNCST); conduct a needs assessment of research ethics knowledge and skills among faculty; strengthen the infrastructure and human resource capacity of the IRB secretariat; design training programmes for induction of new IRB members; maintain continuing education for researchers and IRB members; conduct active monitoring of approved research protocols (as required by national guidelines); innovate strategies for financial sustainability; institute support mechanisms for ethics committee members retention; and conduct operational research on ethical processes (because of increased compliance requirements from international partners).
Status:	Ongoing
Results and Outcomes:	1. Infrastructure / Capacity Development – The following equipment was purchased for Makerere University School of Health Sciences IRB: one laptop, one LCD data projector, two filing cabinets, one office telephone and one photocopier. The IRB and its secretariat were established and are currently functional. A full-time IRB administrator was employed. 2. Training (resources developed (e.g. manuals) and human capacity developed) – The project team and IRB secretariat reviewed and adapted Standard Operating Procedures for the MakSHS-IRB. SOP development and dissemination workshop took place (16 participants; 3 July 2012). A 'human subject protection' course was held by UNCST (35 participants; 19-20 March 2012). Seven IRB members participated in networking activities, including attending the annual research and ethics conference (10-11 July 2012) organised by UNCST and attended workshops with other IRBs. The project team conducted a rapid situational analysis and designed monitoring and evaluation tools for the i) project progress, ii) IRB function and operations, iii) financial monitoring of project. The MakSHS-IRB developed and instituted a

	research fees structure payable to the IRB in order to raise funds to support the operations of the IRB as part of the sustainability after the grant ends. 3. Networking/collaborations developed – Uganda National Council of Science and Technology (UNCST) – CINECA (Italy)

9.1.62 Olupot-Olupot-MRHIRC-Ethics

EDCTP Project Coordinator:	Peter Olupot-Olupot (Mbale Regional Hospital Institutional Review Committee (MRHIRC), Uganda)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening research ethics capacity of the Mbale Regional Hospital Institutional Review Committee
EDCTP Project Code:	CB.2011.41302.016
EDCTP Project Start Date:	9 March 2012
EDCTP Project End Date:	8 March 2013
Collaborators:	• Jeanette Meadway (United Kingdom) • Mark R. Nelson (United Kingdom)
Type of Project:	Institutional Review Board
Goal:	The goal of this project was to have a well-established Mbale Regional Hospital Institutional Review Committee (MRHIRC) equipped with an appropriate team; infrastructure; and guidelines for review and monitoring of research ethics at Mbale Hospital and in the region.
Objectives:	This project aimed to strengthen the ethics capacity at the Mbale Regional Hospital Institutional Review Committee (MRHIRC) to perform high quality research and ethical review as well as monitoring of research through: 1. Training of the MRHIRC members to review and monitor research 2. Development of relevant Standard Operation Procedures (SOPs) 3. Procurement of office furniture, equipment and supplies 4. Development of research review and monitoring tools to enhance standardised systematic protocol review and monitoring of research 5. Development of archival process for all the reviewed research and communication protocols 6. Development of complete review structures at the hospital that will include carrying out Scientific Review (SR), Endpoint Review (ER) and Community Advisory Roles (CAR) to work with the MRHIRC 7. Enhancing electronic ICT capacity for communication, networking and registration of research 8. Recruiting and employing staff to handle the management process of the MRHIRC 9. Network with experienced IRCs, partners and Data Safety Monitoring Boards, both locally and internationally, in order to: promote safe research; exchange ideas and skills on research monitoring and review; as well as transfer skills and technology (as may be deemed appropriate).
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – MRHIRC has a fully functional office that houses the MRHIRC Secretariat at the Mbale Regional Referral Hospital. The following equipment was purchased: six office tables, 12 chairs, two telephones, five desktop computers, two printers, one document scanner and one photocopier. Two administrators were recruited and employed on a full time one year contract 2. Training (resources developed (e.g. manuals) and human capacity developed) – The MRHIRC through consultations, under the guidance of the Chairman and the Secretary General, developed a

	final copy of the SOPs. This was done through holding SOP review and development meetings with all members of the MRHIRC (30 April 2012, 7 May 2012, 14 May 2012, 7-8 June 2012, 10 June 2012 and 29 October 2012). All heads of departments of MRRH were given the first draft of the SOPs and thereafter comments were sent back to the Secretary General who presented them to all members of the MRHIRC. The final copy/version of the SOPs (MRHIRC SOPs manual version 1.2 dated 25 October 2012) was sent to UNCST for review and was approved. On 19 November 2012, members of MRHIRC organised and participated in a research site visit and monitored five studies that were being carried out at MRRH. The MRHIRC secretariat developed a database for archiving submitted study protocols and completed research reports/dissertations to promote confidentiality of participants' information. In addition, the secretariat created filing shelves to store hard copy proposals and research reports. An ethics course curriculum for use as face-to-face training was developed. It is planned that in future this will be an online course. A capacity building training on scientific reviews involving a curriculum on ethics, research review, research monitoring, statistics, biostatistics and epidemiology was conducted for three weeks at Mbale Regional Referral Hospital (30 participants; 21 May-8 June 2012 and 27-31 August 2012). Some members of the MRHIRC enrolled in free online research ethics training courses on ethics, good clinical practices and research. All members of the MRHIRC attended university modules on ethics training. By the 3rd quarter of the project implementation, MRHIRC had attained high level performance standards and was accredited by UNCST as a nationally recognised institutional review committee. The UNCST issued an accreditation certificate on 23 November 2012. The MRHIRC developed a research-monitoring plan to protect the rights and welfare of research subjects as well as minimisation of risks involved in research. MRHIRC developed a brochure to disseminate useful information about the review process for researchers and also visitors to Mbale Hospital. The following is the basic information on the brochure as grouped under the following sub-headings: MRHIRC establishment, composition, administration, mandate, scope, protocol information, requirements for submission for initial and continuing review, requirements for progress reports and/or request to renew, action taken if documentation is not adequate or additional information is required, meetings and proposed review fees. 3. Networking/collaborations developed – Uganda National Council for Science and Technology (UNCST) – St Stephens AIDS Trust – MforM Africa (United Kingdom) – NIMR-Amani Medical Research Centre (Tanzania) – Global Health Trials

9.1.63 Nkandu-Zambia-Ethics

EDCTP Project Coordinator:	Esther Nkandu (University of Zambia (UNZA), Zambia)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening research ethics in Zambia
EDCTP Project Code:	CB.2011.41302.024
EDCTP Project Start Date:	6 February 2012
EDCTP Project End Date:	5 February 2013
Collaborators:	• Fastone Goma (Zambia) • James Munthali (Zambia)
Type of Project:	Institutional Review Board
Goal:	This project proposed to establish an independent Directorate of Research Ethics (DRE) within the University of Zambia (UNZA) headed by a dedicated director who will oversee the activities of all three UNZA research ethics committees (RECs) with the help of the REC Secretariats.
Objectives:	The objectives of this project were to: 1. Strengthen the UNZA (University of Zambia) Research Ethics Committees' review, monitoring, and training capacity by establishing an independent Directorate of Research Ethics with dedicated staff and effective IRB software 2. Support the newly constituted National Health Research Ethics Committee through training and consultation 3. Serve as a resource for researchers in Zambia by providing research ethics and good clinical practices training 4. Conduct training on basic research ethics; community participation in research; and the role of community representatives for two rural communities.
Cofunders:	• Centre for Infectious Disease Research in Zambia (CIDRZ) (Zambia)
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – The following equipment was purchased for the University of Zambia, School of Medicine: Two lap tops, four office chairs, three office desks, one conference table, four filing cabinets, three hanging drawers and nine chairs 2. Training (resources developed (e.g. manuals) and human capacity developed) – An educational visit was made to the University of North Carolina (USA) as a familiarisation tour to activities of a Directorate of Research Ethics. Research ethics training (33 participants; 22-24 February 2012) and training of community members on research ethics in two rural areas in Chongwe (241 participants; 8 March 2012 and 12 March 2012) took place. The Biomedical Research Ethics Committee has been a resource centre for various research groups (academics, non-academics and students). Software for the REC is being developed. SOPs were developed and/or enhanced for UNZA RECs. The establishment of the Directorate of Research Ethics is in progress. 3. Networking/collaborations developed – CIDRZ – University of North Carolina (UNC) – National Health Research Ethics Committee, Zambia

9.1.64 Mutenherwa-BRTI-Ethics

EDCTP Project Coordinator:	Farirai Mutenherwa (Biomedical Research and Training Institute (BRTI), Zimbabwe)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening the ethical review and oversight of health systems and social science research in Zimbabwe
EDCTP Project Code:	CB.2011.41302.014
EDCTP Project Start Date:	15 February 2012
EDCTP Project End Date:	14 June 2013
Collaborators:	• Midion Mapfumo Chidzonga (Zimbabwe) • Exnevia Gomo (Zimbabwe) • Rosemary Musesengwa (Zimbabwe)
Type of Project:	Institutional Review Board
Goal:	This project focused on activities aimed at strengthening the capacity of two research ethics committees (RECs), namely the Biomedical Research and Training Institute Institutional Review Board (BRTI-IRB) and the Joint Research Ethics Committee (JREC) to review two types of studies: (i) health systems research and (ii) social sciences research.
Objectives:	The focus was on three main activities: research; the development of practice guidelines; and training of RECs, Community Advisory Boards (CABs), researchers and research regulators in responding positively to the requirements of communities. Specifically, the project will: 1. Establish the perceptions of REC members, research regulators, researchers and CAB members on health systems and social science research 2. Identify the processes involved and criteria used for the approval of health systems and social science research 3. Determine the attitudes of REC members, CAB members and regulatory bodies towards the review and conduct of health systems and social science research 4. Assess the capacity of, challenges faced by and the training needs of RECs in the review of health systems and social science research 5. Establish the ethical and legal framework guiding health systems and social science research in Zimbabwe.
Status:	Completed
Results and Outcomes:	1. Infrastructure/capacity development – BRTI IRB received the following equipment: 1 full set desktop, 1 printer, 1 laptop, 2 (four tier) lockable cabinets, 1 secretarial chair, 2 visitor's chairs and 1 executive desk. – JREC received the following equipment: 1 full set desktop, 1 printer, 2 (four tier) lockable cabinets, 1 office desk, 1 secretarial chair and 2 visitor's chairs. 2. Training (resources developed (e.g. manuals) and human capacity developed) – A situational analysis on the conduct of ethics review of health systems research and health social science at institutional and national levels was conducted. Development of good practice guidelines on the review of health systems research and social science research is in progress and requires wider consultation than had initially been planned. Once completed, the guidelines will be presented to MRCZ for adoption nationally. A three-day training course entitled 'ethical issues in health

	research in Africa with special emphasis on social science and health systems research' (11-13 September 2012; 18 participants) was conducted by the Biomedical Research and Training Institute (BRTI) in collaboration with the Joint Research Ethics Committee (JREC) of the College of Health Sciences, University of Zimbabwe and the Medical Research Council of Zimbabwe (MRCZ). The course was designed to provide knowledge, concepts and skills appropriate for the review and approval of health systems and social sciences research in Zimbabwe. The second training course ('health research ethics workshop: development of ethics guidelines for social sciences and health systems research') (23-24 May 2013; 32 participants) was a follow up workshop to address issues raised during the first training course. Specifically, the workshop sought to develop a draft framework (guidelines) for ethical review of HSS and HSR as well as to develop an outline for future training courses for reviewers, regulators, researchers and communities. The workshop was also used as a platform for the dissemination of results from the situational analysis. A Microsoft Access database that will be used for capturing, storing and reporting IRB activities was developed. 3. Networking/collaborations developed – Medical Research Council of Zimbabwe (MRCZ) – College of Health Sciences, University of Zimbabwe

9.1.65 Oloo-CREATES-Ethics

EDCTP Project Coordinator:	Florence Oloo (Strathmore University, Kenya)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Establishment of Institutional Review Board at the Centre for Research in Therapeutic Sciences
EDCTP Project Code:	CB.2011.41302.029
EDCTP Project Start Date:	13 August 2012
EDCTP Project End Date:	12 August 2014
Collaborators:	• John Odhiambo (Kenya) • Antoinette Kankindi (Kenya) • Bernhards Ogutu (Kenya)
Type of Project:	Institutional Review Board
Goal:	The project aims at building ethics review and monitoring capacity.
Objectives:	In establishing the Institutional Review Board (IRB), the proposed activities aim at building capacity for ethics review and monitoring research at the Centre for Research in Therapeutic Sciences (CREATES). It is expected that at the end of two years, members of the IRB will have been sufficiently trained to accomplish their function within the committee effectively. The IRB would also have a functional Secretariat and relevant SOPs in place. Objectives: 6. Establishment of an Institutional Review Board within CREATES to approve research protocols in compliance with national and international ethical conduct 7. Recruit and train members of the IRB in line with internationally accepted standards 8. Develop SOPs and guidelines of the IRB in line with international and Kenyan regulatory requirements 9. Develop a registry for the protocols and activities with a robust tracking system.
Status:	Ongoing
Results and Outcomes:	1. Infrastructure/capacity development – The following equipment was purchased: one smart board screen, one desktop computer and one laptop. 2. Networking/collaborations developed – African Centre for Clinical Trials (ACCT) – Council for Scientific and Industrial Research (CSIR) (South Africa) – Kenya Medical Research Institute (KEMRI) – University of Nairobi – Maseno University – Moi University

9.1.66 Ekouevi-Togo-Ethics

EDCTP Project Coordinator:	Didier Koumavi Ekouevi (Université de Lomé, Togo)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening the National Health Research Ethics Committee of Togo
EDCTP Project Code:	CB.2011.41302.032
EDCTP Project Start Date:	23 August 2012
EDCTP Project End Date:	22 June 2014
Collaborators:	• Kossivi Agbelenko Afanvi (Togo) • Alex Mazabalo Aleza (Togo) • Moustapha Mijiyawa (Togo) • François Gado Napo-Koura (Togo) • Vincent P. Pitche (Togo)
Type of Project:	National Ethics Committee
Goal:	To train the National Health Research Ethics Committee in order to set up research procedures that complies with international standards.
Objectives:	The National Health Research Ethics Committee of Togo (NHREC) was set up in 2008, but has not been effective because of lack of funding, inadequate training and poor communication between healthcare workers in Togo and the members of the ethics committee. The proposed project aims to ensure that studies conducted by health researchers and medical students use internationally accepted and standard research procedures. By strengthening the NHREC, the project intends to improve the communication between health researchers and ethics committee members, provide all of the materials needed for conducting ethical research and ensure that training provided is in compliance with national and international bioethics guidelines. The objectives of the project are to: 1. Provide training in health research and bioethics to healthcare workers involved in health research activities 2. Conduct updated training for the NHREC members of Togo who have not had specific instruction in health research ethics. Such training will aim to improve committee members' capacity to properly review health research protocols and contribute to policy formulation in health research ethics in Togo 3. Provide training to medical students as they prepare for their theses 4. Implement the tools for updated training and to improve the communication between the ethics committee members and healthcare workers 5. Create a database for improved monitoring of all studies submitted to the ethics committee 6. Create a website that will include information about how the National Health Research Ethics Committee of Togo functions 7. Renovate and equip the National Ethics Committee for health research office.
Status:	Ongoing
Results and Outcomes:	1. Infrastructure/capacity development – One computer, one printer and one video projector were purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed)

	– Trainers were trained in research ethics (6 April 2013; 52 participants). Final year medical students received training on research ethics (20 July 2013; 120 participants). Website for the Bioethics Committee for Research in Health Sciences (CBRS) was created (http://www.cbrstogo.org/). A pamphlet to increase awareness on the structure of the NHREC for the general public was created. The pamphlet was distributed in the six regions of Togo and more than 300 pamphlets were distributed. A database with a complete list of projects submitted to the ethics committee was created. Members of the ethics committee completed online training from Family Health International (FHI). 3. Networking/collaborations developed – National Bioethics Advisory Council – Ministry of Health (Togo)

9.1.67 Kangwende-Zimbabwe-Ethics

EDCTP Project Coordinator:	Rugare Abigail Kangwende (Africa University, Zimbabwe)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Establishment of an Institutional Review Board at Africa University, Mutare, Zimbabwe
EDCTP Project Code:	CB.2011.41302.034
EDCTP Project Start Date:	1 September 2012
EDCTP Project End Date:	28 February 2014
Collaborators:	• Auxillia Chideme-Munodawafa (Zimbabwe) • Simbirayi Gwaze (Zimbabwe) • Vhumani Magezi (Zimbabwe) • Rosemary Musesengwa (Zimbabwe) • Fadzai Mutseyekwa (Zimbabwe) • Anderson B. Shankanga (Zimbabwe) • Gilbert Utshudienyema M. Wembodinga (Zimbabwe)
Type of Project:	Institutional Review Board
Goal:	The ultimate goal is to have large volumes of ethically and scientifically sound research conducted at Africa University and its surrounding areas.
Objectives:	The main objective of the project is to establish a new Institutional Review Board (IRB) at Africa University (AU) that is competent and independent. There is no IRB at AU, and none in the whole province. The applicants propose to undertake the following activities to set up an IRB at AU: 1. Set up and equip an office for the AU IRB 2. Develop constitution, guidelines and policy documents for the IRB 3. Establish and capacitate the IRB secretariat, with the support of the National Ethics Committee 4. Train a critical mass of citizens from Manicaland Province on research ethics, and from this group appoint the IRB 5. Induct, train and establish internship and benchmark programmes to capacitate the IRB 6. Develop and implement IRB Standard Operating Procedures (SOPs) 7. Sensitise AU faculty, students, surrounding institutions and general public about research ethics, review process, and existence of the newly established IRB 8. Identify and capacitate reviewers 9. Develop a strategic plan to guide the IRB in the period immediately following the end of this project.
Cofunders:	• Africa University
Status:	Ongoing
Results and Outcomes:	1. Infrastructure/capacity development – One laptop, one printer/scanner, one photocopier, one paper shredder, four visitor's chairs, one LCD projector and one mobile phone handset were purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed) – A trainee Research Ethics Programme Officer was recruited to train and serve as the IRB administrator. Terms of Reference (ToRs) were developed for the Africa University Research Ethics Committee (AUREC). Ethics training workshop for potential IRB members and the secretariat was conducted (25 January 2013; 28 participants). A nine member Africa University Research Ethics Committee was appointed by the AU Vice

	Chancellor. The leadership of this AUREC has also been established. A research ethics training and induction workshop was conducted for AUREC members and the secretariat (4-8 March 2013; 15 participants). The IRB administrator successfully completed the online research ethics course with TRREE up to the third level. The IRB Administrator completed an internship at MRCZ (14-23 November 2012). 3. Networking/collaborations developed – Family AIDS Caring Trust (FACT) – Medical Research Council of Zimbabwe (MRCZ) – Joint Research Ethics Committee (J-REC) for the Parirenyatwa Hospital and the University of Zimbabwe College of Health Sciences – Biomedical Research and Training Institute (BRTI) Research Ethics Committee

9.1.68 Mbae-ECSA-Ethics

EDCTP Project Coordinator:	Josephine Kibaru Mbae (East, Central and Southern African Health Community (ECSA-HC), Tanzania)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Establishment of a Regional Scientific and Ethical Review Committee (ECSA-RSEC) in the ECSA region
EDCTP Project Code:	CB.2011.41302.036
EDCTP Project Start Date:	1 September 2012
EDCTP Project End Date:	28 February 2014
Collaborators:	• Francis Kimani (Kenya)
Type of Project:	Institutional Review Board
Goal:	To support the development of quality and consistent research activities to promote collaborative research, safety and to safeguard the interests of research participants.
Objectives:	The East, Central and Southern African Health Community (ECSA HC) is a regional inter-governmental health organisation that fosters and promotes regional cooperation in health among member states. The 10 member states of the ECSA Health community include Kenya, Lesotho, Malawi, Mauritius, Seychelles, Swaziland, United Republic of Tanzania, Uganda, Zambia and Zimbabwe. The ECSA Secretariat proposes to establish a Regional Ethical Research Committee (RERC) that will act as an oversight body charged with the responsibility of approving multi-country research proposals and capacity building of the NECs of the member states. The expected outcome is speedy approval and facilitation of multi-country research proposals within the region. The objectives of the ECSA-RSEC are to: 1. Establish a regional ethical body to facilitate scientific review and ethical approval of multi-country and multisite research studies in the ECSA-region 2. Provide a platform for networking amongst member states and partners and improve south-south and north-south collaborations in research 3. Strengthen research capacity and ethical reviews among collaborating partners through sharing of expertise and knowledge between scientists in different countries in the region 4. Establish and strengthen linkages with local ethics committees of institutions conducting clinical research and with appropriate government agencies and international organisations involved in ethical review 5. Promote the rights, confidentiality, safety and protection of human dignity and well-being of volunteers participating in human research 6. Establish a regional database for multi-country research findings and knowledge sharing within the ECSA region that is easily accessible to member states; to promote data sharing between national and regional databases.
Status:	Ongoing
Results and Outcomes:	

9.1.69 Mombo-Ngoma-MRU-Ethics

EDCTP Project Coordinator:	Ghyslain Mombo-Ngoma (Centre de Recherches Médicales de Lambaréné (CERMEL), Gabon)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening of an Institutional Review Board according to international standards at the Albert Schweitzer Hospital in Lambaréné, Gabon
EDCTP Project Code:	CB.2011.41302.039
EDCTP Project Start Date:	1 September 2012
EDCTP Project End Date:	28 February 2014
Collaborators:	• Rella Manego Zoleko (Gabon) • Pierre Blaise Matsiegui (Gabon) • Afsatou Ndama Traoré (Gabon) • Odile Ouwe Missi Oukem (Cameroon)
Type of Project:	Institutional Review Board
Goal:	The main goal of the initiative is to create a viable IRB that would meet international standards with the purpose of reinvigorating research activities at the Medical Research Unit (MRU) of Lambaréné.
Objectives:	The intention is to use the knowledge gained in the process to promote capacity building in biomedical ethics and to facilitate the development of IRBs at other institutions in Gabon and other African countries. The applicants aim to strengthen the IRB of the MRU according to international standards. To achieve this, a private-public partnership will be developed to support a review of prevailing practice and the development of necessary infrastructure for an effective IRB. An internationally registered and well constituted IRB will be established within 18 months. This project will lead to the development of a designated IRB office at the MRU with appropriate procurement of furniture, needed equipment such as computers, printers, photocopier, scanner, filling cabinets and staff (secretary and clerk) to execute all related activities of the IRB.
Status:	Ongoing
Results and Outcomes:	1. Infrastructure/capacity development – One laptop was purchased. 2. Networking/collaborations developed – University of Tuebingen in Germany (UKT) – Medical University of Vienna (Austria) – University of Leiden (The Netherlands) – University of Barcelona (Spain) – Council on Health Research for Development (COHRED) – Cameroon Bioethics Initiative (CAMBIN)

9.1.70 Nyika-ZIMFRI-Ethics

EDCTP Project Coordinator:	Aceme Nyika (Public Health Projects in Africa (PHPAfrica), Zimbabwe)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening and harmonizing health research ethics through collaborative partnerships and joint training of the Zimbabwean Forum of Research Institutions (ZIMFRI)
EDCTP Project Code:	CB.2011.41302.042
EDCTP Project Start Date:	20 August 2012
EDCTP Project End Date:	19 April 2014
Collaborators:	• Umberto Filibeck (Italy) • Ronnie Matambo (Zimbabwe) • Takafira Mduluza (Zimbabwe) • Rosemary Musesengwa (Zimbabwe) • Paul Ndebele (United States of America)
Type of Project:	Coordination function
Goal:	The goal of the project is to enhance the effectiveness and efficiency of ethical review processes in Zimbabwe.
Objectives:	This project is aimed at strengthening and harmonising health research ethics in Zimbabwe. In order to maximise utilisation of existing expertise and meagre resources, the Public Health Projects in Africa (PHPAfrica) has spearheaded the formation of the Zimbabwe Forum of Research institutions (ZIMFRI) through which strengthening and harmonisation of health research ethics in Zimbabwe will be carried out. ZIMFRI has been formed and is ready to be used as a platform for this project. The institutions that are part of ZIMFRI are (1) University of Zimbabwe, (2) Medical Research Council of Zimbabwe, (3) Africa University, (4) Midlands State University, (5) Chinhoyi University of Technology, (6) City of Harare, and (7) PHPAfrica. The specific objectives are to: 1. Develop and review curriculum and training materials for the basic Health Research Ethics (HRE) workshop for IRB members, researchers and policy makers from ZIMFRI. 2. Train IRB members, researchers and policy makers from ZIMFRI on basic HRE. 3. Disseminate information about the basic HRE to ZIMFRI members and to other stakeholders in Zimbabwe and beyond. 4. Develop and review the curriculum and training materials for the Advanced HRE workshop for IRB members, researchers and policy makers from ZIMFRI. 5. Train IRB members, researchers and policy makers drawn from ZIMFRI on advanced HRE. 6. Disseminate information about the advanced HRE to ZIMFRI members and other stakeholders in Zimbabwe and beyond. 7. Contribute towards harmonisation of health research ethics in Zimbabwe within the MRCZ national framework and through networking and partnerships, firstly within ZIMFRI and, secondly, with international collaborators that include UNICRI-Italy.
Status:	Ongoing
Results and Outcomes:	

9.1.71 Okoye-AGCPN-Ethics

EDCTP Project Coordinator:	Ifeoma Okoye (Association for Good Clinical Practice in Nigeria (AGCPN), Nigeria)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Towards more ethics in ethics committee conduct: Building capacity of ethics committees to conduct research monitoring
EDCTP Project Code:	CB.2011.41302.048
EDCTP Project Start Date:	20 August 2012
EDCTP Project End Date:	19 August 2013
Collaborators:	• Emmanuel Okechukwu Nna (Nigeria) • Uzoma Ijeoma Chinwe (Nigeria)
Type of Project:	Support for courses on ethics
Goal:	To train 36 IRB members in the northern and southern Nigerian States.
Objectives:	This project proposes to assess the capacity of members of ethics committees that have been trained via EDCTP projects in the country in the last five years on how to monitor research and clinical trials. This is important because it could help ensure accountability through research and trials monitoring as well as build the capacity of those who should be conducting the monitoring exercise. The application built on the activities of a previous EDCTP grant, but this time proposed to provide training to laypersons and other members of IRBs. This should help facilitate dialogue and practical discussions. The training will reach out to several additional ethics committee members from institutions in northern Nigeria. Specifically, it shall reach out to three new ethics committees in three northern states in Nigeria. The project will set out to achieve the following objectives: 1. Build the skills of 36 IRB members from 18 IRBs reached through EDCTP funded activities in Nigeria on how to monitor approved research so as to ensure accountability and transparency. 2. Facilitate dialogue between laypersons and other members of the targeted 18 IRBs on how to better conduct the review and monitoring of research. 3. Pilot test and print a developed adaptable training curriculum for IRB members (adaptable for use for both laypersons and clinicians) on monitoring of clinical trials. 4. Step down training for other members of the 18 IRBs participating in the training.
Status:	Completed
Results and Outcomes:	1. Training (resources developed (e.g. manuals) and human capacity developed) – The project was able to build skills in health research ethics and ethical review capacity of 36 IRB members from 18 IRBs in both Northern and Southern Nigeria. The project facilitated dialogue between 22 laypersons and 50 medical persons on best practices for conducting ethical review and monitoring of research. A total of 72 persons (22 laypersons and 50 medical personnel) were trained. The capacity building was designed to reach out to 15 and three new (unregistered) IRBs in Northern and Southern Nigeria respectively. Four new IRBs were registered for the first time with the National Health Research Ethics Committee (NHREC): Federal Medical Centre (FMC) Health Research Ethics (HREC) Gombe; Abubakar Tafawa Balewa University Teaching Hospital HREC; Benue State University Teaching

	Hospital HREC; and FMC Jalingo HREC. A handbook of 'health research ethics' for training IRB members was developed, tested and used in the training – the training training manual was approved by the National Health Research Ethics Committee (NHREC) of the Federal Ministry of Health. 2. Networking/collaborations developed – National Health Research Ethics Committee (NHREC), Nigeria – National Food and Drug Regulatory Agency (NAFDAC) – New HIV Vaccine and Microbicide Advocacy society (NHVMAS)

9.1.72 Sow-CNERS-Ethics

EDCTP Project Coordinator:	Oumou Younoussa Sow (Guinean National Ethic Committee for Health Research (CNERS), Guinea)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Support project for the strengthening of Guinean National Ethic Committee
EDCTP Project Code:	CB.2011.41302.046
EDCTP Project Start Date:	1 October 2012
EDCTP Project End Date:	30 September 2014
Collaborators:	• Alpha Mamadou Barry (Guinea) • Abdoul Habib Beavogui (Guinea) • Alexandre Delamou (Guinea) • Alpha Ahmadou Diallo (Guinea)
Type of Project:	National Ethics Committee
Goal:	To strengthen the Guinean National Ethic Committee's capabilities to appropriately apply ethical principles in their review of research protocols involving human subjects.
Objectives:	The Republic of Guinea established a National Ethic Committee for Health Research (CNERS) in August 1999 by presidential decree. The objectives of this project are to: 1. Evaluate continuously the activities and the functioning of the CNERS 2. Train the CNERS members and researchers in the field of ethics in research involving human subjects 3. Draft Standard Operating Procedures (SOPs) for the CNERS 4. Equip the CNERS with office materials, computers, printers, photocopy machine, website and a high speed and reliable internet connection.
Status:	Ongoing
Results and Outcomes:	1. Infrastructure/capacity development – The following equipment was purchased for CNERS: three desks, two arm chairs, seven chairs, one desktop computer, three laptop computers (with accessories), one printer, one photocopier, two wooden cabinets and two air conditioners. The grant funded internet connectivity for CNERS (a WIFI wireless network was installed). 2. Training (resources developed (e.g. manuals) and human capacity developed) – Research ethics training took place (12-15 June 2013; 17 participants) (training report received in French). A permanent secretary was recruited. SOPs, monitoring and evaluation plan as well as communication plan were developed. A 'knowledge, attitudes and practices' survey was conducted. Three experience sharing visits took place to neighbouring NECs (Cote d'Ivoire, Senegal and Togo). 3. Networking/collaborations developed – Institute of Tropical Medicine (ITM) – Cote d'Ivoire NEC – Senegal NEC – Togo NEC

9.1.73 Atashili-Buea-Ethics

EDCTP Project Coordinator:	Julius Atashili (University of Buea, Cameroon)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Strengthening the capacity of the Faculty of Health Sciences Institutional Review Board, University of Buea, Cameroon
EDCTP Project Code:	CB.2011.41302.038
EDCTP Project Start Date:	1 October 2012
EDCTP Project End Date:	31 March 2014
Collaborators:	• Marceline Djuidje Ngounoue (Cameroon) • Mariana Kruger (South Africa) • Denis Nkweteyim (Cameroon)
Type of Project:	Institutional Review Board
Goal:	To strengthen the capacity of the Faculty of Health Sciences Institutional Review Board (IRB) through training, infrastructure improvement and research on the perception of research ethics in the IRB's target community.
Objectives:	The University of Buea, Faculty of Health Sciences Institutional Review Board (FHS IRB) was created in 2010 to address the research ethics of the wider research community of investigators and participants involved in research conducted by staff and students of the faculty. This project proposes to strengthen the capacity of the FHS IRB by: 1. Increasing human capacity through training on the ethical aspects of research for members of the FHS IRB and FHS investigators 2. Improving the infrastructural capacity of the FHS IRB by setting up an electronic system for receiving, distributing, and reviewing proposals as well as providing feedback to investigators and archiving 3. Setting up an ethical framework to form the basis for review of research proposals by assessing the knowledge, attitudes and practices of researchers, participants and the community at large.
Status:	Ongoing
Results and Outcomes:	1. Infrastructure/capacity development – Internet connectivity was set up for FHS IRB. The following equipment was purchased: Five laptops, one colour printer, one digital camera, two portable DVD writers, one security door, one video projector. 2. Training (resources developed (e.g. manuals) and human capacity developed) – Student researchers received training on the 'ethics of research in human participants' (91 participants; 26-28 September 2013). 3. Networking/collaborations developed – South African Research Ethics Training Initiative (SARETI) – University of Yaounde I

9.1.74 Touko -OCEAC-Ethics

EDCTP Project Coordinator:	Josiane Désirée Etang Touko (Organization for the Coordination of Endemic Disease Control in Central Africa (OCEAC), Cameroon)
EDCTP Call Title:	Support for the Establishment and the Strengthening of African National Ethics Committees or Institutional Review Boards
EDCTP Project Title:	Establishment of a multi-country Institutional Review Board hosted by OCEAC
EDCTP Project Code:	CB.2011.41302.045
EDCTP Project Start Date:	1 November 2012
EDCTP Project End Date:	31 October 2014
Collaborators:	• Hélène Degui (Cameroon) • Parfait Awono (Cameroon) • Abel Mouafo (Cameroon) • Aline Okoko (Cameroon) • Sylvie Kwedi Nolna (Cameroon) • Sidi Brahim Issa (Chad) • Constant Roger Ayenengoye (Gabon)
Type of Project:	Institutional Review Board, National Ethics Committee
Goal:	To create a multi-country Institutional Review Board (IRB) at OCEAC, built on existing ethics committees and Medicine Regulatory Authorities from CEMAC countries with the aim of reviewing multi-country health research protocols in which OCEAC is involved.
Objectives:	1. Set up a multi-country IRB hosted by OCEAC 2. Ensure that the four ethics principles are respected i.e.: autonomy, beneficence, non-maleficence, confidentiality 3. Organise the collaboration between in-countries or National Ethics Committees and Medicines Regulatory Authorities to evaluate the safety of drugs used in the trials with respect of the pharmaceutical functions: registration, pharmacovigilance and post marketing analysis, liberation of batches, follow-up of trials, inspection and quality control of drugs 4. Establish and strengthen a network with existing national or in-countries ethics committees in the central African sub-region, local and international partners (national regulatory authorities, ministries in charge of health research, research institutions, scientists and any other relevant parties) 5. Promote the creation and to assist with the organisation of National Ethics Committees in Chad and Equatorial Guinea.
Cofunders:	• OCEAC: Organisation de Coordination pour la lute contre les Endémies en Afrique Centrale (Organization for the Coordination of Endemic Disease Control in Central Africa) (Cameroon)
Status:	Ongoing
Results and Outcomes:	1. Infrastructure/capacity development – An office was provided by OCEAC for the coordination of the project. The office space is equipped with a computer and accessories used for project work as well as room for storage and archival of documents. OCEAC also provided meeting space for project meetings and other project activities. The following equipment was purchased with the EDCTP grant: one desktop computer (including a monitor, keyboard, mouse and surge protector), one laser printer and one laser copier.

	2. Training (resources developed (e.g. manuals) and human capacity developed) – A multi-country IRB, CERSAC (Comité d'Ethique pour la Recherche en Santé en AfriqueCentrale), was established. A workshop was held (25-27 November 2013; 5 participants) to finalise the documents necessary for the functioning of the CERSAC. These documents were generated to facilitate the creation of CERSAC as well as to outline its operations. These documents are: – Concept note for the creation of CERSAC (English and French versions) providing a brief justification on the rationale of creating the committee and its importance in the CEMAC region – By laws for CERSAC (English and French versions) were generated to serve as a governing tool for the functioning of the committee – Meeting agenda for the first CERSAC meeting (English and French versions). The first meeting will not only consist of convening the members, but it will also include training for the members to enhance their functions of reviewing clinical research protocols – Profile requirements for each individual member of the CERSAC (English and French versions) – Standard Operating Procedures (SOPs) (English and French versions) for CERSAC. This document is intended to serve as the guidance tool for each and every activity conducted by and for CERSAC. 3. Networking/collaborations developed – Central African Network for TB, AIDS and malaria (CANTAM) – Initiative to Strengthen Research for health Capacity in Africa (ISHReCA) – Capacity for Leadership Excellence And Research (CLEAR, Inc.) – Network for the coordination and advancement of sub-Saharan Africa-EU Science and Technology Cooperation (CAAST-Net) – Central African Research and Innovation Management Association (CARIMA)

9.1.75 IJsselmuiden-MARCII-Ethics

EDCTP Project Coordinator:	Carel IJsselmuiden (Council on Health Research for Development (COHRED), Switzerland)
EDCTP Call Title:	Coordination function
EDCTP Project Title:	Mapping African Research Ethics Review and Medicines Regulatory Capacity (MARC II)
EDCTP Project Code:	CB.2013.41303.001
EDCTP Project Start Date:	5 September 2013
EDCTP Project End Date:	4 March 2014
Collaborators:	• Gabriel Caires (Switzerland) • Bruno Coelho (Switzerland) • Mary Kasule (Botswana) • Debbie Marais (South Africa) • Boitumelo Mokgatla-Moipolai (Botswana) • Douglas Wassenaar (South Africa)
Type of Project:	Coordination function
Goal:	To analyse MARC phase I data, publicise the results and expand on the use of Ethicall for multi-centre trials ethics review.
Objectives:	1. To perform a detailed analysis of data collected in MARC Phase I 2. To expand and improve the functionalities of "EthiCall" including putting Ethicall into wider use.
Cofunders:	• Pfizer
Status:	Ongoing
Results and Outcomes:	

10 Networks of Excellence

Table 10-1: EDCTP networks of excellence projects

Project Acronym (Coordinator)	Disease/ Program area	Project goal	Institutions involved	Status
WANETAM	TB, HIV, malaria and networking	Capacity Building	Burkina Faso • Centre Muraz • Centre National de Recherche et de Formation sur le Paludisme The Gambia • Medical Research Council Laboratories, Gambia Nigeria • Nigerian Institute of Medical Research • Innovative Biotech Nigeria Ltd • University of Ibadan Ghana • University of Ghana • Korle-bu Teaching Hospital/ University Of Ghana Medical School, College of Health,College of Health Sciences, University of Ghana, Legon • Noguchi Memorial Institute for Medical Research, Legon Guinea-Bissau • Bandim Health Project Mali • Malaria Research and Training Center (MRTC) • University of Bamako Senegal • Institut Pasteur de Dakar	Ongoing
CANTAM	TB, HIV, malaria and networking	Capacity Building	Cameroon • Organisation de Coordination Pour La Lutte Contre Les Endemies (OCEAC) • University of Buea (UB) • University of Yaoundé • Centre International de Référence Chantal Biya (CIRCB) Republic of Congo • Université Marien Ngouabi • Centre d'Etudes sur les Ressources Vegetales (CERVE) Gabon • Fondation Internationale de l'Hôpital du Docteur Albert Schweitzer Tanzania • Multilateral initiative on Malaria	Ongoing

EACCR	TB, HIV, malaria and networking	Capacity Building	Ethiopia • Armauer Hansen Research Institute (AHRI) Kenya • KEMRI-Wellcome Trust Research Programme, Kilifi • Maseno University • University Of Nairobi • Kenya Aids Vaccine Initiative (KAVI) Sudan • Institute Of Endemic Diseases (IEND) Tanzania • Ifakara Health Institute (IHI) • Kilimanjaro Clinical Research Institute (KCRI) • Muhimbili University of Health and Allied Sciences (MUHAS) • National Institute for Medical Research (NIMR) • NIMR-Mbeya Medical Research Programme • Tabora Medical Center Uganda • Infectious Diseases Institute, Makerere University • Masaka Regional Hospital, Uganda Ministry of Health • Uganda Virus Research Institute (UVRI) • St. Francis Nsambya Hospital, Kampala • Medical Research Council (MRC)	Ongoing
TESA	TB, HIV, malaria and networking	Capacity Building	• Botswana • Botswana- Harvard AIDS Institute Partnership (BHP) • Malawi • College of Medicine • Mozambique • Centro de Investigação em Saúde da Manhiça (CISM) • South Africa • University of Cape Town • University of Stellenbosch • Medical Research Council of South Africa • Zambia • University Teaching Hospital Lusaka • • Zimbabwe • Biomedical Research and Training Institute • University of Zimbabwe College of Health Sciences	Ongoing

10.1.1 WANETAM

EDCTP Project Coordinator:	Souleymane Mboup (University Cheikh Anta DIOP de Dakar (UCAD), Senegal)
EDCTP Call Title:	Networks of Excellence
EDCTP Project Title:	Capacity building to prepare West African sites for clinical trials on HIV, TB and malaria (WANETAM)
EDCTP Project Code:	CB.2007.41700.007
EDCTP Project Start Date:	31 July 2009
EDCTP Project End Date:	31 December 2014
Collaborators:	• Simon Agwale (Innovative Biotech Nigeria) • Toure Aissatou (Institut Pasteur de Dakar, Senegal) • Audrey Forson (Korle-Bu Teaching Hospital, Ghana) • Tumani Corrah (MRC Laboratories, The Gambia) • Sheriffo Jagne (Centre Muraz, Burkina Faso) • Ogobara Doumbo (MRTC, University of Bamako, Mali) • Oni Idigbe (NIMR , Nigeria) • Aderemi Kehinde (University of Ibadan, Nigeria) • Ignatius Baldeh (NPHL, Gambia) • Sodiomon Sirima (Centre national de recherche de Formation sur le Paludisme (CNRFP), Burkina Faso) • Paulo Rabna (Bandim Health Project, Guinea-Bissau) • Nancy Duah (Noguchi Memorial Institute, Ghana)
Objectives:	To establish capacity building and technology transfer to prepare West African institutes for the successful conduct of clinical trials and creation of a network for sub-regional scientific collaborations
Cofunders:	NACCAP, MRC-UK, MRC, The Gambia
Status:	Ongoing
Results and outcomes:	WANETAM website: www.wanetam.org • Malaria incidence and serological marker study linked to the network started in January 2010 in Burkina Faso, Senior • Training includes: – Ethics, Data management and grant writing, Basic Quality Control practices for clinical laboratories, Project Management and GCP/GCLP **Disease-specific training:** – TB: DNA extraction, PCR, Spoligotype analysis, MTBDR for drug resistance testing; DNA sequencing, Bioinformatics – HIV Viral load assay for regional use: optimization of in-house Elona assay and real time PCR.
Publications:	1. Adoga, MP; Pennap, GR; John, PA; Shawulu, PT; Kaba, SV; Forbi, JC; Agwale, SM. CD4-and CD3-T Lymphocyte Reference Values of Immunocompetent Urban and Rural Subjects in an African Nation. Scandinavian Journal of Immunology. 2012: 76 (1):33-38 2. Pennap GR, Adoga MP, Forbi MP, Ojobo F and SM Agwale, CD4+ Immunocompetent reference values of immunocompetent subjects in an African University. Tropical Doctor, 2011:41: 218-221 3. George M Miiro, Odile Ouwe Missi Oukem-Boyer, Ousmane Sarr, Maerangis Rahmani, Francine Ntoumi, Keertan Dheda, Alexander Pym, Souleymane Mboup, Pontiano Kaleebu and on behalf of the NoEs' programme. EDCTP regional networks of excellence: initial merits for planned clinical trials in Africa. BMC Public Health. 2013. 13: 258 (doi:10.1186/1471-2458-13-258)

10.1.2 CANTAM

EDCTP Project Coordinator:	Francine Ntoumi (Congolese Foundation for Medical Research, Congo)
EDCTP Call Title:	Networks of Excellence
EDCTP Project Title:	Central African Network on TB, HIV/AIDS and malaria (CANTAM)
EDCTP Project Code:	CB.2007.41700.006
EDCTP Project Start Date:	19 December 2008
EDCTP Project End Date:	31 December 2014
Collaborators:	• Eric Akum Achidi (University of Buea, Cameroon) • Matthias Frank (University of Tübingen, Germany) • Saadou Issifou (Albert Schweitzer Hospital, Gabon) • Rose Leke (University of Yaounde, Cameroon) • Pierre Blaise Matsiegui (Albert Schweitzer Hospital, Gabon) • Mathieu Ndounga (Centre d'Etudes sur les Ressources Végétales (CERVE), Congo) • Marie-Yvonne Nkodia (CERVE, Congo) • Odile Ouwe Misse Oukem (International Reference Centre Chantal Biya (CIRCB), Cameroon) • Veronique Penlap Beng (University of Yaounde, Cameroon) • Julius Atshali (Buea university, Cameroon) • Akim Adegnika (Medical Research Unit of albert Schweitzer Hospital, Gabon) • Jude Daiga Bigoga (University of Yaounde, Cameroon) • Anissa Sidibe (Congolese Foundation for Medical Research (FCRM), Congo) • Thomas Michel Anana (Centre International de Recherche Chantal Biya, Cameroon) • Carine Kades (Congolese Foundation for Medical Research (FCRM), Congo) • Ange-Antoine Abena (University Marien Ngouabi/faculty of Health Sciences, Congo) • Peter kremsner (University of Tubingen, Germany) • Pembe Issamou Mayengue (Faculté des Sciences de la Santé/FCRM, Congo)
Objectives:	1. To develop human resources in the skills required to conduct safe clinical trials including GCP/GLP training and preparation and development of clinical and standardized protocols from recruitment of participants to the conduct of clinical trials 2. To strengthen laboratories to be able to perform relevant tests for HIV/AIDS and malaria clinical research 3. To strengthen ethical review boards and regulatory authorities in needy collaborating sites; and establish effective community liaison at each site and identify new study cohorts in villages and towns for future clinical trials on HIV/AIDS and malaria.
Cofunders:	NACCAP, TOTAL Congo and Paraxel
Status:	Ongoing
Results and outcomes:	CANTAM website: www.cantam.org Infrastructure update: In Cameroon, University of Yaounde1 established and equipped a TB lab at the biotechnology center. In the Republic of Congo, the first molecular biology lab of the university Marien Ngouabi has been established under CANTAM project and the full renovation and equipment of Parasitology lab as well. A malaria Unit for clinical trials activities has been set up at the Hospital of Makélékélé in Brazzaville.

	Baseline studies: In Cameroon and Congo, epidemiological studies for collecting data on HIV, Malaria and TB infections (prevalence, genotypes of strains, level of resistance to drug, age-distribution,) are on-going. Training: A total of 15, 10 and 7 , MSc, PhD and MD students have been trained respectively at the different institutions in collaboration with Northern Partners. Staff have also been skilled through short term training of laboratory technicians, nurses, etc. More than 300 participants attended 21 workshops organized in Cameroon, Congo and Gabon. Networking: CANTAM consolidated its collaborations with other regional and international networks by sharing knowledge and training activities.
Publications	1. Kilama W, Ntoumi F.2009. Malaria: a research agenda for the eradication era. *The Lancet*. Oct 31;374(9700):1480-2 2. Ntoumi Francine. 2010. Networking and capacity building for health research in Central Africa. *Wien Klin Wochenschr*. 2010 Mar;122 Suppl 1:23-6. 3. Francine Ntoumi, Gunilla Priebe. 2010. Africanizing scientific knowledge: The Multilateral Initiative on Malaria as a model*? Malaria Journal*, 9(Suppl 3):S7 December 2010. 4. Pembe Issamou Mayengue, Mathieu Ndounga, Freddy Vladimir Malonga, Michel Bitemo, Francine Ntoumi. 2011. Genetic polymorphism of merozoite surface protein-1 and merozoite surface protein-2 in Plasmodium falciparum isolates from Brazzaville, Republic of Congo. *Malaria Journal* Sep 22;10(1):276. 5. Francine Ntoumi. The Ant Who Learned to Be an Elephant. 2011. *Science*. 2011 Sep 30;333 (6051):1824-5. 6. Matthias Frank, Nicola Lehners, Pembe I Mayengue, Julian Gabor, Matthias Dal-Bianco, David U Kombila, Ghyslain Mombo Ngoma, Christian Supan, Bertrand Lell, Francine Ntoumi, Martin P Grobusch, Klaus Dietz and Peter G Kremsner. 2011. A thirteen-year analysis of Plasmodium falciparum populations reveals high conservation of the mutant pfcrt haplotype despite the withdrawal of chloroquine from national treatment guidelines in Gabon. *Malaria Journal* 10:365. 7. Selidji T Agnandji, Florian Kurth, Jose F Fernandes, Solange S Soulanoudjingar, Beatrice P Abossolo, Ghyslain Mombo-Ngoma, Arti Basra, Raquel González, Gondo Kizito, Pembe I Mayengue, Lorenz Auer-Hackenberg, Saadou Issifou, Bertrand Lell, Ayola A Adegnika and Michael Ramharter. The use of paediatric artemisinin combinations in sub-Saharan Africa: a snapshot questionnaire survey of health care personnel. *Malaria Journal* 2011, 10:365 8. Koukouikila-Koussounda F, Malonga V, Mayengue PI, Ndounga M, Vouvoungui CJ, Ntoumi F. 2012. Genetic polymorphism of merozoite surface protein 2 and prevalence of K76T pfcrt mutation in Plasmodium falciparum field isolates from Congolese children with asymptomatic infections. *Malar Journal*. Apr 1;11(1):105. 9. Gervais Gouana Tchinda, Julius Atashili, Eric A. Achidi, Henri L. Kamga, Anna L. Njunda, Peter M. Ndumbe. 2012. Impact of Malaria on Hematological Parameters in People Living with HIV/AIDS Attending the Laquintinie, Hospital in

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10.1.3 EACCR

EDCTP Project Coordinator:	Pontiano Kaleebu (Medical Research Council Programme on AIDS - Uganda Virus Research Institute (MRC/UVRI), Uganda)
EDCTP Call Title:	Networks of Excellence
EDCTP Project Title:	East Africa Consortium for Clinical Research (EACCR)
EDCTP Project Code:	CB.2007.41700.001
EDCTP Project Start Date:	14 May 2009
EDCTP Project End Date:	31 December 2014
Collaborators:	• Salim Abdulla (Ifakara Health Research and Development Centre, Tanzania) • Michael Ashton (University of Gothenburg, Sweden) • Muhammad Bakari (Muhimbili University College of Health Sciences, Tanzania) • John Changalucha (National Institute for Medical Research (NIMR), Tanzania) • Alison Elliott (London School of Hygiene and Tropical Medicine (LSHTM), UK) • Howard Engers (rmauer Hansen Research Institute (AHRI), Ethiopia) • Heiner Grosskurth (MRC/UVRI, Uganda) • Michael Hoelscher (Ludwig-Maximilians Universitat Munchen, Germany) • Andrew Kambugu (Makerere University, Uganda) • Edward Katongole-Mbidde (MRC/UVRI, Uganda) • Jonathan Kayondo (MRC/UVRI, Uganda) • Gibson Kibiki (Tanzania) • Stafford Kibona (NIMR, Tanzania) • Japhet Killewo (Muhimbili University College of Health Sciences, Tanzania) • Trudie Anne Lang (Kenya Medical Research Institute (KEMRI) Kenya) • Martha Lemnge (NIMR, Tanzania) • Frank Van Leth (KNCV Tuberculosis Foundation, Netherlands) • Asuman Lukwago (Ministry of Health, Uganda) • Kevin Marsh (KEMRI, Kenya) • Sayoki Godfrey Mfinang (NIMR, Tanzania) • Odd Mørkve (University of Bergen, Norway) • Maowia Mukhtar (University of Khartoum, Sudan) • Patricia Jane Munseri (Muhimbili University College of Health Sciences, Tanzania) • Beatrice Kemilembe Mutayoba (NIMR, Tanzania) • Martin Nsubuga (San Raphael of St. Francis Hospital Nsambya, Uganda) • Ayub V. O. Ofulla (Maseno University, Kenya) • Bernhards Ragama Ogutu (KEMRI, Kenya) • Norbert Peshu (KEMRI, Kenya) • Eric Sandström (Karolinska Institute, Sweden) • Mark Urassa (NIMR, Tanzania) • Andre Van Der Ven (Radboud University Nijmegen, Netherlands) • Dr Abraham Aseffa (AHRI,Ethiopia) • Dr Mwele Malacela (NIMR, Tanzania) • Mr Wandiga (KEMRI/CDC, Kenya) • Dr Walter Godfrey Jaoko (uni. Of Nairobi/KAVI, Kenya) • Prof Eligius Lyamuya (MUHAS, Tanzania) • Dr Benard Ngowi (National Insititute for Medical Research,

	Muhimbili , Tanzania) • Dr Florence Tugumisirize (Masaka Hospital,Uganda) • Dr leonard Maboko (NIMR-Mbeya, Tanzania)
Objectives:	1. To upgrade research capacity and build formal operational links and affiliations among east African and northern partner institutions to form a consortium with enhanced multi-disease (HIV/AIDS, TB and malaria) capacity to conduct ICH-GCP compliant clinical trials. 2. To establish and strengthen East African excellence in the field of clinical trials on HIV/AIDS, Tuberculosis (TB) and Malaria in a well-structured and integrated network, organised and run by the East African research community itself.
Cofunders:	Canadian Global Health Research initiative.
Status:	Ongoing
Results and outcomes:	• EACCR website: http://eaccr.org/ • Long-term trainees: 26 Masters candidates, 2 post-doctoral and 2 PhD have projects in progress. • HIV research activity: Social science study on Health Seeking Behaviour of People on Anti-Retroviral Therapy for at least 3 years in Kenya, Tanzania and Uganda. 2 reports were received from Kenya and Tanzania during this reporting period. Investigators will now write a publication combining the findings from these 3 countries. • Four EDCTP-linked Senior Fellowships: – "Evolution of HIV-1 ARV drug resistance mutations in the ART naïve during therapy; threshold frequency levels and linkage context associated with treatment failure in Uganda " by Dr Jonathan Kayondo in Uganda – "Comparison of efficacy, safety and pharmacokinetics of intravenous artesunate and intravenous quinine followed by oral artemisinin combination therapy for severe malaria treatment in uganda AND evaluation of pharmacokinetic drug interactions of artesunate, quinine, lumefantrine and piperaquine with antiretroviral drugs" by Dr Pauline Byakika-Kibwika in Uganda. She hs been promoted to position of associate professor at Makerere University. – "Clinical trials in HIV/AIDS in Africa: Should they routinely control for mental health factors?" by Dr Eugene Kinyanda – "Short and long term clinical and immunological outcomes of patients with HIV/TB co-infections on ART" by DR William Worodria • Capacity building: maintained a consensus-governed and networked consortium, also registered 2 additional MSc research fellows from Ethiopia and Tanzania; recorded 11 graduated MSc fellows; completed 4 EDCTP senior fellowships and reached at least 100 scientists through 4 short-courses in GCLP, GCP, TB laboratory techniques, clinical monitoring and trial conduct. Five more laboratories of sister sites in Kenya, Sudan and Uganda were upgraded. It has a regional reciprocal monitoring scheme of at least 10 experienced monitors, who have cumulatively conducted 27 site visits to 11 clinical trials and mentored at least 10 new monitors, including 2 from new partner institution in Rwanda. • Networking: Prepared a proposal to EDCTP for a joint planning meeting of stakeholders from EACCR and TESA

	(On-going by date of reporting) . Submitted a research capacity building proposal to WHO/TDR (1Oth May 2013). Distributed over 400 EACCR brochures during national & international meetings (On-going by date of reporting) . Two EACCR members gave oral presentations at the 4th annual East African Health and Science conference following successful peer-review of the submitted abstracts (annexes 7 & 8). This conference took place at Serena Hotel in Kigali, Rwanda(26th - 29th Mar 2013) . Worked with the East Central & Southern Africa Health Community on an EDCTP capacity needs assessment for ethics committees of selected institutions in Uganda (Feb - Mar 2013). EACCR Scientific Liaison Officer attended a scientific meeting in Les Diablerets, Switzerland at the invitation of the TB Vaccine Initiative (TBVI) and the consortium on TB Vaccine Trials in Europe and Africa (TB-TEA), 26th Jan - 1't Feb 2013. Made Advocacy for EACCR in the Afrique one consortium meeting held in NDjamena (29th Sep - 6th Oct 2012). Submitted research & capacity building proposal to the Tropical Health & Education Trust, UK in paftnership with University of Oxford (Sep 2012) . Submitted a proposal for a Youth Community HIV/AIDS (YoCHA) program to funders in Netherlands in collaboration with a South African partner (Aug 2012). Submitted a proposal on a point-of-care diagnostic for Malaria in collaboration with a Canadian industrial partner from Alberta to Grand Challenges-Canada (Jul 2012).
Publications:	1. Byakika-Kibwika, p., Lamorde, M., Mayito, J., Nabukeera, L., Namakula, R., Mayanja-Kizza, N. et al. (2012a). Significant pharmacokinetic interactions between artemether/lumefantrine and efavirenz or nevirapine in HIV-infected Ugandan adults.. I Antimicrob Chemother,6T(9),2213-21. 2. Byakika-Kibwika, p.. Lamorde, M., Mayito, J., Nabukeera, L., 14ayanja-Kizza, H., Katabira, E. et al. (2OI2b). Pharmacokinetics and pharmacodynamics of intravenous artesunate during severe malaria treatment in Ugandan adults.. Malar J., 11(132). 3. Lamorde, M., Byakika-Kibwika, p., Tamale, W., Kiweewa, F., Ryan, M., Amara, A. et al. (2OI2). Effect of Food on the Steady-State Pharmacokinetics of Tenofovir and Emtricitabine plus Efavirenz in Ugandan Adults.. AIDS Res Treat., 2012(105980). 4. Lamorde, M., Byakika-Kibwika, p. & f.4erry, C. (20t2). Pharmacokinetic interactions between antiretroviral druqs and herbal medicines. Br J Hosp Med (Lond),73(3), 732 - 136. 5. bavis-Kibirigel, Richard Ssekitoleko, Edrisa Mutebi and William Worodria. Overt diabetes mellitus among newly diagnosed Ugandan tuberculosis patients: a cross sectional study. BMC Infectious Diseases 2013, 13:.1'22 6. Davis Kibirige, Edrisa Mutebi, Richard Ssekitoleko, William Worodria, and Harriet lvlayanja-Kizza. Vitamin D deficiency among adult patients with tuberculosis: a cross sectionat study from a national referral hospital in Uganda. BMC Res Notes. 2013; 6: 293. 7. Eugene Kinyanda et al. prevalence and risk factors of depression in childhood and adolescence as seen in 4 districts of north-eastern Uganda BMC Int Health Hum

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10. Seeley, lunet PhD, Nkinyigi-Miiro, Jessica PhD;Kamali, Anatoli MSc.'s; Mpendo, Juliet MPHn; Asiki, Gershim MSc-; Abaasa, Andrew MSc.; DeBont, Jan phD,; Nielsen, Leslie-RN; Kaleebu, Pontiano PhD. High HIV Incidence and Socio-Behavioral Risk Patterns in Fishing Communities on the Shores of Lake Victoria, Uganda. Sexually Transmitted Diseases: June 2012 Volume 39 Issue 6 - p 433 439. doi: 10.1097/01Q. 0b013e318251555d
11. David Cooper; Fiona Ewings, Sarah Fidler, AMrtin Fisher, John Frater, Michelle Gabriel, Pontiano Kaleebu, Steve Kaye, Antony Kellerher et al.,Short-course antiretroviral therapy in primary HIV infection. The New England journal of medicine 2OL3;368(3):207-I7.
12. George M Miiro; Francine Ntoumi; Alexander Pym; Maerangis Rahmani; Ousmane Sarr; Odile Ouwe Missi Oukem-Boyer; Keertan Dheda, Souleymane Mboup; Pontiano Kaleebu. EDCTP regional networks of excellence: initial merits for planned clinical trials in Africa. BMC public health 2013;130:258.

10.1.4 TESA

EDCTP Project Coordinator:	Gerhard Walzl (Stellenbosch University, Immunology Research Group , South Africa)
EDCTP Call Title:	Networks of Excellence
EDCTP Project Title:	Trials of Excellence for Southern Africa (TESA)
EDCTP Project Code:	CB.2007.41700.009
EDCTP Project Start Date:	16 November 2009
EDCTP Project End Date:	31 December 2014
Collaborators:	• Keertan Dheda (University of Cape Town, South Africa) • Eusebio Macete (Manhiça Health Research Center, Mozambique) • Peter Robert Mason (Biomedical Research and Training Institute (BRTI), Zimbabwe) • Helen McIlleron (University of Cape Town, South Africa) • Rosemary Musonda (Botswana Harvard Partnership (BHP)/(Botswana-Harvard AIDS Institute Partnership), Botswana) • Peter Mwaba (University Teaching Hospital, Zambia) • Lynn Zijenah (University of Zimbabwe, Zimbabwe) • Dr Duncan Chanda (iMRET) • Newton Kumwenda (University of Malawi, College of Medicine, Research Support Centre, Malawi) •
Objectives:	To build capacity and strengthening of new and established sites including infrastructure for the conduct of clinical trials in HIV/AIDS, TB and Malaria in accordance with the highest ethical and Good Clinical Practice. The network also aims on building experience and infrastructure in clinical trial design, biomarker discovery and research project management.
Cofunders:	South African Medical Research Council (SA-MRC); LUMC to SUN-IRG
Status:	Ongoing
Results and outcomes:	1. TESA website: www.tesafrica.org 2. Establishment of TESA as a functional consortium The network has established itself by linking ten research institutions within six countries of the Southern African region. The network has conducted annual evaluation of the institutions' activities, through general annual meetings. Thus far two annual meetings were held in Mozambique (2010) and Zambia (2011) subsequent to network's initial launch in Durban South Africa in 2009. 3. Capacity building: Fellowships: Two senior researchers attached to TESA research institutions Dr Mark Hatherill (UCT-Lung) and Prof. Takafira Mduluza (Botswana Harvard HIV Partnership (BHP)) respectively were awarded with two EDCTP Senior Fellowships each with value of €200000. 4. 86 research staff are being supported by the NoE grant with 11 working for TESA full time. 5. HIV: HIV incidence baseline study protocol has been finalised in Malawi. The aim of the study is to obtain basleine data for planning HIVvaccine trial.They have enrolled 1014 partcipants and are currently in the analusis phase. An EDCTP funded Senior Fellowship awarded to Dr. Takafira Mduluza attached to BHP, started in 2009 and has now joined BRTI in Zimbwabwe. 6. TB: Preparations for a multi-site epidemiological study are underway. A prevalence study of TB and MDR-TB among HIV+ patients on HAART which will involve all sites is in

	preparation. They have 193 partcipants enrolled and the study is in progress. An EDCTP funded Senior Fellowship awarded to Mark Hatherill attached to UCT, started in 2009. 7. From September 17 to September 20,2012, CISM participated in the Health Conference (Jornadas de Saúde) organized by the National Institute of Health (Ministry of Health of Mozambique) and school of Medicine, Eduardo Mondlane University. The theme of the health conference was "Research Institutions Contributing to the Improvement of Health in Mozambique". CISM presented 15 papers (8 oral and 7 in form of Posters) . 8. Training: over 500 laboratory staff, researchers and investigators, have attended, at least one, TESA short courses. The short course trainings included; Project Management, Laboratory Management, Research Ethics and Methods, TB- DR/TB and HIV lab diagnostic techniques, biomarker studies, PK/PD assay development methods and TB/HIV clinical courses in addition to; GCP /GCLP across all sites. Through the NoE grant 17 MPhil/MSc students, 6 PhD and 2 Post Docs have been identified, registered with universities and supervised within the network of excellence. All sites have strengthened the existing or formed new community advisory boards (CAB). 9. Networking: BRTI has been actively networking with ICHORTA to harmonise trainings. The site is affiliated with the University of Zimbabwe-College of Medicine and also collaborates with the Ministry of Health and Child Welfare to oversee a national TB prevalence survey. BRTI has also started a training program for the National Microbiological reference laboratory staff in Zimbabwe. MRC has been collaborating with the National Department of Health (NDOH) in establishing a MDR-TB surveillance program and has networked with the NDOH on TB program.
Publications:	1. Meredith SA, Smith PJ, Norman J, Wiesner L. 2012. An LC-MS/MSmethod for the determination of ofloxacin in 20 l human plasma. J.Pharm. Biomed. Anal. 58:177–181. 2. Chigutsa E, Meredith S, Wiesner L, Padayatchi N, Harding J, Moodley P, Mac Kenzie WR, Weiner M, McIlleron H, Kirkpatrick CM. Population pharmacokinetics and pharmacodynamics of ofloxacin in South African patients with multidrug-resistant tuberculosis. Antimicrob Agents Chemother. 2012 Jul;56 (7):3857-63. 3. Zvada SP, Denti P, Geldenhuys H, Meredith S, van As D, Hatherill M, Hanekom W,Wiesner L, Simonsson US, Jindani A, Harrison T, McIlleron HM. Moxifloxacin population pharmacokinetics in patients with pulmonary tuberculosis and the effect of intermittent high-dose rifapentine. Antimicrob Agents Chemother. 2012 Aug;56(8):4471-3. 4. Loxton AG, Black GF, Stanley K, Walzl G. Heparin-binding hemagglutinin induces IFN-γ(+) IL-2(+) IL-17(+) multifunctional CD4(+) T cells during latent but not active tuberculosis disease. Clin Vaccine Immunol. 2012 May;19(5):746-51. 5. Chegou NN, Essone PN, Loxton AG, Stanley K, Black GF, van der Spuy GD, van Helden PD, Franken KL, Parida SK, Klein MR, Kaufmann SH, Ottenhoff TH, Walzl G. Potential of host markers produced by infection phase-dependent

	antigen-stimulated cells for the diagnosis of tuberculosis in a highly endemic area. PLoS One. 2012;7(6):e38501. 6. Mihret A, Bekele Y, Loxton AG, Aseffa A, Howe R, Walzl G. Plasma Level of IL-4 Differs in Patients Infected with Different Modern Lineages of M. tuberculosis. J Trop Med. 2012; 2012:518564. Epub 2012 Sep 25.

11 Networking grants

Table 11-1: Summary table of small networking projects supported by EDCTP

Project Acronym (Coordinator)	Disease area	Project goal	Institutions involved	Status
Temmerman	HIV/AIDS	Strengthening laboratory capacity and nutrition skills in the context of an ICH GCP clinical trial for the prevention of mother-to-child transmission of HIV	University of Ghent (Belgium), Laboratoire de bactériologie-virologie (France), IRD (France), ICRH (Kenya), Centre Muraz (Burkina Faso)	Completed
Colebunders	HIV/AIDS	Workshop on Tuberculosis Immune Reactivation Inflammatory Syndrome (TB IRIS)	Institute of Tropical Medicine (Belgium), AMC (Netherlands), Infectious Disease Institute (Uganda), Makerere University (Uganda), Chelsea and Westminster Healthcare NHS Trust (UK), IATEC (Netherlands), JCRC (Uganda), UCT (South Africa), Swedish Institute for Infectious Disease Control, Centre hospitalier de Fann (Senegal), WHO, IUATLD, MSF Belgium	Completed
Kyabayinze	HIV/AIDS	KIDS-ART-LINC: network of clinical centres treating HIV-infected children with antiretroviral therapy in Africa to inform public health care and treatment programs	Regional Center For Quality of Health Care (RCQHC-Uganda), Makerere University, CDC Global AIDS Program (Kenya), INSERM (France), Univ of Bern (Switzerland), USAID (Kenya)	Completed
McCormack	HIV/AIDS	Identifying the common learning needs of investigators working in poverty-related diseases in African settings, and the materials to address these, notably in the areas of project and data management	MRC (UK), EuroVacc Foundation (Switzerland), St Stephen's AIDS Trust International Development Group (UK), AMC-CPCD (Netherlands), PENTA Foundation (Italy), JCRC (Uganda), Makerere University (Uganda), Univ of WITS (South Africa), Univ of Zambia, KEMRI (Kenya), Quintiles Clindepharm (South Africa)	Completed
Jindani	TB	Establishing a network of sites, in sub-Saharan Africa, to conduct clinical trials in tuberculosis and to build their capacity to participate in multicentre trials	Jindani, St George's Medical College (UK), MRC (UK), MRC (South Africa), University Medical Centre St Radboud (Netherlands), WHO-TDR	Completed
Aseffa	TB	Strengthening the National Tuberculosis Research Network in	Abraham, Armauer Hansen Research Institute (AHRI), Addis Ababa University, Ministry of Health,	Completed

		Ethiopia	Ethiopian Health and Nutrition Research Institute (EHNRI), Ethiopian Science and Technology Agency	
Hill	Malaria	A North-South working group to support the design integrated of research proposals for malaria in pregnancy	Liverpool School of Tropical Medicine (UK), University of Barcelona, NIMR (Tanzania), Centre of Innovation against malaria (Gambia)	Completed
Navia	Malaria	Ifakara-Lambarene-Manhiça Partnership	Fundació Clínic per a la Recerca Biomèdica (Spain), Ifakara (Tanzania), Lambarene (Gabon) and Manhica (Mozambique)	Completed
Merry	Pharmacology	Networking of European and sub-Saharan African research and capacity building in pharmacology	Trinity College (Ireland), LSTM (UK), MRC (UK), UCT (South Africa), Makerere University (Uganda) and University of Zambia	Completed
Elbourne	Training	EDCTP Grant to support at least 21 Studentships for distance learning Master-course in clinical trials offered by LSHTM	LSHTM (UK)	Ongoing
Hall	Training	Masters courses in clinical trials for sub-Saharan Africa	LSHTM (UK), Centre Muraz (Burkina Faso), University of Ghana and Montpelier University (France)	Completed

11.1.1 Marleen Temmerman

EDCTP Project Coordinator:	Marleen Temmerman (University of Ghent, Belgium)
EDCTP Call Title:	Providing incentives for joint capacity building programmes in Africa with two or more European institutions
EDCTP Project Title:	Strengthening laboratory capacity and nutrition skills in the context of an ICH-GCP clinical trial for the prevention of mother-to-child transmission of HIV
EDCTP Project Code:	NW.2005.10400.001
EDCTP Project Start Date:	17 May 2006
EDCTP Project End Date:	17 May 2007
Collaborators:	• Stanley Luchters (University of Ghent, Kenya) • Nicolas Meda (Centre Muraz, Burkina Faso) • Phillipe van de Perre (French Research Institute for International Development, France) • Kirsten Simondon (French Research Institute for International Development, France)
Objectives:	1. To strengthen the laboratories at Coast Provincial General Hospital (CPGH) in Mombasa and Centre Muraz in Bobo-Dioulasso 2. To monitor biological endpoints in clinical trials assessing antiretroviral drugs (ARVs) for the care of HIV-infected individuals and the prevention of mother-to-child transmission of HIV (MTCT) 3. To strengthen the capacity of team members to effectively and efficiently implement Good Clinical (Laboratory) Practices (GCP and GCLP) in the two African sites 4. To strengthen the capacity of the research teams in the two sites 5. To monitor anthropometric and nutritional status and develop context-specific nutritional support for infants born to HIV-infected mothers who are not breastfed or are weaned early.
Status:	Completed
Results and Outcomes:	The activities in this project were part of a larger research project (the Kesho Bora project) which included a multicentre randomised clinical trial (RCT), the overall objective of which is to optimise the use of ARVs during pregnancy and breastfeeding to maximally reduce MTCT and to protect the health of the HIV-infected mother. The linked sites now participate in EDCTP funded microbicide trials.

11.1.2 Bob Colebunders

EDCTP Project Coordinator:	Bob Colebunders (Prince Leopold Institute of Tropical Medicine (ITM), Belgium)
EDCTP Call Title:	Sponsorship of meetings or workshops of sustainable networks on an EDCTP relevant subject
EDCTP Project Title:	Workshop on Tuberculosis Immune Reactivation Inflammatory Syndrome (TB IRIS)
EDCTP Project Code:	NW.2005.10401.002
EDCTP Project Start Date:	2 February 2008
EDCTP Project End Date:	13 August 2008
Collaborators:	• L. Arnould (Médecins Sans Frontières, Belgium) • J. Baalwa (Makerere University, Uganda) • P. Clevenberg (International Union Against Tuberculosis and Lung Disease (The Union), France) • B. Gazzard (Chelsea and Westminster Hospital, UK) • L. John (Chelsea and Westminster Hospital, UK)
Objectives:	1. To review ongoing research on TB IRIS 2. To propose, with case definitions for different types of TB IRIS for use in resource limited settings 3. To identify research priorities concerning TB IRIS and develop protocols for multi-centre clinical trials to prevent and treat this condition.
Status:	Completed
Results and Outcomes:	This project organised a 3-day workshop on TB IRIS at the Infectious Diseases Institute (IDI), Makerere University, Kampala, Uganda. During the workshop, a case definition of TB IRIS was proposed that could be used in future TB HIV clinical trials. Such a definition, if eventually universally adopted, could facilitate the comparison of TB IRIS data reported from cohort and clinical trial studies in different parts of the world. The outline for preventive and therapeutic clinical trial protocols developed during the workshop could be used by network participants or other interested scientist to write full clinical trial proposals. The group/network studying TB IRIS is now providing this expertise in other EDCTP funded TB projects, including the Senior fellowships to Jean Nachega and William Worodria of EACCR.

11.1.3 Daniel Kyabayinze

EDCTP Project Coordinator:	Daniel Kyabayinze (Makerere University, Uganda)
EDCTP Call Title:	Coordination and Networking of research activities in Africa
EDCTP Project Title:	KIDS-ART-LINC: network of clinical centres treating HIV-infected children with antiretroviral therapy in Africa to inform public health care and treatment programmes
EDCTP Project Code:	NW.2005.10501.003
EDCTP Project Start Date:	30 Oct 2006
EDCTP Project End Date:	25 May 2007
Collaborators:	• Elise Arrive (Victor Segalen Bordeaux 2 University, France) • Francois Dabuis (Victor Segalen Bordeaux 2 University, France) • Matthias Egger (University of Bern, Switzerland) • Mary Kieffer (U.S. Agency for International Development (USAID), USA) • Benoit Marquis (Makerere University, Uganda)
Objectives:	To create a network of clinical centres that are involved in HIV/AIDS care for children in sub-Saharan Africa and to form a collaboration that will pool routinely collected clinical data into a common regional database upon which evaluation of paediatric HAART treatment outcomes will be based.
Status:	Completed
Results and Outcomes:	This networking grant contributed to the Development of Anti-Retroviral Therapy in Africa (DART) which gave landmark policy on priorities for ART programmes especially monitoring of treatment in resource constrained settings.

11.1.4 Sheena McCormack

EDCTP Project Coordinator:	Sheena McCormack (Medical Research Council, UK)
EDCTP Call Title:	Coordination and Networking of research activities in Africa
EDCTP Project Title:	Identifying the common learning needs of investigators working in poverty-related diseases in African settings, and the materials to address these, notably in the areas of project and data management
EDCTP Project Code:	NW.2005.10501.002
EDCTP Project Start Date:	10 Oct 2006
EDCTP Project End Date:	24 January 2008
Collaborators:	• Julie Bakobaki (MRC, UK) • Chifumbe Chintu (University Teaching Hospital, Zambia) • Sinead Delany Moretlwe (University of the Witwatersrand, South Africa) • Mary Edwards (University of the Witwatersrand, South Africa) • Brian Gazzard (Chelsea and Westminster Hospital, UK) • Carlo Giaquinto (University of Padova, Italy) • Diana Gibb (MRC, UK) • Linda Harper (MRC, UK) • Nicola Kaganson (MRC, UK) • Eeva Kaarina Koskelo (Quintiles Transnational Corp., South Africa) • Jean-Pierre Kraehenbuhl (EuroVacc Foundation, Switzerland) • Hermione Lyall (University of Padova, Italy) • Kathryn Maitland (Imperial College London, Kenya) • Sarah Meredith (MRC, UK) • Jocelyn Moyes (University of the Witwatersrand, South Africa) • Peter Mugyenyi (Joint Clinical Research Center, Uganda) • Veronica Mulenga University Teaching Hospital, Zambia) • Phillipa Musoke (Makerere University, Uganda) • Mark Nelson (Chelsea and Westminster Hospital, UK) • Andrew Nunn (MRC, UK) • Nneka Nwokolo (Chelsea and Westminster Hospital, UK) • Gita Ramjee (MRC, South Africa) • Mary Rauchenberger (MRC, UK) • Helen Rees (University of the Witwatersrand, South Africa) • Janneke van de Wiggert (ICRH-International Centre of Reproductive Health, Netherlands)
Objectives:	1. To identify common learning needs of investigators, scientific administrators and monitors that are conducting, or about to conduct, clinical trial research on poverty-related diseases, notably in the areas of project management, data management and monitoring 2. To identify and develop the materials and tools to meet these learning needs in African settings 3. To strengthen the collaboration between European/African clinical trial networks on poverty-related diseases
Status:	Completed
Results and Outcomes:	The final result was a training programme appropriate for African settings and the development of the necessary learning objectives and materials. The programme also facilitated networking opportunities with North-South and South-South collaborations. In addition, the grantee is a recipient of an EDCTP grant for the strengthening of a microbicide trials site.

11.1.5 Amina Jindani

EDCTP Project Coordinator:	Amina Jindani (St. George's University of London, UK)
EDCTP Call Title:	Coordination and Networking of research activities in Africa
EDCTP Project Title:	A proposal to establish a network of sites, in sub-Saharan Africa, to conduct clinical trials in tuberculosis and to build their capacity to participate in multicentre trials
EDCTP Project Code:	NW.2005.10501.001
EDCTP Project Start Date:	10 October 2006
EDCTP Project End Date:	13 November 2007
Collaborators:	• Martin Boeree (Netherlands) • Thomas Kenyok (WHO, Switzerland) • Thomas Harrison (St. George's University of London, UK) • Andrew Nunn (Medical Research Council (MRC), UK) • Roxana Rustomjee (MRC, South Africa)
Objectives:	To strengthen the capacity of the participants to participate in the design and conduct phase IIb and phase III trials of chemotherapeutic agents for the treatment of tuberculosis.
Status:	Completed
Results and Outcomes:	This project conducted a series of workshops with the objective of strengthening the capacity of the participants to take part in the design and conduct phase IIb and phase III trials of chemotherapeutic agents for the treatment of tuberculosis. The workshops provided training in clinical trial design and conduct, including data management and analyses, GCP and GLP procedures. The meeting was designed so that the participants learned, from experts, how to establish a network to prepare for multicentre trials through the conduct of trials of tuberculosis. In addition, members of this network are involved in conducting clinical trials of Rifapentine in simplification of TB drug regimen (Rifaquin trial) and in the EDCTP-funded PanACEA consortium.

11.1.6 Abraham Aseffa

EDCTP Project Coordinator:	Abraham Aseffa (Armauer Hansen Research Institute (AHRI), Ethiopia)
EDCTP Call Title:	Support to national networking of African scientist working on HIV/AIDS, Malaria and Tuberculosis in Africa
EDCTP Project Title:	Strengthening the national Tuberculosis Research Network in Ethiopia
EDCTP Project Code:	NW.2005.20103.001
EDCTP Project Start Date:	30 Oct 2006
EDCTP Project End Date:	4 March 2008
Collaborators:	• Getachew Aderaye (University of Addis Ababa, Ethiopia) • Tsehainesh Messele (Ethiopian Health and Nutrition Research Institute (EHNRI), Ethiopia) • Zerihun Tadesse (Ministry of Health, Ethiopia) • Yemane Teklai (Ethiopian Science and Technology Agency (ESTA), Ethiopia)
Objectives:	The project aimed to strengthen TB research capacity in Ethiopia through training on epidemiological techniques (Field Research Methods in Epidemiology), the establishment of a National Information Centre on TB control and TB research and organising a National forum for TB researchers (National TRAC TB Workshops) and TB control teams to facilitate implementation of research outputs in the efforts to control TB. Participants included TB researchers, particularly those working in the Ministry of Health TB control programme (or planning to join, collaborate or network with the programme), policy makers, academicians and community workers.
Status:	Completed
Results and Outcomes:	This project succeed to improved capability to address operational challenges in TB control, better coordination of national TB research activities with improved design and collaboration, better dissemination of research output and implementation of improved, validated new tools. Dr Aseffa has ledd an EDCTP funded TB vaccine trial to successful completion. In addition, he coordinates the activities of PABIN and has collaborated with Professor Petros Beyene in training ethics committees in Ethiopia

11.1.7 Jenny Hill

EDCTP Project Coordinator:	Jenny Hill (University of Liverpool, UK)
EDCTP Call Title:	Coordination and Networking of research activities in Africa
EDCTP Project Title:	A North-South working group to support the design integrated of research proposals for malaria in pregnancy
EDCTP Project Code:	NW.2005.10401.001
EDCTP Project Start Date:	3 April 2006
EDCTP Project End Date:	14 January 2008
Collaborators:	• Clara Menendez (University of Barcelona, Spain) • Theonest Mutabingwa (National Institute for Medical Research (NIMR), Tanzania) • Ayo Palmer (Medical Research Council Laboratories, The Gambia)
Objectives:	To conduct a last in a series of three meetings convened by the group which aims to: 1. Develop a global MiP research strategy 2. To develop and initiate studies that contribute to the evidence base for best practices to prevent and control malaria in pregnancy
Status:	Completed
Results and Outcomes:	The working group organised a workshop meeting designed to coordinate and guide the development of Malaria in Pregnancy (MiP) joint research protocols based on priorities identified earlier in the technical reviews and the research strategy. It aimed to develop research protocols for multi-centre trials of interventions for the treatment and prevention of malaria in pregnancy using common methodologies packaged into research clusters, each of which addresses a common theme or research question to ensure a coordinated approach to future research on MiP; and to develop draft protocols through electronic communications, which will then be reviewed at a meeting and submitted to funding agencies. As a result of this protocol development meeting, the African and EU-based partners of the MiP Consortium were able to meet face-to-face to develop three distinct but complementary proposals to EDCTP which will be implemented within the context of the wider MiP Consortium activities. These three proposals request support to implement a comprehensive clinical trials research agenda on MiP in Africa that focuses on areas of research likely to lead in the near future or longer term to improved interventions for malaria control in pregnancy and improved maternal and child health outcomes in malaria endemic areas. In addition, the network has received a malaria treatment grant from EDCTP through Professor Feiko ter Kuile. The network is highly active in malaria in pregnancy research and has received grant support from EDCTP and the Bill & Melinda Gates Foundation for specific clinical trials projects.

11.1.8 Jane Navia

EDCTP Project Coordinator:	Enric Jane (Fundació Clínic per a la Recerca Biomèdica, Spain)
EDCTP Call Title:	Coordination and Networking of research activities in Africa
EDCTP Project Title:	Ifakara-Lambarene-Manhiça Partnership
EDCTP Project Code:	NW.2005.10400.002
EDCTP Project Start Date:	30 November 2006
EDCTP Project End Date:	12 August 2008
Collaborators:	• Salim Abdulla (Ifakara Health Research and Development Centre, Tanzania) • John Aponte (Hospital Clinic of Barcelona, Spain) • Saadou Issoufou (Albert Schweitzer Hospital, Gabon) • Bertrand Lell (University of Tübingen, Genrmany) • Hassan Mshinda (fakara Health Research and Development Centre, Tanzania) • Jahit Sacarlal (Manhiça Health Research Center, Mozambique) • Marcel Tanner (Swiss Tropical Institute, Switzerland)
Objectives:	To develop guidelines and to standardize procedures for malaria vaccine trials at the three sites. Fulfilling this objective would enable the network to set up trials quickly and efficiently. Issues such as laboratory protocols, ethical issues, study design, data management and analysis would be addressed
Status:	Completed
Results and Outcomes:	The aim of this project was to establish a joint capacity building programme between three African sites: Medical Research Unit (Albert Schweitzer Hospital, Lambaréné, Gabon), the Ifakara Health Research and Development Centre (IHRDC), Ifakara, Tanzania, and the Centro de Investigação em Saude de Manhiça (CISM), Manhiça, Mozambique and their three European partners: the Department of Parasitology, University of Tübingen (Tübingen, Germany), the Swiss Tropical Institute (Basel, Switzerland) and the Centre for International Health, (Hospital Clinic/University of Barcelona, Spain). The main objective contemplated by the joint collaboration was to develop guidelines and to standardise procedures and other matters concerning malaria vaccine trials among the three sites. Issues such as laboratory protocols, ethical issues, study design, data management and analysis were addressed. The fulfilment of this objective made it possible to set up trials quickly and efficiently. Currently, the three sites are involved in many EDCTP-funded projects.

11.1.9 Concepta Merry

EDCTP Project Coordinator:	Concepta Merry (University of Dublin, Ireland)
EDCTP Call Title:	Coordination and Networking of research activities in Africa
EDCTP Project Title:	Networking of European and sub-Saharan African research and capacity building in pharmacology
EDCTP Project Code:	NW.2005.10501.004
EDCTP Project Start Date:	13 June 2007
EDCTP Project End Date:	23 September 2008
Site Principal Investigator(s):	Not applicable
Collaborators:	David Back (UK), Saye Khoo (UK), Mairin Ryan (Ireland), Diana Gibb (UK), Gary Maartens (South Africa), Peter Smith (UK), Helen McIlleron (South Africa), Karen Barnes (UK), Paul Waako (Uganda), Pauline Byakika (Uganda), Mohammed Lamorde (Uganda), Peter Coakley (Uganda), Robinah Ngnawa (Uganda), Francis Kamlemeera (Uganda), Chifumbe Chintu (Zambia)
Objectives:	To conduct a meeting to: 1. Review the questions surrounding research in the African continent, with a particular focus on the pharmacology of antiretroviral drugs 2. Shape and discuss initiatives in the area of pharmacology research capacity strengthening 3. Develop a strategy for future research applications.
Status:	Completed
Results and Outcomes:	The aim of this proposal was to host a four day workshop at the University of Makerere, Kampala, Uganda in order to consolidate, co-ordinate and expand the research, training and capacity building activities of clinical pharmacologists who are already working together on a number of projects in Zambia, Uganda, South Africa, England and Ireland in the areas of drug information, clinical pharmacy, clinical pharmacology, pharmacoeconomics and pharmacokinetics, but who have not had an opportunity to meet together. The investigators had an opportunity to present their current research portfolio, outline key priority areas for research, identify opportunities for synergy and outline a strategy for future research applications. Dr Merry coordinates a network of pharmacologists in Africa and is active as a collaborator on several EDCTP grants in Uganda. Other participants in the network are collaborators on several EDCTP grants

11.1.10 Diana Elbourne

EDCTP Project Coordinator:	Diana Elbourne (London School of Hygiene and Tropical Medicine (LSHTM), UK)
EDCTP Call Title:	Development of an MSc course in clinical trials methodology
EDCTP Project Title:	EDCTP Grant to support a minimum of 21 Studentships for a distance learning Masters-course in clinical trials offered by the London School of Hygiene and Tropical Medicine (LSHTM).
EDCTP Project Code:	NW.2005.10403.005
EDCTP Project Start Date:	9 August 2007
EDCTP Project End Date:	20 September 2014
Objectives:	To support postgraduate trainees to undertake a distance learning Masters in Clinical Trials at the through this grant, EDCTP has funded 21 students to follow the distance learning MSc in Clinical Trials course of the LSHTM.
Status:	Ongoing
Results and Outcomes:	Twenty one students are being trained through the London School of Hygiene and Tropical Medicine distant MSc in Clinical trials course. Students benefiting from this course from Ethiopia (1), Ghana (2), Kenya (7), Nigeria (3), South Africa (1), Tanzania (1), Uganda (4), Zambia (1) and Zimbabwe (1). By end of 2011 the academic status of the students was as follows: • 6 have already completed their MSc • 13 have been awarded their postgraduate diploma and have started working on their advanced modules • 1 is still working on core modules • 1 student has withdrawn due to failure to pass the core modules, in line with the policy of LSHTM • In 2012 an additional three students were recruited as part of a no-cost extension of the grant.

11.1.11 Andy Hall

EDCTP Project Coordinator:	Andy Hall (London School of Hygiene and Tropical Medicine (LSHTM), UK)
EDCTP Call Title:	Development of an MSc course in clinical trials methodology
EDCTP Project Title:	Masters courses in clinical trials for sub-Saharan Africa
EDCTP Project Code:	NW.2005.10403.001 / NW.2005.10403.006
EDCTP Project Start Date:	10 Oct 2006
EDCTP Project End Date:	25 May 2007 (French course report released 27 January 2010)
Collaborators:	• Fred Binka (University of Ghana) • Shabar Jaffar (LSHTM, UK) • Nicolas Meda (Centre Muraz, Burkina Faso) • Paul Milligan (LSHTM, UK) • Phillippe van de Perre (France)
Objectives:	To adapt a Masters course developed at the London School of Hygiene and Tropical Medicine (LSHTM) using funds from the Bill & Melinda Gates Foundation to an African setting through: • Translation of the course into French • Provision by African partners in Ghana and Burkina Faso of practical field training in clinical trials
Status:	Completed
Results and Outcomes:	This project aims to strengthen clinical trials capacity in Africa through a mechanism that maximises the likelihood of graduates from the programme remaining to work in Africa. It allowed graduates to obtain degrees from European institutions and ensure the transfer of European teaching quality assurance to Africa. By involving experienced trialists in Ghana and Burkina Faso it ensured the relevance of the content and provided practical field experience in well established African sites. The grant has resulted in establishment of MSc clinical trials courses in English at University of Ghana and University of Witwatersrand and in French at Bobo-Dioulasso in Burkina Faso.

12 Joint Programme Activities

Table 12-1: Joint Programme Activities projects

Project Acronym (Coordinator)	Type fo project/ Phase of trial	Product(s)	Manufacturer/ Developer	Study population	Status
TriMSID (Kalanda)	Networking and capacity building, linking NACCAP and EDCTP funded malaria and TB projects	Not applicable	Not applicable	Not applicable	Completed
PFRGIT (Mordmüller)	Quality control systems related to *P. falciparum* culture; Demographic and clinical data assessment	*In vitro* testing of different malaria drugs and vaccines	-	Blood samples from Gabonese patients older than 6 months	Completed
IMPDIAGNOST (Schön)	TB diagnostic and prognostic tools	Placebo Albendazole		Objective 4: 300 patients Objective 5: Target 400 patients	Ongoing
ITAFR (Sonnerborg)	Training and IT infrastructures	Not applicable	Not applicable	Not applicable	Ongoing

12.1.1 TriMSID

EDCTP Project Coordinator:	Gertrude Kalanda (University of Malawi)
EDCTP Call Title:	Call for Identification and Strengthening of Joint Programme Activities
EDCTP Project Title:	To develop a clinical trial management and support infrastructure at the College of Medicine, Blantyre, Malawi
EDCTP Project Code:	JP.2008.10800.001
EDCTP Project Start Date:	6 April 2009
EDCTP Project End Date:	6 April 2012
Collaborators:	• Exnevia Gomo (University of Malawi) • Christa Janko (Vienna School of Clinical Research, Austria) • Sian Roberts (University of Liverpool, UK) • Feiko ter Kuile, (University of Liverpool, UK) • Boele van Hensbroek (International Centre of Reproductive Health (ICRH), Netherlands)
Trial/Study title:	To develop a clinical trial management and support infrastructure at the College of Medicine, Blantyre, Malawi
Goal:	This project aims to develop clinical trial monitoring, administrative trial coordination and trial data management in Malawi, as recognised roles of clinical trial management require appropriate training, a continuous professional development programme and defined career structure. The project focuses on local training of Malawian clinical trial monitors to monitor trials on behalf of academic trial sponsors; clinical trial coordinators' who support the principal investigators (PIs) in the conduct of clinical trials; and data managers to set up, maintain and operate trial databases.
Primary Objective(s):	The objective is to build on existing developments to provide a comprehensive clinical research support service through development of a programme of training and continuous professional development and the establishment of a defined career structure for clinical trial management and administration which will lead to the proactive positioning of Malawi as a location of choice for conducting good quality clinical trials.
Collaborating site(s):	• College of Medicine (Malawi) • Liverpool School of Tropical Medicine (UK) • Vienna School of Clinical Research (Austria)
Status:	Completed
Results and Outcomes:	With the collaboration between VSCR, LSHTM and CoM, a critical mass of clinical research personnel has been trained by the CTU. The following courses have been given: 1. The Foundations of Clinical Research course (attended by 24 participants) included: – An Introduction to Clinical Research – Introduction to GCP – Safety definitions and reporting – Data management – Ethical Considerations in Clinical Research 2. A Trial Site Management course (12 participants) 3. A GCLP course (21 participants) 4. An online Standard Operating Procedures (12 researchers followed the course)

12.1.2 PFRGIT

EDCTP Project Coordinator:	Benjamin Mordmüller (University of Tübingen, Germany)
EDCTP Call Title:	Call for Identification and Strengthening of Joint Programme Activities
EDCTP Project Title:	Implementation and standardization of in vitro Plasmodium falciparum culture for resistance phenotyping and immune-mediated growth inhibition testing
EDCTP Project Code:	JP.2008.10800.004
EDCTP Project Start Date:	31 March 2009
EDCTP Project End Date:	31 March 2012
Collaborators:	• Saadou Issifou (Albert Schweitzer Hospital, Gabon) • Pierre-Blaise Matsiegui (Centre international de recherches médicales de Franceville (Ngounie), Gabon) • Maria Yazdanbakhsh (Leiden University, Netherlands)
Clinical Trial/Study Sponsor:	The Medical Research Unit of the Albert Schweitzer Hospital in Lambaréné (MRU), Gabon
Trial/Study title:	*In vitro* resistance phenotyping and immune-mediated growth inhibition of *Plasmodium falciparum* clinical isolates.
Goal:	The overall objective of this project is to create a network of mutual exchange of techniques, reagents, protocols, as well as training (face-to-face and internet-based), and set up a quality control system relating to P. falciparum culture.
Primary Objective(s):	1. To implement continuous culture of P. falciparum in malaria endemic countries 2. To standardize parasite culture, perform regular training, and assure quality of results across sites 3. To built-up a repository of frozen parasite stocks, standards, and protocols.
Secondary Objective(s):	1. The development of a methodology to measure immune-mediated growth inhibition within the framework of malaria vaccine trials 2. The development of new drug candidates 3. To compare laboratory and clinical isolates.
Clinical Trial/Study site(s):	The Medical Research Unit of the Albert Schweitzer Hospital in Lambaréné (MRU), Gabon
Collaborating site(s):	• Department of Parasitology of the University of Tübingen (UKT, Germany) • MRU (Gabon) • The Medical Research Center of the province Ngounie in Fougamou (CRMN, Gabon) • Leiden University Medical Center (LUMC, Netherlands) Other associated partners include the EDCTP project "Artesunate Treatment for Severe Malaria in African Children" coordinated by Prof. Kremsner and the Medical University Vienna, Austria Other partners: Members of the CANTAM Project
Study design:	Laboratory and epidemiological studies
Status:	Completed
Results and Outcomes:	Through this JPA grant, the following capacities have ben developed: • Implementation of continuous parasite culture in Lambaréné and Fougamou • The two sites in Gabon are now able to perform laboratory studies on parasite biology and growth properties, including immune-mediated and drug-induced growth inhibition • Provision of equipment and training for parasite culture and sample handling • Capacity to perform parasite cell culture and growth assays

	on site • A workshop on *in vitro* parasite culture and sample tracking was given in Gabon.
Total number of subjects (cohort/epidemiological/ other studies):	Up to 2995
Other/Sub-studies:	Other training: Anne-Marie Nkoma received additional training in parasite culture at the University of Tübingen.
Publications:	1. Joanny F, Held J, Mordmuller B. *In vitro* activity of fluorescent dyes against asexual blood stages of *Plasmodium falciparum*. *Antimicrobial Agents and Chemotherapy* Vol 56, 5982-6985, 2012

12.1.3 IMPDIAGNOST

EDCTP Project Coordinator:	Thomas Schön (Kalmar County Hospital, Sweden)
EDCTP Call Title:	Call for Identification and Strengthening of Joint Programme Activities
EDCTP Project Title:	Improved diagnostic and prognostic tools to combat tuberculosis in high endemic areas from bench to clinical trials
EDCTP Project Code:	JP.2009.10800.006
EDCTP Project Start Date:	27 April 2010
EDCTP Project End Date:	27 April 2013
Collaborators:	• Peter Aaby (Bandim Health Project, Guinea) • Ebba Abate (Linköping University, Sweden) • Abraham Aseffa (Armauer Hansen Research Institute (AHRI), Ethiopia) • Sven Britton (Karolinska Institute, Sweden) • Ermias Diro (Gondar University, Ethiopia) • Daniel Elias (ACE Biosciences, Denmark) • Assefa Getachew (Gondar University, Ethiopia) • Jonna Idh (Linköping University, Sweden) • Paulo Rabna (Bandim Health Project, Guinea-Bissau) • Cesaltina Silva Vieira (Bandim Health Project, Guinea-Bissau) • Olle Stendahl (Linköping University, Sweden) • Christian Wejse (University of Aarhus, Denmark) • Sisay Yifru (Gondar University, Ethiopia)
Site Principal Investigator(s):	• Thomas Schön (Ethiopia) • Christian Wejse (Guinea Bissau)
Trial/Study title:	Immunonutrition and Deworming Against Tuberculosis
Goal:	To develop improved tools for clinical diagnosis and surrogate markers of treatment response in patients with tuberculosis (TB) with a special emphasis on methods that could be easily implemented in high endemic areas.
Primary Objective(s):	1. To evaluate and develop a recently published clinical scoring system adopted for field use in Guinea Bissau and Ethiopia (TB-score: Wejse et al SJID 2008) in relation to outcome and response to chemotherapy 2. To introduce a cost effective, quality controlled methodology for drug susceptibility testing of the first and second line drugs against Mycobacterium tuberculosis adopted for high endemic areas such as Ethiopia and Guinea Bissau (Schön et al, JAC 2009, in press and van Klingeren et al, JCM 2007) 3. Development of a new scoring system for chest x-ray for tuberculosis validated against clinical outcome and adopted for areas where TB/HIV-co infection is high. The present classification originating from 1961 needs to be updated for the use in high endemic areas since it does not consider HIV/TB co-infection 4. To evaluate the role of the biomarker soluble urokinase plasminogen activator receptor (suPAR) as an early prognostic marker of mortality in TB suspects in combination with the TB-score 5. To describe the role of adjuvant deworming in patients with smear-positive TB in relation to clinical outcome and enhanced immune effector functions. The surrogate markers of improvement and diagnostic tools outlined above (1-4) will be integrated in ongoing and planned clinical trials.

Clinical Trial/Study site(s):	Objective 4: Bandim Health Project, Guinea Bissau Objective 5:The College of Medicine and Health Sciences (CMHS), University of Gondar, Ethiopia
Collaborating site(s):	• AHRI (Ethiopia) • Bandim Health Project (Guinea-Bissau) • Gondar University (Ethiopia) • Kalmar County Hospital (Sweden) • Karolinska Institutet (Sweden) • Linköping University (Sweden) • University of Aarhus (Denmark)
Study designs:	Objective 4: Prospective observational clinical study Objective 5: A placebo controlled randomised prospective study
Product(s):	Albendazole
Cofunders:	• Swedish Heart and Lung Foundation (Sweden) • Swedish Association of Medicine (Sweden) • DANIDA (Denmark) • SIDA (Sweden)
Trial Registration number(s):	ATMR2009110001673419 (Objective 4: PREDINAM study) NCT00857116 (Objective 5)
Status:	Ongoing
Results and Outcomes:	Master thesis by Wssihun Wedajo (Ethiopia): "Drug Susceptibility Testing and Molecular Characterization of Mycobacterium tuberculosis Isolates from Pulmonary TB Patients at the End of Two Month Intensive Therapy in Addis Ababa, Ethiopia" See publications
Total number of subjects (clinical trials only):	Objective 4: Target 300 patients Objective 5: Target 400 patients
Total number of subjects (cohort/epidemiological/ other studies):	Objective 1: Target 500 patients Objective 2: Target 200 patient isolates Objective 3: Target 200 patients
PhD studies	Objective 5: Deworming against tuberculosis Candidate: Ebba Abate (Gondar University and Linköping University)
	Objective 4: suPAR as an early prognostic marker in TB and TB suspects Candidate: Frauke Rudolf (Bandim Health Project and Aarhus University)
MSc study	Objective 2: A new strategy for second line drug susceptibility against tuberculosis Candidate: Wassihun Wedajo (Armauer Hansen Research Institute. Addis Abeba, Ethiopia)
Publications:	1. Frauke Rudolf, Grethe Lemvik, Victor Francisco Gomes, Morten Sodemann, Jay Verkuilen, Ebba Abate, Thomas Schön, Jesper Eugen-Olsen, Lars Østergaard, Christian Wejse. TBscoreII: refining and validating a simple clinical score to monitor Pulmonary Tuberculosis patients on treatment. *Scand J Infect Dis*. 2012 accepted 5th July 2013. 2. Helena Janols, Meseret Senbeto, Jonna Idh, Sven Britton, Ebba Abate, Thomas Schön. Early treatment response evaluated by a clinical scoring system correlates with the prognosis of pulmonary tuberculosis patients in Ethiopia: a prospective follow-up study. *Scand J Infect Dis*. 2012 Nov; 44(11):828-34. 3. Schön, Thomas. Stendahl, Olle; Lerm, Maria. Shortening the "short-course" therapy – how insights in host immunity may contribute to new treatment strategies for

	tuberculosis*. J Intern Med*. 2013 Apr;273(4):368-82. Review. 4. Ebba Abate, Jonna Idh, Aschalew Gelaw, Shitaye Alemu, Ermias Diro, Assefa Getachew, Sven Britton,Daniel Elias, Abraham Aseffa, Olle Stendahl, Thomas Schön. Rapid decline in helminth infection after treatment initiation for tuberculosis among HIV positive but not HIV negative patients. *PLoS One*. 2012;7(8):e42901. 5. Rudolf F, Joaquim LC, Vieira C, Bjerregaard-Andersen M, Andersen A, Erlandsen M, Sodemann M, Andersen PL, Wejse C.The Bandim tuberculosis score: reliability and comparison with the Karnofsky performance score. *Scand J Infect Dis*. 2013 Apr;45(4):256-64. **Other publications resulting from this work** 1. PhD Thesis: Ebba Abate. The impact of helminth infection in patients with active tuberculosis. Linköping University June 2013. 2. PhD Thesis: Frauke Rudolf. The Bandim TBscore – reliability, further development and evaluation of potential uses. Århus University June 2013. 3. PhD Thesis: Jonna Idh. The role of nitric oxide in host defence against Mycobacterium tuberculosis. Clinical and Experimental Studies. Linköping University June 2012. 4. Master Thesis: Wassihun Wedajo. Drug susceptibility testing and molecular characterization of Mycobacterium tuberculosis isolates from Pulmonary TB patients at the end of two month intensive therapy in Addis Abeba, Ethiopia (awarded the Tore Godal medal by the Ethiopian Medical Association). Ethiopia 2012.

12.1.4 ITAFR

EDCTP Project Coordinator:	Anders Sonnerborg (Karolinska Institute, Sweden)
EDCTP Call Title:	Call for Identification and Strengthening of Joint Programme Activities
EDCTP Project Title:	Integrated training activities and IT infrastructures to improve capacities in eastern African area
EDCTP Project Code:	JP.2009.10800.002
EDCTP Project Start Date:	26 May 2010
EDCTP Project End Date:	26 May 2013
Collaborators:	• Muhammad Bakari (Muhimbili University College of Health Sciences, Tanzania) • Getachew Aderaye Desta (University of Addis Ababa, Ethiopia) • Daniel Fekade (University of Addis Ababa, Ethiopia) • Gian Franco Morino (Neema Mamy Hospital, Kenya) • Admasu Tenna (University of Addis Ababa, Ethiopia) • Mario Toti (Area Vasta Toscana Sud-Est, Italy) • Maurizio Zazzi (University of Siena, Italy)
Trial/Study title:	Integrated training activities and IT infrastructures to improve capacities in eastern African area
Goal:	To strengthen the capacity building of the ongoing Swedish, Ethiopian and Tanzanian EDCTP project "Optimisation of tuberculosis and HIV co-treatment in Africa: Pharmacokinetic and pharmacogenetic aspects on drug-drug interactions between Rifampicin and Efavirenz" managed by the Karolinska Institute (shortly: the KI project) by integrating it with the ongoing Italian and Kenyan project "NEEMA MAMY, Mothers and Children right to Healthcare in the shantytowns"
Primary Objective(s):	The overall objective of the project is to strengthen the capacities of the involved partners and countries to deal with the emerging issue of resistance to antiretrovirals. The sub-objectives are: 1. To upgrade lab infrastructure at involved sites in order to perform basic resistance measurements and to send amplified proviral DNA to Karolinksa Institute (Sweden) and Area Vasta for viral DNA sequencing. The sequences will be sent back for resistance determination and phylogenetic analysis 2. To upgrade IT infrastructure at the involved sites in order to electronically store relevant clinical and resistance data 3. To train staff at involved sites 4. To merge data into the EuResist Integrated DB (EIDB) and realise a resistance prediction engine able to support doctors in Africa in providing most effective medication based on the specific situation in terms viral population, available drugs and health system.
Collaborating site(s):	• University of Addis Ababa (Ethiopia) • Neema Mamy Hospital (Kenya) • Muhimbili University College of Health Sciences (Tanzania) • Karolinska Institutet (Sweden) • Area Vasta Toscana Sud-Est (Italy) • University of Siena (Italy)
Cofunders:	• Karolinska Institutet (Sweden) • Tuscany Area Vasta Sud-Est (Italy) • EuResist Network (Italy)
Status:	Ongoing

Results and Outcomes:	
Total number of subjects (cohort/epidemiological/ other studies):	800
PhD studies:	Project: Development of HIV drug resistance in HIV-TB co-infected individuals Candidate: Amogne Wondwossen (Addis Ababa University, Ethiopia)
	Project: Genotypic analysis of HIV-I drug resistance associated mutations from plasma of antiretroviraldrug naive patients, Co-receptor tropism, and impact of transmitted drug resistance on Virologicaland immunological response to HAART in Ethiopia Candidate: Amare Worku (Addis Ababa University, Ethiopia)
	Project: Developing and Evaluating a Monitoring Algorithm for Antiretroviral Treatment Efficacy and HIV-1 Drug Resistance Mutations among Failing Patients in Ethiopia Candidate: Nigus Fikrie Telele (Addis Ababa University, Ethiopia)
PostDoctoral study:	Project: Lab analysis of HIV drug resistance Candidate: Doreen Molka (Muhimbili University Hospital, Tanzania)
BSc study:	Project: Early infant HIV Diagnosis Candidate: Silvia Kadima (World Friends, Kenya)
Publications:	

13 Information Management

Table 13-1: Information management project(s) supported by EDCTP.

Project Acronym (Coordinator)	Type of Project	Goal of project	Institutions involved	Status
PACTR (Jimmy Volmink)	Clinical Trial Registry	Clinical trials registration	MRC (South Africa) and Cochrane Centre (South Africa)	Completed

13.1 Pan African Clinical Trial Registry (PACTR)

EDCTP Project Coordinator:	Jimmy Volmink (Medical Research Council South Africa (MRC), South Africa)
EDCTP Call Title:	Coordination and networking of research activities in Africa
EDCTP Project Title:	Pan African Clinical Trials Registry
EDCTP Project Code:	CT.2004.70100.001
EDCTP Project Start Date:	10 June 2006
EDCTP Project End Date:	31 December 2014
Collaborators:	Tamara Kredo (South Africa) Elizabeth Pienaar (South Africa)
Objectives:	1. Provide a repository for prospective registration of clinical trials conducted in Africa 2. Promote prospective clinical trial registration in the African region 3. Ensure the WHO-stipulated minimum dataset for registered trials is publicly and freely available to all users of the registry 4. Provide a searchable database of all clinical trials conducted in Africa. 5. To increase the number of trials in Africa that are registered prospectively. In the initial phase, the registry registered trials in HIV/AIDS, Tuberculosis and Malaria to demonstrate proof of concept. Once established, the goal is that the Registry will become the register of choice for any clinical trial conducted in Africa. The Registry is presently the only Africa member of the WHO Network of Primary Registers and transfers all trial information to the WHO International Clinical Trials Search Portal on a quarterly basis.
Status:	Ongoing
Results and Outcomes:	• PACTR has received positive support and increased registration through its evolution which resulted from a request from the World Health Organization (WHO) and the African Vaccine Regulatory Forum for registration of all randomised controlled and controlled clinical trials regardless of disease type conducted in Africa, thus the HIV/AIDS, Tuberculosis and Malaria Clinical Trials Registry was transformed to the Pan African Clinical Trials Registry (PACTR) in June 2008 • In September 2009 PACTR was officially recognised as a WHO Primary Registry • The web-based portal hosting www.pactr.org currently has an online registration facility that meets the standards required by the WHO International Clinical Trials Platform (ICTRP) and its status as a Primary Registry was renewed in 2010 and in 2011 • By January 2010 the Registry applications had doubled since the official launch and by December 2010, the Registry had received 67 applications, of which 36 eligible trials were registered • By April 2011 application submissions increased to 96 of which 46 were registered, 41 were denied (31 were denied because application was submitted while the trials had already started) and 9 were pending review • In August 2011 the Geographic Information Systems (GIS) component was launched on the database portal to facilitate the visual presentation of trial locations on a map of Africa

	• In March 2012 a flagging system was introduced to mark trials that are retrospectively registered. This enables trial applications previously denied registry numbers due to the timing of their application to be registered. In addition the remit of the Registry has been expanded to accept phase 0-4 trials • By February 2014, 396 applications had been submitted to the Registry of which 263 were registered, 57 were denied or in-eligible and 76 are pending review.
Publications:	1. Abrams A, Siegfried N, Geldenhuys H. 2011. Adolescent Trial Experiences in a vaccine trial: a pilot project. *South African Medical Journal* 2011;101:884-886 2. Abrams A, Opiyo N, Crawley S, Cotton M, Wiysonge C, Okebe J. Supporting registration of child-focused clinical trials in Africa: The Child Strategy project. *S Afr Med J* 2011;101(11):804 3. Abrams A, Siegfried N. Growing Everyday: The Pan African Clinical Trials Registry. *Journal of Evidence-Based Medicine* 2011 Aug 2(4):172-9 4. Abrams A. One of a Kind - The Pan African Clinical Trials Registry, a regional registry for Africa. *The Pan African Medical Journal*. 2011;9:42 5. Lutje V, Siegfried N, Gerritsen A. Randomized controlled trials of malaria intervention trials in Africa, 1948 to 2007: a descriptive analysis. *Malaria Journal* 2011, 10:61 6. Abrams A, Siegfried N. The Pan African Clinical Trials Registry: year one data analysis of the only African member of the World Health Organization Network of Primary Registries. *The Journal of Evidence-Based Medicine,* 2010, 3. pp. 195 – 200 7. Baleta A. African Trials Registry Launches Child Strategy. *The Lancet*, 2010, 375. pp. 1423 8. Abrams A, Siegfried N. A Pan-African Clinical Trials Registry for the specific needs of triallists on the continent. *South African Medical Journal*, 2010, 100(5): 294 -95 9. Abrams A, Siegfried N. "Compliance with the WHO minimum data-set in the first Pan African WHO-endorsed Primary Registry. *Trials* 2009, 10:56 doi:10.1186/1745-6215-10-56 10. Abrams A, Siegfried N. Guest Editorial: Maximising the effectiveness of trial registries in resource-constrained settings, *BMJ Clinical Evidence*, 13 July 2009.

14 Regulatory Authorities

Table 14-1: Projects on capacity strengthening for regulatory authorities and environment supported by EDCTP

Project Acronym (Coordinator)	Type of Project	Goal of project	Institutions involved	Status
WHO National Regulatory phase 1	Implementation of the "WHO programme to strengthen regulatory systems in African countries with focus on clinical trial application and inspection of clinical trials"	Regulatory environment strengthening (first phase)	Regulators from Botswana, Ethiopia, The Gambia, Ghana, Malawi, Nigeria, Tanzania, Uganda, Zimbabwe and Mozambique	Completed
WHO National Regulatory phase 2	Implementation of the "WHO programme to strengthen regulatory systems in African countries with focus on clinical trial application and inspection of clinical trials"	Regulatory environment strengthening (second phase)	Members of AVAREF and joint review team from Gabon, Kenya, Ghana, Tanzania, Mozambique, Malawi and Burkina Faso with expert support by two officials from the Belgium National Regulatory Authority	Completed

14.1.1 WHO-National Regulatory (first phase)

EDCTP Project Coordinator:	Liliana Chocarro (WHO, Switzerland)
EDCTP Project Title:	Implementation of the "WHO programme to strengthen regulatory systems in African countries with focus on clinical trial application and inspection of clinical trials"
EDCTP Project Code:	CB.2005.20900.001
EDCTP Project Start Date:	9 June 2006
EDCTP Project End Date:	15 August 2008
Status:	Completed
Results and Outcomes:	• Training for regulators from Botswana, Ethiopia, The Gambia, Ghana, Malawi, Nigeria, Tanzania, Uganda, Zimbabwe and Mozambique • Establishment of the African Regulators Forum (AVAREF) • Support for two AVAREF meetings and continuation of training activities of the Global Training Network Programme of WHO • Joint review of clinical trials involving Gabon, Kenya, Ghana, Tanzania, Mozambique, Malawi and Burkina Faso with expert support by two officials from the Belgium National Regulatory Authority

14.1.2 WHO-National Regulatory (second phase)

EDCTP Project Coordinator:	Liliana Chocarro (WHO, Switzerland)
EDCTP Project Title:	Implementation of the "WHO programme to strengthen regulatory systems in African countries with focus on clinical trial application and inspection of clinical trials"
EDCTP Project Code:	CB.2005.20900.002
EDCTP Project Start Date:	20 August 2008
EDCTP Project End Date:	31 March 2010
Status:	Completed
Results and Outcomes:	• Training for regulators from Botswana, Ethiopia, The Gambia, Ghana, Malawi, Nigeria, Tanzania, Uganda, Zimbabwe and Mozambique • Establishment of the African Regulators Forum (AVAREF) • Support for two AVAREF meetings and continuation of training activities of the Global Training Network Programme of WHO • Joint review of clinical trials involving Gabon, Kenya, Ghana, Tanzania, Mozambique, Malawi and Burkina Faso with expert support by two officials from the Belgium National Regulatory Authority.