

EDCTP Project Portfolio

A compendium of
clinical trial, capacity building and networking projects



Last updated on: 25 January 2012



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Introduction

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

The document starts with the synopsis of clinical trials in the order of disease type HIV/AIDS, tuberculosis and malaria. Within each disease type a summary of funded projects based on intervention types, treatment, vaccines, microbicides and diagnostics is then given. This is then followed by the fellowships, MSc and PhD scholarships, ethics, regulatory, networks of excellence, other networking grants, joint programme activities and the Pan African Clinical Trial Registry.

Each section begins with a short introduction and a table which gives a summary of funded projects in each category. This is followed by a synopsis which summarises the project including, status, results, outcomes and publications if available.

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

Abbreviations and acronyms

The following abbreviations are used in this document:

3TC	Lamivudine
ART	Anti-retroviral treatment (therapy)
ARV	Anti-retroviral
AZT	Zidovudine
BMGF	Bill and Melinda Gates Foundation
Danida	Danish International Development Assistance
D4T	Stavudine
EC	European Commission
EDCTP	European and Developing Countries Clinical Trials Partnership
EFV	Efavirenz
ETH	Ethambutol
GCLP	Good Clinical Laboratory Practice
GCP	Good Clinical Practice
HAART	Highly Active Antiretroviral Treatment
HLA	Human leucocyte antigen
INH	Isoniazid
ISRCTN	International Standard Randomised Controlled Trial Number
LSHTM:	London School of Hygiene and Tropical Medicine
MRC	Medical Research Council
MS	Member States
NRTI	Nucleoside Reverse Transcriptase Inhibitor
PACTR	Pan African Clinical Trials Registry
P(MTCT)	Prevention of (Mother To Child Transmission)
PZA	Pyrazinamide
RIF	Rifampicin
RNA	Ribonucleic acid
RUTF	Ready-to-use therapeutic lipid-based food
TB	Tuberculosis
TBD	To be defined
TB-IRIS	TB Immune Reconstitution Syndrome
UK	United Kingdom
WHO	World Health Organisation

1 HIV/AIDS

EDCTP portfolio of funded projects on HIV/AIDS covers the areas of drugs, vaccines and microbicides. Also funded are pure capacity building projects (with no investigational products).

1.1 HIV/AIDS treatment clinical trials

Table 1-1: Summary table of HIV/AIDS treatment clinical trials supported by EDCTP

Project Acronym (Coordinator)	Phase of trial	Product(s)	Manufacturer / Developer	Study population	Status
CHAPAS-1 (Chintu)	II	Pedimune	Cipla Pharmaceuticals	PAEDIATRIC 211 HIV-1 infected children (3 months-14 years)	Completed
CHAPAS-3 (Mulenga)	III/IV	Triomune baby and Junior (d4T+3TC+NVP); Lamivir S (d4T+3TC); 3TC+ABC baby and junior scored tablets ZDV+3TC baby and junior scored tablets ZDV+3TC+NVP scored tablets	Cipla Pharmaceuticals	PAEDIATRIC Across the full paediatric age-range, in both previously untreated (ART naïve) children and in children with undetectable viral load who have already been receiving d4T+3TC+NVP as first-line ART. More specifically: 420 children aged 1 month to 13 years will be recruited over 18 months from 2 Ugandan and 1 Zambian paediatric clinical centres (140 children per site) and followed for a minimum of 96 weeks	Ongoing
MONOD (Leroy)	IIb/III	ZDV syrup 3TC syrup NVP syrup ABC syrup EFV syrup Cotrimoxazole syrup	GSK, GSK, Boehringer-Ingelheim, Abbott, BMS, Ratiopharm	PAEDIATRIC HIV-infected children Early diagnosed between age 6 weeks and 24 months of life Initial prospective therapeutic cohort (N=230), then phase 2b-3 trial (n=3*65=195)	Ongoing
EARNEST (Mugenyi)	III/IV	- Aluvia (lopinavir/ritonavir co-formulated) - Truvada (co-formulation of tenofovir 300mg and emtricitabine 200mg) - Lamivudine - Abacavir - Tenofovir - Raltegravir	Merk, Abbott, GSK, Gilead	ADULTS 1200 HIV-infected adults on first- line therapy with an NNRTI-based regimen for at least 12 months, with evidence of treatment failure defined by modified WHO 2010 criteria as one of the following: <ul style="list-style-type: none"> • New WHO Stage 4 event (with CD4 < 200 cells/mm³ and viral load (VL) > 400 copies/ml) • CD4 < 100 cells/mm³, or CD4 fall to pre-treatment baseline or below, or CD4 < 200 cells/mm³ X 2 with previous CD4 > 400 cells/mm³ (with VL > 400 copies/ml) • VL > 5,000 copies/ml x2 	Ongoing
2LADY/ALISA	III	emtricitabine-tenofovir-protease inhibitor boosted (LPV/r or	Gilead Sciences, Janssen	ADULTS 670 HIV adults with virological failure	Ongoing

(Delaporte)		ATZ/r) abacavir-didanosine protease inhibitor boosted (LPV/r or ATZ/r)	Pharmaceutica N.V., Matrix laboratory Ltd		
NUSTART (Filteau)	III	Vitamin and mineral preparations and lipid-based therapeutic foods (RUTF)	Nutriset, France	ADULTS (over 18) 1400 Zambian and 900 Tanzanian participants for a total of 2300 or 1150 per treatment arm. ART-naive (except for single-dose nevirapine to prevent maternal-to-child HIV transmission), BMI < 18.5 kg/m ² , requiring ART as determined by CD4 count < 350/l or WHO stage 3 or 4.	Recruiting
PROMPT (Lange)	III	ARV: Stavudine (d4T) or zidovudine (AZT)/lamivudine (3TC)/efavirenz (EFV) Anti-Tb: Isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), ethambutol (ETH), pyridoxine (vitamin B6)	Available through National Programs	ADULT 334 patients, male or female, HIV-1 positive, eligible for antiretroviral treatment with CD4 T cell count < 50 cells/μl AND BMI < 18	Recruiting
RAFA (Merle)	III	ARV: nucleoside Reverse Transcriptase Inhibitor (NRTI) + EFV TB: INH, RIF, PZA and Ethambutol	Available through National Programs	ADULT, 375 patients per treatment arm = 1125, ARV naïve HIV positive, CD4 cell count ≥ 50 and ≤ 300 cells/mm ³ and bacteriologically-confirmed TB.	Recruiting
REMSTART (Egwaga)	III	Available through National Programs	Available through National Programs	ADULT, 2300 eligible for ART.	Recruiting

1.1.1 CHAPAS-1

EDCTP Project Coordinator:	Chifumbe Chintu
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
Site Principal Investigator(s):	Chifumbe Chintu (University Teaching Hospital [UTH], Zambia)
Clinical Trial/Study Sponsor:	Medical Research Council UK (MRC UK)
Trial/Study title:	Children with HIV in Africa - Pharmacokinetics and Adherence of Simple Antiretroviral Regimens (CHAPAS 1 Trial)
Goal:	Evaluate strategies for giving a new fixed-dose combination paediatric formulation of stavudine (d4T), lamivudine (3TC) and nevirapine (NVP) - Pedimune - to children
Primary Objective(s):	Study the appropriate dosing of, and adherence to, a fixed-dose combination of Pedimune
Secondary Objective(s):	<p>1) To describe toxicity probably or possible 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</p> <p>2) Determine the pharmacokinetics (PK) of NVP, d4T and 3TC in twice daily paediatric-co-formulated fixed-dose crushable/dispersible tablet combinations (Pedimune)</p> <p>3) Determine possible PK interactions between NVP and common concomitant medications in children and adolescents enrolled</p> <p>4) Validity of visual analogue scale as a simple measure of adherence compared to scheduled and unannounced pill counts Evaluate adherence to ART on a subset of children enrolled, by using a visual analogue scale for assessing 28-day adherence and comparing comparing with 3-day recall, pill and bottle counts, unannounced pill counts and Medication Event Monitoring System (MEMS).</p> <p>5) Describe mortality, disease progression, hospital admission rates and laboratory markers after starting effective ART</p> <p>6) Estimate the budget impact and cost-effectiveness of effective ART in HIV infected children in Zambia</p>
Clinical Trial/Study site(s):	UTH (Zambia)
Collaborating site(s):	MRC (UK), Radboud University Medical Centre Nijmegen (Netherlands), San Francisco General Hospital (USA), St James' Hospital (Ireland)
Study design:	Open, randomised, controlled phase I/II trial
Product(s):	Pedimune (Triomune Baby/Junior) tablets: stavudine (d4T), lamivudine (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):	31084535 (ISRCTN) http://www.controlled-trials.com/ISRCTN31084535/31084535
Sub-studies:	Aims 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
1) The CHAP 2 Cohort	
2) CHAPAS RIFNVP	Aims to study the pharmacokinetics of nevirapine (NVP) in HIV-infected children younger than 3 years who are being treated with nevirapine-containing ART and rifampin (RIF) for HIV/TB co-infection
3) Adherence sub-study	Aims to i) 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 ii) 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 " <i>Children with HIV in Africa: Pharmacokinetics and Adherence of Simple Antiretroviral Regimens (CHAPAS Trials)</i> " 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.

1.1.2 CHAPAS-3

EDCTP Project Coordinator:	Veronica Mulenga
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.07.33011.006
EDCTP Project Start Date:	9 December 2009
EDCTP Project End Date:	31 July 2013
Site Principal Investigator(s):	Diana Mary Gibb
Clinical Trial/Study Sponsor:	MRC UK
Trial/Study title:	Children with HIV in Africa Pharmacokinetics and Acceptability/Adherence of simple Antiretroviral regimens: The CHAPAS-3 trial
Goal:	The CHAPAS 3 project aims to conduct a paediatric clinical trial and several substudies (addressing in particular pharmacokinetics (PK) and antiretroviral toxicity) using 4 new simplified paediatric antiretroviral (ARV) solid-based formulations administered according to WHO dosing tables. Alongside the trial, over 4 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 a valuable regional collaboration.
Primary Objective(s):	<ol style="list-style-type: none"> 1) To compare toxicity (grade 3 or 4 laboratory or clinical adverse events) of stavudine (d4T) versus zidovudine (ZDV) versus ABC in combination with lamivudine (3TC) as fixed dose combination (FDC) backbone dual NRTI in ART-naïve HIV-infected children initiating 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 2 years and currently have undetectable HIV viral load. 2) To determine via nested PK substudies: <ol style="list-style-type: none"> a) The plasma PK of ZDV, 3TC and abacavir (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 b) The plasma PK of new EFV 200mg scored tablets administered once daily according to weight-based dosing tables. c) The plasma PK of 3TC and ABC paediatric-formulated fixed-dose crushable-tablet combinations taken with efavirenz (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):	<ol style="list-style-type: none"> 1) To compare skinfold thickness as a measure of lipodystrophy/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),

	<p>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.</p> <p>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).</p> <p>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</p> <ol style="list-style-type: none"> i. to optimize 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; ii. to evaluate the association between PK and adverse drug effects as well as immunological and virological responses; iii. to provide reference population PK models which can be used for individual patient management; and iv. 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. <p>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 randomized arms.</p> <p>7) To undertake an economic analysis comparing the cost-effectiveness of the three randomized regimens, and to model the cost-effectiveness 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)</p>
Clinical Trial/Study site(s):	<ul style="list-style-type: none"> - 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 - the Joint Clinical Research Centre (JCRC) Kampala, Uganda - the satellite site to JCRC at Gulu Hospital in Northern Uganda
Collaborating site(s):	<ul style="list-style-type: none"> - University of Nijmegen - University of Cape Town - Trinity College Dublin
Study design:	CHAPAS 3 is a three-arm phase I/II open-label randomised trial of 420 HIV-infected children, aged one month to 13 years 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).
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
Cofunders:	<ul style="list-style-type: none"> - Cipla Pharmaceuticals Ltd (India) - MRC UK (UK) - Instituto de Salud Carlos III (Spain) - Health Research Board Ireland (Ireland)

	- Istituto Superiore de Sanita (Italy)
Trial Registration number(s):	ISRCTN69078957 PACTR201006000222401
Sub-studies:	<ol style="list-style-type: none"> 1) Full pharmacokinetic curves of new Fixed Dose Combination and Efavirenz tablets in arms ZDV and ABC, but not in children in Arm d4T as extensive pharmacokinetic data has already been acquired for Triomune baby and junior in the CHAPAS-1 trial. <ul style="list-style-type: none"> • <i>PK Substudy 1 in Arm ZDV -twice daily ZDV, 3TC; once daily EFV):</i> • <i>PK Substudy 2 in Arm ABC (twice or once daily ABC, 3TC; once daily EFV):.</i> 2) PK substudy 3: Full PK curves of TB drugs with NNRTIs or abacavir Sparse population sampling pharmacokinetic substudy. <ul style="list-style-type: none"> • Those children not enrolled into the subgroups undergoing intensive pharmacokinetic evaluation 4 weeks after enrolment are instead to undergo sparse sampling at 4 week visit, to enable analyses of the impact of PK on toxicity and efficacy in all randomised children. 3) Clinical and biochemical markers associated with lipodystrophy and lipoatrophy in HIV infected children 4) Effect of the different ART drugs on cardiac and vascular function in HIV infected children.
Status:	Ongoing, screening started in Zambia on 18 October 2010 and in Uganda on 4 January 2011, by 31 st March 2011, 111 children had been recruited across the three sites.
Results and Outcomes:	-
Total number of subjects (clinical trials only):	420 Children
Total number of subjects (cohort/epidemiological/other studies):	NA
PhD study-1	Defining Lipodystrophy in HIV Infected African children on antiretroviral therapy (Dr Victor Musiime)
Other/Sub-studies:	NA
Key Publications:	None

1.1.3 MONOD

EDCTP Project Coordinator:	Valeriane Leroy
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 two once-daily simplified antiretroviral triple therapies among HIV-infected children early treated by a 12-month twice daily triple therapy between 6 weeks and 24 months of age and in virological success in Africa: the MONOD ANRS 12206 Project.
EDCTP Project Code:	IP.07.33011.002
EDCTP Project Start Date:	16 November 2009
EDCTP Project End Date:	18 March 2013
Site Principal Investigator(s):	Valeriane Leroy
Clinical Trial/Study Sponsor:	French National Agency for Research on AIDS and Viral Hepatitis (ANRS)
Trial/Study title:	International phase 2b-3 randomized clinical trial to assess two once-daily simplified antiretroviral triple therapies among HIV-infected children early treated by a 12-month twice daily triple therapy between 6 weeks and 24 months of age and in virological success in Africa: the MONOD ANRS 12206 Project.
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 long-term-survival
Primary Objective(s):	To study the proportion of treatment success (alive, under follow-up and without virologic failure) of a once daily dose of two simplified triple therapies (ABC-3TC-EFV or ABC-3TC-LPV/r) in a phase 2b-3 randomised controlled-trial among HIV-infected children above the age of 15 months old and in virologic success after a 12 months initial phase with a twice daily triple therapy using AZT-3TC-LPV/r.
Secondary Objective(s):	<ul style="list-style-type: none"> - To study the tolerance, the pharmacokinetic properties, treatment observation, the profiles of viro-immunological responses and the cost/efficiency aspects during the randomised phase. - 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. - To study the compliance over time in children treated initially twice-daily, then once-daily. - To study the clinical evolution of the children treated initially twice-daily, then once-daily. - To describe the resistance profiles in children who would develop virological failure. - To study the cost /efficiency aspects of these combinations. - To study the social acceptance of these early antiretrovirals regimens.
Clinical Trial/Study site(s):	<ul style="list-style-type: none"> - Abidjan, Ivory Coast, within the PACCI programmes, FSU Abobo-Avocatier , CEPREF-Yopougon, Yopougon and Cocody hospitals. - Kigali, Rwanda: TRAC plus Center, Kigali University Hospital. - Ouagadougou, Burkina Faso: Yalgado Ouédraogo Hospital and Charles de Gaulle Hospital.
Collaborating site(s):	<ul style="list-style-type: none"> - Inserm U897, Institut de Santé Publique, Epidémiologie et Développement (ISPED), Université Victor Segalen Bordeaux 2, - Centre Hospitalier de Luxembourg (CHU), - Hôpital Universitaire des Enfants Reine Fabiola, Brussels/Belgium (HUDERF); - EA 3620, Faculté de Médecine Necker Enfants Malades and Université

	<p>Paris-Descartes, Paris France;</p> <ul style="list-style-type: none"> - University Montpellier 1, Research Team "EA 4205: Transmission, pathogenesis and prevention of HIV and associated infections", Montpellier, France
Study design:	<p>Open phase 2b-3 randomised, international, multicenter clinical trial, of non inferiority, conducted in two consecutive steps:</p> <p><u>Initial therapeutic cohort of 12 months:</u> Prospective treatment cohort of all HIV-infected children (confirmed with PCR) from six weeks to 24 months of life under triple therapy starting at 10-12 weeks with 2 NRTIs ([AZT, ABC, or 3TC] + LPV/r) twice-daily together with prophylaxis of opportunistic infections with Cotrimoxazole and education regarding treatment.</p> <p>All these children will also receive an anti-pneumococcal vaccine (3 doses of Prevenar13), on the top of the child national immunisation programme schedule.</p> <p><u>Simplified randomised phase from 13 to 25 months:</u> Those children in virological success at the end of phase 1 (HIV-ARN <400 copies/mL on two consecutive samples at three months interval) will be randomised in three arms:</p> <ul style="list-style-type: none"> - Combination without treatment class change in one daily dose (ABC-3TC-LPV/r) - Combination with a treatment class change sparing the 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). <p>Sample size</p> <p>Initial cohort (N=230) for 12 months, then trial phase 2-3 for 12 months (n=[3*65]=195)</p> <p>Before the first randomization, a meeting of the independent trial monitoring board could adapt the trial scheme in relation to the external results expected for 2010: to make a final choice on the most appropriate molecules in a once-daily regimen and adapt the sample size if needed.</p>
Product(s):	<ul style="list-style-type: none"> - ZDV syrup - 3TC syrup - NVP syrup - ABC syrup - EFV syrup - LPV/r syrup - Cotrimoxazole syrup
Manufacturer/Developer:	<ul style="list-style-type: none"> - GSK, - Boehringer-Ingelheim, - Abbott, - BMS, - Ratiopharm
Cofunders:	<p>ANRS (France), INSERM (France) HUDERF (Belgium), CRP Luxembourg, Cooperation Luxembourg, CHU Abidjan, CHU Ouagadougou, TRAC+</p>
Sub-studies:	N/A
Trial Registration number(s):	NCT01127204
Status:	<p>Ongoing, Côte d'Ivoire: recrutement started July 2011 Burkina Faso : recruitment started May 2011</p> <p>Rwanda: not yet recruiting, protocol submitted to the Ethics committee in June 2011</p>
Results and Outcomes:	<p>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.</p>

Total number of subjects (clinical trials only):	N=195
Total number of subjects (cohort/epidemiological/other studies):	N=230
PhD study-1	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.
MSc study-1	MSc Epidemiology: Determinants of early access to care of HIV-infected infants in Africa. Supervisor: V. Leroy, Bordeaux. Candidate: Dr Issa Siribié, Burkina Faso
MSc study-2	MSc Paediatric: Clinical, immunological and virological response to ARV treatment in HIV-infected children started on triple therapy during their first year of life. Candidate : to be identified
MSc study-3	MSc Virology: Baseline NNRTI resistance testing using a highly sensitive resistance assay in infants and virological response to antiretroviral treatment. Supervisor: V. Arendt/C. Devaux. Candidate : to be identified
Other/Sub-studies:	To be developed.
Key Publications:	None

1.1.4 EARNEST

EDCTP Project Coordinator:	Peter Mugenyi
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.07.33011.003
EDCTP Project Start Date:	15 September 2009
EDCTP Project End Date:	31 March 2014 (extended, initially 30 September 2013)
Site Principal Investigator(s):	Nick Paton
Clinical Trial/Study Sponsor:	Medical Research Council (MRC) (UK)
Trial/Study title:	EARNEST – A randomised controlled trial to evaluate options for second-line therapy in patients failing first-line 2NRTI + NNRTI regimen in Africa
Goal:	<p>The EARNEST trial aims to determine the best treatment regimen for patients failing first-line therapy in resource limited settings.</p> <p>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.</p>
Primary Objective(s):	<p>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.</p> <p>More specifically the EARNEST trial aims to determine whether, in patients failing a first-line NRTI and NNRTI-containing regimen</p> <ol style="list-style-type: none"> 1 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. 2 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):	<ol style="list-style-type: none"> 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 standardized 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-recognized 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):	<p>14 sites in 5 countries:</p> <p>Nine sites in Uganda:</p> <ol style="list-style-type: none"> 1. Joint Clinical Research Centre (JCRC), Kampala, 2. Infectious Disease Institute (IDI), Kampala 3. St Francis Nsambya Hospital, Kampala 4. JCRC Fort Portal Regional Centre of Excellence, Fort Portal

	<p>5. JCRC Mbarara Regional Centre of Excellence, Mbarara 6. JCRC Mbale 7. JCRC Gulu 8. JCRC Kakira 9. JCRC Kabale</p> <p>One site in Zimbabwe: University of Zimbabwe Clinical Research Centre (UZCRC), Harare</p> <p>Two sites in Malawi: 1. University of Malawi, Queen Elizabeth Hospital, Blantyre 2. Mzuzu Central Hospital, Mzuzu</p> <p>One site in Kenya: Academic Model for the Prevention and Treatment of HIV/Aids (AMPATH) Centre, Eldoret</p> <p>One site in Zambia: University Teaching Hospital (UTH), Lusaka</p>
Collaborating site(s):	MRC Clinical Trials Unit, UK; University College Dublin, Ireland; Istituto Superiore di Sanita and CINECA, both in Italy; Institute of Tropical Medicine, Belgium; Hospital La Paz, Spain
Study design:	<p>The trial is a three arm, open label randomized trial of 1200 HIV infected adults failing first-line therapy. Patients will be randomized in a ratio of 1:1:1 to one of the following three treatment arms.</p> <ul style="list-style-type: none"> • 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) <p>The bPI will be standardised to Aluvia (lopinavir/ritonavir 400 mg/100 mg b.d.).</p> <p>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:</p> <ul style="list-style-type: none"> • 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):	ISRCTN: 37737787
Sub-studies:	<ol style="list-style-type: none"> 1. EARNEST Virology Substudy 2. EARNEST Resistance Substudy 3. EARNEST Immunophenotyping Substudy 4. EARNEST Quantiferon Substudy 5. EARNEST Bone Mineral Density Substudy 6. EARNEST Socioeconomic Substudy 7. EARNEST PK Rifabutin Substudy 8. EARNEST Genital Secretions Substudy
Status:	Ongoing: Recruitment target reached in April, 2011.
Results and Outcomes:	-

Total number of subjects (clinical trials only):	1200 patients
Total number of subjects (cohort/epidemiological/other studies):	N/A
PhD study-1	Bone Mineral Density Substudy - Bonnie Wanderawho (IDI, Uganda)
PhD study-2	Socioeconomic Substudy - Jupiter Simbeye (University of Malawi)
PhD study-3	Public Health - Willard Tinago (University of Zimbabwe).
PhD study-4	Health Economics - Gibson Mandozana (University of Zimbabwe)
MSc study-1	MSc in clinical trials at the London School of Hygiene and Tropical Medicine (LSHTM) - Ennie Chidziva (UZCRC, Zimbabwe)
MSc study-2	MSc in clinical trials at the London School of Hygiene and Tropical Medicine (LSHTM) - Michael Katwere (IDI, Uganda).
Key Publications:	None

1.1.5 2LADY/ALISA

EDCTP Project Coordinator:	Eric Delaporte
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.07.33011.004
EDCTP Project Start Date:	13 July 2009
EDCTP Project End Date:	12 July 2013
Site Principal Investigator(s):	Sinata Koulla-Shiro
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:	To conduct a phase III clinical trial to evaluate the two WHO recommended second-line treatments and further explore a third strategy which combines emtricitabine-tenofovir-darunavir/ritonavir and not yet evaluated in Sub-Saharan Africa. The expected outcomes are that a recommendation can be made concerning the use of the second line strategy recommended by WHO and secondly concerning an innovative strategy.
Primary Objective(s):	The primary objective of both studies will be to compare in an African setting and 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, primary endpoint) in different groups of patients receiving different antiretroviral combinations: 1) 2LADY TRIAL: 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. The primary endpoint will be the virological response (plasma HIV RNA<50 copies/ml) at 48 weeks and 36 months (post end point). 2) ALISA TRIAL: the combination of emtricitabine-tenofovir- lopinavir/ritonavir in arm A and the combination of lamivudine- tenofovir-atazanavir/ritonavir in arm B. The primary endpoint will be the virological response (plasma HIV RNA<50 copies/ml) at 48 weeks.
Secondary Objective(s):	The secondary objective of the trials will be to compare the following parameters of response to antiretroviral treatment across all arms: clinical outcome, virological response, immunologic response, tolerance, adherence to ARV drugs, treatment discontinuation, resistance pattern for failing patients, drug concentration, lipodystrophy syndrome, metabolic disorders, programmatic issues and prevalence of HBsAg positivity, HBV DNA viremia and drug mutation related to lamivudine at baseline.
Clinical Trial/Study site(s):	2LADY Trial: - The Central Hospital of Yaounde [YCH] (Cameroon) - The University Hospital of Fann (Senegal) ALISA Trial: - Mbeya Medical Research Programme [MMRP] (Tanzania) - University of Limpopo Pretoria (South Africa)
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; Montpellier, France
Study design:	The study designs are both multicentre, international, non-inferiority, randomized, non-blinded phase III trial comparing the virological efficacy and tolerance of different antiretroviral treatment regimens in HIV-1 infected patients having virological failure of a first-line antiretroviral therapy with non-nucleoside reverse transcriptase inhibitor.
Product(s):	ANRS 12169 - 2LADY TRIAL:

	<p>1) Emtricitabine-tenofovir-lopinavir/ritonavir 2) Abacavir-didanosine- lopinavir/ritonavir 3) Emtricitabine-tenofovir-darunavir/ritonavir</p> <p>ANRS 12221 – ALISA TRIAL: 1) Emtricitabine-tenofovir-lopinavir/ritonavir 2) Lamivudine-tenofovir-atazanavir/ritonavir</p>
Manufacturer/Developer:	<ul style="list-style-type: none"> - Gilead Sciences, - Janssen Pharmaceutica N.V. - Matrix laboratory Ltd
Cofunders:	<ul style="list-style-type: none"> - Swiss National Science Foundation (Switzerland) - Hôpitaux Universitaire de Genève (Switzerland) - Deutsches Zentrum fuer Luft und Raumfahrt DLR (Germany) - l'Institut de Recherche pour le Développement IRD (France) - ANRS (France) - Prins Leopold Instituut voor Tropische Geneeskunde (Belgium)
Trial Registration number(s):	<p>2LADY: NCT00928187</p> <p>ALISA: NCT01255371</p>
Sub-studies:	<p>1) Metabody - 2LADY sub-study (Evaluation of lipodystrophy and metabolic disorders in patients on second line antiretroviral treatment in Africa)</p> <p>2) Hepatitis B - ALISA sub-study (Cf. PhD study below)</p>
Status:	<p>1) 2LADY Trial: Ongoing, recruitment started in Cameroun in December 2009, in Senegal in January 2010,</p> <p>2) ALISA Trial: Not yet recruiting</p>
Results and Outcomes:	-
Total number of subjects (clinical trials only):	836 for both studies (2LADY & ALISA)
PhD study	<p>Prevalence of Hepatitis B, Hepatitis C and HBV viremia in HIV infected patients with Hepatitis B antigenaemia on lamivudine containing antiretroviral first line therapy</p> <p>Candidate: Dr. Lucas Maganga Mbeya Medical Research Programme, Hospital Hill, PO Box 2410, Mbeya, Tanzania Tel: +255 25 2503364 Fax: +255 25 2503134 Email: maganga@mmp.org</p>
Other/Sub-studies:	ANRS 12231 cost evaluation of three strategies of second-line antiretroviral therapy in African contexts – 2LADY sub-study
Trainings	<ul style="list-style-type: none"> - 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.
Key Publications:	<p>1) Abstract submitted and accepted for the IAS 2010 in Vienna: Never too late for adherence support: Experience from the recruitment phase in ANRS 12169 - 2LADY TRIAL</p> <p>2) Abstract submitted and accepted for the sixth EDCTP forum: The informed consent: a multi-steps approach. The experience from 2LADY, a second line ART randomised clinical trial</p>

1.1.6 NUSTART

EDCTP Project Coordinator:	Suzanne Filteau
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:	14 November 2013
Site Principal Investigator(s):	Suzanne Filteau
Site Principal Investigator(s):	Lackson Kasonka, University Teaching Hospital, Lusaka, Zambia John Chagalucha, National Institute for Medical Research, Mwanza, Tanzania
Clinical Trial/Study Sponsor:	London School of Hygiene & Tropical Medicine (LSHTM)
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: a) How nutritional metabolism and status interact with HIV and associated infectious diseases; b) How to interpret research findings and bring them into policy and practice.
Primary Objective(s):	The primary objective is to decrease mortality of HIV-infected African adults in the period from referral for ART to 12 weeks after starting ART.
Secondary Objective(s):	An additional objective of the project is to bring the Tanzanian and Zambian sites to a point where they can be fully independent managers of phase III clinical trials.
Clinical Trial/Study site(s):	Zambia University Teaching Hospital (Chilenje and Misisi clinics) Lusaka. (Possible addition of Lusaka, Ndola and Kafue) Tanzania Bugando Medical Centre (BMC), Sekou Toure Regional Hospital, Buzuruga Health Centre, Mwananchi hospital and Butimba hospital (Possible addition of Misungwi Hospital, Kisesa Health Centre and Magu district hospital Mwanza city).
Collaborating site(s):	University of Copenhagen, Copenhagen, Denmark; Barts & The London School of Medicine, London, UK; University Teaching Hospital, Lusaka; Zambia; Mwanza Medical Research Centre, Mwanza City, Tanzania; Jimma University Specialised Hospital, Jimma, Ethiopia; Vanderbilt University, Nashville, USA; Odense University Hospital, Odense, Denmark.
Study design:	The study is a phase III individually 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):	RUTF – ready-to-use therapeutic lipid-based food
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); Vanderbilt School of Medicine (USA); Queen Mary & Westfield College, University of London (UK); University of Copenhagen (Denmark).
Trial Registration number(s):	PACTR201106000300631

Status:	Recruiting.
Results and Outcomes:	
Total number of subjects (clinical trials only):	1400 Zambian and 900 Tanzanian participants for a total of 2300 or 1150 per treatment arm.
Total number of subjects (cohort/epidemiological/other studies):	N/A
Postdoctoral fellow	- George Praygod
PhD study-1	- Jeremiah Kidola
PhD study-2	- Tsinuel Girma (Ethiopian funded by Danish cofunding)
PhD study-3	- Daniel Yilma (Ethiopian funded by Danish cofunding)
PhD study-4	- Markos Tesfaye (Ethiopian funded by Danish cofunding)
PhD study-5	- Alemseged (Ethiopian funded by Danish cofunding)
MSc study-1	- Joshua Siame – MSc in Infectious Diseases – LSHTM (funded by commonwealth grant based in Lusaka)
MSc study-2	- Mutinta Muchimba - MSc in Infectious Diseases – LSHTM
Other/Sub-studies:	-
Key Publications:	None

1.1.7 PROMPT

EDCTP Project Coordinator:	Joep Lange
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
Site Principal Investigator(s):	Yuka Manabe and William Ofuti Worodria, Infectious Diseases Institute, Mulago Hospital Complex, Kampala (Uganda); Josefo J. Ferro, Catholic University of Mozambique, Beira, Mozambique Mahomed Riaz Mobaracaly, Ministry of Health, Provincial Health Directorate of the Sofala Province (Direcção Provincial de Saúde de Sofala DPSS), Beira, (Mozambique) Afsatou Traore, Medical Research Unit, Albert Schweitzer Hospital, Lambaréné, Gabon Zinhle Makatini, University of Limpopo Medunsa Campus, Pretoria, (South Africa)
Clinical Trial/Study Sponsor:	Amsterdam Medical Center, University of Amsterdam
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):	The key objectives are: To determine in a randomized-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. 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. 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. 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. 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. 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):	
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 (Universidade Católica de Moçambique, UCM) Research Center for Infectious Diseases (Centro de Investigações de Doenças Infecciosas; CIDI), Beira, Mozambique; Medical Research Unit, Albert Schweitzer Hospital (MRU-HAS) and satellite site (Lambarene General Hospital – HG), Lambarene, Gabon
Collaborating site(s):	Academic Medical Center at the University of Amsterdam and Amsterdam Institute for Global Health and Development, Amsterdam, Netherlands; University of Limpopo Medunsa Campus, Pretoria, South Africa; Ministry of Health, Provincial Health Directorate of the Sofala Province (Direcção Provincial de Saúde de Sofala), Beira, Mozambique; Medical Research Unit, Albert Schweitzer Hospital, Lambaréné, Gabon; Infectious Diseases Institute, University Makerere, Kampala, Uganda; Universitätsklinikum Institut für Tropenmedizin, Tübingen, Germany; Institute of Tropical Medicine, Antwerp, Belgium; Catholic University of Mozambique, Beira, Mozambique
Study design:	Randomized, open-label controlled clinical trial. Consenting HIV-infected patients with CD4 T cell counts <50 cells/μl and with a body mass index (BMI) <18 will be randomized 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) and German Ministry of Education (BMBF) (Germany); Academic Medical Center at the University of Amsterdam (Netherlands); University of Antwerp (Belgium).
Trial Registration number(s):	Pending
Status:	Not yet Recruiting
Results and Outcomes:	
Total number of subjects (clinical trials only):	334 patients
Total number of subjects (cohort/epidemiological/other studies):	-
PhD study-1	Clinical aspects and chemoprophylaxis of cryptococcal meningitis in patients with HIV infection with CD4 counts <50 cells /μL. Candidate TBD.
PhD study-2	Clinical aspects, diagnosis and treatment delay of tuberculosis in patients with HIV infection with CD4 counts <50 cells /μL. Candidate TBD.
MSc study-1	- MSc in clinical research – University of Makerere – Kampala Uganda
MSc study-2	- MSc in clinical research – University of Makerere – Kampala Uganda
MSc study-3	- MSc in clinical research – University of Makerere – Kampala Uganda
MSc study-4	- MSc studentship – Master in Public Health – Disease Control; Institute of Tropical Medicine, Antwerp, Belgium
Other/Sub-studies:	-
Key Publications:	None

1.1.8 RAFA

EDCTP Project Coordinator:	Corinne Merle
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:	20 January 2014
Site Principal Investigator(s):	Mame Bocar Lo, National TB Control Program, Dakar, Senegal Oumou Bah-Sow, National TB Control Program, Conakry, Guinea Gninafon Martin, National TB Control Program, Cotonou, Benin
Clinical Trial/Study Sponsor:	London School of Hygiene and Tropical medicine (LSHTM)
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):	<ul style="list-style-type: none"> • 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 morbidity and mortality of 3 treatment strategies: <ul style="list-style-type: none"> – 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. • 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. • 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. • 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.
Secondary Objective(s):	
Clinical Trial/Study site(s):	TB centres of MBAO and FAN hospital, Dakar, Senegal Pulmonary department of Ignace 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 Hôpitalier 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 Tropical Institute of Medicine of Antwerp, Belgium
Study design:	This is a 3 parallel arms, multicentre, open-label randomised controlled trial with 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: <ul style="list-style-type: none"> • Early ARV initiation (after week 2 of TB treatment) combined with

	<p>standard TB treatment</p> <ul style="list-style-type: none"> • 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 <p>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.</p>
Product(s):	<p>Early 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 nucleoside Reverse Transcriptase Inhibitor (NRTI) + Efavirenz (600mg) initiated 2 weeks after initiating TB treatment</p> <p>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</p> <p>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</p>
Manufacturer/Developer:	No specific manufacturer information was provided, but all drugs utilised in the study are available through national programmes.
Cofunders:	Prince Leopold Institute of Tropical Medicine (Belgium); MRC (UK); Centre Hôpitalier de Pneumo-Phtisiologie (Benin); National TB Control Program (Senegal)
Trial Registration number(s):	Pending
Sub-studies:	PhD studentship: Anti-tuberculosis drug pharmacokinetics and treatment outcomes among HIV co-infected adult patients with tuberculosis.
Status:	Not yet recruiting
Results and Outcomes:	
Total number of subjects (clinical trials only):	1125 patients
Total number of subjects (cohort/epidemiological/other studies):	
PhD study-1	Anti-tuberculosis drug pharmacokinetics and treatment outcomes among HIV co-infected adult patients with tuberculosis. Dr Dissou Affolabi
PhD study-2	-
MSc study-1	MSC Clinical Trial by Distance Learning – Name of the candidate TBC
MSc study-2	MSC Clinical Trial by Distance Learning – Name of the candidate TBC
Other/Sub-studies:	-
Key Publications:	None

1.1.9 REMSTART

EDCTP Project Coordinator:	Saidi Egwaga
EDCTP Call Title:	Call for the support of clinical trials, capacity building and networking on treatment of HIV/AIDS
EDCTP Project Title:	Reduction of <u>early mortality</u> among HIV-infected <u>subjects starting antiretroviral therapy</u> : a randomised trial. (The REMSTART trial)
EDCTP Project Code:	IP.2009.33011.009
EDCTP Project Start Date:	7 March 2011
EDCTP Project End Date:	6 March 2014
Site Principal Investigator(s):	Peter Mwaba, University Teaching Hospital, Lusaka, Zambia Sayoki G Mfinanga, Muhimbili Medical Research Centre, National Institute for Medical Research, Dar es Salaam, Tanzania
Clinical Trial/Study Sponsor:	WHO-TDR
Trial/Study title:	Reduction of <u>early mortality</u> among HIV-infected <u>subjects starting antiretroviral therapy</u> : 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 i) accelerated initiation of ART when patients with very advanced disease present to clinic, ii) increased involvement of lay-workers in adherence iii) increased frequency of diagnostic testing for cryptococcal meningitis and tuberculosis. A simple and large trial – “lean and mean” will be conducted.
Primary Objective(s):	<p>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.</p> <p>Other objectives are:</p> <p>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.</p> <p>To strengthen the capacity of the health hospital centres in clinical care and diagnostics through the conduct of research.</p> <p>To increase linkages between the different partners such that this consortium can bid for funding in clinical and health services research.</p>
Secondary Objective(s):	<p>The secondary objectives of the research programme are</p> <p>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.</p> <p>To determine the effects of the intervention on patient retention, hospital admissions, outpatient attendance as compared to standard care.</p> <p>To determine the uptake of voluntary counselling and testing services and simple tuberculosis screening among family members of patients on antiretroviral therapy.</p>
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):	Ministry of Health and Social Welfare, Dar es Salaam, Tanzania; LSHTM, London, UK; University of Zambia / Ministry of Health, Lusaka, Zambia.

	LSHTM, London, UK; St Georges Medical School, London, UK; Special Programme for Research and Training in Tropical Disease (TDR), Geneva, Switzerland; Karolinska University Hospital, Huddinge, Sotckholm, Sweden; Unit for Tuberculosis Research, South African Medical Research Council, Durban, South Africa
Study design:	The study is a two arm, randomised trial (both intervention (I) and control (C), which is the current standard of care): 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. The trial is unblinded but the outcomes are objective measures.
Product(s):	Standard treatments for HIV, TB, cryptococcal meningitis will used in this study. These are approved by WHO and are available through national programmes.
Manufacturer/Developer:	All drugs utilised in the study are available through national programmes as essential drugs.
Cofunders:	Ministry of Health (Zambia) Ministry of Health and Social Welfare (Tanzania) Karolinska University Hospital (Sweden) LSHTM (UK) WHO Tropical Diseases Research (Switzerland) MRC (UK)
Trial Registration number(s):	Pending
Sub-studies:	
Status:	Not yet recruiting
Results and Outcomes:	
Total number of subjects (clinical trials only):	2500 patients
Total number of subjects (cohort/epidemiological/other studies):	
PhD study-1	-
PhD study-2	-
MSc study-1	-
MSc study-2	-
Other/Sub-studies:	-
Key Publications:	None

1.2 HIV/AIDS prevention & treatment clinical trials

Table 1-2: Summary table of HIV/AIDS prevention & treatment clinical trials supported by EDCTP

Project Acronym (Coordinator)	Phase of trial	Product(s)	Manufacturer / Developer	Study population	Status
Kesho Bora (Newell)	IV	Zidovudine (ZDV) Nevirapine (NVP) Lamivudine (3TC) Lopinavir/Ritonavir (LPV/r)	Cipla Pharm. Ltd Abbot Lab.	PREGNANT WOMEN+INFANTS HIV-positive (32 to 36 weeks gestation and their newborns from birth up to 1 year old (mother-infant pairs) N=845	Completed
ComTru Study (Katzenstein)	III	Combivir (ZDV & 3TC) Truvada (Emtricitabine & Tenofovir)	GlaxoSmithKline Gilead	PREGNANT WOMEN+INFANTS HIV-positive (>18 years old) and their newborns (mother-infant pairs) N=450	Ongoing (enrolment completed 29 April 2010)
VITA-1 Studies (Kisanga)	II	Viramune® (NVP) Taver® (Carbamazepine) Epanutin (Phenytoin)	Boeringer Ingelheim Medochemie Pfizer	PREGNANT WOMEN+INFANTS HIV-positive (>18 years old) & their newborns (mother-infant pairs) N=144	Completed
VITA-2 Studies (Kisanga)	II	Viramune® (NVP) Taver® (Carbamazepine) Epanutin (Phenytoin)	Boeringer Ingelheim Medochemie Pfizer	PREGNANT WOMEN+INFANTS HIV-positive, ARV naive (>18 years old) and their newborns (mother-infant pairs) N=50	Ongoing
PROMISE-PEP Studies (Van de Perre)	III	Lamivudine (3TC) Lopinavir/Ritonavir (LPV/r)	Generic/ GlaxoSmithKline Abbot Lab.	INFANTS HIV-uninfected infants (7 days old, to be breastfed by their HIV-positive mothers) N=1500	Ongoing

1.2.1 Kesho Bora study

EDCTP Project Coordinator:	Marie Louise Newell
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
Site Principal Investigator(s):	Marie Louise Newell (Mtubatuba, South Africa) Nigel Rollins (Durban, South Africa) Stanley Luchters (Mombasa, Kenya) Marcel Reyners (Mombasa, Kenya) Ruth Nduati (Nairobi, Kenya) Nicolas Meda (Bobo-Dioulasso, 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 randomised controlled trial among women with CD4+ cell counts in the range 200-500 cells/mm ³ 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; and 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

	<p>11) Describe and analyse the social and cultural factors that may increase or reduce HIV rates of transmission through breastfeeding</p> <p>12) Describe family HIV-care needs and accessibility of HIV-care services</p> <p>13) Assess the cost-effectiveness of the ARV prophylaxis and therapy regimens in preventing MTC</p>
Clinical Trial/Study site(s):	<p>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)</p>
Collaborating site(s):	<p>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)</p>
Study design:	<p>Investigational phase IV randomised controlled trial (RCT) of eligible women with CD4+ cell counts between 200 and 500 cells/mm³. 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:</p> <p>A triple-ARV regimen (ZDV, 3TC and LPV/r) beginning at 34-36 weeks gestation, through delivery, until six months postpartum; or</p> <p>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.</p> <p>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.</p>
Product(s):	<p>Zidovudine (ZDV) Lamivudine (3TC) Lopinavir/ritonavir (LPV/r) Nevirapine (NVP)</p>
Manufacturer/Developer:	<p>Cipla Pharmaceuticals Ltd Abbot Laboratories</p>
Cofunders:	<p>World Health Organization [WHO] (Switzerland), French National Agency for Research on AIDS and Viral Hepatitis [ANRS] (France), Centre for Disease Control (CDC), National Institutes of Health (NIH) and Thrasher Research Foundation (USA), Belgium Cooperation (Belgium), GlaxoSmithKline Foundation, Department for International Development [DFID] (UK)</p>
Trial Registration number(s):	<p>71468401 (ISRCTN) http://www.controlled-trials.com/ISRCTN71468401/ISRCTN71468401</p>
Status:	<p>Completed</p>
Results and Outcomes:	<p>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.</p> <p>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.</p>
Total number of subjects (clinical trials only):	<p>845</p>
PhD-1	<p>Title: <i>Primary HIV in Pregnancy and its impact on mother-to-child transmission</i>.</p> <p>Candidate: Stephen Mephram</p> <p>Supervised by Prof. Marie Louise Newell</p> <p>Expected completion date: End 2010</p>

Other/Sub-studies: Key Publications:	<p>Primary HIV in pregnancy and its impact on mother-to-child transmission</p> <ol style="list-style-type: none"> 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, Boule 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. <i>Int J Epidemiol.</i> 2008 Jun;37(3):474-480. Epub 2007 Nov 12. 2. Rouet F, Foulongne V, Viljoenc J, Steegen K, Becquart P, Valéa D, Danaviah S, Segondy M, Verhofstede C, Van de Perre P, & the WHO/ANRS 1289 Kesho Bora Study Group (Newell ML). Comparison of the Generic HIV Viral Load® assay with the Amplicor™ HIV-1 Monitor 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. <i>J. Virol. Methods</i> 2010 Feb;163(2):253-7. Epub 2009 Oct 27. 3. The Kesho Bora Study Group (authors include Mephram S, Naidu K & 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. <i>Contemporary Clinical Trials</i> 32 (2011) 74–85. 4. The Kesho Bora Study Group (authors include Mephram S, Naidu K & 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. <i>Lancet Infectious Diseases</i> 11(3) (2011) 171-180. [doi:10.1016/S1473-3099(10)70288-7] 5. Mephram SO, Bland RM & Newell ML. Prevention of mother-to-child transmission of HIV in resource-rich and -poor settings. <i>International Journal of Obstetrics and Gynaecology</i>, 2010; 118(2), 201-218.[DOI: 10.1111/j.1471-0528.2010.02733.x]
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1.2.2 ComTru Study

EDCTP Project Coordinator:	Terese Lea Katzenstein
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
Site Principal Investigator(s):	Terese Lea Katzenstein (Copenhagen, Denmark) Tine Strand/Zahra Theilgaard (Copenhagen, Denmark) Celine Mandara/ Mercy G Chiduo (Tanga, Tanzania) Martha Lemnge (Tanga, 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):	<ol style="list-style-type: none"> 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. <p>Main study end points will be differences between the study groups in:</p> <ul style="list-style-type: none"> • 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):	<ol style="list-style-type: none"> 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, Bombo Regional Hospital and National Institute of Medical Research (Tanzania)
Collaborating site(s):	University of Copenhagen (Denmark), University Hospital of Malmoe (Sweden), National Institute of Medical Research, Bombo Hospital and Kilimanjaro Christian Medical College [KCMC] (Tanzania)
Study design:	Randomised open study comparing 2 regimens . The study is an open label randomised hospital based clinical 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. <u>Arm 1:</u> 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. <u>Arm 2:</u> 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, Statens Serum Institute and Novo Nordisk (Denmark), University Hospital Malmö and Swedish Orphan (Sweden), Bjorn Astrups, Jens Christensen
Trial Registration number(s):	00346567 (NCT) http://clinicaltrials.gov/ct2/show/study/NCT00346567?term=NCT00346567&rank=1
Status:	Completed
Total number of subjects (clinical trials only):	450
PhD-1	Title: <i>not yet provided</i> Candidate: Zahra Theilgaard, University of Copenhagen (DK). Supervised by Dr Terese Katzenstein. Expected completion date: end 2012.
PhD-2	Title: <i>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</i> Candidate: Mercy Chiduo, University of Copenhagen, (DK) and NIMR (TZ). Supervised by Dr Terese Katzenstein Expected completion date: July 2012.
MSc-1	Title: <i>Exploring how community leaders perceive the effects of antiretroviral treatment: A grounded theory study in Tanga, Tanzania</i> Candidate: Christiane Pahl – MSc at the Lund University, Sweden
Other/Sub-studies:	Not applicable
Status:	Ongoing
Results and Outcomes:	Ongoing
Key Publications:	None

1.2.3 VITA Studies

EDCTP Project Coordinator:	Elton R. Kisanga
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:	<i>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)</i>
EDCTP Project Code:	CT.2006.33020.006
EDCTP Project Start Date:	15 October 2007
EDCTP Project End Date:	01 March 2012
Trial 1	VITA 1 study
Site Principal Investigator(s):	Elton R. Kisanga (Moshi, Tanzania) David Burger (Nijmegen, Netherlands) Chipepo Kankasa (Lusaka, Zambia) Diana Gibb (London, 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):	<ol style="list-style-type: none"> 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):	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:	Open-label, single dose, two-group, pharmacokinetic, phase IIa study. <u>Arm 1</u> (Active Comparator): An oral dose of 400 mg <u>carbamazepine</u> is added to the 200 mg oral dose <u>nevirapine</u> intake prior delivery. <u>Arm 2</u> (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. Boeinger Ingelheim
Cofunders:	NACCAP (Netherlands) and MRC (UK)
Trial Registration number(s):	00294892 (NCT) http://clinicaltrials.gov/ct2/show/study/NCT00294892?term=NCT00294892&rank=1
Total number of subjects (clinical trials only):	144 mother-infant pairs
Sub-studies:	None
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.
Trial 2	VITA 2 study
Site Principal Investigator(s):	Elton R. Kisanga (Moshi, Tanzania) Werner Schimana (Moshi, Tanzania) David Burger (Nijmegen, Netherlands) Andreas J. van der Ven (Nijmegen, 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 (VI ramune®), which is part of ARV prophylaxis for PMTCT in Moshi, T Anzania, 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):	<ul style="list-style-type: none"> - 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). - 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):	<ul style="list-style-type: none"> - 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. - To determine the HIV status of the infant. - 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:	Open-label, multi-centre, two-group, pharmacokinetic, phase IIa/IIb study. ARV prophylaxis for PMTCT follows national guidelines (which differ slightly): <ul style="list-style-type: none"> - Mother: <ul style="list-style-type: none"> • 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 randomized to phenytoin intrapartum: start phenytoin 184 mg (2 tablets of 92mg) OD at onset of labour and continue for seven days. - Child: <ul style="list-style-type: none"> • 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) and MRC (UK)
Trial Registration number(s):	01187719 (NCT) http://clinicaltrials.gov/show/NCT01187719
Total number of subjects (clinical trials only):	VITA 2 pilot study: 50 HIV-positive, ARV naive, African, pregnant women (18 years or older) and their newborns VITA 2 main study: 150 HIV-positive, ARV naive, African, pregnant women (18 years or older) and their newborns
PhD-1	Title: <i>Clinical Pharmacology of ARV agents in resource limited settings</i> Candidate: Ms. Quirine Fillekes, at the Radboud University, Nijmegen (NL). Supervised by Prof. David Burger and Dr. Elton Kisanga. Expected completion date: September 2012.
PhD-2	Title: <i>Clinical Pharmacology of pMTCT</i> Candidate: Ms. Eva Muro, at the Radboud University, Nijmegen (NL). Supervised by Prof. David Burger and Dr. Elton Kisanga. Expected completion date: September 2012.
MSc-1	Title: <i>Age standardization in relative survival</i> Candidate: Mr. Humphrey Mkali – MSc in Biostatistics at the Leicester University (UK). Supervised by Paul Lambert and Nuala Sheehan. Completion date: 26 September 2011. Graduation: 27 January 2012.
MSc-2	Title: Ms. Lutengano George – MSc in Clinical research at KCM College, Moshi (TZ). Dissertation is still under development after successful completion of the taught semesters. Expected completion date: September 2012.
Other/Sub-studies:	Not applicable
Status:	Ongoing
Results and Outcomes:	Ongoing
Key Publications:	Submitted manuscript to <i>AIDS Journal</i> May 2011

1.2.4 PROMISE-PEP Studies

EDCTP Project Coordinator:	Philippe Van de Perre
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 June 2013
Site Principal Investigator(s):	Thorkild Tylleskar (Bergen, Norway) Nicolas Meda (Ouagadougou, Burkina Faso) James K Tumwine (Kampala, Uganda) Chipepo Kankasa (Zambia) Justus Hofmeyr (Western Cape, South Africa) Eva-Charlotte Ekström (Uppsala, Sweden) Stephane Blanche (Paris, 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):	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:	Randomised double-blind controlled trial, interventional, phase III <u>Arm 1</u> (Experimental): infant peri-exposure prophylaxis with <u>lopinavir/ritonavir</u> (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. <u>Arm 2</u> (Active Comparator): infant peri-exposure prophylaxis with <u>lamivudine</u> (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):	00640263 (NCT) http://clinicaltrials.gov/ct2/show/NCT00640263
Status (Major Challenges & Setbacks):	The participant recruitment started in November 2009 in Burkina Faso, in April 2010 in Zambia, in May 2010 in Uganda, and in October 2010 in South Africa. The main challenge is the recruitment rate which was lower than expected in South Africa and to a lesser extent in Burkina and Uganda. Fortunately, the Zambian site recruits more than expected which partly compensates for the difference in accrual with the expectations.
Status:	Ongoing
Total number of subjects (clinical trials only):	1,500
PhD-1	Title: <i>Male involvement in the PMTCT programme in Uganda</i> Candidate: Robert Byamugisha
PhD-2	Title: <i>The social context of prevention of mother-to child transmission of HIV in Mbale District Eastern Uganda</i> Candidate: Joseph Rujumba
PhD-3	Title: <i>Topic to be determined</i> Candidate: Amwe Sunday Aku
PhD-4	Title: <i>Topic to be determined</i> Candidate: Collins Chudi Ekbe-Eza
MSc-1	Title: <i>Assessment of the PMTCT programme in Ouagadougou and impact of the implementation of PROMISE-PEP on this programme</i> Candidate: Hugues Traore
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.
Status:	Ongoing
Results and Outcomes:	Ongoing
Key Publications:	Nicolas Nagot, Chipepo Kankasa, Nicolas Meda, Cheryl Nikodem, James K. Tumwine, Charles Karamagi, Halvor Sommerfelt, Dorine Neveu, Thorkild Tylleskar and Philippe Van de Perre for the PROMISE-PEP group. <i>Lopinavir/Ritonavir (LPV/r) versus Lamivudine peri-exposure prophylaxis to prevent HIV-1 transmission by breastfeeding: the PROMISE-PEP trial Protocol - ANRS 12174</i> . Submitted to BMC Infectious Diseases Tylleskar T. <i>Making it happen</i> , level 2. Glob Health Action. 2010 Jul 1;3. doi: 10.3402/gha.v3i0.5370. Byamugisha R, Tumwine JK, Semiyaga N, Tylleskar T. <i>Determinants of male involvement in the prevention of mother-to-child transmission of HIV programme in Eastern Uganda: a cross-sectional survey</i> . Reprod Health. 2010 Jun 23;7:12. Engebretsen IM, Tylleskar T. <i>[HIV, breast feeding and antiretroviral agents]</i> . Norwegian Tidsskr Nor Laegeforen. 2010 Mar 11;130(5):520-2. Byamugisha R, Tumwine JK, Ndeezi G, Karamagi CA, Tylleskar T. <i>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</i> . J Int AIDS Soc. 2010;13:52. Byamugisha R, Tylleskar T, Kagawa MN, Onyango S, Karamagi CA, Tumwine JK. <i>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</i> . BMC Health Serv Res. 2010;10:290.

1.3 HIV/AIDS microbicides capacity building and clinical trials

HIV/AIDS microbicides capacity building

Table 1-3a: Summary table of HIV/AIDS microbicides capacity building projects supported by EDCTP

Project Acronym (Coordinator)	Capacity Building Goal	Study population	Status of project
Van de Wiggert	Preparing for Phase III vaginal microbicide trials in Rwanda and Kenya: Preparedness studies, capacity building, and strengthening of medical referral systems	Cohort of high-risk women N=?	Completed
TVMTU (Hayes)	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.	Cohort of high-risk women N=2000 (1970)	Completed
MRC CTU (McCormack)	MDP301 : To build additional infrastructure at the RHRU Orange Farm site, Johannesburg; training on ethics, GCP/GCLP training for collaborators, 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	See table 1-3b	Completed
	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.	See table 1-3b	Completed
	Mozambique Feasibility Study : A Feasibility Study to evaluate the population and study site in the Healthcare centres of Mavalane and Manhica in preparation for a phase III randomised controlled trial of a vaginal microbicide for the prevention of HIV (FS Microbicides)	See table 1-3b	Completed
Mandaliya-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	Cohort of women N=430	Ongoing

Table 1-3b: Summary table of HIV/AIDS microbicides clinical trials supported by EDCTP

Project Acronym	Phase of trial	Product(s)	Manufacturer / Developer	Study population	Status	Key Publications
MDP301/Pro 2000 (McCormack)	III	PRO 2000 vaginal gel / HEC Placebo gel	Indevus Pharmaceuticals (ENDO Pharma)/ CONRAD	Adult women Sexually active, HIV-uninfected women from communities with access to primary health care N=9673	completed	
TopUp Pilot study (McCormack)	Feasibility Prospective / COHORT	Hydroxyethyl cellulose (HEC)	CONRAD	Adult women Women from existing MDP301 trial sites and MDP feasibility study site (min 45 per site over 6 sites). Male partners who agree for interview. N=270	ongoing	

Both the MDP301 phase III trial and the TopUp Pilot study were conducted under the MRC CTU project coordinated by Dr Sheena McCormack. Although these were clinical trials, they were funded as part of a call on capacity building for the conduct of clinical trials of vaginal microbicides against sexual transmission of HIV.

1.3.1 Van de Wijgert

EDCTP Project Coordinator:	Janneke van de Wijgert
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:	27 June 2007 (10 April 2007 – Contract Signed)
EDCTP Project End Date:	9 April 2011
Trial 1	
Site Principal Investigator(s):	Janneke van de Wijgert (AMC-CPCD), Anne Buve (ITM), Marleen Temmerman (Gent University), Dr. Kishor Mandalayi (ICRH-K), Joseph Vyankandondera (PU)
Clinical Trial/Study Sponsor:	n/a
Trial/Study titles:	<ol style="list-style-type: none"> 1. The Kigali HIV Incidence Study 2. The Mombasa HIV Incidence Study 3. The Reproductive Health Study 4. The 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):	<p>a) Conduct cross-sectional HIV incidence surveys in Kigali and Mombasa using BED capture enzyme immunoassay (BED-CEIA) measures and Avidity Index (AI) testing, to estimate HIV incidence in potential microbicide trial target populations, and to validate BED/AI testing in African settings.</p> <p>b) 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</p> <p>c) 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.</p>
Secondary Objective(s):	
Clinical Trial/Study site(s):	Projet Ubuzima (Rwanda), ICRHK (Kenya)
Collaborating site(s):	AMC-CPCD (Netherlands), ITM (Belgium), Gent University (Belgium)
Study design:	Cross-sectional HIV incidence surveys; and, preparedness cohorts
Product(s):	n/a
Manufacturer/Developer:	n/a
Status:	Completed
Results and Outcomes:	<p>Both HIV incidence studies 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.</p> <p>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 HPV type-specific distribution post-vaccination.</p> <p>In terms of capacity building, Chantal Ingabire from PU graduated with a MSc Medical Anthropology from the University of Amsterdam in August 2010.</p> <p>The reproductive health clinic established at the Kigali Teaching Hospital</p>

	<p>is still up and running, increasing treatment options for cervical cancer and infertility.</p> <p>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".</p>
Cofunders:	AMC-CPCD (Netherlands), ITM (Belgium), Gent University (Belgium), ICRH (Kenya), Projet Ubuzima (Rwanda), NACCAP (NL)
Total number of subjects (cohort/epidemiological/other studies):	<p>Kigali:</p> <p>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</p> <p>Mombasa:</p> <p>Cross-sectional survey female sex workers: 800 Cross-sectional survey post-partum women: 800 Prospective cohort study HIV-negative female sex workers: 400</p>
PhD study-1	The Epidemiological Utility of antibody-based assays for estimating HIV incidence in Kigali, Rwanda - Sarah Braunstein PhD defense September 2009
PhD study-2	The epidemiology of HIV and HPV among high-risk women and steady couples in Kigali, Rwanda – Nienke Veldhuijzen PhD defense 9 June 2011
PhD study	Clinical, epidemiological and socio-cultural aspects of infertility in resource-poor settings. Evidence from Rwanda – Nathalie Dhont PhD defense 15 April 2011
MSc study-1	<p>MSc Medical Anthropology (University of Amsterdam; 2009-2010) Both health and life matter becoming a sex worker: the experiences of women living in Kigali, Rwanda – Chantal Ingabire</p> <p>Graduation 17 August 2010</p>
MSc study-2	(Study title) (Name of candidate) (Study title) (Name of candidate)
Other/Sub-studies:	<p>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.</p> <p>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).</p>
Key Publications:	See section "List of publications"

1.3.2 TVMTU

EDCTP Project Coordinator:	Richard Hayes
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:	28 February 2008 (5 May 2007 – Grant Agreement Signed)
EDCTP Project End Date:	27 February 2011
Trial 1	
Site Principal Investigator(s):	Richard Hayes, Saidi Kapiga, Judith Vandepitte, Janneke van de Wijgert, Sheena McCormack
Clinical Trial/Study Sponsor:	n/a
Trial/Study title:	<p>1. A Feasibility Study to assess potential cohort suitability for future microbicide trials in North West Tanzania</p> <p>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</p>
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):	<p>a) 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.</p> <p>b) 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.</p>
Secondary Objective(s):	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) and Kampala (Uganda)
Collaborating site(s):	<ol style="list-style-type: none"> 1. Mwanza Intervention Trials Unit (MITU)/National Institute for Medical Research (NIMR) [Tanzania] 2. Medical Research Council/Uganda Virus Research Institute (MRC/UVRI) [Uganda] 3. Academic Medical Center - Center for Poverty-related Communicable Diseases (AMC-CPCD) [The Netherlands] 4. Medical Research Council Clinical Trials Unit (MRC CTU) [UK] 5. London School of Hygiene & Tropical Medicine (LSHTM) [UK]
Study design:	Mwanza: The protocol was developed to recruit 1,000 women who work in recreational facilities in the northwest region of Tanzania. This is a prospective observational 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 behavior in Kampala, of which 500 HIV-negative women contributed to this study.
Product(s):	n/a
Manufacturer/Developer:	n/a
Status:	Completed
Results and Outcomes:	The Final report with the study results and full details of capacity building activities will be submitted in June 2011. The project is currently undertaking the final data analysis of the studies conducted in Mwanza and Uganda.
Cofunders:	UK MRC (UK), NACCAP (NL),
Total number of subjects (cohort/epidemiological/other studies):	1,970
PhD study-1	n/a
PhD study-2	n/a
MSc study-1	n/a
MSc study-2	n/a
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.
Key Publications:	Vandepitte J, Bukenya J, Weiss HA, Nakubulwa S, Francis SC, Hughes P, HAYES R, Grosskurth H. HIV and other sexually transmitted infections in a cohort of women involved in high-risk sexual behavior in Kampala, Uganda. Sexually Transmitted Diseases 2011; 38: 316-323. Other publications are currently being developed.

1.3.3 MRC CTU/MDP 301

EDCTP Project Coordinator:	Sheena McCormack
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
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
EDCTP Funded Activities:	To build additional infrastructure at the RHRU Orange Farm site, Johannesburg; training on ethics, GCP/GCLP training for collaborators, personnel, etc.; database training.
Clinical Trial/Study site(s):	Reproductive Health & HIV Research Unit [RHRU] Orange Farm (South Africa) – trial also conducted at 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:	International multi-centre, randomised, double-blind, placebo-controlled phase III
Product(s):	PRO 2000 vaginal gel / HEC Placebo gel
Manufacturer/Developer:	Indevus Pharmaceuticals (ENDO Pharma)/ CONRAD (USA)
Status:	Completed
Trial Registration number(s):	ISRCTN64716212 http://www.controlled-trials.com/ISRCTN64716212/64716212
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)
Sub studies:	HPV Sub Study: the HPV sub-study target population was women enrolling into the MDP 301 trial of PRO 2000 through the clinics coordinated by the South African (SA) research centres. Owing to delayed approval from the MCC it was no longer viable to conduct this sub-study.
Major Challenges & 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. Unfortunately, the RHRU were unable to purchase the plot for expansion and a certain timeframe was reached (December 2007) with only 3 months remaining for enrolment to the trial, when there seemed little point in pursuing the additional space as the clinical activity would be decreasing from March 2008 onwards when screening and enrolment were scheduled to complete.

	<p>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.</p> <p>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.</p> <p>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.</p> <p>The greatest set back perceived by the project is the threat to sustainability of the network despite proof of efficacy reported by CAPRISA 004 and VOICE due to report in 2013. The challenge has been the lack of a sufficiently large funding scheme to approach for MDP302, designed to critically inform implementation in the most cost-effective and robust way, which is through comparison to placebo.</p>
Results and Outcomes:	<p>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.</p> <p>The following HIV and STIs rates were found at enrolment:</p> <ul style="list-style-type: none"> • HIV positive at screening: 26% • Chlamydia trachomatis: 8% • Neisseria gonorrhoea: 3% • Herpes (serology): 60% • Syphilis: 4% • Trichomonas vaginalis: 10% <p>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%.</p> <p>The key messages of the trial were:</p> <ul style="list-style-type: none"> • 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 <p>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.</p> <p>Two Mozambican clinical research centres (Manhica and Maputo 1 de Junho) now have capacity for HIV prevention trials using unlicensed</p>

	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
PhD study – 1	Jonathan Stadler, PhD Social Anthropology, University of Pretoria
MSc study – 1	Dr Jocelyn Moyes, MSc Epidemiology & Biostatistics, University of the Witwatersrand (Wits)
MSc study – 2	Ananta Nanoo, MSc Epidemiology & Biostatistics, Wits
MSc study – 3	Dr Sibongile Walaza, MSc Epidemiology & Biostatistics, Wits
Other/Sub-studies	<ol style="list-style-type: none"> 1. Mdu Mntambo, Masters in Public Health Wits 2. Dr Lucia Hans & Dr Nokwazi Ndlela trained in Reproductive Health & HIV Research Methods Postgraduate short course 3. Jessica Dhooke trained in Controlled Clinical Trials Postgraduate short course London School of Hygiene & Tropical Medicine (LSHTM) 4. Dr Lucia Hans & Vera Mbatha trained in Clinical HIV Management, RHRU
Key Publications	PENDING
Trial 2	TopUp pilot study
Site Principal Investigator(s):	Robert Pool (CRESIB), on site Khátia Munguambe (CISM)
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):	To inform the way adherence is assessed in a future clinical trial by comparing the following outcomes across three methods for monitoring adherence: <ul style="list-style-type: none"> ◆ Adherence to daily use of gel ◆ Consistency of the adherence measure ◆ Retention of participants
Clinical Trial/Study site(s):	Manhica and Maputo [CISM] (Mozambique), {trial is also being conducted in Durban (South Africa), Mwanza (Tanzania), Masaka (Uganda, Mazabuka (Zambia)}
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 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),
Status:	Completed
Trial Registration number(s):	ATMR2010060002133418 PACTR
Results and Outcomes:	<p>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.</p> <p>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.</p> <p>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.</p>
Trial 3	Mozambique feasibility study
Site Principal Investigator(s):	Sibone Mocumbi
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:	A Feasibility Study to evaluate the population and study site in the Healthcare centres of Mavalane and Manhica 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):	a) Assess the level of HIV/AIDS awareness in the general community & within the target population b) Assess the willingness of women to participate in a microbicide trial
Clinical Trial/Study site(s):	Manhica Health Research Centre (Mozambique)
Collaborating site(s):	MRC (UK), Foundation for the Development of the Community (FDC), Mavalane General Hospital (HGM) (Mozambique), Manhica Health Research Centre (CISM) (Mozambique), Centre for International Health Hospital Clinic Barcelona (Spain)
Study design:	Observational cohort design
Product(s):	n/a
Manufacturer/Developer:	n/a
Cofunders:	MRC (UK), University of Barcelona (Spain), Reproductive Health and Research Unit, University of the Witswatersrand (South Africa)
Status:	Completed
Results and Outcomes:	<p>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).</p> <p>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.</p> <p>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.</p> <p>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.</p>

1.3.4 Mandaliya-Biomarkers HIV Mic

EDCTP Project Coordinator:	Kishor Mandaliya
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:	06 April 2009
EDCTP Project End Date:	05 April 2012
Site Principal Investigator(s):	Mary Mwaura, Sinead Delany-Moretlwe, Gilles Ndayisaba
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):	<ol style="list-style-type: none"> 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 1) in HIV-negative adult women in good health at low risk for HIV with and without bacterial vaginosis
Secondary Objective(s):	<ol style="list-style-type: none"> 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):	<ol style="list-style-type: none"> 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 and MRC CTU (UK)
Study design:	Multi-country, observational, prospective cohort study in 430 women
Product(s):	Pantarhei® screener
Manufacturer/Developer:	Pantarhei Devices
Cofunders:	Medical Research Council (MRC, UK), ITM and Ghent University (Belgium), Pantarhei Devices (Netherlands) – to be confirmed
Sub-studies:	Inflammation sub-study investigates the effects of IVP on the vaginal environment over 28 days in intensive longitudinal study in the sub-sample of 100 women. The study includes colposcopy, testing for cervical and vaginal infections, cervicovaginal lavage for testing for inflammatory cytokines and investigation of novel proteins, cervical cell sampling to investigate HIV target cells and a special vaginal swab for investigating

	vaginal flora species by polymerase chain reaction in real time.
Status:	Ongoing
Results and Outcomes:	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 these results informed the different macrobicide partners to make course collection and therefore saving resources

1.4 HIV/AIDS vaccines capacity building

Table 1-4: Summary table of HIV/AIDS microbicides clinical trials supported by EDCTP

Project Acronym (Coordinator)	Phase of trial	Product(s)	Manufacturer / Developer	Study population	Status
SASHA – HPV vaccine study (Bekker)	Not applicable	GARDASIL	Merck Sharp & Dohme (Pty) Ltd	Adolescents (12-17), up to 200 participants at 6 sites N = 835	Ongoing
SASHA – Community attitudes (Bekker)	Not applicable	Not applicable	Not applicable	Adolescents (12-17) with parents/guardians and stakeholders. Focus group: N=59 (of 6-10 participants each)	Ongoing
TaMoVac – Feasibility of neonatal vaccination in Maputo (Bakari)	Not applicable	Not applicable	Not applicable	200 mothers in Maputo	Protocol under development
HIVTAB (Kapiga)	Not applicable	Not applicable	Not applicable	Tanzania: Adult women (18-44) working in bars, guest houses, hotels or other recreational facilities Burkina Faso: Adult women (18-44) sex workers N= 630	Ongoing
CHIVTUM (Kaleebu)	Not applicable	Not applicable	Not applicable	Malawi: Adult men and women (over 20) and “mature minors” (13-15) who are married or have children working in fishing communities, HIV sero-negative, N = 743 Uganda: Adult men and women (13-49) working in fishing communities, HIV sero-negative, N = 1000	Ongoing
AfrEVacc – Beira study (Weber)	Not applicable	Not applicable	Not applicable	Adult, women at risk of sexual acquisition of HIV, cross sectional survey, N = 1000; prospective cohort, N= 400; BED false negative, N= 400.	Ongoing
AfrEVacc – Manhica EVAS (Weber)	Not applicable	Not applicable	Not applicable	Adults N=70	Ongoing
AfrEVacc - Manhica Epidemiology (Weber)	Not applicable	Not applicable	Not applicable	Adults N= 696	Ongoing
AfrEVacc – Africa Centre (Weber)	Not applicable	Not applicable	Not applicable	Adult men N= 200	Ongoing
AfrEVacc – Joburg (Weber)	Not applicable	Not applicable	Not applicable	Adult, men sero-negative N= 150	Completed

1.4.1 SASHA

EDCTP Project Coordinator:	Linda-Gail Bekker
EDCTP Call Title:	Capacity building in preparation for the conduct of preventive HIV vaccine trials (EDCTP/BMGF/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
HPV vaccine study – 6 sites in South Africa	
Site Principal Investigator(s):	Surita Roux, Desmond Tutu HIV Centre (DTHF), Cape Town, South Africa Glenda Gray, Perinatal HIV Research Unit (PHRU), Johannesburg, South Africa Mary Latka, Klerksdorp Research Site (KOSH), Matlosana district, South Africa Thola Bennie, Centre for the AIDS Programme of Research in South Africa (CAPRISA), Durban, South Africa Maphoshane Nchabeleng, University of Limpopo, Medunsa, South Africa Jimmy Chandia, Walter Sisulu University, Mthatha, 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):	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):	<ol style="list-style-type: none"> 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: <ol style="list-style-type: none"> 1. Desmond Tutu HIV Centre (DTHC), Nyanga district, Cape Town; 2. Perinatal HIV Research Unit (PHRU), Johannesburg; 3. Klerksdorp Research Site (KOSH), Matlosana district; 4. Centre for the AIDS Programme of Research in South Africa (CAPRISA), Durban; 5. Medunsa Clinical Research Unit (MeCRU), Limpopo 6. Walter Sisulu University, Mthatha
Collaborating site(s):	University of KwaZulu Natal & HIV AIDS Vaccines Ethics Group (HAVEG, South Africa), Institute of Public Health, Epidemiology & Development (France)
Study design:	Longitudinal cohort study with self-selecting intervention and control groups.
Number of subjects:	Establishing a cohort group, adolescents (12-17), 200 participants are expected to be enrolled at each site.
Product(s):	GARDASIL

Manufacturer/Developer:	Merck Sharp & Dohme (Pty) Ltd
Cofunders:	BMGF (USA), ANRS (France), Irish Aid (Ireland), NACCAP (Netherlands), SIDA (Sweden), SNSF (Switzerland), MRC (UK), Merck Sharp & Dohme (Pty) Ltd (South Africa)
Trial Registration number(s):	Not applicable
Sub-studies:	Not applicable
Status:	Completed
Results and Outcomes	By enrolling 834 adolescents at 6 sites across South Africa and having 816 of those adolescents choosing to be vaccinated, the project has shown that it is indeed feasible to enrol and retain 12-17 year old adolescents in a clinical trial in South Africa. Another important contribution was developing ethico-legal guidelines for the conduct of adolescent clinical trials in South Africa, which they state is rapidly becoming a nationally and internationally used reference.
Community attitudes focus group study	
Site Principal Investigator(s):	Surita Roux, Desmond Tutu HIV Centre (DTHF), Cape Town, South Africa Glenda Gray, Perinatal HIV Research Unit (PHRU), Johannesburg, South Africa Mary Latka, Klerksdorp Research Site (KOSH), Matlosana district, South Africa Thola Bennie, Centre for the AIDS Programme of Research in South Africa (CAPRISA), Durban, South Africa Maphoshane Nchabeleng, University of Limpopo, Medunsa, South Africa Jimmy Chandia, Walter Sisulu University, Mthatha, South Africa
Clinical Trial/Study Sponsor:	Not applicable
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):	<ol style="list-style-type: none"> 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
Secondary Objective(s):	-
Clinical Trial/Study site(s):	South African AIDS Vaccine Initiative (SAAVI) sites: <ol style="list-style-type: none"> 1. Desmond Tutu HIV Centre (DTHC), Nyanga district, Cape Town; 2. Perinatal HIV Research Unit (PHRU), Johannesburg; 3. Klerksdorp Research Site (KOSH), Matlosana district;

	<p>4. Centre for the AIDS Programme of Research in South Africa (CAPRISA), Durban;</p> <p>5. Medunsa Clinical Research Unit (MeCRU), Limpopo</p> <p>6. Walter Sisulu University, Mthatha</p>
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
Number of subjects:	Adolescents (12-17) 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).
Product(s):	Not applicable
Manufacturer/Developer:	Not applicable
Cofunders:	BMGF (USA), ANRS (France), Irish Aid (Ireland), NACCAP (Netherlands), SIDA (Sweden), SNSF (Switzerland), MRC (UK)
Trial Registration number(s):	Not applicable
Sub-studies:	Not applicable
Status:	Completed
Results and Outcomes	Data processing is still ongoing but preliminary data has shown that 1) communication about sex is difficult between parents and adolescents; 2) there are many misunderstandings and miscommunications between the two; and 3) third parties such as relatives seems to facilitate communication between parents and adolescents.
Total number of subjects (clinical trials only):	
Total number of subjects (cohort/epidemiological/other studies):	N = 1307
PhD study-1	-
PhD study-2	-
MPH study-1	Psychosocial predictors of sexual risk behaviour in a cohort of South African adolescents, Agnes Ronan, Demond Tutu HIV Centre, Cape Town, South Africa
MSc study-2	-
Other/Sub-studies:	-
Key Publications:	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. <i>JAIDS</i> , 54 Suppl 1, S7-S11.

1.4.2 HIVTAB

EDCTP Project Coordinator:	Saidi Kapiga
EDCTP Call Title:	Capacity building in preparation for the conduct of preventive HIV vaccine trials (EDCTP/BMGF/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
Site Principal Investigator(s):	Saidi Kapiga, National Institute for Medical Research, Mwanza, Tanzania; John Shao, Kilimanjaro Christian Medical Centre and National Institute for Medical Research, Tanzania; Nicolas Meda, UFR-SDS University of Ouagadougou & Centre Muraz/Site ANRS du Burkina Faso, Burkina Faso
Clinical Trial/Study Sponsor:	Not applicable
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):	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
Secondary Objective(s):	<ol style="list-style-type: none"> 1. To characterise HIV-1 viral isolates and assess factors associated with viral genotypes among identified target populations 2. To determine immunological and genetic factors that could confer resistance to HIV infections and/or slow down disease progression 3. 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:	Multi-centre study
Number of subjects:	Tanzania: N= 630, Burkina Faso: N= 630
Product(s):	Not applicable
Manufacturer/Developer:	Not applicable
Cofunders:	BMGF (USA), ANRS & IRD (France), Irish Aid (Ireland), Milano University Medical School (Italy), MRC, LSHTM & ImmunoClin (UK)
Trial Registration number(s):	Not applicable
Sub-studies:	Not applicable
Status:	Completed
Results and Outcomes	A report on the results and outcomes is expected in December 2011 when the final report is due.

1.4.3 TaMoVac

EDCTP Project Coordinator:	Muhammad Bakari
EDCTP Call Title:	Capacity building in preparation for the conduct of preventive HIV vaccine trials (EDCTP/BMGF/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:	27 March 2012
Feasibility of Neonatal Vaccination in Maputo	
Site Principal Investigator(s):	Paula Vaz, Hospital Central de Maputo, Maputo
Clinical Trial/Study Sponsor:	Not applicable
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
Secondary Objective(s):	-
Clinical Trial/Study site(s):	Maputo Central Hospital, Maputo, Mozambique Polana Caniço Health Centre, Maputo, Mozambique
Collaborating site(s):	-
Study design:	Mixed qualitative/quantitative
Number of subjects:	200
Product(s):	Not applicable
Manufacturer/Developer:	Not applicable
Cofunders:	Not applicable
Trial Registration number(s):	Not applicable
Sub-studies:	-
Status:	Ongoing
Results and Outcomes	None

1.4.4 CHIVTUM

EDCTP Project Coordinator:	Pontiano Kaleebu
EDCTP Call Title:	Capacity building in preparation for the conduct of preventive HIV vaccine trials (EDCTP/BMGF/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
Malawi epidemiological and social science study	
Site Principal Investigator(s):	Site Principal Investigator(s): Victor Mwapasa, College of Medicine, University of Malawi, Blantyre, Malawi
Clinical Trial/Study Sponsor:	Not applicable
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):	<ol style="list-style-type: none"> 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):	<ol style="list-style-type: none"> 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):	Malawi-Liverpool-Wellcome Trust Clinical Research Programme and WorldFish Center (Malawi)
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)
Study design:	<ol style="list-style-type: none"> 1. 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. 2. 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.
Number of subjects:	<p>1. Participatory and qualitative study: Study population: Adult men and women (over 20) and young women (under 20) from fishing communities of Namaso, Nkope, Malembo, Msaka, Mvunguti and Chirombo villages. N= 382;</p> <p>2. Prospective cohort: Study population: Men and women (15-49) as well as young people classified as "mature minors" (13-15) 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</p>
Product(s):	Not applicable
Manufacturer/Developer:	Not applicable
Cofunders:	BMGF (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)
Trial Registration number(s):	Not applicable
Sub-studies:	Not applicable
Status:	Ongoing
Results and Outcomes	In the social science study, 451 participants involved in the studies. Data analyzed and used as a basis for further indepth qualitative studies. For the epidemiological study, 740 recruits screened for HIV (taget: 743).
Uganda epidemiological, social science and virology study	
Site Principal Investigator(s):	Pontiano Kaleebu, Uganda Virus Research Institute, Entebbe, Uganda
Clinical Trial/Study Sponsor:	Not applicable
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):	<p>Main Cohort Study:</p> <ol style="list-style-type: none"> 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):	<p>Virology sub-study</p> <ol style="list-style-type: none"> 1. Characterise the circulating HIV-1 subtypes in order to better understand the molecular epidemiology in these populations <p>Social and Behavioural Context sub-study</p> <ol style="list-style-type: none"> 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):	UVRI (Uganda)
Collaborating site(s):	MRC/UVRI Uganda Research Unit on AIDS and UVRI-IAVI HIV Vaccine Program (Uganda)
Study design:	<p><i>The main cohort study</i> is a prospective, observational study, through which a demographic, medical history questionnaire will be administered and volunteers requested to provide blood samples at each visit.</p> <p><i>The virology sub-study</i> will have blood collected to be used to describe the molecular epidemiology of circulating viruses.</p> <p><i>The social and behavioural context sub-study</i> will utilise qualitative and quantitative methods, including mapping, semi-structured and in-depth interviews.</p>
Number of subjects:	Main cohort: Male and female volunteers (13-49), n= 1000; Virology sub-study: 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; Social and behavioural context: N= 50
Product(s):	Not applicable
Manufacturer/Developer:	Not applicable
Cofunders:	BMGF (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)
Trial Registration number(s):	Not applicable
Sub-studies:	<p>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.</p> <p>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 <i>Schistosoma mansoni</i> infection in stool (Kato Katz method) and using blood samples for <i>Mansonella perstans</i> (Knott's method) in 50 incident cases of HIV compared to 150 HIV-negative controls from the fisher folk main cohort. To compare prevalence of <i>S. mansoni</i> 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.</p>
Status:	Ongoing
Results and Outcomes	This study nearly complete with the targetted 1000 participants enrolled. High prevalence and high incidence of HIV amongst participants, with retention of approx. 85%. This indicates that this population has a lot of potential to host future large scale HIV prevention research. For the social science study, the work has been completed and the data is being

	analysed
Total number of subjects (clinical trials only):	
Total number of subjects (cohort/epidemiological/other studies):	N = 1000
PhD study-1	Andrew Obuku Akii Immunological interactions between helminths and HIV infection, Makerere University Supervisor: Pontiano Kaleebu, Pietro Pala and Guisseppe Pantaleo
MSc study-1	Aloysious Ssemaganda Monoclonal B-cell lymphocytosis in a rural Ugandan population, Makerere University Supervisor: Dr Noah Kiwanuka
MSc study-2	Paul Kato Kitandwe Hepatitis C Virus Genotypes and Confirmation of Antibody Reactive Serum Samples from East Africa using Reverse Transcriptase and Real Time PCR , Makerere University Supervisor: Fred Lyboga
Other/Sub-studies:	<p><i>Yellow Fever DNA Microarray Assay study</i> 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.</p> <p><i>Schistosomiasis sub study</i> (among those from main cohort) –pending approval of protocol</p> <p>To determine the odds of worm infections diagnosed using stool samples obtained on three consecutive days for intestinal <i>Schistosoma mansoni</i> infection in stool (Kato Katz method) and using blood samples for <i>Mansonella perstans</i> (Knott’s method) in 50 incident cases of HIV compared to 150 HIV-negative controls from the fisher folk main cohort. To compare prevalence of <i>S. mansoni</i> 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.</p> <p>Wellcome Trust funded sub- study: <i>"Addressing communication gaps and needs in HIV prevention research within Lake Victoria fishing communities in Uganda"</i> Main focus was to understand and address communication gaps on HIV prevention research within Lake Victoria fishing communities, specifically in the districts of Wakiso and Masaka.</p>
Key Publications:	Asiki G, Mpendo J, Abaasa A, Agaba C, Nanvubya A, Nielsen L, Seeley J, Kaleebu P , Grosskurth H and Kamali A. HIV and syphilis prevalence and associated risk factors among fishing communities of Lake Victoria, Uganda. Sex Transm Infect , 2011; 87:511-515

1.4.5 AfrEVacc

EDCTP Project Coordinator:	Jonathan Weber
EDCTP Call Title:	Capacity building in preparation for the conduct of preventive HIV vaccine trials (EDCTP/BMGF/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 March 2012
Beira Study	
Site Principal Investigator(s):	Josefo João Ferro and Arlinda Zango, Faculty of Medicine of Universidade Católica de Moçambique, Beira, Mozambique
Clinical Trial/Study Sponsor:	Not applicable
Trial/Study title:	Combined Cross-Sectional and Prospective 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):	<ol style="list-style-type: none"> 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):	<ol style="list-style-type: none"> 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, North Carolina, USA; AMC-CPCD, Amsterdam, The Netherlands
Study design:	<p>Combined cross-sectional survey and prospective cohort:</p> <ol style="list-style-type: none"> 1. Cross-sectional survey: HIV-positive individuals in survey 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-infected individuals were infected within six months of sample collection. 2. 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 sero-conversion. 3. 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.
Number of subjects:	<p>Cross-sectional survey: approximately 1000 women at risk of sexual acquisition of HIV infection;</p> <p>Prospective cohort: approximately 400 women who tested HIV-negative in the cross-sectional survey and who volunteer for follow-up;</p> <p>BED false recent calibration: Approximately 400 HIV-positive individuals (men and women) known to be HIV infected for 12+ months and who have not used ART.</p>

Product(s):	Not applicable
Manufacturer/Developer:	Not applicable
Cofunders:	US Agency for International Development (USAID)
Trial Registration number(s):	Not applicable
Sub-studies:	Not applicable
Status	Ongoing
Results and Outcomes	
Manhica Feasibility Studies (EVAS) (capacity building)	
Site Principal Investigator(s):	Khátia Munguambe, Centro de Investigaçã em Saúde da Manhica (CISM), Manhica, Mozambique; Denise Naniche, Centre de Recerca en Salut Internacional de Barcelona (CRESIB), Barcelona, Spain
Clinical Trial/Study Sponsor:	Not applicable
Trial/Study title:	A feasibility and acceptability study in preparation for phase I/II clinical trials of an HIV vaccine candidate in Manhica, Mozambique (EVAS)
Goal:	To contribute to capacity development and provide information needed for the conduction of HIV vaccine trials in Mozambique
Primary Objective(s):	<ol style="list-style-type: none"> To assess the feasibility and acceptability of future HIV vaccine trials in Manhica by determining: <ul style="list-style-type: none"> 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 drawing); Willingness to participate in future HIV vaccine trials; Potential barriers and motivators to participation of adults in vaccine interventions. To develop the Manhica site in specific procedures related to future HIV vaccine trials by assessing: <ul style="list-style-type: none"> 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
Secondary Objective(s):	-
Clinical Trial/Study site(s):	Centro de Investigaçao em Saúde da Manhica (CISM), Manhica district, Mozambique
Collaborating site(s):	National Health Laboratory Services, Johannesburg, South Africa
Study design:	<p>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.</p> <p>The study population comprises mostly of subsistence farmers and employees of the sugar estates from Maragra and Xinavane. Manhica is a source of migrant labour to South Africa, which contributes to highly mobile population. A significant number of people, mainly women, are engaged in vending activities in markets and on the streets.</p>
Number of subjects:	N = of 70 participants (50 men and 20 women)
Product(s):	Not applicable
Manufacturer/Developer:	Not applicable
Cofunders:	Fondo de Investigaciones Sanitarias (FIS) – Instituto de Salud Carlos III, Madrid, Spain
Trial Registration number(s):	Not applicable
Sub-studies:	Not applicable
Status:	Ongoing
Results and Outcomes	
Manhica Epidemiology Study (capacity building)	
Site Principal Investigator(s):	Khátia Munguambe, Centro de Investigaçã em Saúde da Manhica (CISM), Manhica, Mozambique Denise Naniche, Centre de Recerca en Salut Internacional de Barcelona (CRESIB), Barcelona, Spain

Clinical Trial/Study Sponsor:	Not applicable
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):	<ol style="list-style-type: none"> 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
Secondary Objective(s):	
Clinical Trial/Study site(s):	Centro de Investigaçao em Saúde da Manhiça (CISM), Manhiça district, Mozambique
Collaborating site(s):	-
Study design:	<p>In order to accomplish the objective of HIV incidence determination, 2 cross sectional studies will be conducted with an interval of 2 years between cross sectional studies. The HIV incidence will be estimated from both prevalence measures. The prevalence of selected STI will be determined by a single cross sectional study.</p> <p>The first cross-sectional study to determine age-specific HIV prevalence in the Manhiça region. Second cross sectional study to determine age-specific HIV incidence and prevalence of <u>selected STIs</u> in Manhiça community.</p>
Number of subjects:	<p>First cross sectional study: Adults (men and women), 18-47, part of the Manhiça DSS area, 232 subjects per age group (18-27; 28-37 and 38-47), N= 696;</p> <p>Second cross sectional study: Adults (men and women), 18-47, part of the Manhiça DSS area, 232 subjects per age group (18-27; 28-37 and 38-47), N= 696.</p>
Product(s):	Not applicable
Manufacturer/Developer:	Not applicable
Cofunders:	Fondo de Investigaciones Sanitarias (FIS) – Instituto de Salud Carlos III, Madrid, Spain
Trial Registration number(s):	Not applicable
Sub-studies:	Not applicable
Status:	Ongoing
Results and Outcomes	
Africa Centre Impilo Yamadoda - Men's Health Study (capacity building)	
Site Principal Investigator(s):	John Imrie, Centre for Sexual Health & HIV Research, University College London, London, UK
Clinical Trial/Study Sponsor:	Not applicable
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 <i>AfrEVacc Network Partners</i> 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):	<ol style="list-style-type: none"> 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

	<p>engagement with the Africa Centre and its programme of behavioural and biomedical HIV prevention research;</p> <ol style="list-style-type: none"> 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 <i>AfrEVacc Network Partners</i> 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.
Secondary Objective(s):	-
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
Collaborating site(s):	-
Study design:	<p>Adult men (18-29 years) 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.</p> <p>The men's health fairs will follow a format similar to the Africa Centre's regular roadshows. 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).</p> <p>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.</p>
Number of subjects:	N = 200 men aged 18 -29 years from the community settings in the Hlabisa Health sub-district.
Product(s):	Not applicable
Manufacturer/Developer:	Not applicable
Cofunders:	-
Trial Registration number(s):	Not applicable
Sub-studies:	-
Status:	Ongoing
Results and Outcomes	
Johannesburg study (capacity building)	
Site Principal Investigator(s):	Sinead Delaney-Moretlwe, Reproductive Health and HIV Research Unit (RHRU), University of the Witwatersrand, Johannesburg, South Africa
Clinical Trial/Study Sponsor:	Not applicable
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):	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

	<ol style="list-style-type: none"> 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
Collaborating site(s):	-
Study design:	A prospective, randomised pilot study of vaccination with a surrogate vaccine (hepatitis B vaccine ENGERIX-B or equivalent generic) compared to no vaccination among healthy HIV sero-negative male (over 18) volunteers.
Number of subjects:	N = 150
Product(s):	Heberbiovac HB
Manufacturer/Developer:	GSK Biologicals, Middlesex, UK
Cofunders:	Not applicable
Trial Registration number(s):	Not applicable
Sub-studies:	Not applicable
Status:	Ongoing
Results and Outcomes	
Total number of subjects (clinical trials only):	-
Total number of subjects (cohort/epidemiological/other studies):	N = 3036
PhD study-1	Sebastian Fuller, PhD candidate at University College London Centre for Sexual Health & HIV Research. Supervisors: Prof's Graham Hart & John Imrie.
PhD study-2	-
MSc study-1	Gerald Feldmann – MSc Daa Networks & Security, Birmingham City University, Jan 2009 for 20 months.
MSc study-2	-
Other/Sub-studies:	-
Key Publications:	None

1.5 HIV/AIDS vaccines clinical trials

Table 1-5: Summary table of HIV/AIDS vaccines clinical trials supported by EDCTP

Project Acronym (Coordinator)	Phase of trial	Product(s)	Insert	Virus subtype	Manufacturer / Developer	Study population	Status
TaMoVac I: HIVIS03 continuation	I/II	Plasmid DNA + MVA-CMDR	Env, Rev, Gag, RTmut + Gag, Pol, Gp160	Clade A, B, C + Clade A, E	Vecura	Healthy adults (Police Officers) N = 60	Completed
TaMoVac I Phase I/II Tanzania + AfrEVacc	I/II	Plasmid DNA + MVA-CMDR	Plasmid: Env, Rev, Gag, RTmut + MVA-CMDR: Gag, Pol, Gp150 + MVA-CMDR: rgp140/GLA-AF	Clade A, B, C + Clade A, E + Clade C	Vecura and Imperial College	Healthy adults (Police Officers) N = 120	Ongoing
TaMoVac I Phase I trial in Maputo with youths	I	Plasmid DNA + MVA-CMDR	Env, Rev, Gag, RTmut + Gag, Pol, Gp160	Clade A, B, C + Clade A, E	Vecura at KI, Sweden (DNA) WRAIR of USA (MVA-CMDR)	Youths, N = 24	Protocol approved
TaMoVac II	II	DNA + MVA-CMDR	Env + gp160 (subtype E, CM235), gag and pol (integrase-deleted and reverse transcriptase non-functional, subtype A, CM240).	Clade A, B, C + Clade A	Vecura/ WRAIR	Healthy young adults (Police and Prison officers and high-risk workers) N=1400	Not yet recruiting
PedVacc (PV001)	I	MVA-HIVA	HIVA (Gag+CD8 ⁺ T cell polyepitope)	Clade A	IDT, Germany / University of Oxford, UK	Healthy infants born to HIV-1/2-negative mothers, n= 48	Ongoing
PedVacc (PV002)	I/II	MVA-HIVA	HIVA (Gag+CD8 ⁺ T cell polyepitope)	Clade A	IDT, Germany / University of Oxford, UK	Healthy infants born to HIV-1-positive mothers, n= 72	Ongoing

1.5.1 PedVacc

EDCTP Project Coordinator:	Tomas Hanke
EDCTP Call Title:	Capacity building in preparation for the conduct of preventive HIV vaccine trials (EDCTP/BMGF/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:	6 April 2012
PV001 Gambian trial	
Site Principal Investigator(s):	Katie Flanagan, MRC Laboratories, Banjul, 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):	To evaluate the safety and immunogenicity of MVA-HIVA vaccine in 20-week old healthy Gambian infants born to HIV-1 and HIV-2-uninfected mothers
Secondary Objective(s):	1. To determine the gross impact of MVA-HIVA on the immunogenicity of expanded programme of immunization (EPI) vaccines 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:	Open, randomised, controlled, unblinded phase I 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:	BMGF (USA), SIDA and Karolinska Institut (Sweden), ISC II (Spain), MRC (UK)
Trial Registration number(s):	NCT00982579 http://www.clinicaltrials.gov/ct2/show/NCT00982579?term=NCT00982579&rank=1 ATMR2008120000904116 http://www.pactr.org/ATMWeb/appmanager/atm/atmregistry?_nfpb=true&_windowLabel=basicSearch_1_2&basicSearch_1_2_actionOverride=%2Fpageflows%2Ftrial%2FbasicSearch%2FviewTrail&basicSearch_1_2id=90
Status	Ongoing, recruitment and procedures completed
Results and Outcomes	Recruitment: First patient in: 30 March 2010 Last patient in: 28 June 2010 Final follow-up: 11 October 2010 All 48 infants have been followed up, no SAEs reported. Immunogenicity studies ongoing.
PV002 Kenyan trial	
Site Principal Investigator(s):	Walter Jaoko, University of Nairobi, 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 HIV1-infected mothers
Goal:	To establish safety and immunogenicity of candidate HIV-1 vaccine MVA.HIVA

Primary Objective(s):	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):	Comparison of HIV-1-specific T cell responses between MVA.HIVA-vaccinated and age-matched unvaccinated infants 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 Comparison of immune activation and phenotypic profile of lymphocytes between MVA.HIVA-vaccinated and age-matched unvaccinated infants 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 & MRC, UK; University of Nairobi & 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:	BMGF (USA), SIDA and Karolinska Institut (Sweden), ISC II (Spain), MRC (UK)
Trial Registration number(s):	NCT00981695 http://www.clinicaltrials.gov/ct2/show/NCT00981695?term=NCT00981695&rank=1 PACTR2009010001152787 http://www.pactr.org/ATMWeb/appmanager/atm/atmregistry?_nfpb=true&_windowLabel=basicSearch_1_2&basicSearch_1_2_actionOverride=%2Fpageflows%2Ftrial%2FbasicSearch%2FviewTrail&basicSearch_1_2id=115
Status:	Ongoing (fully recruited, procedures on going)
Results and Outcomes	In total, 73 infants were recruited and follow-up is ongoing. A press release was released through EDCTP and MRC regarding the study: http://www.edctp.org/Announcement.403+M52d7bfcef0b.0.html http://www.mrc.ac.uk/Newspublications/News/MRC007581
PV001+PV002	
Total number of subjects (clinical trials only):	N = 120
Press releases	http://www.edctp.org/Announcement.403+M52d7bfcef0b.0.html http://www.mrc.ac.uk/Newspublications/News/MRC007581
PhD Study	Jorjoh Ndure Regulatory T cells and vaccines: correlation or coincidence?, MRC Gambia Supervisor: Katie Flanagan
MSc Study	Christine Gichuhi MSc in Epidemiology, LSHTM (distance learning) Supervisor: Walter Jaoko
MSc Study	Fatoumatta Darboe The BCG transcriptome signature and relationship with host immune responses, MRC Gambia Supervisor: Katie Flanagan
MSc Study	Dorcas Murei Anxiety and depression in HIV positive mothers whose infants are completing HIV vaccine studies, University of Nairobi Supervisor: Walter Jaoko
MSc Study	Amos Thairu A software system for advanced flow cytometry data analysis, KAVI/KI Supervisor: Marie Reilly
MSc Study	Moses Muriuki Mundia Immune Responses in HIV/Schistoma Mansonii Coinfection and

	Associations to Disease Progression, KAVI/University of Hertfordshire Supervisor: TBA
Other/Sub-studies:	Preparation of GLP grade BCG.HIVA ²²² vaccine for GMP production.
Key Publications:	None

1.5.2 TaMoVac I

EDCTP Project Coordinator:	Muhammad Bakari
EDCTP Call Title:	Capacity building in preparation for the conduct of preventive HIV vaccine trials (EDCTP/BMGF/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:	27 March 2012
HIVIS 03 continuation	
Site Principal Investigator(s):	Fred Mhalu, Muhimbili University College of Health & Allied Sciences, Dar es Salaam, 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:	Randomised, controlled, double-blinded phase I/II 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 at KI in Sweden (DNA); and WRAIR in USA (MVA-CMDR)
Cofunders:	BMGF and Walter Reed Army Institute of Research (WRAIR), BMBF and LMU Munchen (Germany), NACCAP (Netherlands), EU, SIDA and Embassy of Sweden (Sweden), MRC UK and Imperial College (UK)
Trial Registration number(s):	ISRCTN90053831 http://www.controlled-trials.com/ISRCTN90053831/ISRCTN90053831 ATMR2009040001075080 http://www.pactr.org/ATMWeb/appmanager/atm/atmregistry?_nfpb=true&_windowLabel=basicSearch_1_2&basicSearch_1_2_actionOverride=%2Fpageflows%2Ftrial%2FbasicSearch%2FviewTrail&basicSearch_1_2id=107
Sub-studies:	Not applicable
Status:	Completed First patient in: Feb 2009 Last patient out: July 2010 42 volunteers out of 60 received the 2 nd MVA boost. The vaccine was deemed safe, and a total of 11 SAE unrelated to vaccination have been observed. Study closure visit done June 24 2010.
Phase I/II Tanzania combined project with Weber's AfrEVacc (CT.2006.33111.001)	
Site Principal Investigator(s):	Muhammad Bakari, University College of Health & Allied Sciences (MUHAS), Dar es Salaam, Tanzania; Leonard Maboko, NIMR-Mbeya Medical Research Programme (NIMR-MMRP), Mbeya, Tanzania
Clinical Trial/Study Sponsor:	Swedish Institute for Communicable Disease Control & MUHAS

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):	<ol style="list-style-type: none"> 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):	<ol style="list-style-type: none"> 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):	National Institute for Medical Research (NIMR), Tanzania; Swedish Institute for Infectious Disease Control (Sweden), WRAIR (USA), University of Munich (Germany), Imperial College (UK),
Study design:	Randomised, controlled, double-blinded phase I/II trial
Number of subjects:	Healthy adults (Police Officers, no less than 30 females), N = 120
Product(s):	<p>Priming</p> <p>Pool 1: env (HIV-1 subtype A, B, C) and rev (HIV-1 subtype B)</p> <p>Pool 2: gag (HIV-1 subtype A, B) and RTmut (HIV-1, subtype B)</p> <p>Boosting:</p> <p>Modified Vaccinia Ankara vaccine (MVA-CMDR) expressing HIV-1 genes – gp150 (subtype E, CM235) and gag and pol (subtype A, CM240)</p> <p>Further boosting (amended protocol):</p> <p>Recombinant C clade trimeric envelope protein (rgp140) derived from the Chinese isolate CN54 mixed with glucopyranosyl lipid A (GLA)</p>
Manufacturer/Developer:	DNA: Vecura (Sweden) MVA-CMDR: WRAIR (USA) rgp140/GLA: Imperial College (London, UK)
Cofunders:	BMGF and WRAIR (USA); BMBF and LMU Munchen (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):	<p>PACTR2010050002122368</p> <p>http://www.pactr.org/ATMWeb/appmanager/atm/atmregistry?_nfpb=true&_windowLabel=basicSearch_1_2&basicSearch_1_2_actionOverride=%2Fpageflows%2Ftrial%2FbasicSearch%2FviewTrail&basicSearch_1_2id=212</p>
Sub-studies:	Not applicable
Status:	Ongoing
Results and Outcomes	<p>Dar es Salaam:</p> <p>1) DNA/MVA schedule</p> <p>First patient in: May 2010</p> <p>As of 6 October 2010:</p> <p>134 screened</p> <p>30 (8 females) enrolled</p> <p>No SAE encountered</p> <p>Last patient out: expected Q4 2010</p> <p>Rgp140/GLA</p> <p>First patient in: expected Q3 2011</p> <p>Last patient out: expected Q4 2011</p> <p>Mbeya:</p>

	<p>DNA/MVA schedule First patient in: May 2010 As of 6 October 2010: 251 screened 57 (24 females) enrolled, 4 will be replaced due to withdrawal of consent, pregnancy, enrolment/eligibility error. No SAE encountered Last patient out: expected in Q4, 2010</p> <p>Rgp140/GLA First patient in: expected Q3, 2011 Last patient out: expected Q4 2011</p>
Phase I HIV Vaccine Trial in youths	
Site Principal Investigator(s):	Ilesh Vinodrai Jani, Instituto Nacional de Saúde, Maputo, Mozambique Nafissa Bique Osman, Hospital Central de Maputo, Maputo, Mozambique
Clinical Trial/Study Sponsor:	Swedish Institute for Communicable Disease Control (SMI)
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):	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. 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):	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)
Collaborating site(s):	Instituto Nacional de Saúde (INS), Maputo, Mozambique The Swedish Institute for Communicable Disease Control, Stockholm, Sweden U.S. Military HIV Research Program-Walter Reed Army Institute of Research (MHRP-WRAIR), USA Imperial College (IC), London, UK
Study design:	A randomized, double blinded, placebo-controlled Phase I HIV Vaccine Trial among Youths
Number of subjects:	A Phase I/II HIV Vaccine Trial will be performed on 24 consenting youths
Product(s):	<p>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)</p> <p>Boosting: Modified Vaccinia Ankara vaccine (MVA-CMDR) expressing HIV-1 genes – gp150 (subtype E, CM235) and gag and pol (subtype A, CM240)</p>
Manufacturer/Developer:	DNA: Vecura (Sweden) MVA-CMDR: WRAIR (USA)
Cofunders:	Sida-Lusaka Office
Trial Registration number(s):	Still to be completed
Status:	Ongoing
Results and Outcomes	Pending
Total number of subjects (clinical trials only):	204
PhD study-1	Evaluation of HIV testing strategies and Monitoring of Immune Responses in HIV vaccinated individuals in Tanzania, by Said Aboud

PhD study-2	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 by Patricia Munseri
PhD study-3	What motivates participation in HIV vaccine trials: A study among Police Officers in Dar es Salaam, Tanzania by Edith Tarimo
Other/Sub-studies: MSc study-1	<p><i>In Maputo, Mozambique:</i></p> <p><i>Sub-study of HBV (Hepatitis B) frequency:</i> HBV and HPV testing will be performed for both HIV negative and positive volunteers</p> <p><i>Sub-study of Immune response patterns against HIV antigens and control antigens:</i> 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.</p> <p><i>The establishment of reference values:</i> The establishment of reference values for haematological, biochemistry, and immunological parameters</p> <p><i>Strengthening of group for education on prevention:</i> This component aims to improve the functioning and train the existing group in education for prevention.</p>
Key Publications:Other/Sub-studies:	<ol style="list-style-type: none"> 1. Said About, Charlotta Nilsson, Katarina Karlen, Mary Marovich, Britta Wahren, Eric Sandström, Hans Gaines, Gunnel Biberfeld and Karina Godoy-Ramirez. Genes Virus Ankara Expressing HIV-1 Recombinant Modified Vaccinia Vaccine and Boosted with Immunized with an HIV-1 DNA Responses in Healthy Individuals T-Lymphocyte Proliferative. Clinical and Vaccine Immunology, July 2010;17(7):1124–1131. 2. Patricia J. Munseri, Muhammad Bakari, Kisali Pallangyo & Eric Sandstrom. Tuberculosis in HIV voluntary counselling and testing centres in Dar es Salaam, Tanzania. Scandinavian Journal of Infectious Diseases, 30 June 2010; Early Online, 1-8. 3. Tarimo EA, Thorson A, Kohi TW, Bakari M, Sandström E, Mhalu and Kulane A. A qualitative evaluation of volunteers’ experiences in a phase I/II HIV vaccine trial in Tanzania. BMC Infectious Diseases 2011 11: 283 4. Tarimo EA, Thorson A, Kohi TW, Mwami J, Bakari M, Sandström E, Kulane A. Balancing collective responsibility, individual opportunities and risks: a qualitative study on how police officers reason around volunteering in an HIV vaccine trial in Dar es Salaam, Tanzania. BMC Public Health. 2010 May 28;10:292. 5. Edith Tarimo, Anna Thorson, Muhammad Bakari, Abunuwasi Mwami, Eric Sandström, Asli Kulane. Willingness to volunteer in a Phase I/II HIV vaccine trial and associated factors: A study among police officers in Dar es Salaam, Tanzania. Global Health Action 2009. DOI: 10.3402/gha.v2i0.1953 6. Tarimo EA, Thorson A, Kohi TW, Bakari M, Mhalu F, Kulane A. Reasons for Declining to Enroll in a in a Phase I and II HIV Vaccine Trial after Randomization among Eligible Volunteers in Dar es Salaam, Tanzania. PLoS ONE. 2011 Feb 16; 6(2):e 14619.

1.5.3 AfrEVacc

EDCTP Project Coordinator:	Jonathan Weber
EDCTP Call Title:	Capacity building in preparation for the conduct of preventive HIV vaccine trials (EDCTP/BMGF/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 March 2012
Phase I/II Tanzania combined project with Bakari (CT.2006.33111.007). See under TaMoVac I for more information	

1.5.4 TaMoVac II

EDCTP Project Coordinator:	Eligius Lyamuya
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:	1st July 2009
EDCTP Project End Date:	30 June 2014
Site Principal Investigator(s):	Leonard Maboko (NIMR) Muhammad Bakari (MUHAS) Ileshi Jani (INS)
Clinical Trial/Study Sponsor:	Muhimbili University College of Health & Allied Sciences (MUHAS)/Swedish Institute of Infectious Disease Control (SMI)
Trial/Study title:	HIV vaccine trial capacity building in Tanzania and Mozambique by continued exploration of optimal DNA and MVA boosting strategies; TaMoVac II
Goal:	To increase the immunogenicity of DNA plasmid HIV vaccines and to continue EU, EDCTP and Sida/SAREC investments in a DNA prime/ MVA boost HIV vaccine concept in Dar es Salaam, Mbeya and Maputo, in addition to preparations for a comparison with the AfrEVac immunogens
Primary Objective(s):	1) To evaluate if electroporation (or VaxFectin) can augment cellular immune responses and humoral responses to HIV-1 containing plasmid DNA priming
Secondary Objective(s):	1) Further document the immunogenicity and safety of the HIVIS DNA/MVA immunogens 2) Introduce novel delivery technologies of the HIVIS DNA vaccine to induce long-term memory and antibody production in phase I/II trials. 3) Sustain the youth and adult cohorts in Tanzania and Mozambique from which volunteers will be recruited into phase IIa trials for safety and immunogenicity testing 4) Prepare for comparisons between the HIVIS and EuroVacc HIV vaccines by intensive technology sharing 5) Take the first steps to allow integration of parallel DNA prime/pox boost HIV vaccine efforts supported by EDCTP
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 randomized, controlled, double blinded study
Number of subjects:	1400
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 Munchen (Germany), Federal Ministry of Education and Research (Germany)
Trial Registration number(s):	Not yet obtained

Sub-studies:	Baseline Epidemiological Study: Epidemiological and Social-Behavioural Studies Among the 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; and, to study how services can best be tailored so that the risk of transmission of HIV/STIs and unwanted pregnancies is reduced.
Status:	Ongoing
Results and Outcomes:	Not available yet
Total number of subjects (clinical trials only):	Recruitment has not yet started for the clinical trial. Target is 1400
Total number of subjects (cohort/epidemiological/other studies):	N/A
PhD study-1	Dr. Agricola Joachim (MUHAS, Dr. Theodora Mbunda (MUHAS and Dr. Eulalia Macovela (INS) are processing their PhD registration at Karolinska Institute, Sweden. They have, however, started some training related to their PhD studies
MSc study-1	MSc student Erica Sanga of NIMR-MMRP site in the process of developing thesis objectives
Other/Sub-studies:	Enrolment for the Baseline Epidemiological Survey has not started
Key Publications:	None

2 Tuberculosis

2.1 Tuberculosis treatment clinical trials

Table 2-1: Summary table of tuberculosis treatment clinical trials supported by EDCTP

Project Acronym (Coordinator)	Phase of trial	Product(s)	Manufacturer / Developer	Study population	Status
TB SurMark (vanHelden)	Not applicable	Not applicable (Surrogate biomarkers)	Not applicable	Adults Stored samples and cultured isolates N=313	Completed
HIV-TB Pharmagene (Bertilsson)	IV	Efavirenz Rifampicin 3TC D4T	GlaxoSmith Kline	Adults HIV only and HIV/TB adults N= 430	Ongoing
PPK.DDK (Merry)	IV	Efavirenz Nevirapine Lopinavir Ritonavir Rifampicin	DuPont Pharmaceuticals, Tubingen, Boehringer Ingelheim	Adult and Paediatric patients with HIV/TB coinfection N=178	Ongoing
RIFAQUIN (Jindani)	II, III	Ethambutol Isoniazid Moxifloxacin Pyrazinamide Rifampicin Rifapentine	Sanofi-Aventis Bayer	Adults 18 years of age and HIV CD4 count above 150/mm ³ N=1100	Ongoing
REMox I (Gillespie)	III	Moxifloxacin Rifampicin Isoniazid Pyrazinamide Rifampicin Ethambutol	Bayer Tubingen	Adults N=900	Recruitment Completed

PanACEA-ReMox II (Gillespie)	III	Moxifloxacin	Bayer Sanofi Aventis	Adults N=1000 Total Remox I+II=1900	Recruitment Completed
PanACEA-HIGHRIF (Boeree)	II	Rifampicin Moxifloxacin Isoniazid Pyrazinamide Ethambutol	Svizera Sanofi-Aventis	Adults Study 1: max. 68 patients Study 2: 150 patients Study 3: TBD Study 4: TBD	Ongoing
PanACEA SQ-109 (Hoelscher)	II,IIA, IIIB	novel TB drug (SQ109)	Sequella Inc.	Adults N=420	Ongoing

2.1.1 TB SurMark

EDCTP Project Coordinator:	Paul van Helden
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 Code 2004.01.T.d1).
EDCTP Project Title:	Surrogate markers to predict the outcome of antituberculosis therapy
EDCTP Project Code:	CT.2004.32040.001
EDCTP Project Start Date:	19 September 2005
EDCTP Project End Date:	30 June 2009
Trial 1	
Site Principal Investigator(s):	Paul van Helden
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 eventually 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 samples stored 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.
Secondary Objective(s):	N/A
Clinical Trial/Study site(s):	Stellenbosch University
Collaborating site(s):	Stellenbosch University; London School of Hygiene and Tropical Medicine (LSHTM); GlaxoSmithKline; University of Pretoria
Study design:	Prospective study to validate biomarkers
Number of subjects:	313
Product(s):	N/A
Manufacturer/Developer:	N/A
Cofunders:	Medical Research Council South Africa (MRC); Stellenbosch University; NRF Centre of Excellence for Biomedical TB Research
Trial registration number(s):	N/A
Sub studies:	N/A
Status:	Completed
Results and Outcomes:	The main findings are that 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 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 4 weeks of treatment, when compared to patients who would remain disease-free. Around 2000 genes were consistently differentially expressed between relapse and cured patients.

2.1.3 HIV-TB Pharmagene

EDCTP Project Coordinator:	Leif Bertilsson
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 January 2012
Trial 1	
Site Principal Investigator(s):	Getachew Aderaye Addis Ababa University, Ethiopia Ferdinand Mugusi, University of Dar es salaam, Tanzania. Eleni Aklillu, Karolinska Institutet, Stockholm, Sweden
Clinical Trial/Study Sponsor:	Karolinska Institutet
Trial/Study title:	<u>Trial 1</u> Population pharmacokinetics, pharmacogenetics, safety/efficacy of efavirenz (EFV) based HAART, defined as stavudine (d4T) + lamivudine (3TC) + efavirenz, with and with out RIF in Ethiopians and Tanzanians. <u>Trial 2</u> Influence of RIF on detailed plasma and intracellular pharmacokinetics of EFV.
Goal:	<u>Trial 1</u> To investigate 1) 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 2) 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. <u>Trial 2</u> 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):	The main objective is to identify optimal dose of EFV to be used with RIF in patients receiving TB treatment among Africans. Specific objectives are: 1. To identify 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 extent of RIF interaction on detailed EFV pharmacokinetics and treatment outcome. 4. To investigate pharmacogenetics of CYP3A and CYP2B6 and it's 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 educate African clinicians and researchers at Ph.D./MSc 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 network based 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 Institutet, Sweden

	University of Heidelberg, Germany
Study design:	<u>Trial 1</u> Treatment, non-randomised, openlabel, active control, parallel assignment, PK and safety/efficacy, pharmacogenetic study. <u>Trial 2</u> Randomised PK study
Number of subjects:	
Product(s):	Efavirenz, Rifampicin (RIF), d4T, 3TC
Manufacturer/Developer:	GlaxoSmithKline (lamivudine) Bristol Myers Squibb (stavudine) DuPont Pharmaceuticals (efavirenz) Tubingen (rifampicin)
Cofunders:	University of Heidelberg Karolinska Institutet Stockholm County Council
Trial Registration Number(s):	ATMR2009040001261177
Sub studies:	N/A
Status:	Ongoing
Results and Outcomes:	
PhD study-1	(Optimization of HIV/TB co treatment in Ethiopian Patients: Pharmacokinetic and pharmacogenetic aspects of drug interaction between Rifampicin and Efavirenz) (Name of candidate: Abiy Habtewold Eyakem)
PhD study-2	(Study title: <i>Optimization of TB/HIV co-treatment in Ethiopian patients</i>) (Name of candidate: Wondwossen Amogne)
PhD study-3	(Study 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) (Name of candidate: Eliford Ngaimisi)
PhD study-4	(Treatment outcome, Safety and Efficacy in Concomitant use of Efavirenz and Rifampicin in HIV and Tuberculosis patients) (Name of candidate: Sabina Mugusi)
Other/Sub-studies:	Nil
Key Publications:	See list at end of document

2.1.4 PPK.DDK - HIV and TB medications

EDCTP Project Coordinator:	Concepta Merry
EDCTP Call Title:	Phase II-III trials of drug regimens that shorten or simplify current treatment option. 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 coinfecting patients
EDCTP Project Code:	CT.2004.32011.003
EDCTP Project Start Date:	30 June 2006
EDCTP Project End Date:	6 July 2010
Trial 1	
Site Principal Investigator(s):	Concepta Merry
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, in adequately powered studies, 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):	<p>Adult study: To compare PK of EFV, NVP, LPV and RTV in adult HIV-infected 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.</p> <p>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.</p> <p>Paediatric study: 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.</p>
Secondary Objective(s):	<p>Adult study: To develop the University of Cape Town as a regional reference center for the conduct of clinical PK of HIV studies and the determination of ARV drug assays by building human laboratory capacity</p> <p>To develop efficient methods appropriate to a resource constrained setting for estimation of EFV, NVP, LPV, and RTV concentrations.</p> <p>To determine the impact of covariate patient and drug factors on the PK of EFV, NPV, LPV, rifampicin and isoniazid</p> <p>Paediatric study: 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)</p> <p>To determine the impact of covariate patient and drug factors on the pre-dose levels of EFV, NVP, LPV and RTV</p>
Clinical Trial/Study site(s):	<p><u>South Africa</u> Grotte Schuur Hospital – University of Cape Town Red Cross Hospital – University of Cape Town Tygerberg Hospital – Cape Town PK-Laboratory Division of Pharmacology – University of Cape Town</p>

Collaborating site(s):	University of Liverpool; Radboud University Nijmegen; South African Clinical Research Organisation (SACRA); University Teaching Hospital Zambia; Makerere University; University of Cape Town; Trinity College – Ireland; University Teaching Hospital Zambia; University of KwaZulu-Natal
Study design:	Non – Randomised, openlabel study
Number of subjects:	178
Product(s):	efavirenz (EFV), nevirapine (NVP), lopinavir (LPV), ritonavir (RTV), rifampicin
Manufacturer/Developer:	DuPont Pharmaceuticals, Tubingen, Boehringer Ingelheim
Cofunders:	N/A
Trial registration number(s):	PPK.DDK – ATM 2008060000852767
Sub studies:	N/A
Status:	Completed
Results and Outcomes:	<p>The final key findings of this grant 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 coinfecting adults.</p> <p>The project has generated valuable data on the management of HIV/TB coinfecting patients, built capacity both institutionally and for individuals in clinical pharmacokinetics and forged new collaborations north-south.</p> <p>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.</p>

2.1.5 Rifaquin

EDCTP Project Coordinator:	Jindani, Amina
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
Trial 1	
Site Principal Investigator(s):	Amina Jindani
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 simplifying treatment administration
Primary Objective(s):	(1) To evaluate the effect of an increase in rifapentine dose size in reducing or eliminating the risk of rifampicin mono resistance (RMR) in relapse cultures in HIV positive patients (2) To evaluate the effect of an increase in Rpe 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.
Secondary Objective(s):	N/A
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 &Molecular Medicine (South Africa);
Study design:	Randomised, open label study
Number of subjects:	1100
Product(s):	Ethambutol; Isoniazid; Moxifloxacin; pyrazinamide; Rifampicin (RIF); Rifapentine
Manufacturer/Developer:	Bayer Sanofi-Aventis
Cofunders:	
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.
Status:	Ongoing
Trial Registration number(s):	Results not published yet
Results and Outcomes:	ISRCTN 44153044 & ATMR2008060000861040

2.1.6 Remox I

EDCTP Project Coordinator:	Stephen Gillespie
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
EDCTP Project Code:	CT.2004.32011.001
EDCTP Project Start Date:	21 October 2005
EDCTP Project End Date:	31 December 2011
Trial 1	
Site Principal Investigator(s):	Stephen Gillespie, St Andrews University, UK. Andrew Nunn, Medical Research Council Clinical Trials Unit (MRC CTU), London, UK. Timothy McHugh, Centre for Clinical Microbiology, University College London, London, UK. Sarah Meredith, Medical Research Council Clinical Trials Unit (MRC CTU) London, UK. Ali Zumla, Centre for Clinical Microbiology, University College London London, UK.
Clinical Trial/Study Sponsor:	University College London (UCL) UK
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'oto National Tuberculosis Hospital (Tanzania) Tumaini University (Tanzania) University Teaching Hospital, Lusaka (Zambia) SAMRC Tuberculosis Programme, Durban (South Africa)
Collaborating site(s):	University College London, U.K. Medical Research Council U.K. University of Zambia (Zambia) Kilimanjaro Christian Medical Centre (KCMC) (Tanzania) Triclinium Clinical Research (South Africa) Medical Research Council South Africa (MRC) Pharmanet Development Group (United States)
Study design:	Randomised controlled trial 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:	900
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
Sub studies:	nil
Status:	The project is ongoing, recruitment of a combined total between the ReMox I and ReMox II projects reached the amended target of 1904 in January of 2012. A press release from EDCTP was released to highlight this milestone
Results and Outcomes:	Trial is ongoing, as of June 2011 approximately 1400 subjects of the combined ReMox I and ReMox II studies have been enrolled (target total is 1900)

2.1.7 PanACEA-Remox II

EDCTP Project Coordinator:	Gillespie
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
EDCTP Project Code:	IP.2007.32011.011
EDCTP Project Start Date:	29 September 2009
EDCTP Project End Date:	28 September 2013
Trial 1	
Site Principal Investigator(s):	Stephen Gillespie, St Andrews University , UK. Andrew Nunn, Medical Research Council Clinical Trials Unit (MRC CTU), London, UK. Timothy McHugh, Centre for Clinical Microbiology, University College London, London, UK. Sarah Meredith, Medical Research Council Clinical Trials Unit (MRC CTU) London, UK. Ali Zumla, Centre for Clinical Microbiology, University College London, London, UK.
Clinical Trial/Study Sponsor:	University College London (UCL) UK
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):	To evaluate the efficacy, safety, and acceptability of two moxifloxacin-containing regimens To determine whether substitution for ethambutol or isoniazid makes it possible to reduce the duration of chemotherapy To present the data to international regulatory agencies to permit the regimens to be implemented internationally in resource-poor settings.
Secondary Objective(s):	To assess determinants of the pharmacokinetics of the TB drugs used in Regimen 1, Regimen 2, and Regimen 3 of the REMoxTB study 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):	1. University Teaching Hospital Clinics in Lusaka, Zambia 2. SAMRC supported clinics in Durban Kwa-Zulu Natal South Africa 3. The Lung Institute Clinics in Cape Town, South Africa 4. Kibon'oto National Tuberculosis Hospital, Tanzania 5. Tiervlei Centre in Tygerberg, South Africa. 6. Clinics supported by KEMRI in Kibera, Nairobi, Kenya
Collaborating site(s):	Kenya Medical Research Institute (KEMRI); University of Cape Town Lung Institute; Stellenbosch University; University College London; Medical Research Council UK; University of Zambia; Medical Research Council South Africa (MRC); Kilimanjaro Christian Medical Centre (KCMC);
Study design:	A randomised placebo-controlled double blind trial involving (1) 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) (2) 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, Bill & Melinda Gates Foundation (BMGF), Netherlands Organisation for Scientific Research (NWO),

Trial registration number(s):	NCT00864383
Sub studies:	<p>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.</p> <p>Pharmacokinetic (PK) study: A pharmacokinetic study of this potential interaction between rifampicin and moxifloxacin in the context of patients with tuberculosis.</p>
Status:	Recruitment of the ReMox study was completed in January of 2012. In support of this milestone being reached EDCTP in collaboration with The Global TB alliance launched a series of two press releases. The study has now moved into the 18 month follow up phase.
Results and Outcomes:	Not yet available

2.1.8 PanACEA-HIGHRIF

EDCTP Project Coordinator:	Martin Boeree
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 rifampicin and other rifamycins in tuberculosis
EDCTP Project Code:	IP.2007.32011.012
EDCTP Project Start Date:	11 June 2009
EDCTP Project End Date:	10 June 2014
Trial 1	
Site Principal Investigator(s):	Prof. Dr. Diacon and Dr. Rodney Dawson
Clinical Trial/Study Sponsor:	Radboud University Nijmegen Medical Centre, Nijmegen, 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:	<p>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.</p> <p>To find the maximal tolerable dose of rifampicin.</p>
Primary Objective(s):	<ol style="list-style-type: none"> 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, and 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):	<ol style="list-style-type: none"> 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, and 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, Centre for Clinical Tuberculosis Research University of Stellenbosch, Tygerberg, South Africa University of Cape Town Lung Institute, Cape Town, South Africa
Collaborating site(s):	Not applicable
Study design:	<p>an open-label, prospective, two-center, Phase IIA, maximum tolerability dosage (MTD) study that will be conducted in consecutive groups.</p> <p>Study 4: Open-label, one-arm, two-period, and fixed-order pharmacokinetic interaction study</p>
Number of subjects:	68
Product(s):	Rifampicin
Manufacturer/Developer:	Sanofi-Aventis, Paris, France
Cofunders:	Netherlands Organisation for Scientific Research (NWO), Radboud University Nijmegen, Swiss Tropical Institute, Prince Leopold Institute of Tropical Medicine, Medical Research Council South Africa (MRC)
Trial registration number(s):	PACTR201104000281203,
Sub studies:	None identified so far.
Status:	Ongoing

Results and Outcomes:	Not available yet
Trial 2	
Site Principal Investigator(s):	Prof. Dr. Kibiki and Dr. Reither
Clinical Trial/Study Sponsor:	Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands
Trial/Study title:	Pharmacokinetics and pharmacodynamics of high versus standard dose rifampicin in patients with pulmonary tuberculosis in Tanzania (High RIF Study).
Goal:	<p>Study 2 is a small exploratory Phase II study that primarily evaluates 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.</p> <p>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.</p>
Primary Objective(s):	<ol style="list-style-type: none"> 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 <i>Mycobacterium tuberculosis</i>, evaluated by 2 month sputum culture conversion and Serial Sputum Colony Forming Units Count (SSCC), in the same population.
Secondary Objective(s):	<ol style="list-style-type: none"> 1. To compare the accuracy of surrogate markers (SSCC and RNA) with the standard 2 month sputum conversion marker in patients with smear-positive pulmonary tuberculosis in Tanzania. 2. To document the occurrence of mixed <i>Mycobacterium tuberculosis</i> (MTB) strain infections in the same patient population and its influence on treatment response.
Clinical Trial/Study site(s):	<ul style="list-style-type: none"> • Kilimanjaro Clinical Research Centre, Moshi with its field site Kibong'oto National TB Hospital, Sanya Yuu, Tanzania • Ifakara Health Research and Development Centre, Bagamoyo Branch, Tanzania and its associated field sites
Collaborating site(s):	Kibong'oto National TB Hospital, Sanya Yuu, Tanzania
Study design:	Double blind, randomized, controlled, three arm, phase II clinical trial
No of Participants	150
Product(s):	Rifampicin
Manufacturer/Developer:	Sanofi-Aventis, Paris, France
Cofunders:	Netherlands Organisation for Scientific Research (NWO), Radboud University Nijmegen, Swiss Tropical Institute, Prince Leopold Institute of Tropical Medicine, Medical Research Council South Africa (MRC)
Trial registration number(s):	PACTR2009060001493909, NCT00760149
Status:	Ongoing
Results and Outcomes:	Not available yet
Trial 3	
Site Principal Investigator(s):	TBD
Clinical Trial/Study Sponsor:	Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands
Trial/Study title:	TBD
Goal:	<p>Study 3 is a larger follow-up Phase IIb study that should substantiate that high dose rifampicin (doses based on study 1 and study 2) in combination with regular TB drugs is safe and tolerable and associated with improved response (proof of principle), before advancing to a pivotal Phase III study.</p> <p>TBD</p>
Primary Objective(s):	TBD
Secondary Objective(s):	TBD

Clinical Trial/Study site(s):	<ul style="list-style-type: none"> • Kilimanjaro Clinical Research Centre, Moshi with its field site Kibong'oto National TB Hospital, Sanya Yuu, Tanzania • Ifakara Health Research and Development Centre, Bagamoyo Branch, Tanzania and its associated field sites • Makerere University and Mulago Hospital, Kampala, Uganda • Aurum Institute for Health Research; The Tembisa clinical trials unit; Johannesburg, South Africa • TASK applied Science, Centre for Clinical Tuberculosis Research University of Stellenbosch, Tygerberg, South Africa • University of Cape Town Lung Institute, Cape Town, South Africa
Collaborating site(s):	LMU, UCL
Study design:	TBD
Number of subjects:	600
Product(s):	Rifampicin and others
Manufacturer/Developer:	Sanofi-Aventis
Cofunders:	Netherlands Organisation for Scientific Research (NWO), Radboud University Nijmegen, Swiss Tropical Institute, Prince Leopold Institute of Tropical Medicine, Medical Research Council South Africa (MRC)
Status:	Not yet Recruiting
Trial Registration number(s):	TBD
Results and outcomes:	Not available yet
Trial 4	
Site Principal Investigator(s):	Prof. Dr. Kibiki
Clinical Trial/Study Sponsor:	Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands
Trial/Study title:	TBD
Goal:	<p>Study 4 is a pharmacokinetic interaction study that assesses the extent of the pharmacokinetic interaction between rifampicin and moxifloxacin. If high dose rifampicin reaches the stage of evaluation in Phase III of drug development, it seems logical to evaluate its potential in the combination with moxifloxacin. This warrants a pharmacokinetic interaction study.</p> <p>pharmacokinetic interaction study to assesses the extent of the pharmacokinetic interaction between rifampicin and moxifloxacin.</p>
Primary Objective(s):	TBD
Secondary Objective(s):	TBD
Clinical Trial/Study site(s):	Kilimanjaro Clinical Research Centre, Moshi, Tanzania
Collaborating site(s):	TBD
Study design:	Open label
Product(s):	Rifampicin and moxifloxacin
Manufacturer/Developer:	Sanofi-Aventis (Rifampicin)
Status:	Not yet Recruiting/Ongoing/Completed plus comments
Trial Registration number(s):	TBD
Total number of subjects (clinical trials only):	<p>Study 1: max. 68 patients</p> <p>Study 2: 150 patients</p> <p>Study 3: TBD</p> <p>Study 4: TBD</p>
Total number of subjects (cohort/epidemiological/other studies):	TBD
PhD study-1	TBD
PhD study-2	Study title is TBD, Stellah Mpagama
MSc study-1	Not applicable
MSc study-2	Not applicable
Other/Sub-studies:	TBD
Key Publications:	<ol style="list-style-type: none"> 1. Why Do We Use 600 mg of Rifampicin in Tuberculosis Treatment? van Ingen et al., CID 2011:52 (1 May 2011) 2. High dose rifampicin: how do we proceed?" (Correspondence), M. Boeree et al. , The International Journal of Tuberculosis and Lung Disease, accepted

2.1.9 PanACEA-SQ109

EDCTP Project Coordinator:	Hoelscher, Michael
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.2007.32011.012
EDCTP Project Start Date:	16 June 2009
EDCTP Project End Date:	15 June 2014
Trial 1	
Site Principal Investigator(s):	Andreas Diacon, Michael Hoelscher
Clinical Trial/Study Sponsor:	University of Munich Sequella Inc.
Trial/Study title:	<p>Study 1: A Phase 2A Trial to evaluate the extended early bactericidal activity, safety, tolerability and Pharmacokinetics of SQ109 in adult subjects with newly-diagnosed, uncomplicated, smear-positive, pulmonary tuberculosis (N=90)</p> <p>Study 2: A phase 2A, dose-ranging study to assess safety, tolerability, and preliminary efficacy of isoniazid, rifampicin, pyrazinamide, and SQ109 (HRZSQ) for intensive-phase treatment of patients with uncomplicated, smear-positive, pulmonary tuberculosis caused by drug-sensitive <i>Mycobacterium tuberculosis</i> (N=150)</p> <p>Study 3: A phase 2B, double-blind comparison of isoniazid, rifampicin, pyrazinamide, and SQ109 (HRZSQ) and isoniazid, rifampicin, pyrazinamide, and ethambutol (HRZE) intensive-phase DOTS regimen for treatment of patients with uncomplicated, smear-positive, pulmonary tuberculosis caused by drug-sensitive <i>Mycobacterium tuberculosis</i> (N=400)</p>
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):	<p>(1) To evaluate the safety, tolerability, efficacy, and pharmacokinetics of three oral dose levels of SQ109 alone and in combination with standard dose rifampicin</p> <p>(2) To assess safety, tolerability, and preliminary efficacy of isoniazid, rifampicin, pyrazinamide, and SQ109 (HRZSQ)</p> <p>(3) To compare of isoniazid, rifampicin, pyrazinamide, and SQ109 (HRZSQ) with isoniazid, rifampicin, pyrazinamide, and ethambutol (HRZE)</p>
Secondary Objective(s):	Rate of change of logCFU in sputum over three time periods, time to sputum culture positivity
Clinical Trial/Study site(s):	University of Stellenbosch (South Africa); University of Cape Town (South Africa); University of Witwatersrand (South Africa); Aurum Institute for Health Research Studies (Aurum); Mbeya Medical Research Program (Tanzania); University of Zambia; Albert Schweitzer Hospital (Gabon)
Collaborating site(s):	University of Munich (Germany); University College of London (UK); University of Stellenbosch (South Africa); University of Cape Town (South Africa); University of Witwatersrand (South Africa); Aurum Institute for Health Research Studies (Aurum); Mbeya Medical Research Program (Tanzania); University of Zambia; Albert Schweitzer Hospital (Gabon); Sequella Inc.(USA)
Study design:	<p>Study 1 – A two-center, partially blinded, randomized, 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</p> <p>Study 2 - A three-arm, double-blind, Phase 2A study to compare activity (qualitative and quantitative sputum culture of <i>M. tuberculosis</i>) during the intensive treatment phase (first 8 weeks) of a "low dose" (150 mg), and a "high dose" (300 mg) SQ109-containing regimen and the standard 4-drug, 2-month, intensive-phase regimen consisting of isoniazid, rifampicin, pyrazinamide, and ethambutol (HRZE).</p> <p>Study 3 is a two-arm, double-blind, Phase 2B study to compare activity (quantitative sputum cfu of <i>M.</i></p>

	<i>tuberculosis</i>) during the intensive treatment phase (first 8 weeks) of an SQ109 regimen (HRZSQ) selected from Study 2 and the standard 4-drug, 2-month, intensive-phase regimen consisting of isoniazid, rifampicin, pyrazinamide, and ethambutol (HRZE)
Number of subjects:	420
Product(s):	A novel TB drug (SQ109)
Manufacturer/Developer:	Sequella Inc. (Sequella)
Cofunders:	Klinikum der Universitat Munchen, Institute for Medical Bioinformatics, Medical Research Council UK, Bill & Melinda Gates Foundation (BMGF), Sequella, Federal Ministry of Education and Research (BMBF), Netherlands Organisation for Scientific Research (NWO)
Trial registration number(s):	PACTR201009000252144 NCT01218217 (The EBA study)
Sub studies:	Early Bactericidal Activity (EBA)
Status:	Ongoing
Results and Outcomes:	Not yet available

2.2 Tuberculosis vaccines clinical trials

Table 2-2: Summary table of tuberculosis vaccines clinical trials supported by EDCTP

Project Acronym (Coordinator)	Phase of trial	Product(s)	Manufacturer / Developer	Study population	Status
THYB-03 (Aseffa)	Phase Ib	Ag85B-ESAT-6	SSI	TST positive healthy adolescents N=39	Completed
Van't Hoog - TB Vac prep Kenya (Van't Hoog)	Epidemiological Study	N/A - Epidemiological study	N/A	Neonates and adolescents N=7900	Ongoing
Musoke-TB Vac prep-PC to provide (Musoke)	Epidemiological study	N/A - Epidemiological study	N/A	Infants and adolescents N=7500	Ongoing
THYB-04 (Doherty)	II	Ag85B-ESAT-6 + adjuvant (500 nmol KLK and 20 nmol ODN1a)	SSI	TST positive healthy adolescents N= 320	Not yet recruiting
TB-021: Aeras485 MVA85A (Ota)	IIb	MVA85A/AERAS-485	Aeras/ OETC	Healthy, HIV-infected adults N=1400	Not yet recruiting
AERAS 402/Crucell Ad35 (Hussey)	II	AERAS-402	Aeras	BCG vaccinated, HIV-uninfected infants without evidence of TB N=4096	Ongoing
?? SSI H1 PC to provide (Churchyard)	II	Ag85B-ESAT-6 (50 Pg) (SSI H1) + adjuvant (500 nmol KLK and 20 nmol ODN1a)	SSI	HIV-infected, BCG-vaccinated Adults with CD4+ Lymphocyte Counts Greater Than 350 Cells/mm3 N= (48)	Not yet recruiting

2.2.1 TB Vac prep Ethiopia/THYB-03

EDCTP Project Coordinator:	Abraham Aseffa
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
Trial 1	
Site Principal Investigator(s):	Abraham Aseffa, AHRI Ethiopia Jemal Hussein, AHRI Ethiopia
Clinical Trial/Study Sponsor:	Statens Serum Institute (SSI), Copenhagen, 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 formulations at 0 and 2 months (2) To determine the immunogenicity profile of an adjuvanted TB subunit vaccine administered in different antigen 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):	The Armauer Hansen Research Institute (AHRI), Ethiopia Institut Pasteur, Madagascar (IPM), Madagascar Kilimanjaro Christian Medical College (KCMC), Tanzania GlaxoSmithKline Biologicals (GSK), United Kingdom Statens Serum Institute (SSI), Denmark Leiden University, Netherlands Immunovac Consulting, Belgium
Study design:	Phase I Study: Randomized; Uncontrolled; Safety/Efficacy Study; Single Group Assignment; Open Label; Prevention
Number of subjects:	39
Product(s):	ESAT-6/Ag85B
Manufacturer/Developer:	SSI produces ESAT-6/Ag85B Intercell A/S produces IC31adjuvant
Cofunders:	Statens Serum Institut, Leiden University
Trial Registration number(s):	NCT01049282
Sub studies:	nil
Status:	Completed
Results and Outcomes:	Capacity for conducting of TB Vaccine trials now established at AHRI

2.2.2 Van't Hoog-TB Vac prep Kenya

EDCTP Project Coordinator:	Anja van't Hoog
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
Trial 1	
Site Principal Investigator(s):	Videlis Nduba Anja van't Hoog Kayla Laserson
Clinical Trial/Study Sponsor:	The studies are observational cohort studies without an experimental product. There is no formal sponsor, but Aeras Global TB Vaccine Foundation takes on a sponsor role as far as applicable.
Trial/Study title:	1) A Prospective Epidemiological Cohort Study to Evaluate the Incidence of Tuberculosis in Infants in Western Kenya 2) A Prospective epidemiological study of TB in adolescents in Siaya district, Western Kenya, in preparation for future vaccine trials
Goal:	Cohort studies – see Primary objective below
Primary Objective(s):	Neonatal 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 <i>M. tuberculosis</i> 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 Determine all cause mortality and TB specific mortality, through vital events monitoring and verbal autopsies.
Clinical Trial/Study site(s):	Karemo Division, Siaya district, Western Kenya,
Collaborating site(s):	KNCV Tuberculosis Foundation Ministry of Health, Kenya Kenya Medical Research Institute (KEMRI) University of Cape Town Center for Disease Control and Prevention (CDC) Vienna School of Clinical Research San Raffaele del monte Tabor foundation - Milan
Study design:	Prospective Epidemiological study

Number of subjects:	5004 adolescents and 2900 infants
Product(s):	No investigational Project – Cohort study
Manufacturer/Developer:	No investigational Project – Cohort study
Cofunders:	Netherlands Organisation for Scientific Research (NWO) KNCV Tuberculosis Foundation San Raffaele del monte Tabor foundation – Milan Austrian Federal Ministry of Science
Sub studies:	N/A
Trial registration number(s):	Not applicable. These are cohort studies for capacity building in preparation for vaccine trials
Status:	Adolescent cohort closed in December 2010 and data cleaning in progress. Infant cohort study follow up ends in June 2011 and close out in October 2011
Results and Outcomes:	Preliminary results are being shared in conferences locally, regionally and internationally. Manuscripts are currently under progress.
PhD study-1	I. Epidemiology of tuberculosis in adolescents in western Kenya. Candidate: Videlis Nduba II. 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 III. Infectious disease modeling / epidemiology of tuberculosis in infants and care seeking in self reported adult TB patients in western Kenya. Candidate: Lazarus Odeny
MSc study-1	(Peter Nyamthimba – MSc in Clinical Trials) (Walter Mchembere – Master of Public Health) (Patience Oduor – MSc in Clinical Trials)
MSc study-2	(Dr. Grace Kiringa – MSc in Clinical Trials) (Joseph Opole – MA in Project Planning and Management) (Benard Owuor – Master of Business Administration)
BSc/BA study-2	(Susan Musau – Bachelor of Science in Medical Laboratory Sciences) (Charles Lwanga – Bachelor of Arts) (Paul Frederick Otieno – Bachelor of Business Administration)
Other/Sub-studies:	Nil
Key Publications:	None

2.2.3 TB Vac prep Uganda

EDCTP Project Coordinator:	Philippa Musoke
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
Trial 1	
Site Principal Investigator(s):	Philippa Musoke
Clinical Trial/Study Sponsor:	Infectious Diseases Institute (IDI), Makerere University, Uganda
Trial/Study title:	No clinical trial; 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):	<p>1) To determine the incidence of TB disease in infants. Endpoint: Proportion of infant population with clinical TB disease over a 1 year period</p> <p>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</p>
Secondary Objective(s):	<p>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</p> <p>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</p> <p>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</p> <p>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</p> <p>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</p> <p>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.</p>
Clinical Trial/Study site(s):	Iganga/Mayuge Demographic Surveillance Site in Eastern Uganda
Collaborating site(s):	<p>Infectious Diseases Institute (IDI), Makerere University College of Health Sciences, Uganda</p> <p>Mycobacteriology (BSL-3) Lab (MYCO-LAB) – Department of Medical Microbiology, Makerere University College of Health Sciences, Uganda</p> <p>The School of Public Health, Makerere University College of Health Sciences, Uganda</p> <p>The National TB Reference Laboratory (NTRL)-Wandegeya, Uganda</p> <p>The South African Tuberculosis Vaccine Initiative (SATVI), South Africa</p> <p>Swedish Institute for Infectious Disease Control (SMI), Sweden</p> <p>The Karolinska Institutet, Sweden</p> <p>Prince Leopold Institute of Tropical Medicine, Belgium</p>

	The Institute for Medical Immunology, Belgium
	The KNCV Tuberculosis Foundation, Netherlands
Study design:	Epidemiological Cohort Study
Number of subjects:	2500 subjects in the Infant Cohort Study 5000 subjects in the Adolescent Cohort Study 100 subjects in the immunology study
Product(s):	No investigational product
Manufacturer/Developer:	No investigational product
Cofunders:	Swedish International Development Cooperation Agency (SIDA), Sweden Karolinska Institutet, Sweden Prince Leopold Institute of Tropical Medicine, Belgium Aeras Global TB Vaccine Foundation, USA
Sub studies:	
Status:	Ongoing
Results and Outcomes:	
Total number of subjects (clinical trials only):	Not applicable
Total number of subjects (cohort/epidemiological/other studies):	2500 subjects in the Infant Cohort Study 5000 subjects in the Adolescent Cohort Study 100 subjects in the immunology study
PhD study-1	(Vaccine induced immunity in nine-months old infants following BCG vaccination at birth or at 6 weeks of age) (Dr. Fredrick Lutwama)
PhD study-2	(TBD) (Dr. Patrick Nabongo to start later this year at Karolinska)
MSc study-1	(Study title) (Name of candidate) None
Other/Sub-studies:	Nil
Key Publications:	Esther Buregyeya, Asli Kulane, Robert Colebunders, Anne Wajja, Juliet Kiguli, Harriet Mayanja, Philippa Musoke, George Pariyo and Ellen M.H. Mitchell. <i>Knowledge, attitudes and health seeking behavior towards tuberculosis in rural Uganda. International Journal of TB and Lung Diseases (in press)</i>

2.2.4 THYB-04

EDCTP Project Coordinator:	Timothy Mark Doherty (Peter Andersen – pending approval)
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
Trial 1	
Site Principal Investigator(s):	Hassan Mahomed South African Tuberculosis Vaccine Initiative (SATVI) Cape Town
Clinical Trial/Study Sponsor:	Statens Serum Institute (SSI), Copenhagen, 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.
Secondary Objective(s):	nil
Clinical Trial/Study site(s):	1.) Armauer Hansen Research Institute (AHRI) Addis Ababa, Ethiopia 2.) Nazaret/Adama Regional Hospital(Nazaret/Ethiopia) 3.) Debre Zeit Hospital (Debre Zeit/Ethiopia)
Collaborating site(s):	1.) Statens Serum Institute (SSI), Copenhagen, Denmark () 2.) Armauer Hansen Research Institute (AHRI), Addis Ababa, Ethiopia 3.) Leiden University Medical Centre (LUMC) Leiden, Netherlands 4.) Projecto de Saúde de Bandim/SSI, Guinea-Bissau 5.) Bandim Health Project/ Aarhus University Hospital, Århus, Denmark
Study design:	Randomised, double-blind, multicentre trial
Number of subjects:	320
Product(s):	ESAT-6/Ag85B adjuvant IC31
Manufacturer/Developer:	SSI produces ESAT-6/Ag85B and IC13 Intercell A/S developed IC31adjuvant
Cofunders:	Denmark, Netherlands
Trial registration number(s):	Pending
Sub studies:	(See trial 2 below)
Status:	Yet to recruit
Results and Outcomes:	Not available yet
Trial 2	
Site Principal Investigator(s):	Jemal Hussain. Armauer Hansen Research Institute (AHRI) Ethiopia
Clinical Trial/Study Sponsor:	Statens Serum Institute (SSI), Copenhagen, Denmark
Trial/Study title:	Phase I study -
Goal:	To test the time between vaccinations with the TB subunit vaccine
Primary Objective(s):	To evaluate the safety of a TB subunit vaccine administered in volunteers at 0 and 1 months and compare the results with a 0 and 2 month schedule.
Secondary Objective(s):	Immunogenicity. 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.
Clinical Trial/Study site(s):	Armauer Hansen Research Institute (AHRI) Addis Ababa, Ethiopia

Collaborating site(s):	1.) Statens Serum Institute (SSI), Copenhagen, Denmark (2.) Armauer Hansen Research Institute (AHRI), Addis Ababa, Ethiopia 3.) Leiden University Medical Centre (LUMC) Leiden, Netherlands 4.) Projecto de Saúde de Bandim/SSI, Guinea-Bissau 5.) Bandim Health Project/ Aarhus University Hospital, Århus, Denmark
Study design:	Open
Product(s):	ESAT-6/Ag85B adjuvant IC31
Manufacturer/Developer:	SSI produces ESAT-6/Ag85B and IC31 Intercell A/S developed IC31adjuvant
Cofunders:	Denmark, Netherlands
Trial registration number(s):	Pending
Status:	Yet to recruit
Results and Outcomes:	Not yet available
PhD study-1	PhD - Analysis of regulation of immune responses in Tuberculosis. Martha Zewdie
PhD study-2	Frauke Rudolph (site PI sub study)and Grethe Lemvik (PI sub study)
MSc study-1	Cidia Camara
MSc study-2	Demis Arga (MD)
Other/Sub-studies:	
Site Principal Investigator(s):	Grethe Lemvik, Bandim Health Project, Guinea Bissau
Clinical Trial/Study Sponsor:	Statens Serum Institute (SSI), Copenhagen, 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
Tertiary Objective(s):	
Clinical Trial/Study site(s):	Bandim Health Project, Guinea Bissau
Collaborating site(s):	1.) Statens Serum Institute (SSI), Copenhagen, Denmark (2.) Armauer Hansen Research Institute (AHRI), Addis Ababa, Ethiopia 3.) Leiden University Medical Centre (LUMC) Leiden, Netherlands 4.) Projecto de Saúde de Bandim/SSI, Guinea-Bissau 5.) 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
Status:	Recruiting
Trial Registration number(s):	PACTR201101000273931
Cofunders:	Denmark
Site Principal Investigator(s):	Frauke Rudolf, Bandim Health Project, Guinea Bissau
Clinical Trial/Study Sponsor:	Statens Serum Institute (SSI), Copenhagen, Denmark
Trial/Study title:	PREDicting Tuberculosis among TB suspects, Improving triage and Nutritional support to Alter Mortality, PREDINAM
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):	1.) Statens Serum Institute (SSI), Copenhagen, Denmark (2.) Armauer Hansen Research Institute (AHRI), Addis Ababa, Ethiopia 3.) Leiden University Medical Centre (LUMC) Leiden, Netherlands

	4.) Projecto de Saúde de Bandim/SSI, Guinea-Bissau 5.) 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
Status:	Recruiting
Trial Registration number(s):	PACTR201101000273931
Cofunders:	Denmark

2.2.5 TB-021

EDCTP Project Coordinator:	Martin Ota
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:	26 August 2014
Trial 1	
Site Principal Investigator(s):	Robert Wilkinson
Clinical Trial/Study Sponsor:	University of Oxford
Trial/Study title:	A Phase II, Proof-of-concept, Randomized, 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
Goal:	To evaluate the protective efficacy against TB disease and the safety of MVA85A/AERAS-485 in HIV-positive adults. In addition, the immunogenicity of MVA85A/AERAS-485 will be evaluated.
Primary Objective(s):	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.
Secondary Objective(s):	<ol style="list-style-type: none"> 1. To evaluate the safety of MVA85A/AERAS-485 compared to placebo. 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 who received isoniazid preventive therapy compared to control subjects who also received isoniazid preventive therapy but who receive placebo 4. To evaluate the immunogenicity of MVA85A/AERAS-485 compared to placebo as described by the ex vivo IFN-γ ELISPOT assay. 5. 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 6. To identify potential immunological correlates of protection from tuberculosis in subjects vaccinated with MVA85A/AERAS-485 7. 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, Oxford, UK LSHTM, London, UK University of Cape Town, South Africa Centre Hospitalier Universitaire Le Dantec, Dakar, Senegal Pasteur Institute, Brussels, Belgium
Study design:	Phase II, Proof-of-concept, Randomized, Double-blind, Placebo-controlled
Number of subjects:	1400
Product(s):	Candin (Allermed Labs, USA) - placebo MVA85A (IDT GmbH / Oxford) / AERAS – 485 (Impfstoffwerk Dessau-Tornau (IDT) Biologika GmbH, DE – March 2011)
Manufacturer/Developer:	IDT / UoT OETC
Cofunders:	DfID UK (in kind) Aeras Scientific Institute of Public Health (SIPH) Belgium
Trial registration number(s):	US FDA NCT01151189 (tracked by PACTR)
Sub studies:	Nil
Status:	Not yet recruiting
Results and Outcomes:	Not available yet
Total number of subjects	1400

(clinical trials only):	
Total number of subjects (cohort/epidemiological/other studies):	1400
PhD study-1	TBD
MSc study-1	TBD
Other/Sub-studies:	Post-doctoral Fellowshi
Key Publications:	None

2.2.6 AERAS 402/Crucell Ad35

EDCTP Project Coordinator:	Prof. Gregory Hussey
EDCTP Call Title:	Call for support of clinical trials, capacity building and networking in tuberculosis vaccines development
EDCTP Project Title:	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:	24 May 2014
Trial 1	
Site Principal Investigator(s):	Hassan Mahomed (Cape Town) Jahit Sacarlal (Manhica) Videlis Nduba (Kenya) Eric Wobudeya (MU-JHU, Uganda) Philippa Musoke (IDI, Uganda)
Clinical Trial/Study Sponsor:	Aeras
Trial/Study title:	A Phase II, Double-blind, Randomized, 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:	<p>This study will include a dose-finding phase followed by a safety and efficacy phase at a selected dose of AERAS-402. The rationale for the dose selected for use in the safety and efficacy phase will incorporate the safety experience and immunogenicity results from an ongoing Phase I trial in infants as well as from the dose-finding phase in this study.</p> <p>An exploratory objective of this trial will be to evaluate the efficacy of Crucell Recombinant Ad35 TB vaccine in infants at eight discrete sites in Africa</p>
Primary Objective(s):	<ol style="list-style-type: none"> 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
Secondary Objective(s):	<ol style="list-style-type: none"> 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 immunogenicity of AERAS-402 in infants compared to controls by whole blood intracellular cytokine assay developed by the University of Cape Town (UCT) 4. To assess potential immune correlates of protection from TB in infants vaccinated with AERAS-402 5. 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 6. 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):	<p>Name of site: Kampala, Uganda Name of site: Kisumu, Kenya – Siaya district Name of site: Manhica, Mozambique Name of site: Worcester, South Africa. 4 Sites in Africa to be funded by the NIH. Arrangements for these are still to be finalised</p>
Collaborating site(s):	<p>Prince Leopold Instituut voor Tropische Geneeskunde (Institute of Tropical Medicine (ITM), Belgium Swiss Tropical Institute (STI), Basel, Switzerland Swiss Agency for Development and Cooperation (SDC), Berne, Switzerland Karolinska Institutet (KI), Stockholm, Sweden KNCV Tuberculosis Foundation, The Hague, NL University of Cape Town, South Africa</p>

	KEMRI, Kenya CRESIB, Mozambique Infectious Diseases Institute IDI Makerere University, Kampala, Uganda Mulago Hospital, Kampala, Uganda
Study design:	Phase II, Double-blind, Randomized, Placebo-controlled, Multicenter, Proof-of-concept Study
Number of subjects:	Between 2,200 and 4,000 to be enrolled (Adaptive design). 96 from groups 1, 2 and 3 enrolled to date.
Product(s):	AERAS-402/Crucell Ad35
Manufacturer/Developer:	Crucell B.V./ Aeras
Cofunders:	Institute de Salud Carlos III, Madrid, Spain Aeras, USA Vienna School of Clinical Research (VSCR), Austria Swiss Agency for Development and Cooperation (SDC), Berne, Switzerland
Trial registration number(s):	Pending
Sub studies:	Nil
Status:	Ongoing
Results and Outcomes:	Not available yet
Total number of subjects (clinical trials only):	Between 2,200 and 4,000 to be enrolled (Adaptive design). 96 from groups 1, 2 and 3 enrolled to date.
Total number of subjects (cohort/epidemiological/other studies):	Infant TB epidemiological study in Mozambique: 198 enrolled at 14 March 2011 out of a target enrolment of 800-1000.
PhD study-1	PhD studentship by Helen Buteme; Phenotypic analysis of MTB antigen specific T-cells and the evaluation of new point of care TB diagnostic tests
Post Doctoral study-1	Post doctoral fellowship by Benon Asiime; 1. In-vitro cytokine response to Mycobacterium tuberculosis Uganda genotype strain in human monocyte derived macrophages 2. Characterization of isolates from the Iganga-Mayuge district.
Post doctoral study -2	Dr Brian Abel: His research involved the identification of immune correlates of risk of childhood TB disease, following BCG vaccination. He has since left SATVI but the continuation of his work is being planned.
MSc study-1	MSc studentship by Faith Keneko; Integration of HIV services in TB treatment in Uganda. This was completed. Unfortunately Dr Keneko has passed away in August 2010
MSc study-2	MSc studentship by Mark Okwir; Prevalence and factors associated with hepatotoxicity in HIV infected patients on anti-tuberculosis therapy in Mulago Hospital
MSc study - 3	MSc studentship by Moorine Sekadde; Diagnostic accuracy of the Genexpert system among children with possible/probable tuberculosis at Mulago Hospital
MSc study - 4	MSc studentship by Dr Grace Kiringa: MSc in Clinical Trials via distant learning at the LSHTM (London School of Hygiene and Tropical Medicine)
MSc study - 5	MSc studentship by Mr Benson Muchiri: MSc in Laboratory Science/Microbiology at the Kenya Medical Research Institute, KEMRI/CDC programme
Other/Sub-studies:	nil
Key Publications:	None

2.2.7 Churchyard-TBVac SSI H1

EDCTP Project Coordinator:	Gavin Churchyard
EDCTP Call Title:	Call for support of clinical trials, capacity building and networking in tuberculosis vaccines development
EDCTP Project Title:	Phase II Double-Blind, Randomised, 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/mm ³
EDCTP Project Code:	IP.2009.32080.002
EDCTP Project Start Date:	30 September 2010
EDCTP Project End Date:	4 October 2012
Trial 1	
Site Principal Investigator(s):	Gavin Churchyard
Clinical Trial/Study Sponsor:	Statens Serum Institute (SSI), Copenhagen, Denmark
Trial/Study title:	Phase II Double-Blind, Randomized, 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):	To describe the safety and tolerability of H1 in HIV-infected, BCG-vaccinated adult subjects.
Secondary Objective(s):	To assess cellular immunity induced by H1 in HIV-infected, BCG-vaccinated adult subjects. Exploratory Objective: To describe the effect of H1 on the CD4+ lymphocyte count and HIV-1 viral load in HIV-infected, BCG-vaccinated adult subjects
Clinical Trial/Study site(s):	Ifakara Health Institute/Bagamoyo Research Centre, Bagamoyo Tanzania The Aurum Institute (Johannesburg, South Africa.
Collaborating site(s):	1.) The Aurum Institute (Johannesburg/South Africa) 2.) Aeras Global TB Vaccine Foundation (Cape Town/South Africa); 3.) KNCV Tuberculosis Foundation (The Hague/The Netherlands); 4.) Swiss Tropical Institute (Basel/Switzerland) 5.) Ifkara Health Institute (Bagamoyo/Tanzania); 6.) Statens Serum Institut (Kopenhagen/Denmark); 7.) University of Amsterdam-Academic Medical Centre (Amsterdam/The Netherlands);
Study design:	Phase II Double-Blind, Randomized, Placebo-Controlled Study
Number of subjects:	48
Product(s):	Ag85B-ESAT-6 (50 Pg) + adjuvant (500 nmol KLK and 20 nmol ODN1a)
Manufacturer/Developer:	SSI, Norway
Cofunders:	Swiss Tropical Public Health Institute, Switzerland SIDA, Sweden Swiss National Science Foundation (SNSF), Switzerland
Trial registration number(s):	Pending
Sub studies:	Nil
Status:	-
Results and Outcomes:	-

2.3 Tuberculosis diagnostics clinical trials

Table 2-3: Summary table of tuberculosis diagnostics clinical trials supported by EDCTP

Project Acronym (Coordinator)	Phase of trial	Product(s)	Manufacturer / Developer	Study population	Status
TB NEAT (Dheda)	Not applicable	Optimised smear microscopy with LED-illuminated microscopes Urine LAM lateral flow strip test (Determine TB®)	Carl Zeiss MicroImaging GmbH, Germany Inverness Medical Professional Diagnostics	ADULT (18 and older) HIV-positive patients with suspected TB, 500 recruits per site	Not yet recruiting
TB NEAT (Dheda)	Not applicable	Point-of-treatment GeneXpert MTB/RIF assay	Cepheid, Sunnyvale, California USA	ADULT 18 years and older. 300 patients per site	Not yet recruiting
TB-NEAT (Dheda)	Not applicable XACT (Xpert active case-finding trial)	Xpert MTB/Rif assay Urine LAM lateral flow strip test (Determine TB®)	Cepheid, Sunnyvale, California USA. Inverness Medical Professional Diagnostics	ADULT 18 and over, N=4000	Not yet recruiting
TB CHILD (Lwilla)	Not applicable	<ol style="list-style-type: none"> LHSD Rapid test to detect LAM in sputum or urine Loop-mediated isothermal amplification (LAMP) GeneXpert Diagnostic potential of IP10 and other biomarkers in blood and urine T cell activation markers on <i>Mycobacterium tuberculosis</i> (MTB) specific T cells (TAM-IGRA) Mtb DNA extraction from stool Lab-on-chip based new platform (In-check™) for the molecular diagnosis Ustar TB IAD Kit Pari eFlowrapid nebulizer Newly developed TB diagnostics 	<ol style="list-style-type: none"> LIONEX Eiken Chemical Co. Ltd Cepheid Not applicable Not applicable Not applicable STMicroelectronics Biotech Pari Pharma Not applicable 	<p>Study A: 18 years and older. 180 TB cases (90 smear positive TB cases and 90 smear negative but Xpert MTB positive /culture positive TB cases) 120 healthy cases</p> <p>Study B: Children TB suspects, 6 weeks - 14 years old. 600 paediatric TB suspects</p>	<p>Study A: Ongoing</p> <p>Study B: Not yet recruiting</p>
AE TBC (Walzi)	Not applicable	<ol style="list-style-type: none"> QuantIFERON® TB Gold In-Tube T SPOT TB 	<ol style="list-style-type: none"> Cellestis Oxford Immunotec 	HIV uninfected adult TB suspects N=800 HIV infected adults TB suspects N=400	Ongoing

2.3.1 TB NEAT

EDCTP Project Coordinator:	Keertan Dheda
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:	16 May 2013
Clinical Trial/Study Sponsor:	Institute of Infectious Diseases and Molecular Medicine, University of Cape Town, Cape Town, South Africa
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 Institutet, Stockholm, Sweden
Determine TB® Point-of-care urine LAM RCT	
Site Principal Investigator(s):	Keertan Dheda, University of Cape Town, Cape Town, South Africa Mark Patrick Nicol, University of Cape Town, Cape Town, South Africa Alexander Pym, Medical Research Council, , Durban, South Africa, Unit for Clinical and Biomedical TB Research, South Africa Peter Mwaba, University Teaching Hospital, Lusaka, Zambia Lynn Sodai Zijenah, University of Zimbabwe, Harare, Zimbabwe Andrea Rachow, NIMR-Mbeya Medical Research Programme (MMRP), Mbeya, Tanzania
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:	The study will examine whether 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):	<ol style="list-style-type: none"> 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.
Secondary Objective(s):	None
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.
Number of subjects:	ADULT (18 and older) HIV-positive patients with suspected TB, 500 recruits per site
Product(s):	Optimised smear microscopy with LED-illuminated microscopes Urine LAM lateral flow strip test (Determine TB®)
Manufacturer/Developer:	Carl Zeiss MicroImaging GmbH, Germany Inverness Medical Professional Diagnostics
Cofunders:	Foundation for Innovative New Diagnostics (FIND; Switzerland)

	<p>Swedish International Development Cooperation Agency (SIDA) Sweden)</p> <p>German Ministry for Education and Research (BMBF; Germany)</p> <p>Computer-Aided Detection of Tuberculosis (CAD4TB; Netherlands)</p> <p>Evaluation of transrenal-DNA detection to diagnose tuberculosis (TB trDNA) - a FP6-funded project from the University College London (UCL) UK)</p> <p>Medical Research Council (MRC) UK</p> <p>Active Diagnosis of Active TB [ADAT, EU-funded consortium between Zambia, Tanzania, UCL and Ludwig Maximilian University of Munich (LMU; Germany);</p> <p>Netherlands-African partnership for capacity development and clinical interventions against poverty-related diseases (NACCAP; Netherlands)</p>
Trial Registration number(s):	Not applicable
Status:	Ongoing
Results and Outcomes	First patient in: 15 April 2011
Point-of-treatment GeneXpert MTB/RIF Assay	
Site Principal Investigator(s):	<p>Keertan Dheda, University of Cape Town, Cape Town, South Africa</p> <p>Mark Patrick Nicol, National Health Laboratory Service and University of Cape Town, Cape Town, South Africa</p> <p>Alexander Pym, Medical Research Council, Durban, South Africa, Unit for Clinical and Biomedical TB Research, South Africa</p> <p>Peter Mwaba, University Teaching Hospital, Lusaka, Zambia</p> <p>Lynn Sodai Zijenah, University of Zimbabwe College of Health Sciences, Harare, Zimbabwe</p> <p>Andrea Rachow, NIMR-Mbeya Medical Research Programme (MMRP), Mbeya, Tanzania</p>
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:	This study examines if 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):	<ol style="list-style-type: none"> 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.
Secondary Objective(s):	Not applicable
Clinical Trial/Study site(s):	<p>University of Cape Town, Cape Town, South Africa;</p> <p>National Health Laboratory Service and University of Cape Town, Cape Town, South Africa</p> <p>Medical Research Council, Durban, South Africa, Unit for Clinical and Biomedical TB Research, South Africa</p> <p>University Teaching Hospital, Lusaka, Zambia;</p> <p>, NIMR-Mbeya Medical Research Programme (MMRP), Mbeya, Tanzania</p> <p>University of Zimbabwe College of Health Sciences, Harare, Zimbabwe;</p>
Collaborating site(s):	<p>University College London, London, UK;</p> <p>Radboud University, Nijmegen Medical Center, Nijmegen, Netherlands</p> <p>Klinikum der Universität München, Department of Infectious Diseases & Tropical Medicine, Munich, Germany</p> <p>MTC, Karolinska Institutet, Stockholm, Sweden</p>
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.
Number of subjects:	ADULT 18 and over, 300 patients per site
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); 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(s):	Not applicable
Sub-studies:	Not applicable
Status:	Not yet recruiting
Results and Outcomes	First patient in: 15 April 2011
TB NEAT– XACT (Xpert Active Case-finding Trial)	
Site Principal Investigator(s):	Keertan Dheda, University of Cape Town, Cape Town, South Africa Mark Patrick Nicol, National Health Laboratory Service and University of Cape Town, Cape Town, South Africa Lynn Sodai Zijenah, University of Zimbabwe College of Health Sciences, Harare, Zimbabwe Andrea Rachow, NIMR – Mbeya Medical Research Programme (MMRP), Mbeya, Tanzania
Trial/Study title:	The utility of intensified case finding combined with a package of novel TB diagnostics performed at community-based clinics in Africa- a multi-centric prospective cohort study (XACT study).
Goal:	The study will examine whether community-based symptom screening and point-of-care urine LAM lateral flow strip testing combined with down-stream targeted clinic referral and a package of TB diagnostic technologies will significantly improve the diagnostic yield of intensified case-finding and diminish time to treatment initiation in a cost-effective manner.
Primary Objective(s):	<ol style="list-style-type: none"> 1. To determine the diagnostic yield, impact and feasibility of community-based intensified TB case finding using symptom screening, HIV testing and urine LAM (if HIV-infected) testing together with a clinic-based diagnostic package (sputum smear microscopy, point-of-treatment GeneXpert® MTB/RIF Assay and chest radiograph). 2. To determine the incremental diagnostic yield and feasibility of a single point-of-treatment Xpert® MTB/RIF Assay over routine smear-microscopy in this context. 3. To determine the incremental diagnostic utility and feasibility of the urine LAM lateral flow test for HIV-infected TB patients during community-based symptom screening. 4. To examine the feasibility of performing the Xpert® MTB/RIF Assay at the point-of-treatment when used in conjunction with intensified case finding programmes. 5. To evaluate the cost-effectiveness of using a novel package of TB diagnostic tools for intensified case finding compared to conventional methods.
Secondary Objective(s):	Not applicable
Clinical Trial/Study site(s):	University of Cape Town, Cape Town, South Africa; National Health Laboratory Service and University of Cape Town, Cape Town, South Africa

	University of Zimbabwe College of Health Sciences, Harare, Zimbabwe; NIMR –MMRP, Mbeya, 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 Institutet, Stockholm, Sweden
Study design:	A prospective cohort study evaluating the incremental benefits of novel diagnostic technologies at point-of-care (urine LAM Determine TB lateral flow strip test) and point-of-treatment (GeneXpert MTB/RIF Assay) together with a WHO advised community clinical screening algorithm incorporating conventional screening approaches for intensified case finding. Patients will be recruited at one clinic site in each country (SA and Zimbabwe). All patients will receive all diagnostic tests where possible.
Number of subjects:	Adult (over 18 years), N= 4000 in Harare and N= 4000 in Cape Town (Total N=4000)
Product(s):	1. Xpert MTB/Rif assay 2. Urine LAM lateral flow strip test (Determine TB®)
Manufacturer/Developer:	1. Cepheid, Sunnyvale, California USA. 2. Inverness Medical Professional Diagnostics
Cofunders:	Foundation for Innovative New Diagnostics (FIND) Switzerland) Swedish International Development 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 Munich (LMU; Germany); Netherlands-African partnership for capacity development and clinical interventions against poverty-related diseases (NACCAP; Netherlands)
Trial Registration number(s):	Not applicable
Sub-studies:	Not applicable
Status:	Not yet recruiting
Results and Outcomes	-
Total number of subjects (clinical trials only):	
Total number of subjects (cohort/epidemiological/other studies):	N = 4000
PhD study-1	Cuthbert Musarurwa Performance outcomes of LED technology (Lumin) for microscopic detection of mycobacteria in a high HIV seroprevalence setting in Africa, University of Zimbabwe College of Health Sciences, Zimbabwe
PhD study-2	Hojoon Sohn Cost and cost-effectiveness of New TB Diagnostics, University of Cape Town, South Africa, and McGill University, Montreal, Canada Supervisor: Madhukar Pai
PhD Study-3	Duncan Chandra Predictive value of quantitative T cell responses for progression to active TB in HIV co-infected individuals, University Teaching Hospital, Lusaka, Uganda Supervisor:
PhD Study-4	Richard Nellis Van Zyl-Smit Population specific risks for TB infection and the variable performance characteristics of novel diagnostic technologies, University of Cape Town, South Africa Supervisor: Keertan Dheda
PhD Study-5	Shahieda Adams 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 Supervisor: Keertan Dheda
PhD Study-6	Jonny Peter Sputum induction, and novel emerging technologies to improve TB diagnosis, in a high HIV prevalence primary care setting (SINET study), University of Cape Town, South Africa Supervisor: Keertan Dheda
MSc study-1	Jennifer Allen Evaluation and validation of TB-BEAD Diagnostic assay in both smear positive and negative TB Suspects, MRC Durban, Durban, South Africa Supervisor: Dr Alexander Pym
Other/Sub-studies:	-
Key Publications:	None

2.3.2 TB CHILD

EDCTP Project Coordinator:	Fred Lwilla
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:	1 August 2010
EDCTP Project End Date:	31 July 2013
Study A: Trial for early evaluation in adults	
Chief Trial investigator	Klaus Reither, Swiss Tropical and Public Health Institute and Ifakara Health Institute
Site Principal Investigator(s):	Nahya Salim Masoud, Ifakara Health Institute, Dar es Salaam, Tanzania; Martin Nusubuga/ Franscesco Aloï, Nsambya Hospital, Kampala, Uganda; Nyanda Elias/Petra Clowes, NIMR-Mbeya Medical Research Programme (MMRP), 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):	<ol style="list-style-type: none"> 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.
Secondary Objective(s):	None
Clinical Trial/Study site(s):	Bagamoyo Research and Training Centre / Ifakara Health Institute, and NIMR-Mbeya Medical Research Programme, Tanzania; Saint Raphael of St. Francis, Nsambya Hospital, Kampala, Uganda.
Collaborating site(s):	Swiss Tropical and Public Health Institute, Basel, Switzerland Klinikum of the University of Munich (LMU), Munich, Germany Italian National Institute for Infectious Diseases, Rome, Italy Fondazione Centro San Raffaele del Monte Tabor, Milan, Italy Foundation for Innovative New Diagnostics (FIND) Geneva, Switzerland Stellenbosch University, Cape Town, South Africa Health Sciences Research Ltd, London, UK LIONEX GmbH, Braunschweig, 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):	<ol style="list-style-type: none"> 1. LHSD Rapid test to detect LAM in sputum or urine 2. Diagnostic potential of IP10 and other biomarkers in blood and urine 3. T cell activation markers on Mycobacterium tuberculosis (MTB) specific T cells (TAM-IGRA) 4. Lab-on-chip based new platform (In-check™) for the molecular diagnosis 5. Newly developed TB diagnostics
Manufacturer/Developer:	<ol style="list-style-type: none"> 1. LIONEX, Braunschweig, Germany 2. Not applicable 3. Not applicable

	4. STMicroelectronics, Geneva, Switzerland 5. Not applicable
Status	Ongoing
Results and Outcomes	Recruitment started 28 March 2011
Study B: New diagnostics for childhood TB	
Chief Trial investigator	Klaus Reither, Swiss Tropical and Public Health Institute and Ifakara Health Institute
Site Principal Investigator(s):	Nahya Salim Masoud, Ifakara Health Institute, Dar es Salaam, Tanzania; Martin Nusubuga/ Franscesco Aloi, Nsambya Hospital, Kampala, Uganda; Nyanda Elias/Petra Clowes, NIMR-Mbeya Medical Research Programme (MMRP), Tanzania
Clinical Trial/Study Sponsor:	Ifakara Health Institute, Dar es Salaam, 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):	<ol style="list-style-type: none"> 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.
Secondary Objective(s):	None
Clinical Trial/Study site(s):	Bagamoyo Research and Training Centre / Ifakara Health Institute, and NIMR-Mbeya Medical Research Programme, Tanzania; Saint Raphael of St. Francis, Nsambya Hospital, Kampala, Uganda
Collaborating site(s):	Swiss Tropical and Public Health Institute, Basel, Switzerland Klinikum of the University of Munich (LMU), Munich, Germany Italian National Institute for Infectious Diseases, Rome, Italy Fondazione Centro San Raffaele del Monte Tabor, Milan, Italy Foundation for Innovative New Diagnostics (FIND) Geneva, Switzerland Stellenbosch University, Cape Town, South Africa Health Sciences Research Ltd, London, UK LIONEX GmbH, Braunschweig, 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.
Number of subjects	Children (between 6 weeks and 14 years old) with suspected TB N=600
Product(s):	<ol style="list-style-type: none"> 1. LHSD Rapid test to detect LAM in sputum or urine 2. Loop-mediated isothermal amplification (LAMP) 3. GeneXpert 4. Diagnostic potential of IP10 and other biomarkers in blood and urine 5. T cell activation markers on Mycobacterium tuberculosis (MTB) specific T cells (TAM-IGRA) 6. Mtb DNA extraction from stool 7. Lab-on-chip based new platform (In-check™) for the molecular diagnosis 8. Ustar TB IAD Kit (Biotech) 9. Pari eFlowrapid nebulizer

	10. Newly developed TB diagnostics
Manufacturer/Developer:	<ol style="list-style-type: none"> 1. LIONEX, Braunschweig, Germany 2. Eiken Chemical Co. Ltd., Tokyo, Japan 3. Cepheid, Sunnyvale, USA 4. Not applicable 5. Not applicable 6. Not applicable 7. STMicroelectronics, Geneva, Switzerland 8. Biotech, China 9. Pari pharma, Germany 10. Not applicable
Cofunders:	<p>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 Universität München (Germany); Swiss Agency for Development and Cooperation (SDC; Switzerland)</p>
Trial Registration number(s):	Not applicable
Status:	Ongoing
Results and Outcomes	First patient in: 28 April 2011
Total number of subjects (clinical trials only):	Total: 1200 (Study A: 300; Study B: 600; PhD 1 : 300)
Total number of subjects (cohort/epidemiological/other studies):	
PhD study-1	<p>Title: Evaluation of Xpert™ 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</p>
PhD study-2	<p>Title: Serum microRNAs as biomarkers for active and latent tuberculosis infection in immunocompetent and immunodeficient hosts. Candidate: Grace Mwangoka</p>
MSc study-1	<p>Title: MSc Applied Microbiology, University Dar es Salaam; Thesis title: Prevalence and Environment sources of Atypical Mycobacteria among Tuberculosis suspects Candidate: Sarah Mswata</p>
MSc study-2	<p>Title: MSc Infectious Diseases, Liverpool School of Tropical Medicine Candidate: Nyanda Elias Ntinginya</p>
Other/Sub-studies:	-
Key Publications:	None

2.3.3 AE TBC

EDCTP Project Coordinator:	Gerhard Walzl
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 <i>Mycobacterium tuberculosis</i> 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 June 2013
Site Principal Investigator(s):	Gerhard Walzl, Stellenbosch University, Tygerberg, South Africa Martin Ota and Jayne Sutherland, Medical Research Council, Banjul, The Gambia Rawleigh Howe, Armauer Hansen Research Institute, Addis Ababa, Ethiopia Desta Kassa, Ethiopian Health and Nutrition Research Institute, Addis Ababa, Ethiopia Harriet Mayanja-Kizza, Makerere University, Kampala, Uganda Neil French, Karonga Prevention Study/LSHTM, Karonga, Malawi Marieta Van der Vyver, University of Namibia, Windhoek, Namibia
Clinical Trial/Study Sponsor:	Stellenbosch University, Tygerberg, South Africa
Trial/Study title:	The evaluation of <i>Mycobacterium tuberculosis</i> 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 <i>Mtb</i> antigens and the measurement of a combination of up to three markers ((EGF, IL-1 α and MIP-1 β) by lateral flow upconverting phosphor technology.
Primary Objective(s):	To evaluate the performance of the combination of levels of EGF, IL-1 α and MIP-1 β 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: <ul style="list-style-type: none"> 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 <i>Mtb</i> 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, Tygerberg, South Africa; Medical Research Council, Banjul, The Gambia; Armauer Hansen Research Institute, Addis Ababa, Ethiopia; Makerere University, Kampala, Uganda; Karonga Prevention Study/LSHTM, Karonga, Malawi; University of Namibia, Windhoek, Namibia Ethiopian Health and Nutrition Research Institute, Addis Ababa, Ethiopia
Collaborating site(s):	Max Planck Society for the Advancement of Science/Max Plank Institute for Infection Biology, Berlin, Germany; LUMC, Leiden, Netherlands; LSHTM, London, UK European Research & Project Office GmbH (Eurice), Saarbruecken, Germany Statens Serum Institute, Denmark
Study design:	Group I: TB suspects (adult, >14 to 65) will be recruited and followed up

	<p>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).</p> <p>Group II: TB suspects (Adult, >14 to 65) 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.</p> <p>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.</p>
Number of subjects	Group I: 800 HIV uninfected TB suspects Group II: 400 HIV infected TB suspects
Product(s):	Commercial <i>in vitro</i> interferon gamma (IFN- γ) release assays (IGRAs): 1. QuantiFERON [®] TB Gold In-Tube 2. T SPOT.TB
Manufacturer/Developer:	1. Cellestis, Victoria, Australia 2. 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)
Trial Registration number(s):	-
Sub-studies:	One MSc studentship: Project title: Mycobacteria-specific cytokine profile in pediatric tuberculosis One PhD studentship: Gene expression and cytokine pattern of pulmonary tuberculosis patients and their contacts in Ethiopia. One Post-Doctoral fellow: Project title: Global transcriptome analyses of blood leukocytes
Status:	Ongoing
Results and Outcomes	First patient in: 9 November 2010
Total number of subjects (cohort/epidemiological/other studies):	N = 1200
PhD study-1	Gene expression and cytokine pattern of pulmonary tuberculosis patients and their contacts in Ethiopia. Adane Mhired Bekele
PhD study-2	-
MSc study-1	Innate immune responses in protection against MTB infection. Khutso Phalane
MSc study-2	Diagnostic potential of memory T cell subtypes in MTB infection. Paulin Essone
MSc study 3	Josephina Nolongo. The evaluation of MTB specific host cytokine signatures in whole blood culture supernatants as diagnostic biomarkers.
Other/Sub-studies:	Global transcriptome analyses of blood leukocytes. Maria Esterhuysen (post-doctoral fellowship)
Key Publications:	1. Chegou NN, Hoek KG, Kriel M, Warren RM, Victor TC, Walzl G.

	<p>Tuberculosis assays: past, present and future. <i>Expert Rev Anti Infect Ther.</i> 2011; 9(4):457-469. (PMID: 21504402)</p> <p>2. Walzl G, Ronacher K, Hanekom W, Scriba TJ, Zumla A. Immunological biomarkers of tuberculosis. <i>Nat Rev Immunol.</i> 2011 Apr 8. [Epub ahead of print] (PMID: 21475309)</p>
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3 Malaria

3.1 Malaria treatment clinical trials

Table 3-1: Summary table of malaria treatment clinical trials supported by EDCTP

Project Acronym (Coordinator)	Phase of trial	Product(s)	Manufacturer / Developer	Study population	Status
4ABC (D'Alessandro)	III	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=4112	Completed
SMAC-II (Kremsner)	II	Artesunate (iv)	WRAIR Sigma-Tau	CHILDREN with severe malaria (6 months to 10 years) N=197	Completed
SMAC-III (Kremsner)	III	Artesunate (iv and im)	Guillin Pharm.	CHILDREN with severe malaria (≤ 14 years) – N=1044	Ongoing
PREGACT (D'Alessandro)	III	Artesunate-amodiaquine Dihydroartemisinin-piperaquine Artesunate-mefloquine Artemether-lumefantrine	Sanofi-Aventis Sigma-Tau Farmanguinhos Novartis	PREGNANT WOMEN+INFANTS (>15 years old) & their newborns N=3480	Ongoing
MiPPAD (Menéndez)	IV	Mefloquine Sulphadoxine-pyrimethamine Cotrimoxazole Placebo	Hoffman-La Roche UCB Pharma Carreras/Bonals	PREGNANT WOMEN+INFANTS (>15 years old) & their newborns N=5783	Ongoing
IPTp – SP (ter Kuile)	IIIb/IV	Sulfadoxine-pyrimethamine Dihydroartemisinin-piperaquine	Durbin PLC Sigma-Tau	PREGNANT WOMEN+INFANT (>16 years old) N=5000	Ongoing
WANECAM (Djimde)	IIIb/IV	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=4032	Not yet recruiting
ADAPT	IIIb	Amodiaquine-artesunate	Sanofi-Aventis	ADULTS HIV+ individuals (step 1 study)	Ongoing

(Mwapasa)		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)]	Sigma-Tau Novartis	N= 66	
FosClin (Issifou)	II/III	Fosmidomycin Clindamycin	Jomaa Pharma	Children N=100	Terminated

3.1.1 4ABC study

EDCTP Project Coordinator:	Umberto D'Alessandro
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:	05 December 2005
EDCTP Project End Date:	30 June 2010
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 Kamyia (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-piperazine (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:

	<p>63 days)</p> <p>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 issues)</p> <p>11) Safety profiles including significant changes in relevant laboratory values (time frame: up to 7 months as described as a safety issue)</p>
Clinical Trial/Study site(s):	Nanoro (Burkina Faso), Afokang and Pamol (Nigeria), Fougamou and Lambaréné (Gabon), Mbarara, Jinja and Tororo (Uganda), Rukara and Mashsha (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:	<p>phase III randomised, controlled, open-label study</p> <p>Randomised controlled trial, comparing 4 combinations of artesunate derivatives:</p> <p><u>Arm 1:</u> 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 <i>Coarsucam</i> by Sanofi-Aventis).</p> <p><u>Arm 2:</u> 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 <i>Eurartekin</i> by Sigma-Tau).</p> <p><u>Arm 3:</u> Intervention with artemether-lumefantrine (AL) consisting of tablets containing 20 mg of Artemether and 120 mg of Lumefantrine (other names for AL are <i>Coartem</i> and <i>Riamet</i> by Novartis)</p> <p><u>Arm 4:</u> 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.</p>
Product(s):	<p>Amodiaquine-artesunate (ASAQ)</p> <p>Dihydroartemisinin-piperaquine (DHAPQ)</p> <p>Artemether-lumefantrine (AL)</p> <p>Lapdap (Chlorproguanil-Dapsone) + artesunate (AS) (CDA)</p>
Manufacturer/Developer:	<p>Sigma-Tau</p> <p>Sanofi-Aventis</p>

	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)
Status:	Completed
Results and Outcomes:	<p>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</p> <p>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</p> <p>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</p> <p>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).</p>
Trial Registration number(s):	00393679 (NCT) http://clinicaltrials.gov/ct2/show/NCT00393679?term=NCT00393679&rank=1
Total number of subjects (clinical trials only):	4,116 children 6-59 months old with uncomplicated <i>P. falciparum</i> malaria
PhD (1)	Adoke Yeka PhD title: <i>The best approach for retreating patients with recurrent malaria in the era of ACT</i> In progress
PhD (2)	Innocent Valéa PhD title: <i>Antimalarial treatment policies in Africa: How to improve the existing strategies? The experience of Burkina Faso</i> In progress
PhD (3)	Sarah Donegan PhD title: <i>The value of individual patient data for mixed treatment comparison meta-analysis</i> In progress
Other/Sub-studies:	Efficacy of quinine, artemether-lumefantrine and dihydroartemisinin-piperazine for recurrent uncomplicated malaria in Ugandan children
Key Publications:	1. 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 Randomized Trial. <i>PLoS Med</i> 8(11): e1001119. doi:10.1371/journal.pmed.1001119

3.1.2 SMAC-II and III (Dose Optimisation Study)

EDCTP Project Coordinator:	Peter G. Kremsner
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:	03 July 2006
EDCTP Project End Date:	05 October 2012
3.1.2.1	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, Geneva (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
Study Timelines:	September 2007 – December 2008
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):	The primary objective of the study is 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 <i>P. falciparum</i> 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 <i>P. falciparum</i> malaria. The study will also evaluate the pharmacokinetic profile of artesunate in pediatric patients. Patients will be randomised to 1 of 2 cohorts. <u>Cohort 1</u> : artesunate 2.4 mg/kg on admission, and at 12, 24, 48, and 72 hours (12 mg/kg total dose); or <u>Cohort 2</u> : 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.

	<p>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.</p> <p>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.</p> <p>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.</p>
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):	00522132 (NCT) http://clinicaltrials.gov/ct2/show/study/NCT00522132?term=NCT00522132&rank=1
Status:	Completed
Results and Outcomes:	<p>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).</p> <p>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.</p>
Total number of subjects (clinical trials only):	200 patients planned, 182 patients analysed (ITT population)
Total number of subjects (cohort/epidemiological/other studies):	93 patients analysed in cohort 1 89 patients analysed in cohort 2
PhD study-1	Matthias Duscha PhD title: <i>Efficacy, Safety and Tolerability of two different regimen of intravenous Artesunate therapy in children with severe malaria</i>
PhD study-2	N/A
MSc study-1	N/A
Other/Sub-studies:	N/A
Key Publications:	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. <i>Journal of Infectious Diseases</i> (published online December 2011).
3.1.2.2	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
Study Timelines	December 2010 – October 2012 (Recruitment period from July 2011 until Aug 2012)
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 im 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: To assess non-invasive oto-acoustic tests linked to disease. To assess predictability of fatal malaria by means of the Lambaréné-Organ-Dysfunction Score (LODS). To analyze genetic polymorphisms in humans and parasites linked to disease and treatment. To assess <i>in vitro</i> 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 <i>P. falciparum</i> 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 randomized to 1 of 3 cohorts.

	<p><u>Cohort 1</u>: iv artesunate 4 mg/kg initially, and at 24 and 48 hours (12 mg/kg total dose); or <u>Cohort 2</u>: im artesunate 4 mg/kg initially, and at 24 and 48 hours (12 mg/kg total dose), or <u>Cohort 3</u>: im artesunate 2.4 mg/kg initially, and at 12, 24, 48, and 72 hours (12 mg/kg total dose).</p> <p>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.</p> <p>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 12h), 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).</p> <p>Recurrent malarial infection within 28 days will be treated with artemether/lumefantrine.</p>
Product(s):	Artesunate
Manufacturer/Developer:	Guillin Pharmaceuticals, Shanghai (China)
Cofunders:	Federal Ministry of Education and Research [BMBF] (Germany),
Status (Major Challenges & Setbacks):	Study sites in Lambaréné, Kumasi, Banjul and Kisumu are actively recruiting, site in Blantyre will start-up in Jan 2012. In order to support the main sites in recruitment, the sister sites in Libreville and Kilifi will also be opened by the end of 2011 or beginning of 2012
Status:	Ongoing
Results and Outcomes:	Ongoing
Trial Registration number(s):	PACTR-registration number: PACTR201102000277177
Total number of subjects (clinical trials only):	1044 patients to be included
Total number of subjects (cohort/epidemiological/other studies):	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 <i>in vitro</i> -sensitivity assay
PhD study-1	N/A
PhD study-2	N/A
MSc study-1	N/A
MSc study-2	N/A
Other/Sub-studies:	<ol style="list-style-type: none"> 1. PK- and exploratory analysis will not be performed on the whole study population but only in selected centers on a limited number of patients: <ol style="list-style-type: none"> a. PK: 300 patients to be analysed from the population recruited in Lambaréné, Kumasi and Kisumu. b. Genetic Polymorphisms: 300 patients to be analysed from the population recruited in Lambaréné, Kumasi and Kisumu. c. Oto-acoustic tests: 200 patients to perform these tests from the populations recruited in Lambaréné, Kumasi and Kisumu. d. In vitro-sensitivity: 200 patients to be analysed from the population recruited in Lambaréné.
Key Publications:	None

3.1.3 PREGACT

EDCTP Project Coordinator:	Umberto D'Alessandro
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:	06 February 2009
EDCTP Project End Date:	05 February 2013
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 (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 <i>P. falciparum</i> 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 <ul style="list-style-type: none"> - 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 <i>P. falciparum</i> malaria; - Birth weight measured within 72 hrs of delivery; 2) To describe the safety profile of AL, AQAS, MQAS and DHAPQ in terms of <ul style="list-style-type: none"> - 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 <i>P. falciparum</i> 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, 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:	<p>phase III randomised, controlled, open label study</p> <p>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”.</p> <p><u>Arm 1</u> (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 <i>Eurartesim</i> and was developed by Sigma Tau in partnership with Medicines for Malaria Venture).</p> <p><u>Arm 2</u> (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).</p> <p><u>Arm 3</u> (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 <i>Winthrop</i>®).</p> <p><u>Arm 4</u> (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 <i>Coartem</i>®, <i>Riamet</i>).</p>
Product(s):	Dihydroartemisinin-piperaquine Artesunate-mefloquine Artesunate-amodiaquine Artemether-lumefantrine
Manufacturer/Developer:	Sigma-Tau

	Farmanguinhos (with the mediation of 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 (BMGF)
Trial Registration number(s):	00852423 (NCT) http://clinicaltrials.gov/ct2/show/NCT00852423?term=NCT00852423&rank=1 201008000248160 (PACTR) http://www.atmregistry.org/ATMWeb/appmanager/atm/atmregistry?_nfb=true&_windowLabel=basicSearch_1_2&basicSearch_1_2_actionOverride=%2Fpageflows%2Ftrial%2FbasicSearch%2FviewTrail&basicSearch_1_2id=248
Status:	In progress
Status (Major Challenges & Setbacks):	Summary of achievements (from February 2009 until February 2011) 1. Recruitment has started in all four countries [Burkina Faso (n = 220) by January 2011; Malawi (n = 41) by January 2011; Zambia (n = 176) by January 2011; Ghana (n >1 ?) by March 2011], with a total of 603 patients enrolled by 03/2011. However, they are behind on their schedule according to their work plan. 2. Thirty-four SAEs have been reported by January 2011. 3. All study sites had a monitoring visit up to date. 4. The Data Safety Monitoring Board (DSMB) had a first meeting on 07 January 2011 and after recruitment started in most of the study sites (please note that the DSMB minutes are provided as annex 8 to the report). 5. Development of a third amendment to the study protocol (and provided as annex 1 to the report), which covers a change in administration of DHAPQ, a change in field site in Malawi and a reduction in the percentage of data to be verified. Previous protocol amendments received ethical approvals in all study sites and this third one has been recently submitted to the ITMA (Antwerp, Belgium) and if approved, it will be submitted to the ethical local authorities of all field sites. 6. In capacity development: 6.1 MSc training for 1 students, PhD training for 3 students are ongoing, including a practical training on parasite genotyping (as part of knowledge exchange) 6.2 Data Management workshop carried out in December 2010. 6.3 Good Clinical Practice training course given by VSCR held in Blantyre (Malawi).
Results and Outcomes:	Ongoing
Total number of subjects (clinical trials only):	3,480
PhD study-1	Michael Nambozi (BF) PhD title: <i>Antimalarial treatment safety and efficacy in pregnant women</i> (Registered at the University of Antwerp, Belgium) In progress
PhD study-2	Marc Tahita (ZM) PhD title: <i>Antimalarial treatment safety and efficacy in pregnant women</i> (Registered at the University of Antwerp, Belgium) In progress

PhD study-3	Christine Manyando (ZM) PhD title: <i>The role of drugs in the control of malaria in pregnancy</i> (Registered at the University of Ghent, Belgium & Zambia) In progress
MSc study-1	Sebastian Hachizovu MSc title: <i>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?</i> (MPH, Diseases Control, 2009-2010, Institute of Tropical Medicine, Antwerp, Belgium) Completed
Other/Sub-studies:	None
Key Publications:	None

3.1.4 MiPPAD

EDCTP Project Coordinator:	Clara Menéndez Santos
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 2013
Trial 1	IPTp-SP versus IPTp-MQ (in HIV non-infected women receiving LLITNS)
Site Principal Investigator(s):	Clara Menéndez Santos (Barcelona, Spain) Achille Massougbodji (Cotonou, Benin) Ghyslain Mombo -Ngoma(Lambaréné, Gabon) Eusebio Macete (Manhiça, Mozambique) Salim Abdulla (Ifakara, Tanzania) Michel Cot (Paris, IRD) Michael Ramharter (Tuebingen, Germany)
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):	1) 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 Développement, 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

	<p>effects of malaria during pregnancy and to compare MQ tolerability of 2 different MQ administration regimens. The three arms of the study will be:</p> <ol style="list-style-type: none"> 1. <u>IPTp with SP + LLITNs</u> (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. <u>IPTp with MQ given as full dose + LLITNs</u> (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. <u>IPTp with MQ given as a split dose + LLITNs</u> (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. <p>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.</p>
Product(s):	Mefloquine (MQ) Sulfadoxine-pyrimethamine (SP)
Manufacturer/Developer:	Hoffman-La Roche Sterop UCB Pharma (GSK manufacturer)
Status:	In progress (recruitment step completed)
Results and Outcomes:	In progress
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):	<ol style="list-style-type: none"> 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), Manhica Health Research Centre, Manhica (Mozambique), Ifakara Health Institute (IHI), Ifakara (Tanzania), Vienna School of Clinical Research (VSCR), Vienna (Austria)
Study design:	<p>Trial 2: phase IV randomised, double-blind Comparing IPTp-MQ versus IPTp- placebo in HIV infected women receiving CTX and LLITNs.</p> <p>This is a randomized double-blind superiority clinical trial to compare the efficacy of MQ as IPTp with placebo-IPTp in HIV-infected pregnant women receiving CTX prophylaxis.</p> <ol style="list-style-type: none"> 1. <u>CTX+IPTp-Placebo+LLITNs</u> (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. <u>CTX + IPTp-MQ+ LLITNs</u> (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. <p>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%.</p>
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)
Status:	In progress
Results and Outcomes:	In progress
Trial Registration number(s):	<p>00811421 (NCT) http://clinicaltrials.gov/ct2/show/study/NCT00811421?term=NCT00811421&rank=1</p> <p>2010020001813440 (PACTR) http://www.atmregistry.org/ATMWeb/appmanager/atm/atmregistry?_nfpb=true&_windowLabel=basicSearch_1_2&_basicSearch_1_2_actionOverride=%2Fpageflows%2Ftrial%2FbasicSearch%2FviewTrail&_basicSearch_1_2id=181</p> <p>2010020001429343 (PACTR) http://www.atmregistry.org/ATMWeb/appmanager/atm/atmregistry?_nfpb=true&_windowLabel=basicSearch_1_2&_basicSearch_1_2_actionOverride=%2Fpageflows%2Ftrial%2FbasicSearch%2FviewTrail&_basicSearch_1_2id=142</p>
Status (Major Challenges & Setbacks):	<p>Summary of the major achievements (from 28 November 2008 until 27 November 2010):</p> <ol style="list-style-type: none"> 1. After a slow start due to long regulatory processes in several sites, both trials are actively recruiting in all 5 African sites since April 2010.

	<p>2. To date more than 50% of Trial 1 and 30% of Trial 2 participants have been recruited.</p> <p>3. Clinical monitoring is carried out in all study sites by the study monitor as well as a subcontracted CRO. Study data are being collected from sites by the monitors and sent to the Central database where data is checked and entered. Safety monitoring covers all reports of serious adverse effects with the support of an independent Data and Safety Monitoring Board. To date there have not been any significant safety concerns in the study.</p> <p>And the main challenges concern mainly achieving the recruitment objectives within the study timelines, because:</p> <p>1. In Trial 1, recruitment in Gabon has been very slow and will hopefully take off with the opening of a second site in 11/10.</p> <p>2. In Trial 2, the low prevalence of HIV/AIDS in Tanzania has obliged a transfer of all but 45 of 360 patients. The financial and logistic aspects of this transfer in addition to the burden of recruiting additional participants in the recipient site remain to be managed. The impact of these setbacks on study timelines shall be better assessed during 2011.</p>																								
Total number of subjects (clinical trials only):	Trial 1: 4716 subjects Trial 2: 1070 subjects																								
PhD study-1	Dominic Mosha (TZ) PhD title: <i>Safety profile of antimalarial drugs during pregnancy in the evaluation framework of alternative antimalarial drugs to sulfadoxine-pyrimethamine in Su-saharan Africa</i> (registered at the University of Basel, the Swiss Tropical Institute, Basel, Switzerland) In progress																								
MSc study-1	Kephas Otieno (KE) MSc title: <i>Effect of cotrimoxazole alone or in combination with mefloquine on antibodies to variant surface antigens (VSAs) in pregnant women in Western Kenya</i> (Kenya Medical Research Institute/Center for Global Health Research, Kisumu, Kenya) In progress																								
Other/Sub-studies:	<p>Ancillary studies</p> <p>The Ancillary studies approved to date by the MiPPAD ExCom are listed below:</p> <table border="1"> <tr> <td>1</td> <td>Benin</td> <td>Aetiology of anemia in pregnancy and consequences on the infants in a malaria endemic area.</td> </tr> <tr> <td>2</td> <td>Gabon</td> <td>Immunological changes related to Helminth co-infections and association with malaria pregnancy outcomes</td> </tr> <tr> <td>3</td> <td>Gabon</td> <td>HHV-8 infection in pregnant women and the potential for in utero transmission to newborns</td> </tr> <tr> <td>4</td> <td>Gabon</td> <td>Mefloquine pharmacogenetics</td> </tr> <tr> <td>5</td> <td>Gabon</td> <td>Effects of IPTp with mefloquine and sulfadoxine pyrimethamine on sexually transmitted diseases (STDs) and group B streptococcal colonization</td> </tr> <tr> <td>6</td> <td>Gabon</td> <td>Effect of mefloquine on urinary schistosomiasis</td> </tr> <tr> <td>7</td> <td>Kenya</td> <td>Determine whether the coadministration of mefloquine changes steady-state concentrations of sulfamethoxazole and trimethoprim in pregnant HIV-infected women</td> </tr> <tr> <td>8</td> <td>Kenya</td> <td>Determine the effect of daily cotrimoxazole prophylaxis on genital-tract bacterial carriage and postpartum morbidity in HIV-infected women</td> </tr> </table>	1	Benin	Aetiology of anemia in pregnancy and consequences on the infants in a malaria endemic area.	2	Gabon	Immunological changes related to Helminth co-infections and association with malaria pregnancy outcomes	3	Gabon	HHV-8 infection in pregnant women and the potential for in utero transmission to newborns	4	Gabon	Mefloquine pharmacogenetics	5	Gabon	Effects of IPTp with mefloquine and sulfadoxine pyrimethamine on sexually transmitted diseases (STDs) and group B streptococcal colonization	6	Gabon	Effect of mefloquine on urinary schistosomiasis	7	Kenya	Determine whether the coadministration of mefloquine changes steady-state concentrations of sulfamethoxazole and trimethoprim in pregnant HIV-infected women	8	Kenya	Determine the effect of daily cotrimoxazole prophylaxis on genital-tract bacterial carriage and postpartum morbidity in HIV-infected women
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	9	Mozambique	Molecular markers of antimalarial drug resistance in the context of the intermittent preventive treatment trials for malaria in pregnant women: <i>P. falciparum</i> genetic background, immunity, trial efficacy and development of resistance
	10	Mozambique	Role of maternal immuno-endocrine factors on delivery outcomes of malaria-exposed pregnant women in the context of intermittent preventive treatment trials in Africa
	11	Tanzania	The contribution of dual infection with malaria and HPV virus on pregnancy outcome in sub-Saharan Africa
	12	Gabon	Infection Biology and Epidemiology of Staphylococci and Staphylococcal Diseases in sub-Saharan Africa
	13	Mozambique	Perceptions and behaviours related to prevention of MiP in Manhiça District, Mozambique (MiP-Soc)
	14	Mozambique	Malaria resistance during pregnancy
	15	Gabon	Population Pharmacokinetics of Mefloquine AS Intermittent Preventive Treatment FOR MALARIA in Pregnancy
	16	Mozambique	Malaria decline in the context of pregnancy (MiPredux)
Key Publications:	None		

3.1.5 IPTp-SP

EDCTP Project Coordinator:	Feiko ter Kuile
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 2012
3.1.5.1	IPTp-Mon study
Site Principal Investigator(s):	Kassoum Kayentao (Malaria Research and Training Centre, Mali), S.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 adverse effect 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 <i>P. falciparum</i> 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 recrudescence, 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' <i>in-vivo</i> data from the weekly follow-up to determine the potential validity of a 'sparse' 'population' sampling methodology for future therapeutic <i>in-vivo</i> 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), Vienna School of Clinical Research (VSCR, Austria), 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:	<p>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.</p> <p>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:</p> <ol style="list-style-type: none"> 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 antifolate resistance mutations in <i>P. falciparum</i>) 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 will be followed weekly for 42 days to assess the parasitological response (therapeutic efficacy) and the ability to prevent new infection. Parasites will be genotyped to distinguish between recrudescence 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 [BMGF] (USA)
Status:	Ongoing
Results and Outcomes:	Not yet applicable
Trial Registration number(s):	NA
Total number of subjects (clinical trials only):	256 per site (in-vivo module), and up to 1100 deliveries per site
3.1.5.2	ISTp-Malawi
Site Principal Investigator(s):	Linda Kalilani-Phiri (Blantyre, Malawi). 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):	4 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). Manhica Health Research Centre (Mozambique),
Study design:	<p>Phase IIIb, two arm multi-centre randomised controlled superiority trial to be conducted at 4 sites in southern Malawi with high levels of SP resistance and high ITN coverage.</p> <ol style="list-style-type: none"> <u>Arm 1</u> (IPTp-SP): 3 or 4-dose regimen of IPTp with SP. <u>Arm 2</u> (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). <p>Participants will be 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 will be given an insecticide-treated bed net if they do not already have one. Women enrolled in the trial will 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.</p> <p>Newborns will be seen at approximately seven days and six weeks after delivery, to assess the health of the infant.</p> <p>The study will be open label as it will not be possible to blind the participants to their allocation, although where possible laboratory staff undertaking trial-related diagnostic tests will be blinded.</p> <p>Participants will be HIV-negative pregnant women. They will be screened for eligibility and enrolled at 16 to 29 weeks gestation.</p> <p>The study will recruit 1655 participants and is expected to start in the 2nd quarter of 2011 and recruit for a period of 18 to 24 months, with a further six months follow-up.</p>

Product(s):	Sulphadoxine-pyrimethamine (SP) Dihydroartemisinin-piperaquine (DHA-PQ or DP)
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 [BMGF] (USA)
Status:	Not yet Recruiting
Results and Outcomes:	Not yet applicable.
Trial Registration number(s):	ISRCTN69800930 PACTR201103000280319
Total number of subjects (clinical trials only):	1665
3.1.5.3	IST – IPTp study West Africa
Site Principal Investigator(s):	Harry Tagbor (Ghana), Abraham Hodgson (Ghana), Kassoum Kayentao (MRTC, Mali), Sheick 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) and 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), Manhica Health Research Centre (Mozambique)
Study design:	Phase IV, two-arm, multi-centre, open, randomised, controlled, non-inferiority trial comparing two malaria control strategies in pregnancy is proposed. The study groups will be as follows: 1. <u>Arm 1</u> (SP-IPTp SP according to WHO recommendations): women will receive at least two doses of SP during their

	<p>pregnancy, one at each of the recommended ante-natal visits during the 2nd and 3rd trimester. Women in this arm will be the reference group.</p> <p>2. <u>Arm 2</u> (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.</p> <p>All study women will be provided with an LLIN at their first attendance at the ANC and given instructions on how to use it. Random home visits will be made to check on net usage during the pregnancy.</p>
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 [BMGF] (USA)
Status:	In progress
Status (Major Challenges & Setbacks):	<p>Summary of major achievements (from 18 December 2008 until 17 December 2010)</p> <p>West-Africa: Trial 2 (IPTp-SP vs Intermittent-screening-treatment [ISTp]) initiation with 1731 women recruited until December 2010. Three coordination meetings held in Burkina Faso, Tanzania, and Ghana. Two monitoring visits conducted in each site, and networking functions facilitated by the MiP Consortium secretariat in Liverpool are working well.</p> <p>Malawi: Trial 1 was redesigned in 2010 into 'Trial-1b' and is comparing IPTp-SP with ISTp in areas with high SP-resistance. Study Clinical Protocol received ethics approval, and trial initiation awaits final trial authorisation from the Malawian regulatory authorities, however, it can be anticipated a start date of March 2011.</p> <p>SP-resistance (IPTp-Mon): combines data across sites to assess impact of SP resistance on IPTp-SP effectiveness. Completed baseline observational studies in Malawi and Mali and molecular typing for resistance markers ongoing.</p> <p>In capacity development:</p> <ol style="list-style-type: none"> MSc training for 2 students and PhD training for 2 students are ongoing. IPTp-Mon baseline studies ongoing in the sister site in Burkina Faso: 47% of recruitment completed. Three centralised training courses given by VSCR were held in Nairobi and attended by all 5 sites (Project Management and Foundations in Clinical Research; Introduction to Good Clinical Laboratory Practice; Introduction to Clinical Research & Epidemiology. Additional workshop on trial site management held in Malawi). Additional Data Management workshop and Histology onsite training has been undertaken for trial 2 sites. Infrastructural upgrading is ongoing in all sites. <p>WP4 Networking:</p> <ol style="list-style-type: none"> Project meeting took place in June 2010 in Dar-es-Salaam (Tanzania). Preliminary results of the SP-resistance study presented at ASTMH 2010.
Results and Outcomes:	In progress

Trial Registration number(s):	01084213 (NCT) http://clinicaltrials.gov/ct2/show/NCT01084213?term=nct01084213&rank=1
Total number of subjects (clinical trials only):	4500
Total number of subjects (cohort/epidemiological/other studies):	512 in-vivo follow-up of women receiving SP for IPTp
PhD study-1	Kassoum Kayentao (Mali) PhD title: <i>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</i> (Liverpool School of Tropical Medicine, Liverpool, UK & Medical Research and Training Centre, University of Bamako, Mali) In progress
PhD study-2	John Williams (Ghana) PhD title: <i>The Diagnosis of malaria in pregnancy in west-Africa</i> (London School of Hygiene and Tropical Medicine, London, UK & Navrongo Health Research Centre, Navrongo, Ghana) In progress
MSc study-1	MBA (distance learning) - Mamkumba Sanneh (The Gambia)
MSc study-2	Master Clinical trials (distance learning)- Gerald Mwapasa (Malawi)
Other/Sub-studies:	<u>Economic</u> : 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. <u>Acceptability and implementability</u> : to explore the implementability, acceptability, feasibility and potential for scale-up of ISTp in Malawi.
Key Publications:	None

3.1.6 WANECAM

EDCTP Project Coordinator:	Abdoulaye Djimdé
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
EDCTP Project Code:	IP.2007.31060.002
EDCTP Project Start Date:	15 September 2009
EDCTP Project End Date:	15 March 2013
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 <i>Plasmodium</i> 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 will be 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 will be 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:	<p>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.</p> <p>Patients will be followed for 2 years starting from the first enrolment with the randomised study drug.</p> <p>In each site, eligible subjects will be randomised into 3 treatments arms:</p> <ol style="list-style-type: none"> 1. <u>Arm 1</u>: dihydroartemisinin-piperaquine (DHA-PQP), 2. <u>Arm 2</u>: pyronaridine tetrphosphate/artesunate (pyramax, PA), 3. <u>Arm 3</u>: either artemether-lumefantrine (AL) or artesunate-amodiaquine (ASAQ) (as first line ACT treatment). <p>The total number of patients to be randomized per country is 448. Depending on the study site, DHA-PQP on one hand and PA on the other hand 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) will be 1344.</p> <p>The total number of patients being randomized in the comparator drug (AL or ASAQ) will be 1344. The comparator 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.</p> <p>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.</p>
Product(s):	<p>Pyramax: pyronaridine tetrphosphate/artesunate (PA) combined tablet or granule for oral administration.</p> <p>Eurartesim: dihydroartemisinin-piperaquine (DHA-PQP) combined tablet for oral administration.</p> <p>ASAQ-Winthrop/Coarsucam: artesunate-amodiaquine (ASAQ) combined tablet for oral administration.</p> <p>Coartem or Coartem-D: artemether-lumefantrine (AL) combined tablet or dispersible tablet for oral administration.</p>
Manufacturer/Developer:	<p>Novartis Sanofi-Aventis Sigma Tau Shin Poong Pharmaceutical</p>
Cofunders:	<p>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)</p>
Status:	<p>Recruiting as of 24 October 2011 for the Pyramax arm in the study site of Sotuba (Mali)</p>
Status (Major Challenges & Setbacks):	<p>The major achievements of these studies to date have been:</p> <ul style="list-style-type: none"> - The observational study conducted in Guinea has been completed and a total of 606 subjects were recruited. The active and passive surveillance of that cohort has resulted in 122 cases of malaria, which were included in the prospective artesunate-amodiaquine <i>in vivo</i> efficacy study. - Negotiations with the pharmaceutical partners have been now successfully completed. Agreements were signed with MMV and Shin Poong and signatures are pending with Sigma Tau and Sanofi-Aventis. - The longitudinal study has been registered with PACTR (with code PACTR201105000286876, and linked to ICTRP website, i.e. http://apps.who.int/trialsearch/trial.aspx?trialid=PACTR201105000286876) - The clinical trial started on 25 October 2011 in the study site of Sotuba (Mali), where patient recruitment for the Pyramax arm is ongoing (site initiation visits are underway for the remaining study

	<p>sites in Mali and Burkina Faso).</p> <ul style="list-style-type: none"> - Site upgrades have been completed in all trial participating sites. - All PhD and MSc students are progressing in their respective hosting universities. - Several short-term trainings were carried out in each of the participating institutions. - Several Networking activities including North-South, South-South and North-North Networking activities have been carried out during this reporting period, including an Investigators Meeting attended by 44 collaborators and MMV in Bobo Dioulasso (Burkina Faso). - A publication accepted in the <i>Malaria Journal</i> (November 2010) on measurement of parasite clearance by qPCR (see attached annex 2 for a copy of the publication). - Three abstracts resulting from project activities were presented at the 6th EDCTP Forum held in Addis Ababa (8-12 October 2011). - Three additional abstracts were accepted for presentation at the upcoming American Society of Tropical Medicine and Hygiene Annual meeting to be held in Philadelphia in December 2011. <p>Setbacks:</p> <ul style="list-style-type: none"> - The longitudinal trials were originally scheduled to begin at the commencement of the malaria transmission season in Mali and Burkina Faso in June 2011; however, as the study drugs delivery was delayed, patient recruitment was starting in October 2011. This delay will be mitigated by the additional study site in Mali.
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
Trial Registration number(s):	PACTR201105000286876 http://www.atmregistry.org/ATMWeb/appmanager/atm/atmregistry?_nfpb=true&_windowLabel=basicSearch_1_2&basicSearch_1_2_actionOverride=%2Fpageflows%2Ftrial%2FbasicSearch%2FviewTrail&basicSearch_1_2id=286
Total number of subjects (clinical trials only):	4032
Total number of subjects (cohort/epidemiological/other studies):	600
PhD -1	<i>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.</i> Name of candidate: Mr. Issaka Sagara (Mali) Training University: Universite de Marseille, France
PhD -2	<i>A pilot study of the efficacy of artesunate in the treatment of uncomplicated malaria in Bougoula-Hameau, Sikasso, Mali</i> Name of candidate: Mrs. Aminatou Kone Training University: Karolinska Institute, Stockholm, Sweden
PhD -3	Study title: <i>Pharmacodynamic-pharmacokinetic analysis of the effect of artemisinin-based combination therapies on recurrent episodes of uncomplicated P. falciparum malaria</i> Name of candidate: Mr. Mamadou Tekete (Mali) Training Institution: Heidelberg University
MSc -1	Study title: <i>Epidemiology, Clinical Research</i> Name of candidate: Ms. Esperance Ouedraogo (Burkina Faso) Training Institution: Vienna School of Clinical Research, Vienna, Austria
MSc -2	Study title: <i>Medical Parasitology & Entomology</i> Name of candidate: Mr. Moussa Sylla (Guinea) Training Institution: University of Bobo Dioulasso, Burkina Faso
MSc -3	Study title: <i>Molecular Parasitology</i> Name of Candidate: Ms. Elizabeth Diawara (Guinea) Training Institution: University of Bamako, Mali
Other/Sub-studies:	Baseline malaria epidemiology and normal references ranges for biological parameters in Maferya, Guinea.

	<p><u>Objectives:</u> 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.</p> <p><u>Study Design:</u> 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.</p>
Key Publications:	<p><i>Measuring the efficacy of anti-malarial drugs in vivo: quantitative PCR measurement of parasite clearance.</i> Khalid B Beshir, Rachel L Hallett, Alice C Eziefula, Robin Bailey, Julie Watson, Stephen G Wright, Peter L Chiodini, Spencer D Polley, Colin J Sutherland. <i>Malaria Journal</i> 2010, 9:312</p>

3.1.7 ADAPT

EDCTP Project Coordinator:	Victor Mwapasa
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:	13 July 2014

Theme 1	ARV – ACT trial
Site Principal Investigator(s):	Victor Mwapasa (Malawi)
Clinical Trial/Study Sponsor:	Liverpool School of Tropical Medicine, Liverpool (UK)
Trial/Study title:	Pharmacokinetic studies of interactions between Artemisinin-based Combination Therapies and Antiretroviral Therapies in Malawi.
Goal:	<p>This study aims to assess the safety or efficacy of ACTs such as AL, AQ-AS and DHA-PPQ in HIV-infected individuals who are on ART and examine the nature of interaction between ARVs and ACTs.</p> <p>To reduce malaria-associated morbidity and mortality in three special populations by determining the most appropriate ACT treatment for each of these groups and to improve the research capacity of three African countries, Malawi, Mozambique and Zambia to conduct ICH-GCP compliant clinical trials.</p>
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):	<p>1) To compare the pharmacokinetic parameters (Area Under time-concentration Curve [AUC_{0-t}], maximum concentration [C_{max}], time to maximum concentration [t_{max}], terminal elimination half life [t_{1/2}]) 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.</p> <p>2) To compare the pharmacokinetic parameters (C_{max}, AUC_{0-t}, t_{max} and t_{1/2}) 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.</p> <p>3) To compare the pharmacokinetic parameters (C_{max}, AUC_{0-t}, t_{max} and t_{1/2}) 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.</p> <p>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.</p>
Clinical Trial/Study site(s):	ART Clinic at Queen Elizabeth Central Hospital (QECH, Blantyre Malawi), Ndola, (Zambia), and Manhica (Mozambique).
Collaborating site(s):	Malawi-Liverpool-Wellcome Trust Clinical Research Programme and

	Department of Medicine, College of Medicine (Malawi), Manhica Health Research Center (CISM), Manhica, (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)
Study design:	<p>Phase IIIb studies.</p> <p>Single centre, open-label, dose-escalation, drug-drug interaction pharmacokinetic study. The study will be implemented in the following two steps:</p> <ol style="list-style-type: none"> 1. In Step 1, half adult dose of the ACTs will be 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 will serve as a safety evaluation step in drug interaction studies, checking for unexpected clinical toxicities or interactions. Blood samples for data-rich pharmacokinetic assays will be collected over 72 hours alongside real time clinical, biochemical and haematological monitoring for severe adverse events. Pharmacokinetic parameters including AUC, C_{max}, T_{max} and t_{1/2} will be determined and compared with existing historical data to establish the nature and extent of any drug interaction. Initial data-rich PK studies of interactions between ART and different ACT options in HIV infected participants (N=120) will be followed by efficacy and safety studies of the selected ACTs with suitable PK profiles (N=900) (labelled as Project 1). 2. In Step 2 (assuming that no significant adverse events or high drug levels occur in step 1), a data-rich pharmacokinetic study of full dose ACT will be undertaken over 72 hours 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. <p>It is expected that the study participants will be receiving any of the following nationally recommended ART regimes;</p> <ol style="list-style-type: none"> 1. 3TC (150mg) -d4T (30mg)-NVP (200mg), 1 tablet 12-hourly. Most of our 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) every 12 hours because of d4T toxicity. 2. 3TC (150mg) -d4T (30mg) 12-hourly plus Efavirenz (EFV; 600mg) every 24 hours 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. 3. 3TC (150mg) -AZT (300mg) every 12 hours plus Tenofovir (TDF; 300mg) once daily plus Lopinavir (200mg)/ritonavir (50mg) 2 tablets every 12 hours.
Product(s):	<p>Artemether-Lumefantrine (AL), (Coartem®, Novartis)</p> <p>Artesunate-Amodiaquine, (Coarsucam™, Sanofi-Aventis)</p> <p>DHA-piperaquine, ((Euratesim®), Sigma Tau)</p> <p>Antiretroviral drug combinations: 3TC-d4T-NVP, Trioimmune, Cipla), 3TC-AZT-EFV (combivir plus efavirenz, 3TC-AZT-NVP (combivir plus NVP)TDF-3TC-AZT-LPV/r (tenofovir, combivir plus lopinavir/ritonavir).</p>
Manufacturer/Developer:	<p>Novartis</p> <p>Sanofi-Aventis</p> <p>Sigma Tau</p>
Trial Registration number(s):	<p>ATMR 2010030001871293 (Phase I, step 1 study)</p> <p>ATMR 2010030001971409 (Phase I, step 2 study)</p>
Cofunders:	<p>Carlos III Health Institute (Spain), MRC UK (UK), Austrian Federal Ministry of Science (Austria)</p>

Status (Major Challenges & Setbacks):	<p>Major achievements:</p> <ul style="list-style-type: none"> - Setting up of shared management structure at MLW and LSTM. - DSMB constituted and operational, with two DSMB meetings held on 17 August 2010 and 04 November 2010. - Enrolment and followed up of study participants for Phase 1 Step 1 study completed with the exception for the PI-based ARV arm. - Infrastructure upgrades at Queen Elizabeth Central Hospital completed, including acquisition of most study equipment. - Two PhD candidates enrolled on their long-term training programmes (one at University of Liverpool and the second one at University of Antwerp) and 1 MSc candidate enrolled at the University of Antwerp. - Completed training of relevant study staff in GCP, GCLP, Research Ethics and Clinical Trial Site Management. Two MLW Lab Scientists trained in conducting HPLC assays at LSTM. <p>And the main challenges concern mainly achieving the recruitment objectives within the study timelines, because:</p> <ul style="list-style-type: none"> - Delays in signing sub-contracts with collaborating institutions; however, this does not delay the progress of the overall project. - Temporary suspension of enrolment of study participants has delayed completion of Phase 1 Step 1 study resulting in delay in all subsequent activities. - Difficulties in finding eligible study participants on EFV and PI-based ARVs. - Delays in completing the setting up of the HPLC machine due to delayed procurement and delivery of RapidVap vacuum Evaporation system for the HPLC machine.
Results and Outcomes:	In progress

Theme 2	<i>Label Expansion studies</i>
Site Principal Investigator(s):	Victor Mwapasa (Malawi)
Clinical Trial/Study Sponsor:	Liverpool School of Tropical Medicine, Liverpool (UK)
Trial/Study title:	Facility-based pharmacokinetic and pharmacodynamic studies of ACTs in severely malnourished children and young infants.
Goal:	<p>Theme 2, Project 2: Paediatric special groups This study aims to determine the appropriate dose and regimen severely malnourished children and young infants.</p> <p>Theme 2, Project 3 This study aims to determine evidence for translation of the weight-based dosing regimens to age-based regimens.</p>
Primary Objective(s):	To optimize the dose in mg/kg body weight the antimalarials artemether-lumefantrine, artesunate-amodiaquine and dihydroartemisinin-piperaquine: of for use in young infants and malnourished children as part of a regulatory process leading to drug label expansion or restriction.
Secondary Objective(s):	<p>To determine</p> <ol style="list-style-type: none"> 1. Whether young infants (As-AQ and DHA-PPQ: <6 months, AL<5 kg) or severely malnourished children require dose adjustment because of differences in their pharmacokinetics compared to the older or better nourished populations. 2. To investigate the relationship between drug pharmacokinetics and pharmacodynamics in 150 young infants and 150 severely malnourished children (i.e. the relationship between drug exposure and drug efficacy and safety).
Clinical Trial/Study site(s):	Blantyre and Zomba (Malawi)
Collaborating site(s):	Malawi-Liverpool-Wellcome Trust Clinical Research Programme and Department of Medicine, College of Medicine (Malawi), Manhica Health Research Center (CISM), Manhica, (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)
Study design:	<p>Theme 2 includes label expansion studies in very young infants, malnourished children (labelled as Project 2) and age-based dosing studies (labelled as Project 3).</p> <p>The proposed work involves an open label rich PK phase followed by 3 open label single arm trials (one for each ACT). Rich pharmacokinetic data will be collected from small groups of infants and an equal number of severely malnourished children < 5 years of age Maximum individual blood volumes will not exceed 1ml and over the sampling period will not exceed 10ml.</p> <p>The resulting data will be compared with published or background data from the pharmaceutical developers on PK profiles and known drug exposure levels associated with drug efficacy (e.g. AUC or day 7 drug levels for lumefantrine). Subject to the results it may be necessary to consider a dosage adjustment at this stage. This will take 12 months to complete with the option for a subsequent study in the case of any rational dosage adjustment.</p> <p>The subsequent study will involve the evaluation of the PK: PD relationship in terms of safety and efficacy and will involve sparse PK sampling and population PK:PD modelling. The study will be open label and single arm. i.e. three identical studies one for each ACT.</p> <p><u>Project 2:</u> Pharmacokinetic (PK) studies with the 3 ACTs are performed in special paediatric populations consisting of (a) infants<6 months of age or <5kg and (b) in severely malnourished children in Malawi (N=110). A subsequent large two centre pharmaco-dynamic study of ACTs with a suitable PK profiles is done in the same subgroups to assess safety and efficacy in 450 young infants and 450 severely malnourished children. This larger trial includes sparse (population) sampling for drug assays to further define the determination of the PK profile and to correlate achieved drug levels to tolerance, safety and efficacy.</p> <p><u>Project 3:</u> 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. 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).</p>
Product(s):	Artemether-Lumefantrine (AL), (Coartem®, Novartis) Artesunate-Amodiaquine, (Coarsucam™, Sanofi-Aventis) DHA-piperazine, ((Euratesim®), Sigma Tau)
Manufacturer/Developer:	Novartis Sanofi-Aventis Sigma Tau Antiretroviral drug combinations: 3TC-d4T-NVP, Trioimmune, Cipla), 3TC-AZT-EFV (combivir plus efavirenz, 3TC-AZT-NVP (combivir plus NVP)TDF-3TC-AZT-LPV/r (tenofovir, combivir plus lopinavir/ritonavir).
Cofunders:	Carlos III Health Institute (Spain), MRC UK (UK), Austrian Federal Ministry of Science (Austria)
Status:	–
Results and Outcomes:	–
Trial Registration number(s):	NA
PhD (1)	Mavuto Mukaka (MW) PhD title: <i>Review and development of statistical methodologies for handling missing observations in comparative and non-comparative anti-malarial efficacy and pharmacokinetic /pharmacodynamic studies</i> (Registered at the LSTM, UK)
PhD (2)	Victor Chalwe (ZM)

	PhD title: <i>Interaction between HIV and malaria: implications for public health and medical decision making</i> (Registered at ITM, Antwerp, BE)
MSc (1)	Rueben Dickman Ndindi, MSc in Computer Science focussed on Data Management (training institution: University of Edinburg, UK)
MSc (MPH)	Sebastian Hachizovu (ZM), MPH in Public Health Disease Control (training institution: ITM, BE) Status: Completed
Key Publications:	None

3.1.8 FosClin

EDCTP Project Coordinators:	Saadou Issifou, Peter Kremsner
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 <i>plasmodium falciparum</i> malaria. <i>Clinical Trial terminated because data from another study demonstrated low efficacy in children under the age of three years.</i>
EDCTP Project Code:	IP.2008.31060.003
EDCTP Project Start Date:	29 January 2010
EDCTP Project End Date (Initially planned):	31 December 2013
Clinical trial termination date:	15 July 2011
Capacity Building	PhD studentship: Dr José Francisco FERNANDES "Resistance phenotyping and transmission kinetics of clinical <i>P. falciparum</i> isolates under fosmidomycin treatment"

3.2 Malaria vaccines clinical trials

Table 3-2: Summary table of malaria vaccines clinical trials supported by EDCTP

Project Acronym (Coordinator)	Phase of trial	Product(s)	Manufacturer / Developer	Study population	Status of trial
GMZ2 (Ejigu)	II	GLURP + MSP3 hybrid	EMVI/SSI, Denmark	Adults N=1840	Ongoing
MVVC (Imoukhuede)	I/II	Adenovirus TRAP + MSP1 and MVA TRAP + MSP1	Impfstoffwerke Dessau-Tornau in Germany	Adults and young children N= 1526	Ongoing

3.2.1 GMZ2

EDCTP Project Coordinator:	Dawit Ejigu
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
Site Principal Investigator(s):	Sodiomon Sirima, Saadou Issifou, Fred Kironde, Atuguba Frank
Clinical Trial/Study Sponsor:	AMANET
Trial/Study title:	<p>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.</p> <p>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.</p>
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):	<p>1) 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.</p> <p>2) 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.</p>
Secondary Objective(s):	<p>1) Phase IB</p> <ol style="list-style-type: none"> i. 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. ii. 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. <p>2) Phase IIB</p> <ol style="list-style-type: none"> i. 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. ii. 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. iii. 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

	<p>and 48 hours of stimulation using Th1/Th2 Cytometric Bead Arrays.</p> <p>iv. 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</p>
Clinical Trial/Study site(s):	<ul style="list-style-type: none"> - MRU Lambaréné- Gabon - CNRFP - Burkina Faso - Makerere University - Uganda - Navrongo Medical Research Centre (NMRC) - Ghana
Collaborating site(s):	<ul style="list-style-type: none"> - Medical Research Council Laboratories Gambia - London School of Hygiene and Tropical Medicine (LSHTM) (UK) - Staten Serum Institut (Denmark) - Albert Schweitzer Hospital-Gabon - Makerere University-Uganda - Centre national de recherche de Formation sur le Paludisme (CNRFP) – Burkina Faso - Navrongo Medical Research Centre (NMRC) - Ghana - University of Tübingen - Germany
Study design:	<p>Phase IB: Double-blind, randomised, and controlled trial</p> <p>Phase IIB: Double-blind, randomised, controlled, Multi-centre trial</p>
Product:	GMZ2
Manufacturer/Developer:	SSI, Denmark
Cofunders	<ul style="list-style-type: none"> - University of Tübingen - Statens Serum Institut - European Vaccine Initiative (former EMVI), - Federal Ministry of Education and Research (BMBF) - Germany - African Malaria Network Trust - Department for International Development (DFID)
Trial Registration number(s):	ATMR2010060002033537
Status	Ongoing, the baseline studies have been completed at all sites. Phase IIB began in Gabon, the next site to start recruitment for phase IIB is Burkina Faso in April 2011, Both the Ugandan and Ghanaian sites have already received all the required approvals and soon will initiate their phase IIB studies.
Results and Outcomes:	The results of baseline studies provided guidance for the sample size of phase IIB.
Total number of subjects (clinical trials only):	1840 subjects to be recruited in total
Total number of subjects (cohort/epidemiological/other studies):	Baseline studies of at least 300 children per site have been completed
PhD study-1	Humoral Immune Responses and Immunological Memory Against Plasmodium Falciparum Malaria Antigens - Dr Kaddumark Mukasa
PhD study-2	Protective role of IgG and FcγR in malaria - Tiendrebeogo Régis Wendpayangde
MSc study-1	MSc IT Professional (Databases) - Abubakar Ismaela
Other/Sub-studies:	NA
Key Publications:	<ol style="list-style-type: none"> 1) B. Mordmüller et al. Safety and immunogenicity of the malaria vaccine candidate GMZ2 in malaria-exposed, adult individuals from Lambaréné, Gabon. <i>Vaccine</i> 28 (2010) 6698–6703 2) Belard S, Issifou S, Hounkpatin AB, Schaumburg F, Ngoa UA, et al. (2011) A Randomized Controlled Phase Ib Trial of the Malaria Vaccine Candidate GMZ2 in African Children. PLoS ONE 6(7): e22525. doi:10.1371/journal.pone.0022525

3.2.2 MVVC

EDCTP Project Coordinator:	Egeruan Babatunde Imoukhuede,
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-Dec-09
EDCTP Project End Date:	17-Dec-13
Site Principal Investigator(s):	Bojang Kalifa, Caroline Ogwang
Clinical Trial/Study Sponsor:	University of Oxford
Trial/Study title:	Safety, Immunogenicity and Efficacy Study of Adenoviral-MVA prime-boost Vaccination for Preventing Clinical Malaria in Young African Children: a large multi-site phase IIB trial following two initial phase Ib trials.
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):	<ul style="list-style-type: none"> - Demonstration of the safety and immunogenicity of a new adenovirus encoding malaria antigens in adults and young children in sub-Saharan Africa. - 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. - 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):	<ul style="list-style-type: none"> - The phase I trial in Kenyan adults and children will be undertaken at the KEMRI coastal research unit at Kilifi, Kenya. - The phase I study in Gambians will be undertaken at the Sukuta site near to Banjul in The Gambia. - The phase IIB study will be undertaken at two or three sites following a small lead-in safety study at each site. These sites are: the University of Dakar site in Kerr Soce, Senegal; the CNRFP Banfora site in Burkina Faso and the KEMRI Kilifi site in Kenya
Collaborating site(s):	<ul style="list-style-type: none"> - The Centre National de Recherche et de Formation sur le Paludisme (CNRFP) - Burkina Faso - KEMRI Wellcome Trust Centre, Kilifi - MRC The Gambia, Farafenni and Sukuta Field Stations; - Université Cheikh Anta Diop (UCAD) - The European Vaccine Initiative (EVI) - University of Oxford (UOXF) - Okairòs s.r.l. - Vienna School of Clinical Research
Study design:	Randomised, controlled, double-blind phase IIB efficacy trial
Product:	Adenovirus ME-TRAP and MVA ME-TRAP
Manufacturer/Developer:	Impfstoffwerke Dessau-Tornau in Germany
Cofunders:	<ul style="list-style-type: none"> - 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 - Okairòs s.r.l - Italy - Vienna School of Clinical Research - Austria - Centre national de recherche de Formation sur le Paludisme

	(CNRFP) – Burkina Faso - Medical Research Council Laboratories Gambia - Austrian Federal Ministry of Science - Austria - European Vaccine Initiative (former EMVI) - Université Cheikh Anta DIOP de Dakar (UCAD) – Senegal
Trial Registration number(s):	- Trial K (Phase Ib trial in Kenyan adults): ATMR2010020001771828 - Trial G (Phase Ib trial in Gambian adults): PACTR201008000221638
Sub-studies:	Evaluation of the impact of clinical trials on quality of health care delivery in Africa and Asia
Status:	Ongoing, phase Ib trials in adults started in June 2010 in Kenya and Gambia, the protocol for trial G paediatric arm is being prepared for submission, baseline epidemiological studies started in Senegal and Burkina Faso in November 2010
Results and outcomes:	-
Total number of subjects (clinical trials only):	1526
Total number of subjects (cohort/epidemiological/other studies):	680
PhD study-1	Evaluation of the impact of clinical trials on quality of health care delivery in Africa and Asia - Dr Mohammed Afolabi)
PhD study-2	(Study title to be determined) - David Kagoye
PhD study-3	(Study title to be determined) - Dr Aly Gueye
MSc study-1	(Study title to be determined) - Dr Massamba Syll
MSc study-2	(Study title to be determined) - Yaro Jean Baptiste
Other/Sub-studies:	NA
Key Publications:	<i>Ref: S. Bakshi & EB Imoukhuede. Malaria Vected Vaccines Consortium. Human Vaccines 6:6, 1-6; June 2010</i>

4 Career Development/Senior fellowships

4.1 HIV/AIDS Career development and Senior fellowships

Table 4-1: Summary table of HIV/AIDS fellowship projects supported by EDCTP

Project Acronym (Coordinator)	Type of project /Phase of trial	Product(s)	Manufacturer / Developer	Study population	Status
Alabi SF -HIV	Laboratory assay development	In-house viral load assays	In-house (based on Roche HIV versión)	none	completed
Ekouevi SF -HIV	II	Truvada (Emtricitabine + Tenofovir), Niverapine and Zidovudine/Azidothymid	Gilead Sciences, Boehringer Ingelheim and Tubigen respectively	30 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 (Kebba) - 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 delivery, and both mother and baby followed until the child is 12 months old	Ongoing
Njai- SF	HIV immunology	none	Not applicable	The proposed study will use the unique Rural Clinical Cohort established in 1990	Ongoing
Ndembi -SF	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	Ongoing
Mwinzi - SF	IRIS in schistosomiasis on HAART	standard regimen (Stavudine, lamuvidine and niverapine)	WHO pre-qualified drugs	HIV-schistosome co-infection patients undergoing HAART In western Kenya.	Ongoing
Kiepela - SF	HIV mucosal immunity and KIR:HAL genes	none	Not applicable		Ongoing
Kityo -SF	Observational 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	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	Ongoing
Mduluza -SF	Evolution of neutralising	None	Not applicable	Stored samples of 70 individuals aged between 15 - 55 years old with acute/recent	Ongoing

	antibodies in HIV -C			stages of HIV-1C infection followed up to day 440 in Botswana	
Kayondo -SF	ART resisters 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	Ongoing
Kinyanda - SF	Clinical trials in HIV/AIDS and mental health factors	None	Not applicable	HIV patients on HAART in Uganda	On going
Ndouna - SF	Establishment of a HIV positive cohort for site preparation for HIV and malaria clinical trials in the Republic of Congo	None	Not applicable	HIV infected individuals	In negotiation
Delany Moretlwe - SF	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	In negotiation
Nchinda - SF	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

4.1.1 Abraham Alabi

EDCTP Project Coordinator:	Abraham Alabi
EDCTP Call Title:	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
Objectives:	To developing 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
EDCTP Project Code:	TA.2004.40200.001
EDCTP Project Start Date:	1 January 2005
EDCTP Project End Date:	28 September 2008
Site Principal Investigator(s):	Clayton Onyango, Modou Camara, Steve Kaye, Samuel MacConkey, Sarah Rowland Jones (Gambia)
Collaborators:	Simon Agwale (Nigeria)
Clinical Trial/Study Sponsor:	Medical Research Council, UK
Product(s):	In-house viral load assay
Manufacturer/Developer:	Not applicable
Cofunders:	None

4.1.2 Didier Ekouevi

EDCTP Project Coordinator:	Didier Ekouevi
EDCTP Call Title:	Senior Fellowship
EDCTP Project Title:	Phase II trial, multicentre, opened label evaluating the pharmacokinetics and the safety and toxicity of the Tenofovir-Emtricitabine combination in pregnant women and infants in Africa and Asia
Objectives:	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
EDCTP Project Code:	TA.2004.40200.003
EDCTP Project Start Date:	1 January 2005
EDCTP Project End Date:	30 October 2007
Site Principal Investigator(s):	Thérèse N'dri-Yoman (Côte d'ivoire); Eric Nerrienet, Leang Sim Kruy (Cambodia) and James McIntyre (South Africa)
Collaborators:	Marie-Laure Chaix, Christine Rouzioux, Jean-Marc Treluyer, Elisabeth Rey, Stéphane Blanche, Elise Arrive (France ANRS)
Clinical Trial/Study Sponsor:	French Agence Nationale de Recherches
Product(s):	Truvada (Emtricitabine + Tenofovir), Niverapine and Zidovudine/Azidothymid
Manufacturer/Developer: respectively	Gilead Sciences, Boehringer Ingelheim and University of Tubingen
Cofunders:	ANRS (France) 500,000 euros)

4.1.3 Jenifer Serwanga (Kebba)

EDCTP Project Coordinator:	Jenifer Serwanga
EDCTP Call Title:	Career Development Fellowship
EDCTP Project Title:	Pattern of HIV-induced T-cell response Influencing Viral Load Course following HIV infection
Objectives:	<p>i) To determine the plasma viral load pVL trajectory from primary infection through viral set point and beyond;</p> <p>ii) To evaluate the relationship between HLA class I polymorphisms and pVL trajectory</p> <p>iii) To evaluate the pattern and magnitude of HIV-1 specific CD8 T-cell response longitudinally following infection</p> <p>iv) To sequence the virus at specified intervals following HIV-1 infection to assess viral evolution and escape from HIV specific responses.</p>
EDCTP Project Code:	TA.2005.40203.003
EDCTP Project Start Date:	30 October 2006
EDCTP Project End Date:	23 May 2010
Site Principal Investigator(s):	Heiner Grosskurth, Pontiano Kaleebu, Pietro Pala, Daniel Bugembe Lule (Uganda)
Collaborators:	Andrew McMichael (UK)
Clinical Trial/Study Sponsor:	Not applicable
Product(s):	Not applicable
Manufacturer/Developer:	Not applicable
Cofunders:	Not applicable
Status:	Completed
Results and Outcomes:	

4.1.4 Esperança Sevene

EDCTP Project Coordinator:	Esparanca Sevene
EDCTP Call Title:	Career Development Fellowship
EDCTP Project Title:	Intensive safety monitoring of antimalarial and anti-retroviral drugs used during pregnancy in Manhica
Objectives:	To describe potential adverse drug reactions to anti-malarial and anti-retroviral drugs in pregnant women including adverse pregnancy outcomes 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
EDCTP Project Code:	TA.2005.40203.007
EDCTP Project Start Date:	23 April 2010
EDCTP Project End Date:	27 February 2010
Site Principal Investigator(s):	Alda do Rosário Mariano(Mozambique) Sonia Machevo(Mozambique) Sureia Hassamo(Mozambique) Ana Sofia Roberto(Mozambique) Lidia Laço(Mozambique) Joaquina do Rosário (Mozambique)
Collaborators:	Alexander Doodoo (Ghana) Clara Menendez (Spain) Xavier Carné (Spain)
Clinical Trial/Study Sponsor:	Not applicable
Product(s):	Sulphadoxine-Pyrimithamine + standard regimen (Stavudine, lamuvidine and niverapine)
Manufacturer/Developer:	(WHO prequalified regimen drugs)
Cofunders:	Not applicable

4.1.5 Harr Freeya Njai

EDCTP Project Coordinator:	Harr Freeya Njai
EDCTP Call Title:	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
Objectives:	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.
EDCTP Project Code:	TA.2007.40200.001
EDCTP Project Start Date:	13 August 2008
EDCTP Project End Date:	12 August 2010
Site Principal Investigator(s):	Pontiano Kaleebu (Uganda), Heiner Grosskurth(Uganda), Anatoli Kamali (Uganda)
Collaborators:	David Montefiori (USA), Helen Donners (Belgium)
Clinical Trial/Study Sponsor:	Not applicable
Product(s):	Not applicable
Manufacturer/Developer:	Not applicable
Cofunders:	MRC (93, 232.29 euros)

4.1.6 Nicaise Ndembi

EDCTP Project Coordinator: Nicaise Ndembi

EDCTP Call Title: 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

Objectives: To evaluate the 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

Site Principal Investigator(s): Pontiano Kaleebu (Uganda)

Collaborators: George Shaw (UK)

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

Manufacturer/Developer: Not applicable

Cofunders: Not applicable

4.1.7 Pauline Mwinzi

EDCTP Project Coordinator:	Pauline Mwinzi
EDCTP Call Title:	Senior Fellowship
EDCTP Project Title:	Immune reconstitution inflammatory syndrome (IRIS) in schistosomiasis patients undergoing HAART
Objectives:	To study the Immunopathogenesis, 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.
EDCTP Project Code:	TA.2008.40200.007
EDCTP Project Start Date:	24 November 2009
EDCTP Project End Date:	24 November 2011
Site Principal Investigator(s):	Diana Karanja(Kenya), Erick Muok (Kenya)
Collaborators: (Belgium)	Bob Colebunders(Belgium), Luc Kestens(Belgium), Katja Polman(Belgium)
Clinical Trial/Study Sponsor:	Not applicable
Product(s):	Standard regimen (Stavudine, lamuvidine and niverapine) and anti-schtistosmes
Manufacturer/Developer:	Prequalified regimens
Cofunders:	Not applicable

4.1.8 Photini Kiepela

EDCTP Project Coordinator: Photini Kiepela

EDCTP Call Title: Senior Fellowship

EDCTP Project Title: Training in mucosal immunity and the evaluation of KIR:HLA genes in HIV-1 clade c infection: key components to hiv vaccine design

Objectives: 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.

EDCTP Project Code: TA.2008.40200.015

EDCTP Project Start Date: 25 March 2010

EDCTP Project End Date: 25 March 2012

Site Principal Investigator(s): S Ganesh, Sharika Gappoo, R Govinden, Thumbi Ndung'U, Thesla Palanee

Collaborators: Not applicable

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

Manufacturer/Developer: Not applicable

Cofunders: Not applicable

4.1.9 Cissy Kityo Mutuluuza

EDCTP Project Coordinator:	Cissy Kityo
EDCTP Call Title:	Senior Fellowship
EDCTP Project Title:	Evaluating antiretroviral drug desistance in HIV infected children in Africa
Objectives:	To determine what proportion of a paediatric cohort achieve HIV drug resistance (HIVDR) prevention as measured by viral load suppression, and what HIVDR mutations and mutational patterns are observed in patients not achieving undetectable viral load.
EDCTP Project Code:	TA.2008.40200.022
EDCTP Project Start Date:	23 November 2009
EDCTP Project End Date:	23 November 2011
Site Principal Investigator(s):	Joshua Kiyiwa, Peter Mugenyi, Victor Musiime, Lillian Nakatudda (Uganda)
Collaborators:	Diana Gibb (UK)
Clinical Trial/Study Sponsor:	Not applicable
Product(s):	Standard regimen (Stavudine, lamuvidine and niverapine)
Manufacturer/Developer:	Prequalified regimens
Cofunders:	Not applicable

4.1.10 Wendy Burgers

EDCTP Project Coordinator: Wendy Burgers

EDCTP Call Title: Senior Fellowship

EDCTP Project Title: The effect of HIV co-infection on the immune response to *Mycobacterium tuberculosis* (M.tb) in the lung

Objectives: 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 coinfection.

EDCTP Project Code: TA.2008.40200.020

EDCTP Project Start Date: 09 October 2009

EDCTP Project End Date: 09 October 2011

Site Principal Investigator(s): Gerhard Walzl, Robert Wilkinson, Barbara Karlsdof, Willem Hanekom

Collaborators: Not applicable

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

Manufacturer/Developer: Not applicable

4.1.11 Takafira Mduluza

EDCTP Project Coordinator: Takafira Mduluza

EDCTP Call Title: Senior Fellowship

EDCTP Project Title: Evolution of neutralizing antibodies among acute to early HIV Subtype C infected individuals in Botswana: One Year Longitudinal Study.

Objectives: 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

EDCTP Project Code: TA.2009.40200.005

EDCTP Project Start Date: 14 May 2010

EDCTP Project End Date: 14 May 2012

Site Principal Investigator(s): Rosemary Musonda, Joseph Makhema, Vladmir Novitsky, Keikantse Mathlagela, Sikhulile Moyo

Collaborators: Not applicable

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

Manufacturer/Developer: Not applicable

4.1.12 Jonathan Kayondo

EDCTP Project Coordinator: Jonathan Kayondo

EDCTP Call Title: Senior Fellowship

EDCTP Project Title: 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

Objectives: To complement the just commenced Wellcome Trust-funded UVRI 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 the ART-naïve.

EDCTP Project Code: TA.2009.40200.011

EDCTP Project Start Date: 30 March 2010

EDCTP Project End Date: 30 March 2012

Site Principal Investigator(s): Pontiano Kaleebu, Nicaise Ndembu

Collaborators: UK (Pillay Deenam)

Clinical Trial/Study Sponsor: Not applicable

Product(s): Combivir plus niverapine or tenofivir

Manufacturer/Developer: Prequalified formulations

4.1.13 Stephen Kennedy

EDCTP Project Coordinator: Steven Kennedy

EDCTP Call Title: Senior Fellowship

EDCTP Project Title: Building Research Infrastructure and Capacity to Implement an HIV/STD Prevention Trial in Post-Conflict Liberia

Objectives: To support research infrastructure, training and partnerships to prevent HIV/AIDS in rural Liberia and to implement and evaluate an HIV/AIDS program for high risk rural youth 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

Site Principal Investigator(s): none

Collaborators: Not applicable

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

Manufacturer/Developer: Not applicable

4.1.14 Eugene Kinyanda

EDCTP Project Coordinator: Eugene Kinyanda

EDCTP Call Title: Senior Fellowship

EDCTP Project Title: Clinical trials in HIV/AIDS in Africa: Should they routinely control for mental health factors?

Objectives: The study aims to answer the following questions: 1) What is the prevalence of the mental health problems of major depressive disorder (MDD) and maladaptive coping style (MACS) among HIV-infected patients in the African setting of Uganda, and what is the incidence of MDD in HIV/AIDS? 2) Do the mental health problems of MDD and MACS significantly impact on HIV disease progression in the African socio-cultural environment in Uganda including via non-adherence to ART? 3) What would be the potential impact of the mental health covariates MDD and MACS 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?

EDCTP Project Code: TA.2010.40200.011

EDCTP Project Start Date: 12 April 2011

EDCTP Project End Date: 12 April 2013

Site Principal Investigator(s): none

Collaborators: none

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

Manufacturer/Developer: Not applicable

Cofunders: None

4.1.15 Mathieu Ndounga

EDCTP Project Coordinator: Mathieu Ndounga

EDCTP Call Title: 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

Objectives: 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

EDCTP Project Code: TA.2010.40200.011

EDCTP Project Start Date:

EDCTP Project End Date:

Site Principal Investigator(s): Pembe Issamou Mayengue, Rock Fabien Niama, Celine Samba Louka, Francine Ntoumi, Roth Cecile Laure Mapapa Miakassissa

Collaborators: None

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

Manufacturer/Developer: Not applicable

Cofunders: None

4.1.16 Sinead Delany Moretlwe

EDCTP Project Coordinator: Sinead Delany Moretlwe

EDCTP Call Title: 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.

Objectives: To show the epidemiology of HPV infection in men by HIV status and provide data that would therefore be useful to inform models that predict the impact of HPV vaccination (e.g. using Gardasil) in various African settings, including South Africa.

EDCTP Project Code: TA.2010.40200.034

EDCTP Project Start Date:

EDCTP Project End Date:

Site Principal Investigator(s): David Lewis

Collaborators: None

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

Manufacturer/Developer: Not applicable

Cofunders: None

4.1.17 Godwin Nchinda

EDCTP Project Coordinator: Godwin Nchinda

EDCTP Call Title: 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

Objectives: 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 and 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.

EDCTP Project Code: TA.2010.40200.016

EDCTP Project Start Date: 10 March 2011

EDCTP Project End Date: 10 March 2013

Site Principal Investigator(s): Vitorio Colizzi

Collaborators: Ralph M Steinman (Rokerfeller University) and Klaus Uerberla (Ruhr University – Germany)

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

Manufacturer/Developer: Not applicable

Cofunders: None

4.2 Tuberculosis Career Development and Senior fellowships

Table 4-2: Summary table of Tuberculosis fellowship projects supported by EDCTP

Project Acronym (Coordinator)	Type of project /Phase of trial	Product(s)	Manufacturer / Developer	Study population	Status
Mukhtar - SF	TB epidemiology	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	BCG-induced immune correlates of protection against tuberculosis	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	Completed
Adetifa -CDF	Comparison of immunologic and molecular TB diagnostics techniques	None	Not applicable	188 stored samples (73 smear positive, 93 smear negative, 22 progressors)	Completed
Dheda - SF	TB Lung innate immunity pathways	None	Not applicable	74 TB patients and health contacts	Completed with ongoing sub-studies
Nicol - SF	Genotypic diagnosis of TB and drug resistance	GeneXpert	Cepheid, Sunnyvale, CA, USA	2522 patients	Ongoing
Nachegea -SF	TB-IRIS prevention with steroids	None	Not applicable	TB patients on HAART	Ongoing
Oyakhrome -SF	TB, TB-HIV and MDR prevalence in Brazzaville	None	Not applicable	General population	Ongoing
Hatherill -SF	Association of TB and intestinal helminthes infection	None	Not applicable	800 children in South Africa and Kenya	Ongoing
Worodria -SF	Treatment outcomes of TB patients on ART	None	Not applicable	230 TB patient on HAART in Kampala	On going

4.2.1 Maowia Mukhtar

EDCTP Project Coordinator:	Maowia Mukhtar
EDCTP Call Title:	Senior Fellowship
EDCTP Project Title:	The burden of tuberculosis in eastern Sudan: epidemiology and drug resistance patterns of Mycobacterium tuberculosis isolates
Objectives:	To conduct epidemiological studies to identify suitable sites for future diagnostic, treatment and vaccine trials on tuberculosis in Sudan
EDCTP Project Code:	TA.2004.40200.005
EDCTP Project Start Date:	1 January 2005
EDCTP Project End Date:	30 June 2007
Site Principal Investigator(s):	None
Collaborators:	Patrick van der Styft, Greet Dieltiens, Nageed Saeed
Clinical Trial/Study Sponsor:	Not applicable
Product(s):	Not applicable
Manufacturer/Developer:	Not applicable
Cofunders:	None

4.2.2 Willem Hanekom

EDCTP Project Coordinator: Willem Hanekom

EDCTP Call Title: Senior Fellowship

EDCTP Project Title: The BCG-induced immune correlates of protection against tuberculosis

Objectives: To identify BCG immune correlates of protection against TB in children whose understanding is critical for TB vaccine development

EDCTP Project Code: TA.2004.40200.004

EDCTP Project Start Date: 1 January 2005

EDCTP Project End Date: 6 October 2008

Site Principal Investigator(s): Greg Hussey

Collaborators: Gilla Kaplan (USA), Adrian Hill (UK)

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

Manufacturer/Developer: Not applicable

Cofunders: None

4.2.3 Molebogang Rangaka

EDCTP Project Coordinator: Molebogang Rangaka

EDCTP Call Title: Career Development Fellowship

EDCTP Project Title: Immunological investigation of the HIV-tuberculosis associated immune reconstitution

Objectives: 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

EDCTP Project Code: TA.2005.40203.005

EDCTP Project Start Date: 15 December 2006

EDCTP Project End Date: 31 January 2009

Site Principal Investigator(s): Gary Maartens, Graham Meintjes, Kathrine Wilkinson, Robert Wilkinson

Collaborators: None

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

Manufacturer/Developer: Not applicable

Cofunders: None

4.2.4 Ifedayo Adetifa

EDCTP Project Coordinator: Ifedayo Adetifa

EDCTP Call Title: Career Development Fellowship

EDCTP Project Title: A double blind, placebo controlled randomised trial of vitamin A supplementation for modulation of Mycobacterium tuberculosis immune responses in children aged 5-14 years with latent Tuberculosis

Objectives: 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

EDCTP Project Code: TA.2005.40203.001

EDCTP Project Start Date: 15 March 2007

EDCTP Project End Date: 1 July 2010

Site Principal Investigator(s): Richard Adegbola, Phillip Hill, Martin Antonio

Collaborators: None

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

Manufacturer/Developer: Not applicable

Cofunders: None

4.2.5 Keertan Dheda

EDCTP Project Coordinator: Keertan Dheda

EDCTP Call Title: Senior Fellowship

EDCTP Project Title: Human lung innate immune pathways regulating the stasis and killing of *M. tuberculosis* in a high burden setting

Objectives: To compare compartment-specific IFN- antigen-specific responses in TB versus non-TB patients; 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) and 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

EDCTP Project Code: TA.2007.40200.010

EDCTP Project Start Date: 28 July 2008

EDCTP Project End Date: 27 July 2010

Site Principal Investigator(s): Greg Hussey

Collaborators: Graham Rook (UK), Alimuddin Zumla (UK)

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

Manufacturer/Developer: Not applicable

Cofunders: None

4.2.6 Mark Nicol

EDCTP Project Coordinator: Mark Nicol

EDCTP Call Title: 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

Objectives: 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

EDCTP Project Code: TA.2007.40200.009

EDCTP Project Start Date: 29 August 2008

EDCTP Project End Date: 20 September 2011

Site Principal Investigator(s): None

Collaborators: None

Clinical Trial/Study Sponsor: Not applicable

Product(s): GeneXpert

Manufacturer/Developer: Cepheid, Sunnyvale, CA, USA

Cofunders: None

4.2.7 Jean Nachega

EDCTP Project Coordinator: Jean Nachega

EDCTP Call Title: Senior Fellowship

EDCTP Project Title: A Multi-Site Double-Blind Placebo Controlled Randomized Clinical Trial to Prevent Immune Reconstitution Inflammatory Syndrome with Non-Steroid Anti-Inflammatory Drugs

Objectives: To investigate immune-modulation of non-steroidal anti-inflammatory treatment in TB IRIS among HIV infected patients

EDCTP Project Code: TA.2008.40200.021

EDCTP Project Start Date: 9 February 2010

EDCTP Project End Date: 9 February 2012

Site Principal Investigator(s): Mzileni Mogiyana, Ingrid Wilson

Collaborators: Bob Colebunders (Belgium)

Clinical Trial/Study Sponsor: Not applicable

Product(s): None

Manufacturer/Developer: Not applicable

Cofunders: None

4.2.8 Sunny Oyakhirome

EDCTP Project Coordinator:	Sunny Oyakhirome
EDCTP Call Title:	Senior Fellowship
EDCTP Project Title:	Career development and strengthening institutional capacity for clinical research in TB at the Faculty of Health Sciences in Brazzaville
Objectives:	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
EDCTP Project Code:	TA.2009.40200.010
EDCTP Project Start Date:	13 April 2010
EDCTP Project End Date:	13 April 2012
Site Principal Investigator(s):	Pembe Mayengue and Francine Ntoumi
Collaborators:	Veronique Penlap and Benjamin Mordmueller
Clinical Trial/Study Sponsor:	Not applicable
Product(s):	Not applicable
Manufacturer/Developer:	Not applicable
Cofunders:	None

4.2.9 Mark Hatherill

EDCTP Project Coordinator: Mark Hatherill

EDCTP Call Title: 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

Objectives: To determine whether prevalent infection with intestinal helminths is associated with increased risk of pulmonary tuberculosis disease in children; to determine whether maternal infection with intestinal helminths is associated with increased risk of pulmonary tuberculosis disease in children and to compare the risk above between the research site in Breede Valley, South Africa, and the research site in Karemo Division, Kenya

EDCTP Project Code: TA.2009.40200.015

EDCTP Project Start Date: 20 April 2010

EDCTP Project End Date: 20 April 2012

Site Principal Investigator(s): Videlias Nduba, Eric Muok, Diana Karanja, Pauline Mwinzi,

Collaborators: William Evan Secor, Greg Hussey, Willem Hanekom, William Horsnell

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

Manufacturer/Developer: Not applicable

Cofunders: None

4.2.10 William Worodria

EDCTP Project Coordinator: William Worodria

EDCTP Call Title: Senior Fellowship

EDCTP Project Title: Short and Long term clinical and immunological outcomes of patients with HIV/TB coinfections on ART

Objectives: 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

EDCTP Project Code: TA.2010.40200.007

EDCTP Project Start Date: 11 April 2011

EDCTP Project End Date: 11 April 2013

Site Principal Investigator(s): Yuka Munabe, Robert Lukande, Alice Nakiwogga Mwanga, Harriet Mayanja Kizza

Collaborators: Bob Colebunders, Luc Kerstens, Jean Pierre Van geertruyden, Frank Cobelens

Clinical Trial/Study Sponsor: University of Amsterdam

Product(s): Prequalified TB regimens and HAART

Manufacturer/Developer: Not applicable

Cofunders: None

4.3 Malaria Career Development and Senior fellowships

Table 4-3: Summary table of malaria fellowship projects supported by EDCTP

Project Acronym (Coordinator)	Type of project /Phase of trial	Product(s)	Manufacturer / Developer	Study population	Status
Djimde - SF	Public health benefits of artemisinin therapy in Mali	AS/AQ, AS/SP and AR-L	Pre-qualified drugs	973 malaria episodes studied	Closed
Nzila - SF	Understanding the mechanism of piperazine resistance	None	Not applicable	In vitro cultures	Closed
Talisuna - SF	Pharmacovigilance of anti-malarial drugs in Uganda	None	Not applicable	None (training of health staff and comparison by health facility/region)	Completed
Nebie -SF	Role of T cells in malaria endemicity	None	Not applicable	219 adults and children in Burkina Faso	Closed
Moukoko -CDF	Malaria virulence markers	None	Not applicable	In vitro assays	closed
Nwakanma - SF	PCR diagnosis of malaria	None	Not applicable	Out patients with malaria symptoms in Gambia	Completed
Cisse - SF	IPT with community participation	Dualkin, AS and AQ	Pre-qualified drugs	1893 children	Completed
Dodoo - SF	In vitro assessment of malaria antibodies	None	Not applicable	In vitro assays	Ongoing
Happi - SF	Biomarkers of artemisinin resistance	None	Not applicable	In vitro and in vivo assays	Ongoing
Phiri - SF	Appropriate dosing period of iron in malaria treatment	Iron and iron isotopes	International Atomic Energy Agency	Children under 3 with malaria	Ongoing
Achidi - SF	Baseline studies	None	Not applicable	General population in Cameroon	Ongoing
Tiono - SF	Impact of nets, home management and rapid diagnosis on malaria mortality in children	None	Not applicable	40 clusters of 40 children each and followed for 2 years	Ongoing
Byakika Kibwika - SF	Safety, efficacy, PK and interaction	Iv artesunate and (Quinine, ACT	Gilead (for iv artesunate only)	330 patients	Ongoing

	with ART of iv artesunate and iv quinine	(Artemether-Lumefantrine or Dihydroartemisinin-piperaquine)			
Kouriba - SF	Role of monocytes in protection against malaria in Mali	None	Not applicable	In vitro assays	In negotiation
Toure - SF	Evaluation of malaria immunity and merozoite vaccine candidates	None	Not applicable	In vitro assays	In negotiation
Ndiaye - SF	IPT and home management of malaria in Senegal	None	Not applicable	24 clusters of villages randomised to each intervention	In negotiation

4.3.1 Abdoulaye Djimde

EDCTP Project Coordinator:	Abdoulaye Djimde
EDCTP Call Title:	Senior Fellowship
EDCTP Project Title:	Assessment of the Public Health Benefit of artemisinin based combination therapies for uncomplicated malaria treatment in Mali
Objectives:	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 unclompllicated malaria and malaria attributable malaria and to measure the impact of repeated administration of the drugs on malarial immunity and malaria transmission
EDCTP Project Code:	TA.2004.40200.003
EDCTP Project Start Date:	1 January 2005
EDCTP Project End Date:	8 February 2009
Site Principal Investigator(s):	Demba Dembele, Bakary Fofana, Bakari Sidibe, Sekou Toure
Collaborators:	Not applicable
Clinical Trial/Study Sponsor:	Not applicable
Product(s):	AS/AQ, AS/SP and AR-L
Manufacturer/Developer:	Not applicable

4.3.2 Alexis Nzila

EDCTP Project Coordinator: Alexis Nzila

EDCTP Call Title: Senior Fellowship

EDCTP Project Title: Understanding the mechanism of piperaquine resistance

Objectives: To identify the molecular markers of PQ resistance

EDCTP Project Code: TA.2004.40200.003

EDCTP Project Start Date: 1 January 2005

EDCTP Project End Date: 25 November 2008

Site Principal Investigator(s): None

Collaborators: Xin-Zhuan Su (USA), Steve Ward (UK)

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

Manufacturer/Developer: Not applicable

4.3.3 Ambrose Talisuna

EDCTP Project Coordinator:	Ambrose Talisuna
EDCTP Call Title:	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
Objectives:	The objective was to develop a PV system for monitoring the safety of antimalarial treatment at health facilities and within communities
EDCTP Project Code:	TA.2005.40200.001
EDCTP Project Start Date:	25 May 2007
EDCTP Project End Date:	1 June 2010
Site Principal Investigator(s):	Moses Kanya, Fred Wabwire
Collaborators:	Umberto d'Allesandro (Belgium)
Clinical Trial/Study Sponsor:	Not applicable
Product(s):	Not applicable
Manufacturer/Developer:	Not applicable

4.3.4 Issa Nebie

EDCTP Project Coordinator:	Issa Nebie
EDCTP Call Title:	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
Objectives:	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
EDCTP Project Code:	TA.2005.40200.008
EDCTP Project Start Date:	30 October 2006
EDCTP Project End Date:	31 May 2010
Site Principal Investigator(s):	Diadier Diallo, Amadou Diara, Alphone Ouedraogo, Sodiomon Sirima
Collaborators:	David Modiano (Italy), Maria Gabriela Torcia (Italy)
Clinical Trial/Study Sponsor:	Not applicable
Product(s):	Not applicable
Manufacturer/Developer:	Not applicable

4.3.5 Emboumbou Moukoko

EDCTP Project Coordinator:	Emboumbou Moukoko
EDCTP Call Title:	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
Objectives:	To perform the combined epidemiological, clinical and genetic analysis (gene mapping of several loci of <i>P. falciparum</i> 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)
EDCTP Project Code:	TA.2005.40203.006
EDCTP Project Start Date:	21 November 2006
EDCTP Project End Date:	20 November 2008
Site Principal Investigator(s):	Eric Achidi, Albert Sammy Ekobo
Collaborators:	Ogobara Doumbo (Mali), Peter Kremsner (Germany), Christophe Rogier (France)
Clinical Trial/Study Sponsor:	Not applicable
Product(s):	Not applicable

4.3.6 Davis Nwakanma

EDCTP Project Coordinator:	Davis Nwakanma
EDCTP Call Title:	Senior Fellowship
EDCTP Project Title:	Evaluation and implementation of high throughput PCR-based method for diagnosis and measurement of <i>P. falciparum</i> parasitaemia in clinical trials
Objectives:	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. In addition to conduct a cost analysis to assist towards a decision on whether slide microscopy, which has been the gold standard for malaria diagnosis for over a hundred years now, can be replaced by more modern methodologies, for the conduct of clinical trials in central laboratories in disease endemic regions
EDCTP Project Code:	TA.2005.40200.006
EDCTP Project Start Date:	27 November 2006
EDCTP Project End Date:	27 May 2009
Site Principal Investigator(s):	David Conway, Natalia Gomez-Escobar, Michael Walther
Collaborators:	Not applicable
Clinical Trial/Study Sponsor:	Not applicable
Product(s):	Not applicable
Manufacturer/Developer:	Not applicable

4.3.7 Badara Cisse

EDCTP Project Coordinator: Badara Cisse

EDCTP Call Title: Senior Fellowship

EDCTP Project Title: A pilot study of the Implementation of Seasonal Intermittent Preventive Treatment with Community Participation in Senegal

Objectives: 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).

EDCTP Project Code: TA.2005.40200.004

EDCTP Project Start Date: 14 May 2007

EDCTP Project End Date: 8 August 2010

Site Principal Investigator(s): Omar Gaye, Pape Moussa Thior

Collaborators: Brian Greenwood (UK), Paul Milligan (UK), Jean Francois Trape (France)

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

4.3.8 Daniel Dodoo

EDCTP Project Coordinator:	Daniel Dodoo
EDCTP Call Title:	Senior Fellowship
EDCTP Project Title:	Assessment of functionality of antibodies that associate with protection from clinical malaria using the <i>in-vitro</i> <i>P.falciparum</i> growth inhibition assay
Objectives:	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 <i>in vitro</i> 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
EDCTP Project Code:	TA.2007.40200.012
EDCTP Project Start Date:	24 July 2008
EDCTP Project End Date:	30 March 2011
Site Principal Investigator(s):	Not applicable
Collaborators:	Klaus Berzins (Sweden), Michael Theisen (Denmark)
Clinical Trial/Study Sponsor:	Not applicable
Product(s):	Not applicable

4.3.9 Christian Happi

EDCTP Project Coordinator: Christian Happi

EDCTP Call Title: 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

Objectives: To identify and validate new biomarkers/molecular determinants of parasites response to artemisinin derivatives (ARTs) and partner drugs *in vitro* and *in vivo*

EDCTP Project Code: TA.2007.40200.016

EDCTP Project Start Date: 13 December 2008

EDCTP Project End Date: 12 December 2010

Site Principal Investigator(s): Not applicable

Collaborators: Not applicable

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

4.3.10 Kamija Phiri

EDCTP Project Coordinator: Kamija Phiri

EDCTP Call Title: Senior Fellowship

EDCTP Project Title: A randomised controlled trial of oral iron therapy for treatment of post-malaria iron-deficiency anaemia in Malawian children comparing immediate post-discharge versus delayed treatment on iron uptake and haematological response

Objectives: 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

EDCTP Project Code: TA.2008.40200.016

EDCTP Project Start Date: 29 September 2009

EDCTP Project End Date: 29 September 2011

Site Principal Investigator(s): Sarah White

Collaborators: Patrick van Rheenen (Netherlands), Feiko Ter Kuile (UK)

Clinical Trial/Study Sponsor: Not applicable

Product(s): Iron tonic/ iron isotopes

4.3.11 Eric Achidi

EDCTP Project Coordinator: Eric Achidi

EDCTP Call Title: Senior Fellowship

EDCTP Project Title: Malaria baseline studies towards characterising and establishing a clinical trial site at Mutengene, South West Region of Cameroon

Objectives: The epidemiological study is designed to provide data on baseline malarionometric parameters valuable for future intervention studies aimed at validating disease control tools

EDCTP Project Code: TA.2009.40200.008

EDCTP Project Start Date: 22 March 2010

EDCTP Project End Date: 22 March 2012

Site Principal Investigator(s): Julius Atashili, Samuel Wanji, Njua Yafi, Judith Anchang

Collaborators: Not applicable

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

4.3.12 Alfred Tiono

EDCTP Project Coordinator: Alfred Tiono

EDCTP Call Title: Senior Fellowship

EDCTP Project Title: A cluster-randomized 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

Objectives: 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

EDCTP Project Code: TA.2009.40200.019

EDCTP Project Start Date: 29 April 2010

EDCTP Project End Date: 29 April 2012

Site Principal Investigator(s): Sodiomon Sirima, Issa Nebie, Alphonse Ouedraogo, Abdoulaye Traore,

Collaborators: Simon Cousens

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

4.3.13 Pauline Byakika Kibwika

EDCTP Project Coordinator: Pauline Byakika Kibwika

EDCTP Call Title: 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 piperazine with antiretroviral drugs

Objectives: 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-piperazine) 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 piperazine with the antiretroviral drugs (Nevirapine, Efavirenz, Lopinavir/ritonavir) in Ugandan patients

EDCTP Project Code: TA.2009.40200.020

EDCTP Project Start Date: 14 March 2011

EDCTP Project End Date: 14 March 2013

Site Principal Investigator(s): Elly Katabira, Moses Kanya, Concepta Merry, Harriet Mayanja Kizza, Mohammed Lamorde, Noah Kiwanuka

Collaborators: David Back, Saye Khoo

Clinical Trial/Study Sponsor: Institute of Infectious Diseases

Product(s): Quinine, ACT (Artemether-Lumefantrine or Dihydroartemisinin-piperazine) and IV artesunate

4.3.14 Bourema Kouriba

EDCTP Project Coordinator:	Bourema Kouriba
EDCTP Call Title:	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
Objectives:	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
EDCTP Project Code:	TA.2010.40200.007
EDCTP Project Start Date:	In negotiations
EDCTP Project End Date:	Not applicable
Site Principal Investigator(s):	Kourane Sissoko, Abdoulaye Kone, Issa Diara, Amadou Niangaly, Charles Arama, Mahamadou Sissoko
Collaborators:	Not applicable
Clinical Trial/Study Sponsor:	Not applicable
Product(s):	Not applicable

4.3.15 Aissatou Toure

EDCTP Project Coordinator: Aissatou Toure

EDCTP Call Title: 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

Objectives: i) 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; ii) to compare ADRB results with those of other commonly used functional assays such as the growth inhibition assay (GIA); iii) 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

EDCTP Project Code: TA.2010.40200.027

EDCTP Project Start Date: In negotiations

EDCTP Project End Date: Not applicable

Site Principal Investigator(s): Adama Tall, Shirley Longacre, Sylvie Bay

Collaborators: Not applicable

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

4.3.16 Jean Louis Ndiaye

EDCTP Project Coordinator: Jean Louis Ndiaye

EDCTP Call Title: 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

Objectives: 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)

EDCTP Project Code: TA.2010.40200.032

EDCTP Project Start Date: 11 April 2011

EDCTP Project End Date: 11 April 2013

Site Principal Investigator(s): Badara Cisse, Oumar Gaye, Pape Thior, Youssoupha Ndiaye

Collaborators: Paul Milligan

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

5 PhD and MSc scholarships

Table 5-1: Summary table of stand-alone (individual) PhD and MSc scholarships in HIV/AIDS, tuberculosis and malaria
Other PhD and MSc grants are included under their respective integrated/clinical trial projects

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

5.1.1 Alasan Jobe

EDCTP Project Coordinator: Alasan Jobe

EDCTP Call Title: MSc Studentship

EDCTP Project Title: Masters in Reproductive and Sexual Health Research

Objectives: TBD

EDCTP Project Code: TA.2005.40205.001

EDCTP Project Start Date: 10 August 2006

EDCTP Project End Date: 30 October 2007

Site Principal Investigator(s): Malang Fofana (Gambia)

Collaborators: Joanne Cooper (UK)

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

Manufacturer/Developer: Not applicable

5.1.2 Sunny Oyakhirome

EDCTP Project Coordinator: Sunny Oyakhirome

EDCTP Call Title: MSc Studentship

EDCTP Project Title: MSc in Public Health

Objectives:

EDCTP Project Code: TA.2005.40205.002

EDCTP Project Start Date: 27 June 2006

EDCTP Project End Date: 27 June 2007

Site Principal Investigator(s):

Collaborators:

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

Manufacturer/Developer: Not applicable

5.1.3 Bornwell Sikateyo

EDCTP Project Coordinator:	Bornwell Sikateyo
EDCTP Call Title:	PhD Studentship
EDCTP Project Title:	An assessment of the understanding of the informed consent process by participants in microbicide intervention trials in Zambia
Objectives:	To interrogate the consent undertaken by participants in an Enterotoxigenic vaccines trial in Misisi in Lusaka – Zambia through an ethnographic approach to explore the evolving relationships between researchers and participants’ expectations over the course of the trial, and the responsibilities these inspired
EDCTP Project Code:	TA.2005.40204.026
EDCTP Project Start Date:	1 November 2006
EDCTP Project End Date:	30 March 2011
Site Principal Investigator(s):	None
Collaborators:	Not applicable
Clinical Trial/Study Sponsor:	Not applicable
Product(s):	Not applicable
Manufacturer/Developer:	Not applicable

5.1.4 Louis Marie Yindom

EDCTP Project Coordinator:	Louis Marie Yindom
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
Objectives:	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
EDCTP Project Code:	TA.2005.40204.013
EDCTP Project Start Date:	1 August 2006
EDCTP Project End Date:	31 August 2009
Site Principal Investigator(s):	None
Collaborators:	Not applicable
Clinical Trial/Study Sponsor:	Not applicable
Product(s):	Not applicable
Manufacturer/Developer:	Not applicable

5.1.5 Getnet Yimer

EDCTP Project Coordinator: Getnet Yimer

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

Objectives: 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.

EDCTP Project Code: TA.2005.40204.005

EDCTP Project Start Date: 2 August 2006

EDCTP Project End Date: 2 December 2010

Site Principal Investigator(s): None

Collaborators: Not applicable

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

Manufacturer/Developer: Not applicable

5.1.6 Thuli Mthiyane

EDCTP Project Coordinator: Thuli Mthiyane

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)

Objectives: 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

EDCTP Project Code: TA.2005.40204.025

EDCTP Project Start Date: 10 November 2006

EDCTP Project End Date: 31 October 2011

Site Principal Investigator(s): None

Collaborators: Alexander Pym, Phillip Onyebujoh

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

Manufacturer/Developer: Not applicable

5.1.7 Leah Mwai

EDCTP Project Coordinator: Leah Mwai

EDCTP Call Title: PhD Studentship

EDCTP Project Title: Understanding the mechanism of resistance to lumefantrine by Plasmodium falciparum

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

EDCTP Project Code: TA.2005.40204.011

EDCTP Project Start Date: 18 July 2006

EDCTP Project End Date: 1 October 2010

Site Principal Investigator(s): None

Collaborators: Kevin Marsh

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

Manufacturer/Developer: Not applicable

5.1.8 Janha Ramatouli

EDCTP Project Coordinator: Janha Ramatouli

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

Objectives: To investigate whether CYP2C9 and its genetic polymorphs participate in the biotransformation of the antimalarial biguanides

EDCTP Project Code: TA.2005.40204.018

EDCTP Project Start Date: 23 August 2006

EDCTP Project End Date: 1 March 2010

Site Principal Investigator(s): None

Collaborators: Robert Walton

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

Manufacturer/Developer: Not applicable

5.1.9 Charles Arama

EDCTP Project Coordinator: Charles Arama

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

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

EDCTP Project Code: TA.2005.40204.003

EDCTP Project Start Date: 10 August 2006

EDCTP Project End Date: 10 December 2010

Site Principal Investigator(s): None

Collaborators: None

Clinical Trial/Study Sponsor: Not applicable

Product(s): Not applicable

Manufacturer/Developer: Not applicable

6 Member States Initiated projects

Table 6-1: Summary table of member states initiated projects in HIV/AIDS, tuberculosis, capacity building and networking projects
Summary of individual projects can be found in the relevant sections as 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=20	Ongoing
Ekouevi MSI - HIV Treatment (Ekouevi)	III	AtriplaR and CombivirR Aluvia	<i>Please see details below</i>	<i>Please see details below</i>	Pending Revision
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	Not yet recruiting
FATI (Hoelscher)	II	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.	Not yet recruiting
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			1800 children per site (Democratic Republic of Congo and Uganda) between 6 and 59 months with non-severe malaria	Not yet recruiting

Project Acronym (Coordinator)	Capacity Building Goal	Study population	Status of project
Fomsgaard MSI-HIV vaccine (Fomsgaard)	<ul style="list-style-type: none"> 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)	<ul style="list-style-type: none"> 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)	<ul style="list-style-type: none"> 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 rationale for selecting the appropriate doses to be carried forward in more advanced clinical development 	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.	Not yet recruiting

	<ul style="list-style-type: none"> 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. 		
TBTEA (Kaufmann)	<ul style="list-style-type: none"> 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 be 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 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). 	n/a	Ongoing
WANETAM PLUS (Jaye)	<ul style="list-style-type: none"> 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)	<ul style="list-style-type: none"> 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 between 6 and 59 months with non-severe malaria.	Not yet recruiting

6.1.1 Fomsgaard AFO-18

EDCTP Project Coordinator:	Anders Fomsgaard
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
Trial 1	
Site Principal Investigator(s):	David de Silva Te (Anders Fomsgaard)
Clinical Trial/Study Sponsor:	SSI
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):	Evaluate 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):	Bissau, Guinea-Bissau
Collaborating site(s):	University Cheikh Anta DIOP, Dakar Senegal MRC Faluja, The Gambia SSI, Denmark
Study design:	Single-Blinded, placebo-controlled phase 1 trial
Product(s):	HIV vaccine peptide and CAF01 adjuvant
Manufacturer/Developer:	SSI (Denmark)
Cofunders	Denmark UK
Status:	Ongoing
Results and Outcomes:	
Trial Registration number(s):	
Sub-studies	
Capacity Building	
Site Principal Investigator(s):	Amabelia Rodrigues
Clinical Trial/Study Sponsor:	SSI
Trial/Study title:	Baseline Epi Studies: Site Infrastructure: Short term training:
Goal:	Introduce and maintain technology and GCP procedures
Primary Objective(s):	Introduce and maintain hematology and clinical chemistry and viral and immunology measures
Secondary Objective(s):	Educate key persons in English and GCP
Clinical Trial/Study site(s):	Bandim health Project, Simao Mendes Hospital, National Laboratory Bissau
Collaborating site(s):	The John Radcliffe MRC Human Immunology Unit (University of Oxford) 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 SSI Department of Virology, Denmark
Study design:	n/a
Product(s):	n/a

Manufacturer/Developer:	
Total number of subjects (clinical trials only):	(20-25)
Total number of subjects (cohort/epidemiological/other studies):	Cohort: app 300 HIV-1 positive healthy individuals
PhD study-1	none
PhD study-2	none
MSc study-1	(HIV-1 subtypes in Republic Guinea Bissau) (Sanne Skov Jensen) (Study title) (Name of candidate)
MSc study-2	(Study title) (Name of candidate) (Study title) (Name of candidate)
Other/Sub-studies:	Bachelor: In house real-time PCR for HIV-1 viral load testing in Guinea Bissau (stud: Christian Leo-Hansen)
Key Publications:	None

6.1.2 Ekouevi MSI - HIV Treatment

EDCTP Project Coordinator:	Didier Ekouevi
EDCTP Call Title:	Call for the support of member states initiated projects within the scope of EDCTP activity areas
EDCTP Project Title:	Safety and efficacy of the universal use of the Efavirenz-Tenofovir-Emtricitabine and Zidovudine-Lamivudine-Lopinavir/ritonavir combinations in pregnant and breastfeeding women to prevent mother-to-child transmission of HIV-1 in resource-limited settings
EDCTP Project Code:	MS.2009.10800.003
EDCTP Project Start Date:	30 September 2010
EDCTP Project End Date:	15 September 2013
PROJECT UPDATE	<i>The clinical trial aspect of the project has been cancelled as of December 2011 on account of difficulties in securing insurance for the clinical trial. The project is currently working on revising their proposal to ensure the capacity building element is maintained.</i>
Trial 1	
Site Principal Investigator(s):	Renaud Becquet
Clinical Trial/Study Sponsor:	ANRS
Trial/Study title:	Safety and efficacy of the universal use of the Efavirenz-Tenofovir-Emtricitabine and Zidovudine- Lamivudine- Lopinavir/ritonavir combinations in pregnant and breastfeeding women to prevent mother-to-child transmission of HIV-1 in resource-limited settings. A multicentre randomized phase III clinical trial.
Goal:	To assess the maternal and infant safety of a single daily fixed-dose combination of TDF/FTC/EFV (Atripla®), compared to the association of LPV/r (Aluvia®) and 3TC/ZDV (Combivir®) given to African women to prevent MTCT overall in populations practicing breastfeeding.
Primary Objective(s):	To compare the safety of two maternal triple ARV combinations in the first 6 and 12 months following delivery/birth with regard to the cumulative occurrence of: <ul style="list-style-type: none"> • adverse pregnancy outcome (stillbirth, premature delivery, low birthweight); • paediatric HIV infection; • infant mortality.
Secondary Objective(s):	To document the 5 following outcomes at 6 and 12 months following delivery / birth: <ul style="list-style-type: none"> • the occurrence of grade 3 or 4 events in treated women, and of grade 3 or 4 events in ARVexposed • infants; • the tolerability of the ARV combinations in treated women, defined as the absence of modification • of the initial ARV treatment; • the frequency of virological failure (viral load >300 copies/ml) at 6-month post HAART initiation • or 6 and 12-months post-delivery, and the viral resistance profile; • the frequency of premature delivery and the frequency of low birth weight; • the cumulative incidence of paediatric HIV infection; • the health-related quality-of-life of women assessed with a newly validated scale for HIV-infected • patients on HAART in resource-constrained settings and to take into account the following • outcomes: physical health and symptoms, ARV treatment impact, social and intimate • relationships, and emotional distress
Clinical Trial/Study site(s):	PAC-CI Abidjan, Côte d'Ivoire <ul style="list-style-type: none"> • Formation Sanitaire Urbaine Abobo-Avocatier • Formation Sanitaire Urbaine Niangon-Sud • Formation Sanitaire Urbaine Sainte Thérèse –enfant Jésus CIDRIZ Lusaka, Zambia <ul style="list-style-type: none"> • Kanyama clinic • Kamwala clinic
Collaborating site(s):	INSERM, France

	Universite Descartes, France Hopital Fabiola, Belgium ANRS, France
Study design:	Multicentric, non-inferiority, randomized controlled trial
Product(s):	AtriplaR and CombivirR Aluvia
Manufacturer/Developer:	Drugs will be provided by the following laboratories free of charge Atripla® (Tenofovir + Emtricitabine+ efavirenz) by MerckSharp & Dhome (MSD) Combivir® (Zidovudine+ Lamivudine) by Glaxo-Wellcome Kaletra® (Lopinavir/ritonavir) will be paid by the Sponsor
Status:	Not yet recruiting
Cofunders:	ANRS, France
Trial Registration number(s):	NCT 00 93 61 95 http://clinicaltrials.gov/ct2/show/NCT00936195
Results and Outcomes:	
Trial 2	AS APPLICABLE
Site Principal Investigator(s):	
Clinical Trial/Study Sponsor:	
Trial/Study title:	
Goal:	
Primary Objective(s):	
Secondary Objective(s):	
Clinical Trial/Study site(s):	
Collaborating site(s):	
Study design:	
Product(s):	
Manufacturer/Developer:	
Status:	Not yet Recruiting
Results and Outcomes:	
Total number of subjects (clinical trials only):	0
Total number of subjects (cohort/epidemiological/other studies):	Not applicable
PhD study-1	Dr Juan BURGOS
PhD study-2	
MSc study-1	
MSc study-2	
Other/Sub-studies:	
Key Publications:	<ul style="list-style-type: none"> • Becquet R, Ekouevi DK. Breastfeeding, triple ARV prophylaxis, and MTCT prevention. <i>Lancet Infect Dis.</i> 2011 Jan 13. • Ekouevi DK, Coffie PA, Ouattara E, Moh R, Amani-Bosse C, Messou E, Sissoko M, Anglaret X, Eholié SP, Danel C, Dabis F; International Epidemiological Database to Evaluate AIDS West Africa; ANRS 1269 and ANRS 12136 Study Groups in Abidjan. Pregnancy outcomes in women exposed to efavirenz and nevirapine: an appraisal of the IeDEA West Africa and ANRS Databases, Abidjan, Côte d'Ivoire. <i>J Acquir Immune Defic Syndr.</i> 2011 Feb 1;56(2):183-7 • Becquet R, Bland R, Ekouevi DK, Dabis F, Newell ML. Universal antiretroviral therapy among pregnant and postpartum HIV-infected women would improve maternal health and decrease postnatal HIV transmission. <i>AIDS.</i> 2010 May 15;24(8):1239-41 • Becquet R, Ekouevi DK, Arrive E, Stringer JS, Meda N, Chaix ML, Treluyer JM, Leroy V, Rouzioux C, Blanche S, Dabis F. Universal antiretroviral therapy for pregnant and breast-feeding HIV-1-infected women: towards the elimination of mother-to-child transmission of HIV-1 in resource-limited settings. <i>Clin Infect Dis.</i> 2009 Dec 15;49(12):1936-45

6.1.3 Magesa MSI-Malaria Capacity Building

EDCTP Project Coordinator:	Stephen Magesa
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
EDCTP Project Code:	MS.09.10800.002
EDCTP Project Start Date:	29 July 2010
EDCTP Project End Date:	28 August 2013
Capacity Building	
Site Principal Investigator(s):	Stephen Magesa
Clinical Trial/Study Sponsor:	n/a
Trial/Study title:	n/a
Goal:	<p>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 HRM system through JMP.</p> <p>2. To build capacity for laboratory support of clinical trials. To strengthen the infrastructure for clinical trials at Teule Hospital through the refurbishment of a research laboratory. The research laboratory facilities in Teule Hospital are cramped and have no attached office space needed for management of the laboratory. We therefore propose to refurbish the current research laboratory and will be equipped through resources from the host institution (NIMR). The facility will meet the exacting demands of GCLP and external quality assurance to international standards</p> <p>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 NMCP and MOH, health service providers. In addition there will be meetings specifically directed to new proposals from young Tanzanian scientists and a 1-week proposal writing workshop will be linked at the end of the scientific meeting.</p> <p>Training</p> <p>4. To improve capacity of junior staff to participate in clinical research. We will hold regular short courses on good clinical practice, good laboratory practice, clinical research ethics, biosafety with certification for qualifying staff in order to improve the quality of research. In addition we will hold short courses in research administration and financial management.</p>
Primary Objective(s):	n/a
Secondary Objective(s):	n/a
Third Objective	n/a
Clinical Trial/Study site(s):	
Collaborating site(s):	LSHTM, UK University of Copenhagen, Denmark NIMR, Tanzania Kilimanjaro Christian Medical College (KCMC), Tanzania Radboud University of Nijmegen, Netherlands
Cofunders	Denmark UK Netherlands
Status:	Ongoing
Results and Outcomes:	
Sub-studies	
Total number of subjects	n/a

(clinical trials only):	
Total number of subjects (cohort/epidemiological/other studies):	n/a
PhD study-1	n/a
PhD study-2	n/a
MSc study-1	n/a
MSc study-2	n/a
Other/Sub-studies:	n/a
Key Publications:	None

6.1.4 Strub-Wourgaft - Malaria Treatment

EDCTP Project Coordinator:	Nathalie Strub-Wourgaft
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:	15 August 2012
Trial 1	
Site Principal Investigator(s):	Carn Gwanaelle
Clinical Trial/Study Sponsor:	DNDi
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 5 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):	<ul style="list-style-type: none"> • To measure the parasite reduction ratio on Day 1, 2 and 3 • To compare the proportion of patients with parasitaemia on Day 2 and 3 • To compare the proportion of patients with fever on Day 2 and 3 • To compare the gametocyte carriage at Day 2 and 3, and Day 28, 42 and 63 • To evaluate cure rate at 28 and 42 days • To evaluate the population-pharmacokinetics of Artesunate-Mefloquine in under-5 children • To evaluate the incidence and severity of adverse events • To evaluate the incidence of Serious Adverse Events and adverse events leading to treatment discontinuation • To analyze the time description of time course and vomiting frequency
Third Objective	
Clinical Trial/Study site(s):	Kilosa, Tanzania Kisumu, Kenya Balonghin, Burkina Faso Banfora, 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
Product(s):	Artesunate Mefloquine (ASMQ) Artemether – Lumefantrine (Coartem®)
Manufacturer/Developer:	
Cofunders	United Kingdom (DFID) The Netherlands (DGIS) Switzerland (ARPE Foundation)
Status:	Not yet recruiting
Results and Outcomes:	
Trial Registration number(s):	Information have been entered into www.pactr.org website, registry number pending
Sub-studies	
Capacity Building	n/a
Site Principal Investigator(s):	
Clinical Trial/Study Sponsor:	n/a
Trial/Study title:	n/a
Goal:	n/a
Primary Objective(s):	n/a

Secondary Objective(s):	n/a
Clinical Trial/Study site(s):	n/a
Collaborating site(s):	
Study design:	n/a
Product(s):	
Manufacturer/Developer:	
Total number of subjects (clinical trials only):	940 planned
Total number of subjects (cohort/epidemiological/other studies):	
PhD study-1	n/a
PhD study-2	n/a
MSc study-1	n/a
MSc study-2	n/a
Other/Sub-studies:	No
Key Publications:	None

6.1.5 FATI

EDCTP Project Coordinator:	Michael Hoelscher
EDCTP Call Title:	Call for the support of member states initiated projects within the scope of EDCTP activity areas
EDCTP Project Title:	Fozivudine in Africa trials initiative (FATI) – a stepwise drug development programme for an improved AZT treatment
EDCTP Project Code:	MS.2010.18000.001
EDCTP Project Start Date:	6 October 2011
EDCTP Project End Date:	30 June 2013
Trial 1	
Site Principal Investigator(s):	Arne Kroidl, NIMR-MMRP, Mbeya, Tanzania Serge Eholie, PACCI Program, Abidjan, 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):	The primary objective of this study is to confirm a sustained virological suppression (HIV RNA <50 copies/ml) after 24 weeks of treatment between four different doses of Fozivudine (FZD) based antiretroviral 1st line treatment regimen in context to a standard Zidovudine (AZT) based treatment regimen in non subtype B HIV-1 infected individuals from Africa.
Secondary Objective(s):	<ol style="list-style-type: none"> 1. Virological response (HIV RNA <50 copies/ml) at 2, 4, 8 and 12 weeks of treatment between different arms 2. Virological response (HIV RNA <400 copies/ml) at 2, 4, 8, 12 and 24 weeks of treatment between different arms 3. Immunologic response: variation in CD4 lymphocytes between different arms 4. Fozivudine drug concentration (C_{trough} drug levels) at 2, 4, 8 and 12 weeks of treatment 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, the Arabic region, Africa and Europe.
Clinical Trial/Study site(s):	The NIMR-Mbeya Medical Research Programme (MMRP) supporting the Mbeya Referral Hospital (MRH) in Mbeya, 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:	The study will be an open-label, multicenter, prospective, randomized Phase IIa proof of concept and dose evaluating study. The study will evaluate 5 different oral 1st line antiretroviral regimens: four study arms will contain different doses of Fozivudine (FZD) plus Lamivudine (3TC) in a twice daily (BD, Arms A and B) or once daily (OD, Arms C and D) application plus once daily Efavirenz. The 5th study arm (Arm E) will contain standard Zidovudine (AZT)/Lamivudine (3TC) twice daily in a fixed dose combination plus once daily Efavirenz.
Number of subjects:	150 ART naïve HIV-infected adults (15 participants per arm per site)
Product(s):	Fozivudine (FZD) Lamivudine (3TC) Efavirenz 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	
Sub studies:	
Status:	Not yet recruiting
Results and Outcomes:	
Total number of subjects (clinical trials only):	150
Total number of subjects (cohort/epidemiological/other studies):	-
PhD study-1	Name of candidate: to be determined, NIMR-MMRP, Tanzania "Cross sectional viral load assessment in HIV infected patients on antiretroviral therapy (ART) evaluating the treatment efficacy defined by virological endpoint as provided by different levels of health facilities and health care provider in rural and urban southern Tanzania" Supervisor: Michael Hoelscher
PhD study-2	-
MSc study-1	-
MSc study-2	-
Other/Sub-studies:	-
Key Publications:	None

6.1.6 TBTEA

EDCTP Project Coordinator:	Stefan Kaufmann
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.2010.18000.002
EDCTP Project Start Date:	2 September 2011
EDCTP Project End Date:	30 June 2013
Site Principal Investigator(s):	Stefan Kaufmann, Max Planck Institution for Infection Biology, Berlin, Germany
Clinical Trial/Study Sponsor:	n/a
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):	<ol style="list-style-type: none"> 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 be 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 (MGIA)s.
Secondary Objective(s):	-
Clinical Trial/Study site(s):	n/a
Collaborating site(s):	Tuberculosis Vaccine Initiative (Netherlands), University of Oxford (UK), Staens 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)
Study design:	n/a
Number of subjects:	n/a
Product(s):	n/a
Manufacturer/Developer:	n/a
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),
Trial Registration number	n/a
Sub studies:	n/a
Status:	Ongoing
Results and Outcomes:	
Total number of subjects (clinical trials only):	n/a
Total number of subjects	n/a

(cohort/epidemiological/other studies):	
Post-doc 1	Abebech Demissie Aero, AHRI, Ethiopia "Control of pathology during chronic TB infection: host-pathogen interaction"
Post-doc 2	Candidate TBA, Max Planck Society of the Advancement of Science Global Transcriptome Analyses
Post-doc 3	Iman Satti, University of Oxford, UK " 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."
Post-doc 4	Benjamin Kagina, University of Oxford, UK " 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."
Post-doc 5	Juan Ignacio Aguiló, University of Zaragoza, Spain "Search for immunological correlates of protection for MTBVAC"
Other/Sub-studies:	-
Key Publications:	None

6.1.7 WANETAM plus

EDCTP Project Coordinator:	Assan Jaye
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:	30 June 2013
Site Principal Investigator(s):	Assan Jaye
Clinical Trial/Study Sponsor:	n/a
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):	<ol style="list-style-type: none"> 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):	<ol style="list-style-type: none"> 1. Establishment of links with the newly formed BE-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
Clinical Trial/Study site(s):	n/a
Collaborating site(s):	n/a
Study design:	n/a
Number of subjects:	n/a
Product(s):	n/a
Manufacturer/Developer:	n/a
Cofunders:	FOD Buitenlandse Zaken (Belgium), Institut of Tropical Medicine (Belgium), MRC (UK)
Trial Registration number	n/a
Sub studies:	-
Status:	Ongoing
Results and Outcomes:	
Total number of subjects (clinical trials only):	n/a
Total number of subjects (cohort/epidemiological/other studies):	n/a
MSc 1	Candidate TBD, Institut of Tropical Medicine Antwerp, Belgium Master Public Health – Including 8-week Short Course Health Policy, Health Systems Management, Disease Control Supervisor: Marleen Boelaert, Umberto D'Alessandro and Marie Laga (Institut of Tropical Medicine)

Post-doc 2	
Post-doc 3	
Post-doc 4	
Post-doc 5	
Other/Sub-studies:	
Key Publications:	None

6.1.8 QuinACT

EDCTP Project Coordinator:	Jean-Pierre Van geertruyden
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:	30 June 2013
Site Principal Investigator(s):	Moses Kamya and Carolyne Nabasumba, University Makerere, Uganda Hypolyte Muhindo, University of Kinshasa, RD Congo
Clinical Trial/Study Sponsor:	University of Antwerp
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):	<ol style="list-style-type: none"> 1. To determine the safety and efficacy of 2 ACTs (ASAQ and AL) vs quinine when administered to children under five with recurrent <i>P. falciparum</i> 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.
Secondary Objective(s):	-
Clinical Trial/Study site(s):	Lisungi Health Center, Kinshasa, Democratic Republic of Congo University Makerere, 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 Center at the University of Amsterdam (Netherlands)
Study design:	Bi-centre, non inferiority, phase III, randomized, open label, 3-arm trial
Number of subjects:	1800 children (between 12 and 59 months inclusively).
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	
Sub studies:	
Status:	Not yet recruiting
Results and Outcomes:	
Total number of subjects (clinical trials only):	3600
Total number of subjects (cohort/epidemiological/other studies):	
MSc	-
PhD-1	Hypolite Muhindo, University of Kinshasa "The impact of retreatment with an artemisinin-based combination on malaria incidence and its potential selection of resistant strains?" Supervisors: Pascal Lutumba, Halidou Tinto and Jean-Pierre Van

	geertruyden
PhD-2	Carolyn Nabasumba, Epicentre Mbarara Research Base "Antimalarial treatment in the Greater Mbarara district, Uganda: efficacy, use and access" Supervisors: Umberto D'Alessandro and Moses Kanya
Post-doc	-
Other/Sub-studies:	
Key Publications:	None

7 Ethics (IRB and NEC)

Table7-1: Summary table of ethics (Institutional Review Boards (IRBs) and National Ethics Committees (NECs) projects)

Project Acronym (Coordinator)	Type of Project (NEC or IRB)	Project goal	Institutions involved	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 Project was stopped on PB recommendation in May 2008
SPRUMONT-TREEE-1-ETHICS	Support for courses on ethics	Capacity Building	University of Neuchâtel	Completed
MATSIEGUI-MPH-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-STELLENBOSCH-ETHICS	Support for courses on ethics	Capacity Building	University of Stellenbosch	Completed
KILAMA-AMANET-1-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-MRCb&c-ETHICS	NEC, IRB	Capacity Building	Medical Research Council of Zimbabwe (MRCZ)	Completed
HOUNGNIHIN-MH-BENIN-ETHICS	NEC	Capacity Building	Ministry of Health (Benin)	Completed
PETROS-ETBIN-1-ETHICS	IRB	Capacity Building	Addis Ababa University	Completed
ADEBAMOWO-WABT-ETHICS	NEC	Capacity Building	West African Bioethics Training Program (WAB), University of Ibadan	Delayed
WANE (KAYITENKORE)-RWANDA-NEC-ETHICS	NEC	Capacity Building	Rwanda National Ethics Committee, Ministry of Health	In progress
CHANGALUCHA-NIMR-	IRB	Capacity Building	National Institute for Medical Research (NIMR)	Completed

2-NEC-ETHICS				
CHILENGI (KILAMA)-AMANET-2-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	Delayed
ONAPA-UNCST-ETHICS	NEC	Capacity Building	Uganda National Council for Science and Technology (UNCST)	In progress
MASON-BRTI-ETHICS	IRB	Capacity Building	Biomedical Research and Training Institute (BRTI)	Completed
KHULUMANI (KASULE)-HRU-BOTSWANA-ETHICS	NEC, IRB	Capacity Building	Health Research Unit, Ministry of Health Botswana	In progress
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	In progress
BOATENG-NMIMR	NEC, IRB	Capacity Building	Noguchi Memorial Institute for Medical Research, College of Health Sciences, University of Ghana	In progress
WASUNNA-KEMRI-ETHICS	IRB	Capacity Building	Kenya Medical Research Institute (KEMRI)	In progress
FUMANE-MH-MOZAMBIQUE-ETHICS	NEC	Capacity Building	Ministry of Health, National Health Institute, Comité Nacional de Bioética para Saúde (CNBS)	In progress
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)	In progress
WASSENAAR-SARECCER	Support for courses on ethics	Capacity Building	University of KwaZulu-Natal	In progress
IJSSELMUIDEN-COHRED-ETHICS	Support for courses on ethics	Capacity Building	Council on Health Research for Development (COHRED)	In progress
MBIDDE-UVRI-ETHICS	IRB	Capacity Building	Uganda Virus Research Institute (UVRI)	In progress
SPRUMONT-TREEE-2-ETHICS	Support for courses on ethics	Capacity Building	Institute of Health Law, University of Neuchâtel	In progress
MATSIEGUI-CAEN-ETHICS	NEC	Capacity Building	Comité National d'Éthique pour la Recherche du Gabon	In progress
KOLLIE-UNI-LIBERIA-IRB-ETHICS	IRB	Capacity Building	University of Liberia-Pacific Institute for Research and Evaluation Africa Center (PIRE)	In progress
RULISA-KUTH-ETHICS	IRB	Capacity Building	Kigali University Teaching Hospital (KUTH)	In progress
MUGYENYI-JCRC-IRB-ETHICS	IRB	Capacity Building	Joint Clinical Research Centre (JCRC)	In progress
NDEBELE-BOTSWANA-IRB-ETHICS	IRB	Capacity Building	University of Botswana	In progress
KAPTUE-CAMEROON-ETHICS	NEC	Capacity Building	Cameroon National Ethics Committee (CNEC)	In progress
WOLDEAMANUEL (PETROS)-ETBIN-2-ETHICS	IRB	Capacity Building	Ethiopian Bioethics Initiative (ETBIN), Addis Ababa University	In progress
YEVOO-GHANA-IRB-ETHICS	IRB	Capacity Building	Dodowa Health Research Centre (DHRC)	In progress

BHATT-KENYA-ETHICS	NEC	Capacity Building	University of Nairobi	In progress
BUKUSI-KENYA-ETHICS	IRB	Capacity Building	Kenya Medical Research Institute (KEMRI)	In progress
OTIENO-KENYA-ETHICS	IRB	Capacity Building	Centre for Research and Technology Development (RESTECH)	In progress
MANDA-MALAWI-ETHICS	IRB	Capacity Building	College of Medicine, University of Malawi	In progress
OTUONYE-NIMR-NIGERIA-ETHICS	IRB	Capacity Building	Nigerian Institute of Medical Research (NIMR)	In progress
OYEDEJI-NIMR-NIGERIA-ETHICS	IRB	Capacity Building	Nigerian Institute of Medical Research (NIMR)	In progress
KRUGER-SOUTH AFRICA-ETHICS	Support for courses on ethics	Capacity Building	University of Stellenbosch	In progress
MSAMBICHAKA-IFAKARA-TANZANIA-ETHICS	IRB	Capacity Building	Ifakara Health Institute	In progress
TEMU-LZIRB-TANZANIA-ETHICS	IRB	Capacity Building	National Institute for Medical Research (NIMR)	In progress
BIRUNGI-TASO-UGANDA-IRB-ETHICS	IRB	Capacity Building	The AIDS Support Organization (TASO)	In progress
ZIMBA-ZIMBABWE-ETHICS	IRB	Capacity Building	Harare City Health Department	In progress

7.1.1 Janko-VSCR–Ethics

EDCTP Project Coordinator:	Christa Janko
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:	01 December 2006
EDCTP Project End Date:	30 November 2008
Collaborators:	1) Michel Anoumou Missinou (Gabon) 2) Pierre Blaise Matsiegui (Gabon) 3) Maryvonne Kombila (Gabon) 4) Ulrick Bisvigou (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 INDEPTH Network
Results and Outcomes:	1. Training (resources developed (e.g. manuals) and human capacity developed) Trained 8 participants in the "Train the Trainer" course and 18 participants in the "Ethical Aspects of Clinical Research" course. 2. Networking / Collaborations Developed <ul style="list-style-type: none"> • Medical Research Unit, Albert Schweitzer Hospital Lambarene (MRU) • University of Health Sciences (USS), Libreville • National Centre for Medical Research (CIRMF), Franceville
Key Publications:	Not applicable

7.1.2 Aseffa-PABIN–Ethics

EDCTP Project Coordinator:	Abraham Aseffa
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 (Project was stopped on PB recommendation in May 2008.)
Collaborators:	<ol style="list-style-type: none"> 1) Wenceslaus Kilama (Tanzania) 2) Pierre Effa (Cameroon) 3) Juntra Karbwang (WHO / TDR) 4) Francis Crawley (Belgium) 5) Josef Glasa (Slovakia) 6) Christa Janko (Austria) 7) Reider Lie (Norway) 8) Gunnar Bjune (Norway) 9) Emilio Modini (Italy) 10) Christian Herve (France)
Type of Project:	Support for courses on ethics
Goal:	This project intends 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 is 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 develops research ethics capacity that promotes national capacity for carrying out clinical trials with the support of European and international partners. Specifically, the project will 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.
Cofunders:	Not applicable
Results and Outcomes:	Not applicable
Key Publications:	Not applicable

7.1.3 Sprumont–TRREE-1-Ethics

EDCTP Project Coordinator:	Dominique Sprumont
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:	01 November 2006
EDCTP Project End Date:	01 November 2008
Collaborators:	<ol style="list-style-type: none"> 1) Marcel Tanner (Switzerland) 2) Dirk Lanzareth (Germany) 3) Marie Hirtle (Canada) 4) Wenceslaus Kilama (Tanzania) 5) Peter Ndumbe (Cameroon) 6) Ogobara Doumbo (Mali) 7) Marie-Charlotte Bouèsseau (Switzerland) 8) John Williams (Canada) 9) Douglas Wassenaar (South Africa) 10) Charles Becker (Senegal) 11) Clement Adebamowo (Nigeria)
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, regulators).
Objectives:	<ol style="list-style-type: none"> 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. <p>Overall, this will strengthen the research ethics evaluation capacities in African and other participating countries.</p>
Cofunders:	<p>Swiss National Science Foundation KFPE – Commission for Research Partnership Swiss Academy of Science (SCNAT) Swiss Academy of Medical Sciences (SAMS) Health Law Institute Canadian Institute for Health Research</p>
Results and Outcomes:	<ol style="list-style-type: none"> 1. Infrastructure / Capacity Development The 3 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: <ul style="list-style-type: none"> • Mali • Cameroon • Tanzania • Switzerland All collaborators received personal coaching and 2 completed 3 month internships. 3. Networking / Collaborations Developed <ul style="list-style-type: none"> • AMANET (Tanzania) • MRTC (Mali) • University of Yaoundé (Cameroon) • Institute of Health Law, University of Neuchâtel (Switzerland) • SARETI (South Africa) • West African Bioethics (Nigeria)
Key Publications:	<ol style="list-style-type: none"> 1. Ateudjieu Jérôme, 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, in <i>Developing World Bioethics</i>, 2009 on-line, Vol. 10

(2) August 2010, Pages: 88–98

<http://onlinelibrary.wiley.com/doi/10.1111/j.1471-8847.2009.00266.x/full>

2. Dominique Sprumont, Formation de base en éthique de la recherche: retour aux sources avec le projet TRREE, in Bioethica Forum (2009) Vol. 2, n° 2, pp. 79-81

7.1.4 Matsiegui-MPH-Gabon-Ethics

EDCTP Project Coordinator:	Pierre-Blaise Matsiegui
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:	<ol style="list-style-type: none"> 1) Dominique Collin (Gabon) 2) Saadou Issifou (Gabon) 3) Christa Janko (Austria) 4) Eduard Ngou Milama (Gabon) 5) Appolinaire Essono (Gabon) 6) Constant Roger Aynangoye (Gabon) 7) Rufin Dikoumba (Gabon) 8) Peter Kremsner (Germany) 9) Fidèle Pierre Nze-Nguema (Gabon) 10) Marie Charlotte Bouésseau (Switzerland) 11) Paul Bekale (Gabon) 12) Dominique Sprumont (Switzerland) 13) Aissatou Toure (Senegal)
Type of Project:	NEC
Goal:	<p>Gabon is an important country with respect to clinical research in Central Africa. Several academic and private institutions, partly in collaboration with the pharmaceutical industry, conduct clinical trials in Gabon. Nevertheless Gabon still lacks a National Ethics Committee (NEC) that ensures high quality review of clinical trial documents and therefore patient safety and data credibility. The Ministry of Public Health of the Republic of Gabon in collaboration with the Institutional Review Board at the Albert Schweitzer Hospital, the Medical Research Unit of the Albert Schweitzer Hospital and the Vienna School of Clinical Research (VSCR) will form a group of members for the future Gabonese Ethics Committee. This NEC will be responsible for all clinical trials conducted in Gabon and with an interregional approach. Additionally this project aims to develop a strategy for designing and implementing the necessary laws and regulations.</p>
Objectives:	<ol style="list-style-type: none"> (i) Establishment of a Gabonese National Ethics Committee (NEC). (ii) Establishment of an administrative structure. (iii) Establishment of procedures. A set of SOPs were implemented. The establishment of the NEC had an important impact on clinical research activities in Gabon as for the first time independent ethical review infrastructures have been implemented. Research institutions without local ethics committees in the country received the possibility to shift the review process from mainly European ethics committees (responsible for European partner research institutions) to a Gabonese ethics committee with the necessary background about the local population, including cultural habits. Furthermore the establishment of the NEC and the presence of the process of establishing the NEC in the national media had a positive impact on the perception of medical research on a governmental level as well as on the population/community level. (iv) Training of NEC members.
Cofunders:	Not applicable
Results and Outcomes:	<ol style="list-style-type: none"> 1. Infrastructure / Capacity Development Computer and printer purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed) <ol style="list-style-type: none"> (i) establishment of a Gabonese NEC (ii) establishment of an administrative structure (iii) establishment of procedures, including implementation of SOPs (iv) training of NEC members - 64 participants received training on ethics. (v) A webpage has been designed: http://www.cner-gabon.org/cner/ 3. Networking / Collaborations Developed

	<ul style="list-style-type: none"> • 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
Key Publications:	Not applicable

7.1.5 Tindana-Navrongo-Ethics

EDCTP Project Coordinator:	Paulina Tindana
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:	1) Okyere Boateng (Ghana)
Type of Project:	IRB
Goal:	The aim of this project was to strengthen the capacity of administrators and members of the 6 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 6 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.
Cofunders:	Not applicable
Results and Outcomes:	<ol style="list-style-type: none"> 1. Infrastructure / Capacity Development Each of the 6 RECs were provided with a set of computers, printers, universal power systems (UPS) and filing cabinets. 2. Training (resources developed (e.g. manuals) and human capacity developed) National Research Ethics conference was held in February, 2007. 3. Networking / Collaborations Developed <ul style="list-style-type: none"> • PABIN • AMANET
Key Publications:	Not applicable

7.1.6 Bengo-Malawi-Ethics

EDCTP Project Coordinator:	Joseph Mfutso-Bengo
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.2005.41300.011
EDCTP Project Start Date:	20 October 2006
EDCTP Project End Date:	19 October 2007
Collaborators:	<ol style="list-style-type: none"> 1) Paul Ndebele (Zimbabwe) 2) Lie Reidar (Norway) 3) Rosemary Musesengwa (Zimbabwe) 4) Willard Kazembe (Malawi) 5) Mike Kachedwa (Malawi)
Type of Project:	NEC, IRB
Goal:	The main goal of the project was to strengthen the 2 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:	<ul style="list-style-type: none"> - To strengthen the capacities of NHSRC and COMREC in ethical review and clinical trials monitoring. - To adequately equip the Ethics Committee offices so that they can be able to perform all their tasks without limitations.
Cofunders:	Not applicable
Results and Outcomes:	<ol style="list-style-type: none"> 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 4 day workshop was held during which members of the 2 ethics committees developed standard operating procedures for the 2 ethics committees. The standard operating procedures covered various issues including ethical review and clinical trials monitoring so as to ensure that the 2 committees are using internationally acceptable standard operating procedures. 3. Networking / Collaborations Developed <ul style="list-style-type: none"> • PABIN
Key Publications:	<ol style="list-style-type: none"> 1. Report on the workshop "Enhancing Clinical Trial Oversight in Malawi" conducted on 19th June – 20th June 2008 at Nkopola Lodge in Mangochi, Malawi Medical Journal – MMJ 20(2): 63 – 64 June 2008. www.mmj.medcol.mw. 2. Ethical challenges in conducting research in humanitarian crisis situations, research ethics paper published in the Malawi Medical Journal – MMJ 20(2) 2008: 46 – 49 June 2008. www.mmj.medcol.mw

7.1.7 Bengo (Ndebele)-Malawi-Ethics

EDCTP Project Coordinator:	Joseph Mfutso-Bengo (Paul Ndebele)
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:	1) Lie Reidar (Norway) 2) Rosemary Musesengwa (Zimbabwe) 3) Willard Kazembe (Malawi) 4) Mike Kachedwa (Malawi)
Type of Project:	NEC, IRB
Goal:	This project aims 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 2 bodies are the only ethics committees in Malawi.
Objectives:	<p>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:</p> <p><u>Strengthening national capacity for ethical review in Malawi</u> Intermediate steps:</p> <ul style="list-style-type: none"> - Training workshops in Research Ethics, GCP and ethical review were conducted in all regions and an Annual National Conference was held during the project's duration. - <u>Introduction and strengthening of clinical trial monitoring in Malawi</u> Intermediate steps: - Two clinical trial monitors were employed for the 2 committees (1 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.
Cofunders:	Not applicable
Results and Outcomes:	<p>1. Infrastructure / Capacity Development</p> <ul style="list-style-type: none"> • Overhead projector • Consumables and supplies for the COMREC Secretariat were provided <p>2. Training (resources developed (e.g. manuals) and human capacity developed)</p> <p>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 Good Clinical Practice 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</p>

	<p>the 2 ethics committees (NHSRC and COMREC) and the regulatory authority (PMPB) has been harmonised. Members of Medical Rights Watch received funding and training.</p> <p>3. Networking / Collaborations Developed</p> <ul style="list-style-type: none"> • PABIN (Pan African Bioethics Initiative) • SARETI (Southern African Research Ethics Training Initiative) • PEHRP AFRICA (Partnership for Enhancing Human Research Protection in Africa) • AMANET (African Malaria Network Trust)
Key Publications:	<ol style="list-style-type: none"> 1. Report on the workshop “Enhancing Clinical Trial Oversight in Malawi” conducted on 19th June – 20th June 2008 at Nkopola Lodge in Mangochi, Malawi Medical Journal – MMJ 20(2): 63 – 64 June 2008. www.mmj.medcol.mw. 2. Mfutso-Bengo, J. M., Masiye, F., & Muula, A., Ethical challenges in conducting research in humanitarian crisis situations, research ethics paper published in the Malawi Medical Journal – MMJ 20(2) 2008: 46 – 49 June 2008. www.mmj.medcol.mw 3. Ndebele, P., Mfutso-Bengo, J., Mduluza, T., Compensating clinical trial participants from limited resource settings in internationally sponsored clinical trials, a proposal, Malawi Medical Journal; 20(2): pp. 42 – 45. www.mmj.medcol.mw

7.1.8 Falusi-Ibadan-Ethics

EDCTP Project Coordinator:	Adeyinka Falusi
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:	<ol style="list-style-type: none"> 1) Prince U. Ele (Nigeria) 2) O. Ojuawo (Nigeria) 3) O. Ogunbodede (Nigeria) 4) Paulina Tindana (Ghana) 5) Paul Ndebele (Malawi) 6) John R. Williams (Canada) 7) Marie-Charlotte Bouesseau (Switzerland)
Type of Project:	IRB
Goal:	The goal of this project was to provide technical, administrative and material support to the 3 Research Ethics Committees (RECs) for effective and efficient capacity building for research oversight to their institutions and possibly others in their localities.
Objectives:	<ol style="list-style-type: none"> 1. To document the existing infrastructure, manpower capacity and operational details of the selected RECs to appropriately assess their needs. 2. To develop an intervention package of a training programme and provision of a seed grant to improve capacity building and infrastructural facilities to the 3 sites. 3. To monitor and evaluate the outcomes of the intervention package. 4. To empower the core group trained to become trainers in their localities. 5. To stimulate the development of ethics guidelines with the incorporation of African concepts.
Cofunders:	Not applicable
Results and Outcomes:	<ol style="list-style-type: none"> 1. Infrastructure / Capacity Development Desktop computer, printer, UPS, power surge arrestor, scanner and photocopier were provided to each of the 3 RECs. 2. Training (resources developed (e.g. manuals) and human capacity developed) A four-day training workshop was held. RECs developed Operational Guidelines. 3. Networking / Collaborations Developed <ul style="list-style-type: none"> • WHO • World Medical Association (WMA)
Key Publications:	Workshop Proceedings on Strengthening The Capacity of Research Ethics Committees in Africa. (ISBN 978 978 083 544 6)

7.1.9 Manafa-NIMR-Ethics

EDCTP Project Coordinator:	Ogenna Manafa
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:	1) Kolawole Solomon Oyedeji (Nigeria) 2) ST Abolarinwa (Nigeria) 3) Olumide Ogundahunsi (Switzerland)
Type of Project:	IRB
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 5-10 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.
Cofunders:	Not applicable
Results and Outcomes:	1. Training (resources developed (e.g. manuals) and human capacity developed) A 5 day training workshop on Human Subject Protection and Standard Operating Procedures (SOPs) writing for investigators and members of RECs/IRBs took place. A second 5 day workshop was held for investigators and members of RECs/IRBs in northern Nigeria. Evaluation of 3 ethics committees. 2. Networking / Collaborations Developed <ul style="list-style-type: none"> • TDR/WHO which houses the Scientific Initiative for Developing Capacity in Ethical Review (SIDCER) • West African Bioethics Initiative (Nigerian Institute of Medical Research (NIMR))
Key Publications:	Not applicable

7.1.10 Moodley-Stellenbosch-Ethics

EDCTP Project Coordinator:	Keymanthri Moodley
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:	<ol style="list-style-type: none"> 1) Landon Myer (South Africa) 2) Lyn Horn (South Africa) 3) Gordon Payne (South Africa) 4) Dawn Kolbe (South Africa) 5) Johan Hattingh (South Africa)
Type of Project:	Support for courses on ethics
Goal:	The ERECCA project focuses on capacity development in 2 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 2-3 years).
Objectives:	<p><u>Intermediate objectives:</u></p> <ul style="list-style-type: none"> • To extend refresher GCP courses to a wider audience via WEB CT. • To develop new capacity for ethics review. <p><u>Final objectives:</u></p> <ul style="list-style-type: none"> • 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.
Cofunders:	Not applicable
Results and Outcomes:	<ol style="list-style-type: none"> 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 <ul style="list-style-type: none"> • University of Ibadan, Nigeria • University of Zambia • Pan African Bioethics Initiative (PABIN) • Medicines Control Council (MCC) • University of Cape Town (UCT)
Key Publications:	Not applicable

7.1.11 Kilama-AMANET-1-Ethics

EDCTP Project Coordinator:	Roma Chilengi (Wenceslaus Kilama)
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:	01 June 2006
EDCTP Project End Date:	13 June 2007
Collaborators:	<ol style="list-style-type: none"> 1) Wencesalus Kilama (Tanzania) 2) Joseph Mfutso-Bengo (Malawi) 3) Francis Crawley (Belgium) 4) Paul Ndebele (Malawi) 5) Godfrey Tangwa (Cameroon) 6) Juntra Karbwang (Switzerland) 7) Joyce Ikingura (Tanzania) 8) Alwyn Mwinga (Zambia) 9) Souleman Mboup (Senegal) 10) Edphose Nfuka (Tanzania) 11) Saad Ramathan (Tanzania)
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 tailor-made 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.
Cofunders:	Not applicable
Results and Outcomes:	<ol style="list-style-type: none"> 1. Training (resources developed (e.g. manuals) and human capacity developed) <p>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.</p>
Key Publications:	Not applicable

7.1.12 Sewankambo-Makerere-Ethics

EDCTP Project Coordinator:	Nelson Sewankambo
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:	1) Elly Katabira (Uganda) 2) Steven Kiwuwa (Uganda) 3) Paul Kutwabami (Uganda) 4) Ronald Kiguba (Uganda)
Type of Project:	IRB
Goal:	The goal is to train faculty staff in ethical processes; establish a tracking system for research activities; strengthen the infrastructure of the 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:	<ol style="list-style-type: none"> 1. Establish a tracking system for research activities at the Faculty of Medicine. Institutional Review Board (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. Staff has undergone continued ethics training including an EDCTP-funded health research ethics workshop held 15-17 June 2009 as well as a National Ethics Committee workshop organised in July 2009 by the Uganda National Council for Science and Technology.
Cofunders:	Not applicable
Results and Outcomes:	<ol style="list-style-type: none"> 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. Staff have undergone continued ethics training including an EDCTP-funded health research ethics workshop as well as a National Ethics Committee workshop. 3. Networking / Collaborations Developed <ul style="list-style-type: none"> • University of Antwerp Ethics Committee • AMANET
Key Publications:	Not applicable

7.1.13 Holm-Cardiff-Ethics

EDCTP Project Coordinator:	Søren Holm
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:	1) Azaveli Lwaitama (Tanzania) 2) Heta Gylling (Finland) 3) 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 10 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. 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 3 years after the end of the project period.
Cofunders:	Not applicable
Results and Outcomes:	1. Training (resources developed (e.g. manuals) and human capacity developed) Online training course developed. 2. Networking / Collaborations Developed • University of Dar Es Salaam • University of Helsinki • University of Oslo
Key Publications:	Not applicable

7.1.14 Munyati-MRCZb&c-Ethics

EDCTP Project Coordinator:	Shungu Munyati (Rosemary Musesengwa)
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:	01 March 2010
Collaborators:	<ol style="list-style-type: none"> 1) Paul Ndebele (Malawi) 2) Peter Makuhunga (Zimbabwe) 3) Priscilla Nyambayo (Zimbabwe) 4) J. Matenga (Zimbabwe) 5) Simba Rusakaniko (Zimbabwe)
Type of Project:	NEC, IRB
Goal:	The main goal is 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:	<ol style="list-style-type: none"> 1. Strengthening national and institutional ethical review processes and ethics review capacity in Zimbabwe. 2. Strengthening of clinical trial monitoring in Zimbabwe.
Cofunders:	Not applicable
Results and Outcomes:	<ol style="list-style-type: none"> 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) Trained 762 researchers, students, IRB and CAB members. 3. Networking / Collaborations Developed <ul style="list-style-type: none"> • MCAZ • BRTI • AMANET • WHO • Professor E. Gomo, College of Medicine, Malawi
Key Publications:	Not applicable

7.1.15 HOUNGNIHIN-MH-BENIN-ETHICS

EDCTP Project Coordinator:	Roch A. Hounghinin
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:	<ol style="list-style-type: none"> 1) Raouf A. Osséni (Benin) 2) Flore Gangbo (Benin) 3) Dorothee Kinde Gazard (Benin) 4) Jules Affodji (Benin) 5) Michelle Hountondji (Benin)
Type of Project:	NEC
Goal:	This project aims to contribute to reinforce the capacities of the National Ethics Committee (NEC) in Benin.
Objectives:	This project will contribute to the setting up and the reinforcement of the capacities of the National Ethics Committee (NEC). For this objective, many workshops and meetings will be 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 will be elaborated and carried out.
Cofunders:	Not applicable
Results and Outcomes:	<ol style="list-style-type: none"> 1. Infrastructure / Capacity Development Equipment and computers for the Secretariat were purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed) <ul style="list-style-type: none"> - the law on the creation of a National Ethics Committee was revised and adopted by the Parliaments, - 100% of the members of the National Ethics Committee were trained in Benin (Cotonou) and in Kenya (Nairobi) (40 researchers); - 50% of the researchers were trained on the role of an ethics committee (for its good knowledge and its perception in Benin) (45 members) - Information leaflets were developed - Development of a website: www.ethiquesante.org 3. Networking / Collaborations Developed <ul style="list-style-type: none"> • 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)
Key Publications:	Not applicable

7.1.16 Petros-ETBIN-1-Ethics

EDCTP Project Coordinator:	Beyene Petros
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:	1) Fisseha Hailemeskel (Ethiopia) 2) Abraham Aseffa (Ethiopia)
Type of Project:	IRB
Goal:	Research departments in the 5 newly established universities do 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 is to establish and strengthen Health Research Ethics Committees in Ethiopia.
Objectives:	- Establishing Institutional Review Boards (IRBs) in 5 newly established universities. - Strengthening 3 existing IRBs. - Popularising Health Research Ethics in the country.
Cofunders:	Armauer Hansen Research Institute (AHRI)
Results and Outcomes:	1. Infrastructure / Capacity Development Eleven printers, 12 computers, 1 photocopier and 1 scanner were purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed) Manuscript on Human Participant Protection and Good Clinical Practice (GCP). Human Participant Protection, GCP and SOP Bioethics Training Workshop took place. Seventy-six individuals trained in total. 3. Networking / Collaborations Developed <ul style="list-style-type: none"> • Bioethics Unit, School of Medicine, Addis Ababa University (AAU) • Pan African Bioethics Initiative (PABIN)
Key Publications:	Not applicable

7.1.17 Adebamowo-WABT-Ethics

EDCTP Project Coordinator:	Clement Adebamowo
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:	1) Yakubu Aminu (Nigeria) 2) Yemisi Ajibose (Nigeria)
Type of Project:	NEC
Goal:	The objective of this work is to provide training for members of the National 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:	a) Provide training in health research ethics for those members of the NHREC who have not had specific training in health research ethics. b) 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
Results and Outcomes:	1. Training (resources developed (e.g. manuals) and human capacity developed) In April 2009, 13 individuals received training in a course on Informed Consent and Management of an Ethics Committee. In June 2010, 10 members from the National Health Research Ethics Committee (NHREC) received training. Ten NHREC members received materials (e.g. books) and training towards a diploma in research ethics. 2. Networking / Collaborations Developed <ul style="list-style-type: none"> Federal Ministry of Health of Nigeria
Key Publications:	Not applicable

7.1.18 Wane (Kayitenkore)-Rwanda-NEC-Ethics

EDCTP Project Coordinator:	Justin Wane (Kayitesi Kayitenkore)
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:	1) Emmanuel Nkeramihigo (Rwanda) 2) Dariya Mukamusoni (Rwanda)
Type of Project:	NEC
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 7 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). Three months ago; an administrator was recruited with the responsibility of running the office on a day-to-day basis. The Ministry of Health has 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 intends 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: <ul style="list-style-type: none"> • Training in human subject's protection course. • Completion of SOPs. <ul style="list-style-type: none"> • Training in SOPs. • Improvement of the infrastructure, internet and telephone connectivity. • Acquisition of shelves and metal lockable cabinets for archiving documents. • Providing a stable salary to the administrator. • Publish guidance documents, such as RNECs SOPs National Guidelines on the Ethics of Health Related Research in Rwanda. • Setting up a website providing access to guidance documents and important links. • Meeting to discuss with research community, national workshop to explain procedures, e.g. SOPs, forms. • Propose National Guidelines for Ethical Review. • Organise training of local IRBs and teaching of ethics in health training institutions. • Networking activities with dissemination of information. • Archiving and development of a database.
Cofunders:	Not applicable
Results and Outcomes:	In progress
Key Publications:	Not applicable

7.1.19 Changalucha-NIMR-2-NEC-Ethics

EDCTP Project Coordinator:	John M. Changalucha
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:	1) Saidi Kapiga (Tanzania) 2) Joyce Ikingura (Tanzania) 3) Zaba Basia (United Kingdom)
Type of Project:	IRB
Goal:	The establishment of a well-functioning local 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 National Ethics Committee.
Objectives:	The main objective of this project is to establish a local Institutional Review Board (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 will be formed to guide the establishment of a local Ethics Review Board (ERB) in Mwanza, Tanzania. Members of the ERB will be trained in research ethics.
Cofunders:	Not applicable
Results and Outcomes:	1. Infrastructure / Capacity Development Equipment including 2 computers, 1 laser printer, 3 filing cabinets and 1 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 2 day training workshop was conducted in order to orient IRB members on Health Research Ethics (HRE), their duties and responsibilities. A 1 day national meeting was held in order to share experiences between all active IRBs in Tanzania. 3. Networking / Collaborations Developed <ul style="list-style-type: none"> • Bugando Medical Centre • African Medical and Research Foundation (AMREF) • Sekou Toure Hospital • Tanzania Essential Strategies Against AIDS (TANESA)
Key Publications:	Not applicable

7.1.20 Chilengi (Kilama)-AMANET-2-Ethics

EDCTP Project Coordinator:	Roma Chilengi (Wenceslaus Kilama)
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:	<ol style="list-style-type: none"> 1) Aceme Nyika (Tanzania) 2) Godfrey Tangwa (Cameroon) 3) Ramadhani Noor Abdalla (Tanzania) 4) Saad Ramadhani (Tanzania) 5) Paul Ndebele (Malawi) 6) Joyce Ikingura (Tanzania) 7) Edephonse Nfuka (Tanzania) 8) Joseph Mfutso-Bengo (Malawi) 9) William Mwatu (Kenya) 10) Paulina Tindana (Ghana) 11) Djouaka Rousseau (Benin)
Type of Project:	Support for courses on ethics
Goal:	This 1 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:	<p>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:</p> <ul style="list-style-type: none"> • Improved delivery of the web based course with new features; • Increased francophone Africa participation on the basic course; • Further training for individuals interested in higher understanding of research ethics; and • Using the web learning to deliver GCP training.
Cofunders:	African Malaria Network Trust (AMANET)
Results and Outcomes:	<p>1. Training (resources developed (e.g. manuals) and human capacity developed)</p> <p>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.</p>
Key Publications:	Not applicable

7.1.21 Massaga (Mashalla)-TANHER-Ethics

EDCTP Project Coordinator:	Julius J. Massaga
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:	1) Mwele Malecela (Tanzania) 2) Leonard Mboera (Tanzania)
Type of Project:	NEC
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 plans 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 by doing the following activities: <ul style="list-style-type: none"> • 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. • To 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, photocopier machine, scanner with advanced document feeder), for facilitating storage and retrieval of information. • To develop national guidelines for insurance and compensation of research participants involved in clinical trials. • Organise a stakeholders meeting to disseminate the revised guidelines, SOPs and guidelines on insurance and compensation of clinical trials research participants.
Cofunders:	Not applicable
Results and Outcomes:	1. Infrastructure / Capacity Development Office furniture (2 tables and 2 office chairs), cabinets (2 units), desktop computers (2 units), laptop (1 unit), printer (1 unit), photocopier (1 unit), scanner with advanced document feeder (1 unit) and UPS (2 units) were purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed) Stakeholder's workshop (September 2008), Stakeholder's meeting (June 2010), Workshop to develop proposal on reduction of maternal and newborn mortality in Tanzania (August 2010) and a Symposium on research ethics in clinical studies in sub-Saharan Africa (5-7 April 2011) was held. Revision of National Guidelines: Guidelines on ethics for health research in Tanzania (2nd version, 2009). Standard Operating Procedures for the National Ethics Review Committee in Tanzania (www.nimr.or.tz/ethical_guidelines.html). Development of Guidelines on Insurance of Clinical Trial Participants.
Key Publications:	Not applicable

7.1.22 Onapa-UNCST-Ethics

EDCTP Project Coordinator:	Maxwell Otim Onapa
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:	05 September 2008
EDCTP Project End Date:	04 September 2011
Collaborators:	1) Julius Ecuru (Uganda) 2) Leah Nawegulo (Uganda) 3) Jane Nabuto (Uganda) 4) Winfred Badanga (Uganda)
Type of Project:	NEC
Goal:	The goal of this project is to strengthen the Uganda National Council for Science and Technology's committees, but also to improve the efficiency, effectiveness and coordination of the national system for scientific and ethical review of research protocols.
Objectives:	<ul style="list-style-type: none"> • To ensure that a minimum standard is applied for post-approval monitoring of research. • To develop the accreditation standards for all institutional review/ethics committees (IRCs) based on the existing national and international human subjects protection guidelines. • To develop standard operating procedures (SOPs) for the National AIDS/HIV Research committee (NARC) in Uganda. • To establish a network of IRC chairpersons for an improved coordination of the ethical review system in Uganda. • To organise and launch the First Annual Research Ethics conference. • To improve the infrastructure for the NARC and Health Sciences Committee.
Cofunders:	Not applicable
Results and Outcomes:	In progress
Key Publications:	Not applicable

7.1.23 Mason-BRTI-Ethics

EDCTP Project Coordinator:	Peter Mason
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:	<ol style="list-style-type: none"> 1) Farirai Mutenherwa (Zimbabwe) 2) Alphege Maisiri (Zimbabwe) 3) Innocent Gangaidzo (Zimbabwe) 4) Mandla Sigogo (Zimbabwe) 5) Ian McVey (Zimbabwe)
Type of Project:	IRB
Goal:	The conduct of ethical review of human subjects 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 improve this situation.
Objectives:	<ol style="list-style-type: none"> 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.
Cofunders:	Not applicable
Results and Outcomes:	<ol style="list-style-type: none"> 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. 2. Training (resources developed (e.g. manuals) and human capacity developed) Publication of an ethics handbook and ARENA newsletter. Workshop and training course were held.
Key Publications:	Not applicable

7.1.24 Khulumani (Kasule)-HRU-Botswana-Ethics

EDCTP Project Coordinator:	Pilate Khulumani (Mary Kasule)
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:	<ol style="list-style-type: none"> 1) Pilate Khulumani (Botswana) 2) Paul Ndebele (Botswana) 3) David Guwatudde (Uganda) 4) Keymanthri Moodley (South Africa)
Type of Project:	NEC
Goal:	<p>The goal of this project is to strengthen the capacity of Botswana's National Research Ethics Committee (BNREC) through training its members in the 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 is 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) will also be set up as part of this project to sensitise communities in Botswana about health research, especially clinical trials conducted in their communities. This project aims 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.</p>
Objectives:	<ol style="list-style-type: none"> 1. To strengthen the Botswana National Research Ethics Committee (NREC) and establish Institutional Review Boards (IRBs). 2. To 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. To establish IRBs in all Health Training Institutions and Districts in Botswana. 4. To 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. To develop review guidelines, Standard Operational Procedures (SOPs) and Clinical Trial Guidelines. 6. To improve office infrastructure through purchasing equipment and stationery.
Cofunders:	Not applicable
Results and Outcomes:	<ol style="list-style-type: none"> 1. Infrastructure / Capacity Development One laptop, 1 heavy duty photocopier, 1 camera and 1 shredder were purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed) Three workshops for NREC members and 1 audit training for 14 participants took place. Community advisory boards have been established in 3 districts. Five out of 7 Institutes of Health Sciences have established their own ethics committee. Review guidelines and SOPs were developed. 3. Networking / Collaborations Developed <ul style="list-style-type: none"> • University of Pennsylvania

	<ul style="list-style-type: none"> • University of Botswana • University of Stellenbosch • Botswana Harvard Partnership • Harvard School of Public Health • Boehringer-Ingelheim • Makerere University • Baylor College of Medicine
Key Publications:	Not applicable

7.1.25 Mupenda-CIBAF-Mzadi-Ethics

EDCTP Project Coordinator:	Bavon Mupenda
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:	<ol style="list-style-type: none"> 1) Jean-Vivien Mombouli (Congo Brazzaville) 2) Moyikoua (Congo Brazzaville) 3) Félicien Munday (Democratic Republic of Congo) 4) Emery Ndwelo (Democratic Republic of Congo) 5) Laurent Ravez (Belgium) 6) Stuart Rennie (United States)
Type of Project:	IRB
Goal:	The primary aim of this project is 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:	<ol style="list-style-type: none"> (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.
Cofunders:	Not applicable
Results and Outcomes:	<ol style="list-style-type: none"> 1. Infrastructure / Capacity Development Desks and tables (4 in total), 1 laptop and 1 inkjet printer were purchased. 2. Training (resources developed (e.g. manuals) and human capacity developed) SOPs were finalised, national guidelines were developed and a researcher's brochure was developed. A webpage on the existing website was created to assist researchers with the ethical review process. A 2-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 3 technical assistants) of experienced researchers, clinicians, nurses and university administrators involved in biomedical research. 3. Networking / Collaborations Developed <ul style="list-style-type: none"> - Marien Ngouabi University - Kinshasa School of Public Health - University of North Carolina – Chapel Hill - University of Namur, Belgium
Key Publications:	Not applicable

7.1.26 Okitolonda-CIBAF-Palabre-Ethics

EDCTP Project Coordinator:	Emile Okitolonda Wemakoy
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:	<ol style="list-style-type: none"> 1) Pierre Lokadi Opetha (Democratic Republic of Congo) 2) Aimé Malonga Mulenda (Democratic Republic of Congo) 3) Kiyombo Mbela (Democratic Republic of Congo) 4) Samuel Mampunza (Democratic Republic of Congo) 5) Didine Kaba (Democratic Republic of Congo) 6) Lapika Dimomfu (Democratic Republic of Congo) 7) Félicien Munday (Democratic Republic of Congo) 8) Bavon Mupenda (Democratic Republic of Congo) 9) Marcel Blanchard Mukengeshayi (Democratic Republic of Congo) 10) Hypolite Kalambayi (Democratic Republic of Congo) 11) Kadima Ebeja (Democratic Republic of Congo) 12) Pélagie Babakazo (Democratic Republic of Congo)
Type of Project:	NEC
Goal:	This project aimed at strengthening the capacity of the National Health Ethics Council (NHEC) and developing national ethics guidelines.
Objectives:	<ol style="list-style-type: none"> 1. Strengthening the capacity of the National Health Ethics Council. Activities in support of this aim include: <ul style="list-style-type: none"> - 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: <ul style="list-style-type: none"> - 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.
Cofunders:	Not applicable
Results and Outcomes:	<ol style="list-style-type: none"> 1. Infrastructure / Capacity Development Two laptops, 4 desks/ tables and 1 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 developed. Members of the National Health Ethics Council received training. 3. Networking / Collaborations Developed <ul style="list-style-type: none"> • Human African Trypanosomiasis Platform
Key Publications:	Not applicable

7.1.27 Boateng-NMIMR-Ghana-Ethics

EDCTP Project Coordinator:	Okyere Boateng
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:	1) Paulina Tindana (Ghana) 2) John Gyapong (Ghana) 3) Isaac Adams (Ghana)
Type of Project:	NEC, IRB
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:	a) Enhance the quality of the scientific and ethical review of proposals/protocols involving human subject/participants by ethical review committees through capacity building. b) To develop National Ethical Guidelines in the conduct of research involving human subjects. c) Establish a database for Institutional Review Boards (IRB)/Research Ethics Committees in the country. d) Promote networking and sharing of ideas among IRB/REC and researchers. e) Resource IRBs/RECs which were not covered by the earlier grant from EDCTP by providing them with office equipment.
Cofunders:	Not applicable
Results and Outcomes:	1. Infrastructure / Capacity Development Four computers, 4 printers, 4 cabinets and 5 shredders were purchased. The target institutions for the supply of equipment were: <ul style="list-style-type: none"> • 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 2-day Health Research Ethics Seminar was held in November 2010 for researchers, IRB members and lecturers. The training and mentoring of IRB administrators from the 8 IRBs took place. A 2-day National Research Ethics Review Conference was held on 8 and 9 March 2011. National Research Ethics Guidelines were drafted. A Secretariat to work towards establishment of the National Health Research Ethics Board was put in place. Improved databases for the IRBs. 3. Networking / Collaborations Developed <ul style="list-style-type: none"> • AMANET (Africa Malaria Network Trust) • KEMRI (Kenya Medical Research Institute) • Networking among the local IRBs
Key Publications:	Not applicable

7.1.28 Wasunna-KEMRI -Ethics

EDCTP Project Coordinator:	Christine Wasunna
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:	17 December 2011
Collaborators:	1) Juma Rashid (Kenya) 2) Jayesh Pandit (Kenya)
Type of Project:	IRB
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 1 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 2 include establishing a research audit package and initiating a joint electronic clinical trials database between the 2 institutions.
Objectives:	<p>1. Improve ethical review process at KEMRI through:</p> <p>a) Training KEMRI ERC members in international health research ethics; b) Facilitating health research ethics workshops for researchers at KEMRI and PPB twice a year.</p> <p>2. Develop a system for auditing research approved for implementation by the KEMRI ERC in order to provide important research safeguards by:</p> <p>a) Facilitating 3 Clinical Research Monitoring and Good Clinical Practice workshops (3 workshops) for Site Auditors (Senior research officers selected from 3 KEMRI Research Centres in Nairobi, Kisumu and Kilifi); KEMRI ERC and PPB ECCT members; b) Developing an auditing checklist for project initiation, interim project evaluation and project completion.</p> <p>3. Promote high standards of clinical research oversight through partnership with the Pharmacy and Poisons Board of Kenya by:</p> <p>a) Launching a database on all clinical trials in Kenya; b) Promoting pharmacovigilance through adverse drug reaction reporting within the study sites.</p>
Cofunders:	Not applicable
Results and Outcomes:	In progress
Key Publications:	Not applicable

7.1.29 Fumane-MH-Mozambique-Ethics

EDCTP Project Coordinator:	João Manuel de Carvalho Fumane
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:	1) Xavier Carne (Spain) 2) Raquel Hernandez (Spain) 3) Nuria Sanz (Spain)
Type of Project:	NEC
Goal:	The Mozambican National Ethic Committee, called CNBS (Comité Nacional de Bioética para Saúde), was created in 2002. The CNBS will coordinate the proposed activities, which will consist 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 will be 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 is 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 will receive African Malaria Network Trust (AMANET) and European Clinical Research Infrastructures Network (ECRIN) / Vienna School of Clinical Research (VSCR) training and will exchange capacity building expertise with ECRIN. And on a second step, already trained CNBS and IEC members will train researchers, health professionals, health authorities and medical school students. The second objective is to create a network of Mozambican Institutional Ethics Committees (IECs).
Cofunders:	Not applicable
Results and Outcomes:	In progress
Key Publications:	Not applicable

7.1.30 Ukpong-NHVMS-Ethics

EDCTP Project Coordinator:	Morenike Ukpong
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:	<ol style="list-style-type: none"> 1) Kolawole Oyedeki (Nigeria) 2) Oliver Ezechi (Nigeria) 3) Ademola Ajuwon (Nigeria) 4) Adebisi Adejumo (Nigeria) 5) Kayode Dada (Nigeria) 6) Olayide Akanni (Nigeria) 7) Augustina Amumuziam (Nigeria) 8) Florita Durueke (Nigeria) 9) Aisha Adaraniyo (Nigeria)
Type of Project:	Support for courses on ethics
Goal:	<p>This project is a proposed follow up to an earlier pilot project with grant support from SIDACTION, France. This project is 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 1 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.</p>
Objectives:	<ol style="list-style-type: none"> 1. To 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 8 months. 2. To familiarise 20 lay members of Ethics Committees in Nigeria with the operational guidelines for conducting ethical research in Nigeria over a period of 8 months. 3. To 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. To 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 8 months.
Cofunders:	Not applicable
Results and Outcomes:	<ol style="list-style-type: none"> 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 <ul style="list-style-type: none"> • National Health Research Ethics Committee • National Bioethics Society of Nigeria
Key Publications:	Not applicable

7.1.31 Sarr-CNRS-Ethics

EDCTP Project Coordinator:	Samba Cor Sarr
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:	02 December 2009
EDCTP Project End Date:	01 December 2011
Collaborators:	<ol style="list-style-type: none"> 1) Aïssatou Toure (Senegal) 2) Charles Becker (Senegal) 3) Oumar Faye (Senegal) 4) Mohamadou Lamine Mane (Senegal) 5) Doulo Der (Senegal) 6) Assane Diouf (Senegal)
Type of Project:	NEC
Goal:	The expected outcomes of this project are 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:	<p>The broad objective of the project is 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.</p> <p>The specific objectives are:</p> <ul style="list-style-type: none"> - To improve the human resources of the CNRS secretariat. - To improve the infrastructure of the CNRS secretariat. - To train the different stakeholders in research ethics: ethic committee members and researchers. - To improve the review process of health research proposals. - To establish a tracking system for research proposals. - To create a website for adequate information for all the stakeholders, awareness and discussion on ethics issues.
Cofunders:	Not applicable
Results and Outcomes:	In progress
Key Publications:	Not applicable

7.1.32 Wassenaar-SARECCER-Ethics

EDCTP Project Coordinator:	Douglas Wassenaar
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:	1) Mariana Kruger (South Africa) 2) Catherine Slack (South Africa) 3) Nicole Mamotte (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 is funding 5 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 proposed 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.
Cofunders:	Not applicable
Results and Outcomes:	In progress
Key Publications:	Not applicable

7.1.33 Ijsselmuiden-COHRED-Ethics

EDCTP Project Coordinator:	Carel Ijsselmuiden
EDCTP Call Title:	Support for Courses and Seminars on Ethics
EDCTP Project Title:	Mapping of ethics review and trial regulatory capacity in sub-Saharan 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:	Support for courses on ethics
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:	<p>The core deliverables of this project are:</p> <ol style="list-style-type: none"> 1) A continuously updated ('self-updating'), systematic map of African research ethics review committees and clinical trial related regulatory activities that are linked to the 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 research ethics committees through Health Research Web (HRWeb) and developing the content and display of research ethics committee information in ways that suit the key audiences best. 4) Developing sustainability and capacity, in specific: <ol style="list-style-type: none"> a. Agreement on criteria for ethics committee registration on HRWeb; b. Support from donors and research sponsors to demand review by registered research ethics committees; c. Mechanisms for 'self-funding', additional donors in place; and d. Beginnings of a pan African accreditation mechanism.
Cofunders:	<ol style="list-style-type: none"> 1) NIH 2) Pfizer
Results and Outcomes:	<ol style="list-style-type: none"> 1. Mapping <ol style="list-style-type: none"> 1.1) 116 RECs have been mapped in 30 African Countries, with a further 56 RECs identified. 1.2) The Ethics Pages of HRWeb are developed with various analysable functionalities. 1.3) MARC now has an independent website: www.researchethicsweb.org 2. Networking <ol style="list-style-type: none"> 2.1) MARC will soon launch the Research Ethics social network platform, which will allow for online interaction of RECs across Africa. 2.2) The social network will be an African based tool and serve as a platform for questions and debate, and also facilitate the standards and quality of RECs and ethics review. 3. Medicines Regulatory Authorities Mapping of Medicines Regulatory authorities will commence in June, a research officer has already been appointed.
Key Publications:	A first paper has been submitted and accepted by the Developing World Bioethics Journal

7.1.34 Mbidde-UVRI-Ethics

EDCTP Project Coordinator:	Edward K. Mbidde
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:	07 February 2010
EDCTP Project End Date:	06 February 2012
Collaborators:	1) Tom Lutalo, Uganda 2) Robert Ssekubugu, Uganda
Type of Project:	IRB
Goal:	There is 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 is also an urgent need to put together guidelines for running the secretariat.
Objectives:	The main objective of the project is to strengthen the review capacity and process of the UVRI Science and Ethics Committee. This requires continuing training of the current and potential future members, the scientific staff from the collaborating programs and core UVRI departments. The funds will be used to train trainers who will continue with the training process. The funds will also be used to strengthen the UVRI Secretariat such 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 will also be shared with the other IRBs in the country such that the review process in the country is strengthened. The following is a break-down of the planned process: <ul style="list-style-type: none"> - Equip the science and ethics office with necessary office tools. - Prepare the Standard Operating Procedures (SOPs) and regulations for the Science and Ethics Committee. - Disseminate SOPs and regulations to the partner programmes. - Perform research site visits to ensure compliance, offer support, supervision and continuous training. - Facilitate science and ethics review meetings. - Establish an IRB forum in the country and liaise with PABIN to strengthen the review process.
Cofunders:	1. Uganda Virus Research Institute (UVRI)
Results and Outcomes:	In progress
Key Publications:	Not applicable

7.1.35 SPRUMONT-TRREE-2- Ethics

EDCTP Project Coordinator:	Dominique Sprumont
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:	<ol style="list-style-type: none"> 1) Clement Adebamowo (Nigeria) 2) Samba Cor Sarr (Senegal) 3) Aïssatou Toure (Senegal) 4) Eusebio Macete (Mozambique) 5) Peter M. Ndumbe (Cameroon) 6) Ogobara Doumbo (Mali) 7) Wenceslaus Kilama (Tanzania) 8) Marie Hirtle (Canada) 9) John R. Williams (Canada) 10) Marcel Tanner (Switzerland) 11) Dirk Lanzerath (Germany) 12) Marie Charlotte Bouësseau (Switzerland) 13) Douglas Wassenaar (South Africa) 14) Charles Becker (Senegal) 15) 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:	<p>1. Training (resources developed (e.g. manuals) and human capacity developed)</p> <p>The online training programme (www.trree.org) was extended with four new national modules:</p> <ol style="list-style-type: none"> 1. Senegal 2. Nigeria 3. Mozambique 4. Germany <p>There is also an additional module on informed consent. The programme has been translated into Portuguese.</p> <p>2. Networking / Collaborations Developed</p> <ul style="list-style-type: none"> • AMANET (Tanzania) • Comité d'Ethique National de la Recherche en santé (CNRS) (Senegal) • EURECNET (European Network of Research Ethics Committees) • Institute of Health Law, University of Neuchâtel (Switzerland) • Manhica Health Research Center (Mozambique) • MRTC (Mali) • SARETI (South Africa) • University of Yaoundé (Cameroon) • West African Bioethics (Nigeria)
Key Publications:	Not applicable

7.1.36 Matsiegui-CAEN-Ethics

EDCTP Project Coordinator:	Pierre-Blaise Matsiegui
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 May 2013
Collaborators:	<ol style="list-style-type: none"> 1) Sophie Bipolo (Gabon) 2) Adèle Sambo (Gabon) 3) Jean Baptiste Moussavou Kombila (Gabon) 4) Jaqueline Obone Mba (Gabon) 5) Saadou Issifou (Gabon) 6) Jean Paul Akue (Gabon) 7) Christiane Mbili (Gabon) 8) Véronique Nianguï (Gabon) 9) Dafna Feinholz (France)
Type of Project:	NEC
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 (i) investing in infrastructure, (ii) providing tailor-made training, (iii) raising public awareness in Gabon on ethical issues in (clinical) research as well as the role and responsibilities of the NEC, and (iv) 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:	<ol style="list-style-type: none"> 1) Ministry of Public Health, Republic of Gabon 2) Ministry of Research and Science, Republic of Gabon 3) Vienna School of Clinical Research
Results and Outcomes:	<ol style="list-style-type: none"> 1. Infrastructure / Capacity Development An office table was 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 installed in Libreville. 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 from 27 September to 01 October 2010. Additionally, 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. A website for the NEC has been set up: <http://www.cner-gabon.org/cner/>

3. Networking / Collaborations Developed

A. 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

B. International institutions:

- UNESCO
- WHO
- Ethics Committee of the Chantal Biya International Reference Centre for Research on HIV/AIDS Prevention and Management (CIRCB), Cameroon
- Comité d’Ethique de la Recherche en Sciences de la Santé (CERSSA), Republic of Congo
- Comité d’Ethique 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, Austria

Key Publications:	Not applicable
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7.1.37 KOLLIE-Uni-Liberia-IRB-ETHICS

EDCTP Project Coordinator:	James Kollie
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:	1) Cecelia Morris (Liberia) 2) Robert Draper (Liberia) 3) Ellen George-Williams (Liberia) 4) Pearl Fahnbulleh (Liberia) 5) Jemee Tegli (Liberia)
Type of Project:	IRB
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 is 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:	- To increase and build the capacity of the UL-IRB. - To introduce the UL Deans, Coordinators, Researchers to human research ethics. - To appraised the ethical knowledge of the UL Graduate and Professional programmes.
Cofunders:	Not applicable
Results and Outcomes:	In progress
Key Publications:	Not applicable

7.1.38 Rulisa-KUTH-Ethics

EDCTP Project Coordinator:	Stephen Rulisa
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:	04 May 2010
EDCTP Project End Date:	03 May 2011
Collaborators:	1) Heinrich Klech (Austria) 2) Christine Druml (Austria) 3) Pierre-Blaise Matsiegui (Gabon)
Type of Project:	IRB
Goal:	The current ethical review system in Rwanda consists of 1 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 very limited resources, which hinders a rapid realisation of this plan. The EDCTP grant will therefore provide an important impetus to speed up the re-organisation of the Rwandan ethical review system.
Objectives:	The Kigali University Teaching Hospital (KUTH) has been chosen to be the first Rwandan research institution where an IRB will be established. OnQ Research Company will be in charge of organising a training course on ethics and for providing access to an on-line course on Good Clinical Practice (GCP). The training course will be combined with a train-the-trainer where candidates will be instructed in training skills so that they can put together and conduct their own training sessions. Additionally this project aims 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 a 1-year long (part-time) administrative support and coordination of the IRB (1 meeting per month) and the knowledge exchange between European and African ethics committees.
Cofunders:	1) University Central Hospital of Kigali 2) OnQ Research Company
Results and Outcomes:	In progress
Key Publications:	Not applicable

7.1.39 Mugenyi-JCRC-IRB-Ethics

EDCTP Project Coordinator:	Peter Mugenyi
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:	<ol style="list-style-type: none"> 1) Cissy Kityo (Uganda) 2) Jesse Kagimba (Uganda) 3) Jasper Ogwal Okeng (Uganda) 4) Ferrie Nangobi (Uganda) 5) Emilio Ovuga (Uganda) 6) Julius Ecuru (Uganda) 7) Emmanuel Kyagaba (Uganda)
Type of Project:	IRB
Goal:	To enhance the capacity of the JCRC-IRB to oversee bioethical issues in human research.
Objectives:	<ol style="list-style-type: none"> a. Improving policies and Standard Operating Procedures (SOPs) for pre- and post-approval of research. b. Mentorship of Gulu University IRB Members. c. Facilitating and supporting education in biomedical research ethics related to research reviews. JCRC proposes to conduct an annual 5 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. d. 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. e. 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
Results and Outcomes:	<ol style="list-style-type: none"> 1. Infrastructure / Capacity Development A LCD projector, one laptop computer, one desktop computer, one printer, one desk, one shredder 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. The first workshop was held in November 2010 in Kampala and targeted 40 IRB members and researchers from within Kampala, Gulu and Mbarara IRBs. The second GCP and RE training was held in Gulu in northern Uganda, targeting 25 IRB members and researchers. 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 of the GCP and RE was held – 25 participants were trained. A video conference with the research counterparts in the USA was held. Draft SOPs were developed. 3. Networking / Collaborations Developed <ul style="list-style-type: none"> • Center for Social Science Research (CeSSRA), USA • Uganda National Council for Science and Technology (UNCST) • Strategic Initiative for Development of Capacity in Ethical Review (SIDCER) • Gulu University • Mbarara University • Mukono University • Mildmay Uganda • Uganda Virus Research Institute (UVRI)

	<ul style="list-style-type: none">• Makerere University
Key Publications:	Not applicable

7.1.40 Ndebele-Botswana-IRB-Ethics

EDCTP Project Coordinator:	Paul Ndebele
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:	28 February 2013
Collaborators:	<ol style="list-style-type: none"> 1) Isaac Mazonde (Botswana) 2) Mary Kasule (Botswana) 3) Rosemary Musesengwa (Zimbabwe) 4) Mike Kachedwa (Malawi)
Type of Project:	IRB
Goal:	The proposed project aims to ensure that studies conducted by UB staff and students conform to internationally accepted standards. In addition, the project will ensure that the UB IRB plays a more central role in coordinating human research in UB and is in a better position to respond to both national and international challenges in research oversight.
Objectives:	<p>The main objective is to strengthen the University of Botswana's Institutional Review Board (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 will ultimately contribute towards the independence, competence and transparency of the UB IRB. To address this objective, the project will include 5 components:</p> <ol style="list-style-type: none"> 1. Enhancing the ethical review and monitoring of studies conducted by UB staff, students and affiliates. 2. Streamline 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.
Cofunders:	Not applicable
Results and Outcomes:	In progress
Key Publications:	Not applicable

7.1.41 Kaptue-Cameroon-Ethics

EDCTP Project Coordinator:	Lazare Kaptue
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:	28 February 2013
Collaborators:	<ol style="list-style-type: none"> 1) Jerome Ateudjieu (Cameroon) 2) Marceline Djuidje Ngounoue (Cameroon) 3) Dominique Sprumont (Switzerland) 4) Timéleon Tchuinkam (Cameroon) 5) Sylvie Hansel-Esteller (France) 6) Jonas Tchakoa (Cameroon) 7) Albert Same-Ekobo
Type of Project:	NEC
Goal:	EDCTP support to the CNEC (Cameroon National Ethics Review Committee) will be 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:	<p>This project will support the Cameroon National Ethics Committee in strengthening its capacity in reviewing research protocols by:</p> <ul style="list-style-type: none"> • Updating Standard Operating Procedures (SOPs) for protocol review and monitoring, and contribute to the harmonisation of SOPs of other ethics committees in Cameroon. • Ensuring on-going training of its members in protocol evaluation, site visits monitoring and follow-up of protocols implementation. • Improving the access to infrastructure for its activities. • Improving the condition of protocols and informed consent evaluation and follow-up. • Organising training at the university level.
Cofunders:	Cameroon National Ethics Committee
Results and Outcomes:	In progress
Key Publications:	Not applicable

7.1.42 Woldeamanuel (Petros)-ETBIN-2-Ethics

EDCTP Project Coordinator:	Yimtubezinash Woldeamanuel (Beyene Petros)
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:	28 February 2013
Collaborators:	1) Fisseha Haile Meskal (Ethiopia) 2) Abraham Aseffa (Ethiopia)
Type of Project:	IRB
Goal:	This project is a continuation of the Ethiopian Bioethics Initiative (ETBIN's) EDCTP supported project towards establishing and strengthening IRBs in Ethiopia.
Objectives:	<p>a) Assist 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.</p> <p>b) 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.</p> <p>c) Translate the ethics booklet written in Amharic (with EDCTP support) into at least 2 more Ethiopian languages, thus contributing to much broader awareness creation.</p> <p>d) 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.</p> <p>e) Organise ETBIN's General Assembly to enhance its organisational capacity.</p> <p>f) Provide administrative support to organising PABIN's General Assembly.</p>
Cofunders:	Armauer Hansen Research Institute (AHRI)
Results and Outcomes:	In progress
Key Publications:	Not applicable

7.1.43 Yeveo-Ghana-IRB-Ethics

EDCTP Project Coordinator:	Lucy Yeveo
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:	28 February 2013
Collaborators:	1) Margaret Gyapong (Ghana) 2) Sheila Addei (Ghana) 3) Okyere Boateng (Ghana) 4) Miriam Diana Abagal (Ghana)
Type of Project:	IRB
Goal:	The Dodowa Health Research Centre (DHRC) is 1 of the 3 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 aims to establish and strengthen the activities of an IRB for the DHRC.
Objectives:	a) Establish an Ethical Review Board for the Dodowa Health Research Centre. b) Develop Standard Operating Procedures (SOPs) for the IRB. c) Promote networking and sharing of ideas among IRB members and researchers to ensure high standards. d) Train ethics review board members. e) Catalogue protocols. f) Educate community members about their ethics rights in research activities. g) Establish institutional structures and communication strategies for the IRB. h) Set up field monitoring processes by committee members for on-going research.
Cofunders:	Dodowa Health Research Centre (DHRC)
Results and Outcomes:	In progress
Key Publications:	Not applicable

7.1.44 Bhatt-Kenya-Ethics

EDCTP Project Coordinator:	Kirana Bhatt
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:	1) Micah Oyaro (Kenya) 2) Christine Kigundu (Kenya) 3) Anastasia Guantai (Kenya) 4) Simon Lang'at (Kenya)
Type of Project:	NEC
Goal:	This project is aimed at improving the efficiency and expansion of Ethical Research Committees (ERC) in Kenya.
Objectives:	An inventory of all ethics review committees will be taken. It also seeks to expand 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 will be designed to take inventory of various ethics committees in Kenya, their location, facilities and composition of its members. The study will also identify 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, established long-term sustainability plan 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.
Cofunders:	Not applicable
Results and Outcomes:	In progress
Key Publications:	Not applicable

7.1.45 Bukusi-Kenya-Ethics

EDCTP Project Coordinator:	Elizabeth Bukusi
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:	28 February 2013
Collaborators:	<ol style="list-style-type: none"> 1) Gerald Mkoji (Kenya) 2) Caroline Kithinji (Kenya) 3) Sammy Njenga (Kenya) 4) Christine Wasunna (Kenya)
Type of Project:	IRB
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:	<ol style="list-style-type: none"> 1) US National Institute of Health through the University of California San Francisco 2) US National Institute of Health through the University of Cape Town
Results and Outcomes:	In progress
Key Publications:	Not applicable

7.1.46 Otieno-Kenya-Ethics

EDCTP Project Coordinator:	Wellington Otieno
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:	03 March 2011
EDCTP Project End Date:	31 January 2013
Collaborators:	<ol style="list-style-type: none"> 1) Wilson Odero (Kenya) 2) Kawango Agot (Kenya) 3) Erick Nyambedha (Kenya) 4) Spala Ohaga (Kenya)
Type of Project:	IRB
Goal:	<p>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 1 of the 3 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.</p>
Objectives:	<ol style="list-style-type: none"> 1. Sensitise academic staff and students on research ethics. 2. Train faculty and postgraduate students on research ethics. 3. Establish and register an Institutional Research and Ethics Committee (IREC) with the National Science for Council and Technology (NCST) as a recognised IRB. 4. Obtain Kenya Shillings 300,000 start-up seed money from partner institutions. 5. Set up IREC Secretariat at RESTECH centre. 6. Negotiate South-to-South partnership with the South Africa Research and Ethics Committee (SAREC) at UNISA. 7. Nominate and train IREC members on formation and function of IRBs. 8. Prepare Terms of Reference (TOR) for committee members and operational guidelines for running IREC. 9. Launch IREC among university staff, National Research Institutes and postgraduate students. 10. Generate sufficient funds to run IREC activities.
Cofunders:	<ol style="list-style-type: none"> 1) Maseno University 2) Centre for Research and Technology Development (RESTECH) 3) Impact Research and Development Organization (Impact-RDO)
Results and Outcomes:	In progress
Key Publications:	Not applicable

7.1.47 Manda-Malawi-Ethics

EDCTP Project Coordinator:	Lucinda Manda-Taylor
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:	28 February 2013
Collaborators:	1) Linda Kalialani-Phiri (Malawi) 2) Joseph Mfutso-Bengo (Malawi) 3) Victor Mwapasa (Malawi) 4) Tamara Chipasula (Malawi)
Type of Project:	IRB
Goal:	The aim of this project is 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 subjects 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. Firstly, the aim is to develop and/or adapt 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.
Cofunders:	Not applicable
Results and Outcomes:	In progress
Key Publications:	Not applicable

7.1.48 Otuonye-NIMR-Nigeria-Ethics

EDCTP Project Coordinator:	Ngozi Otuonye
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:	28 February 2013
Collaborators:	1) Nwaokorie Franka (Nigeria) 2) Dominique Sprumont (Switzerland) 3) Tinto Halidou (Burkina Faso)
Type of Project:	IRB
Goal:	This project will build on projects previously funded by EDCTP by improving the capacity of researchers' to enable the conduct of ethically sound research in Nigeria. The aim of the current project is to establish new RECs at Mainland Hospital Yaba (MHY) and Ambrose Ali University (AAU); and to enhance the capacity of medical professionals, such as doctors, nurses, medical laboratory scientists, pharmacists, and researchers to effectively conduct research that is ethically regulated and of international standard.
Objectives:	This project will establish competent, operational and independent RECs that will protect the wellbeing of research participants, especially the highly vulnerable groups by the year 2011 and 2012. In addition, the infrastructural capacity will be strengthened and the REC administrators' capacity will be improved to enable them to understand the operations of a research ethics committee and how to adequately review research protocols and monitor research.
Cofunders:	Not applicable
Results and Outcomes:	In progress
Key Publications:	Not applicable

7.1.49 Oyedeji-NIMR-Nigeria-Ethics

EDCTP Project Coordinator:	Kolawole Solomon Oyedeji
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:	1) Morenike Ukpong (Nigeria) 2) Oliver Ezechi (Nigeria) 3) Timothy Abolarinwa (Nigeria) 4) Johnson David (Nigeria)
Type of Project:	IRB
Goal:	This project aims to provide some basic support and training for 3 ethics review committees in 2 geopolitical zones in Nigeria, namely North Central and South Western.
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 3 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.
Cofunders:	Not applicable
Results and Outcomes:	In progress
Key Publications:	Not applicable

7.1.50 Kruger-South Africa-Ethics

EDCTP Project Coordinator:	Mariana Kruger
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:	28 February 2013
Collaborators:	1) Lyn Horn (South Africa) 2) Phil Hans-Jörg Ehni (Germany) 3) Urban Wiesing (Germany)
Type of Project:	Support for courses on ethics
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 2 or 3 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 <i>Institutional Review Board: Member Handbook</i> 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.
Cofunders:	Not applicable
Results and Outcomes:	In progress
Key Publications:	Not applicable

7.1.51 Msambichaka-I fakara-Tanzania-Ethics

EDCTP Project Coordinator:	Beverly Msambichaka
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:	03 March 2011
EDCTP Project End Date:	31 January 2013
Collaborators:	1) Abdallah Mkopi (Tanzania) 2) Saumu Ahmed (Tanzania) 3) Mwifadhi Mrisho (Tanzania) 4) Aceme Nyika (Tanzania) 5) Sherry Armstrong Wilkinson (Austria)
Type of Project:	IRB
Goal:	The IHI – IRB (Ifakara Health Institute Institutional Review Board) seeks to establish a training unit in health research ethics serving Tanzanian institutions and others in Africa.
Objectives:	<p>1. <u>Customise the IHI-IRB office</u> 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.</p> <p>2. <u>Establish a well-managed database and archiving system for IHI-IRB</u> 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.</p> <p>3. <u>Support personnel cost and IRB members allowance</u> 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 managers 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.</p> <p>4. <u>Promote HRE awareness among clinical trial communities</u> 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.</p> <p>5. <u>Facilitate effective clinical trial oversight visits</u> 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.</p> <p>6. <u>Build capacity of IRB members and IHI staff on HRE</u> 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.</p>

Cofunders:	Not applicable
Results and Outcomes:	In progress
Key Publications:	Not applicable

7.1.52 Temu-LZIRB-Tanzania-Ethics

EDCTP Project Coordinator:	Mansuet Temu
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:	28 February 2013
Collaborators:	<ol style="list-style-type: none"> 1) John M. Chagalucha (Tanzania) 2) Joseph R. Mwanga (Tanzania) 3) Mark Urassa (Tanzania) 4) Joyce K. Ikingura (Tanzania)
Type of Project:	IRB
Goal:	This project aims 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:	<p>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 1 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.</p> <p><u>The specific objectives are:</u></p> <ol style="list-style-type: none"> 1) To provide additional health research ethics training to the members of the LZIRB. 2) To train and mentor a group of protocol reviewers, especially in clinical trials protocols. 3) To train a resource person within the country. 4) To attach a secretary and recorder from within the Institute to support operations of the LZIRB office. 5) To refurbish and furnish the secretariat office. <p><u>The intermediate steps will include:</u></p> <ol style="list-style-type: none"> 1) Identification of a trainer who will offer continued training to the members and a group of protocol reviewers. 2) To identify a person with an interest in research ethics who will be trained within the country as a resource person in research ethics. 3) To identify a secretary within the Institute. 4) To procure furniture and other items for the secretariat office.
Cofunders:	Not applicable
Results and Outcomes:	In progress
Key Publications:	Not applicable

7.1.53 Birungi-TASO-Uganda-IRB-Ethics

EDCTP Project Coordinator:	Josephine Birungi
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:	28 February 2013
Collaborators:	1) Shabbar Jaffar (United Kingdom) 2) Edward Mills (Canada) 3) Concepta Merry (Ireland)
Type of Project:	IRB
Goal:	The goal of this project is 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:	a) Developing clear procedures for identifying and recruiting members of the TASO IRB. b) Reviewing and further developing TASO IRB Standard Operating Procedures (SOPs). c) Developing a curriculum for training members of the TASO IRB and other IRBs. d) Documenting and disseminating relevant lessons learned about the establishment and strengthening of IRBs in Uganda at national and international conferences/meetings.
Cofunders:	Not applicable
Results and Outcomes:	In progress
Key Publications:	Not applicable

7.1.54 Zimba-Zimbabwe-Ethics

EDCTP Project Coordinator:	Moses Zimba
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:	1) Stanley Mungofa (Zimbabwe) 2) Prosper Chonzi (Zimbabwe) 3) Clemence Duri (Zimbabwe) 4) Richard Chigerwe (Zimbabwe)
Type of Project:	IRB
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 is limited due to inadequate knowledge and trained manpower. The goal is to establish an Institutional Review Board (IRB) for the health facilities in City of Harare.
Objectives:	The objective of this project is to establish an Institutional Review Board (IRB) for health facilities in the City of Harare through training 40 health workers, including doctors, nurses, pharmacists, laboratory scientists and the clergy. At the end of the project, 10 of the trained health workers will become members of the IRB and the other 30 will assist the IRB with the general monitoring of compliance by researchers in the respective health facilities as they perform their normal duties and will 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 will seek to improve the conduct of health research and ensure that proposed disease intervention clinical trials are conducted using internationally accepted standards. The project also aims 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.
Cofunders:	Not applicable
Results and Outcomes:	In progress
Key Publications:	Not applicable

8 Networks of Excellence

Table 8-1: Summary table of EDCTP networks of excellence projects

Project Acronym (Coordinator)	Disease/ Program area	Project goal	Institutions involved	Status
WANETAM	TB, HIV, malaria and networking	Capacity Building	<ul style="list-style-type: none"> -Innovative Biotech, Nigeria -Medical Research Council Laboratories, Bacterial Diseases Programme, Gambia -Centre Muraz, Burkina Faso -Korle-bu Teaching Hospital/ University Of Ghana Medical School, College of Health, Ghana -National Public Health Reference Laboratory, Ghana -Bandim Health Project, Guinea-Bissau -College of Medicine, University of Ibadan, Ibadan, Nigeria -Nigerian Institute of Medical Research, Nigeria -Centre National de Recherche et de Formation sur le Paludisme, Burkina Faso -Malaria Research and Training Center (MRTC)/Department of Epidemiology of Parasitic Diseases (DEAP)/Faculty of Medicine, Pharmacy and Dentistry (FMPOS), the University of Bamako, Mali -Pasteur Institute (Senegal), Senegal 	On schedule
CANTAM	TB, HIV, malaria and networking	Capacity Building	<ul style="list-style-type: none"> - Organisation de Coordination pour la lute Contre les Endemies en Afrique Centrale (OCEAC), Cameroon - University Marien Nguabi, Congo -University of Beua, Cameroon -University of Yaounde 1, Cameroon -Agence Nationale de la Recherche sur le SIDA (ANRS), Cameroon -Centre International de Reference Chantal Biya (CIRCB), Cameroon -Centre d'Etudes des Ressources Vegetales – Groupe de Recherches Biomedicales (CERVE/GRBM), Congo - Medical Research Unit of Albert Schweitzer (ASH/MRU), Gabon 	On schedule
EACCR	TB, HIV, malaria and networking	Capacity Building	<ul style="list-style-type: none"> -Medical Research Council (MRC) Unit of Uganda -Infectious Diseases Institute, Makerere University, Uganda -Masaka Regional Hospital, Uganda Ministry of Health, Uganda -Nsambya Hospital, Kampala, Uganda -Kenya Medical Research Institute, Kilifi, Kenya -Maseno University, Kenya -University Of Nairobi, Kenya Aids Vaccine Initiative (KAVI), Kenya -Ifakara Health Research and Development Centre, Tanzania -National Institute for Medical Research (NIMR), Tanzania -Muhimbili University of Health and Allied Sciences, Tanzania -Tabora Medical Center, Tanzania -Mbeya Medical Research Programme, Tanzania -Kilimanjaro Clinical Research Centre (KCRC), Tanzania -Armauer Hansen Research Institute (AHRI), Ethiopia -Institute Of Endemic Diseases (IEND), Sudan 	On schedule

TESA	TB, HIV, malaria and networking	Capacity Building	<ul style="list-style-type: none"> -Botswana- Harvard AIDS Institute Partnership for Research and Education, Botswana -University of Stellenbosch, South Africa -University of Cape Town, South Africa -University Teaching Hospital, Zambia -Biomedical Research Training Institute, Zimbabwe -University of Zimbabwe College of Health Sciences, Zimbabwe -College of Medicine Research Support Centre, Malawi -Direccao De Saude da Cidade de Maputo, Mozambique -Centro de Investigação em Saúde da Manhica (CISM), Mozambique 	On schedule

8.1.1 WANETAM

EDCTP Project Coordinator:	Souleymane Mboup
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)
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
EDCTP Project Code:	CB.2007.41700.007
EDCTP Project Start Date:	31 July 2009
EDCTP Project End Date:	31 July 2012
Collaborators:	Simon Agwale (Nigeria), Martin Antonio (Gambia), Tumani Corrah (Gambia), Richard Adegbola (Gambia), Bouke Bojang (Gambia), Abraham Alabi (Gambia), Kalifa Bojang (Gambia), Kalifa Manneh (Gambia), Sarah Rowland Jones (Gambia), Potiandi Diagbouga (Burkina Faso), Audrey Forson (Ghana), Awewura Kwara (Ghana), Ekow Biney (Ghana), Aderemi Kehinde (Nigeria), Emmanuel Idigbe (Nigeria), Issa Nebie (Burkina Faso), Ogbara Doumbo (Mali), Aissatou Toure (Senegal)
Results and outcomes:	<p>(http://www.wanetam.org)</p> <ul style="list-style-type: none">• The capacity development plan was approved in June 2010 and a contract amendment signed in September 2010• Malaria: Incidence and serological marker study linked to the network started in January 2010 in Burkina Faso, Senior Fellowship funded by EDCTP started in 2009• HIV: One workshop on Research Capacity in HIV Network for Prevention Trials conducted. Some institutions have submitted proposals for HIV surveillance through dried blood spots to ECOWAS and have approval for funding (details in next report), Senior Fellowship funded by EDCTP started in 2009• TB: BACTEC and MGIT training conducted. MDR-TB surveillance in Guinea Bissau is linked to MRC Laboratories through NoE grant• Training: GCP and GCLP training conducted. Ethics training done in Dakar in January 2011. Other planned trainings for 1st quarter of 2011 included:- HIV drug resistance surveillance, data management, grant writing and project management.
Key publications:	To be compiled

8.1.2 CANTAM

EDCTP Project Coordinator:	Francine Ntoumi
EDCTP Call Title:	Networks of Excellence
EDCTP Project Title:	Central African Network on TB, HIV/AIDS and malaria (CANTAM)
Objectives:	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; strengthen laboratories to be able to perform relevant tests for HIV/AIDS and malaria clinical research; 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
EDCTP Project Code:	CB.2007.41700.006
EDCTP Project Start Date:	19 December 2008
EDCTP Project End Date:	19 December 2011
Collaborators:	Peter Ndoumbe (Cameroon), Mathieu Ndounga (Congo), Elie Mavhoungou (Gabon), Sinatta Koulla- Shiro (Cameroon), Odile Ouwe Missi Oukem (Cameroon), Pierre-Blaise Matsiegui (Gabon), Rose Leke (Cameroon), Frank Mathias (Germany), Eric Achidi (Cameroon), Parfait Awono (Cameroon), Issifou Saadou (Gabon), Leonardo Basco (Cameroon), Veronique Penlap (Cameroon) and Marie-Yvonne Nkodia (Congo)
Results and outcomes:	<p>(www.cantam.org)</p> <ul style="list-style-type: none">• Malaria: The studies done so far include 2 prevalence studies, 2 entomology surveys and 1 socio-demographic survey. Details of some of these studies are given below. 4 MSc students and 3 MD students are in training. In preparation for conduct of malaria trials a cohort of children less than 10 years and malaria surveillance studies in the childhood cohort have been completed. An EDCTP funded malaria Senior Fellowship awarded to Eric Achidi started in 2009• TB: Activities are aimed at capacity building for future vaccine and drug trials. A laboratory has refurbished and equipped, 2 PhD and 2 MSc students have been recruited. Once the details of studies by students are known they will be published in the next update of this report. The scientists have established links with Novartis and Aeras. An EDCTP funded TB Senior Fellowship awarded to Sunny Oyakhirome started in 2009• HIV: Baseline studies in HIV-malaria co-infection started at CIRCB in Cameroon (details are not yet available). An HIV laboratory was renovated and equipped and a cohort for HIV positive mother-child was started. Four HIV community studies were completed (see below). An EDCTP funded Senior Fellowship awarded to Mathieu Ndounga will start in 2011• TB and HIV: Co-infection baseline studies and social science studies have commenced. Details of these studies are yet to be reported.• Training: These include GCP, ethics (through AMANET and TRREE), data management, on line diploma in statistics, training of an FP7 funded project on Young African Scientist initiative• Collaboration with other NoE:<ul style="list-style-type: none">i) EACCR: Training in HIV researchii) TESA: discussions on joint grants application have taken place
Key publications:	To be compiled

8.1.3 EACCR

EDCTP Project Coordinator:	Pontiano Kaleebu
EDCTP Call Title:	Networks of Excellence
EDCTP Project Title:	East Africa Consortium for Clinical Research (EACCR)
Objectives:	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. 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
EDCTP Project Code:	CB.2007.41700.001
EDCTP Project Start Date:	14 May 2009
EDCTP Project End Date:	14 May 2012
Site Principal Investigator(s):	None
Collaborators:	Gibson Kibiki (Tanzania), Howard Engers (Ethiopia), Maowia Mukhtar (Sudan), Andrew Kambu (Uganda), Andre Van Der Ven (Netherlands), Pontiano Kaleebu (Uganda), Edward Katongole-Mbidde (Uganda), Jonathan Kayondo (Uganda), Heiner Grosskurth (Uganda), Eugene Kinyanda (Uganda), Elie Katabira (Uganda), Asuman Lukwago (Uganda), Martin Nsubuga (Uganda), Kevin Marsh (Kenya) Norbert Peshu (Kenya), Trudie Anne Lang (Kenya), Bernhards Ragama Ogutu (Kenya), Kayla Laserson (Kenya), Ayub V. O. Ofulla (Kenya), Walter Godfrey Jaoko (Kenya), Salim Abdulla (Tanzania), Andrew Yona Kitua (Tanzania), John Changalucha (Tanzania), Mark Urassa (Tanzania), Sayoki Godfrey Mfinang (Tanzania), Beatrice Kemilembe Mutayoba (Tanzania), Japhet Killewo (Tanzania), Innocent Semali (Tanzania), Candida Moshiro (Tanzania), Muhammad Bakari (Tanzania), Patricia Jane Munseri (Tanzania), Stafford Kibona (Tanzania), Martha Lemnge (Tanzania), Leonard Maboko (Tanzania), Michael Hoelscher (Germany), Eric Sandström (Sweden), Anna Ekstrom (Sweden), Odd Mørkve (Norway), Frank Van Leth (Netherlands), Michael Ashton (Sweden), Alison Elliott (UK), Philippa Easterbrook (UK)
Results and outcomes:	<p>(http://eaccr.org/)</p> <ul style="list-style-type: none">• Malaria: Node Committee coordinated from Kilifi was formed in 2010. An EDCTP funded Senior Fellowship awarded to Pauline Byakika-Kibwika will start in May 2011 (contract signed in March 2011)• HIV: Node Committee coordinated from UVRI was formed in 2010. An EDCTP funded Senior Fellowship awarded to Jonathan Kayondo started in 2009• TB: Node Committee coordinated from KCMC was formed in 2010. An EDCTP funded Senior Fellowship awarded to William Worodria is under negotiation and will start in second quarter of 2011• Training: Since capacity building budget was approved by EDCTP in August 2010 the network expected to deliver on key milestones between this date and May 2011.
Key publications:	To be compiled

8.1.4 TESA

EDCTP Project Coordinator:	Alexander Pym
EDCTP Call Title:	Networks of Excellence
EDCTP Project Title:	Trials of Excellence for Southern Africa (TESA)
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 to the highest ethical and Good Clinical Practice. The network also aims on building experience, and infrastructure in clinical trial design, biomarker discovery and project management
EDCTP Project Code:	CB.2007.41700.009
EDCTP Project Start Date:	16 November 2009
EDCTP Project End Date:	16 November 2012
Collaborators:	Rosemary Musonda (Botswana), Gerhard Walzl (South Africa), Keertan Dheda (South Africa), Helen McIlleron (South Africa), Peter Mwaba (Zambia), Peter Robert Mason (Zimbabwe), Lynn Zijenah (Zimbabwe), Exnevia Gomo (Zimbabwe), Zulmira Almeida da Silva (Mozambique), Eusebio Macete (Mozambique), Stefan Kauffman (Germany), Tom Ottenhoff (Netherlands), Alimuddin Zumla (UK), Amina Jindani (UK), Christian Lienhardt (France) and Anneka Erhust (Sweden)
Results and outcomes:	<p>(www.tesafrica.org)</p> <ul style="list-style-type: none">• Management: Upgrade in infrastructure and IT systems have taken place in Mozambique and Zimbabwe. 51 personnel are being supported by the NoE grant• Malaria: Currently there are no ongoing malaria activities. The network has failed twice to get EDCTP senior fellowship grants• HIV: HIV incidence study protocol has been finalised in Malawi. An EDCTP funded Senior Fellowship awarded to Takafira Mduluza started in 2009• 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. An EDCTP funded Senior Fellowship awarded to Mark Hatherill started in 2009• Training: 349 persons have received some form of training through the NoE grant. 5 PhD and 1 Post Doc have been identified. The training that has taken place that includes project management, ethics and GCP. All sites have formed community advisory boards (CAB)
Key publications:	To be compiled

9 Networking grants

Table 9-1: 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
Dr 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 Ethiopia	Abraham, Armauer Hansen Research Institute (AHRI), Addis Ababa University, Ministry of Health, Ethiopian Health and Nutrition Research Institute (EHNRI), Ethiopian Science and Technology Agency	Completed
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	Trinity College (Ireland), LSTM (UK), MRC (UK), UCT (South Africa), Makerere University (Uganda) and University of Zambia	Completed

		African research and capacity building in pharmacology		
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 Montpellier University (France)	Completed

9.1.1 Marleen Temmerman

EDCTP Project Coordinator:	Marleen Temmerman
EDCTP Call Title:	Networking
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
Objectives:	<ol style="list-style-type: none"> 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.
EDCTP Project Code:	NW.2005.10400.001
EDCTP Project Start Date:	17 May 2006
EDCTP Project End Date:	17 May 2007
Collaborators:	Stanley Luchters (Kenya), Nicolas Meda (Burkina Faso) Phillipe van de Perre (France) Kirsten Simondon (France)
Results and Outcomes:	
Key Publications	

9.1.2 Bob Colebunders

EDCTP Project Coordinator:	Bob Colebunders
EDCTP Call Title:	Networking
EDCTP Project Title:	Workshop on Tuberculosis Immune Reactivation Inflammatory Syndrome (TB IRIS)
Objectives:	<ol style="list-style-type: none"> 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.
EDCTP Project Code:	NW.2005.10401.002
EDCTP Project Start Date:	2 February 2008
EDCTP Project End Date:	13 August 2008
Collaborators:	<p>J. Baalwa (Uganda) L. Arnould (Belgium) P. Clevenberg (France) B. Gazzard (UK) L. John (UK)</p>
Results and Outcomes:	The group/network studying TB Iris is now on other EDCTP funded TB projects providing this expertise, including the recently awarded TB Senior fellowships to Jean Nachega and William Worodria of EACCR
Key Publications	See publication list

9.1.3 Daniel Kyabayinze

EDCTP Project Coordinator:	Daniel Kyabayinze
EDCTP Call Title:	Coordination and Networking of research activities in Africa
EDCTP Project Title:	KIDS-ART-LINC: network of clinical centers treating HIV-infected children with antiretroviral therapy in Africa to inform public health care and treatment programs
Objectives:	To network of clinical centres that are involved in HIV/AIDS care for children in Sub-Saharan Africa and 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.
EDCTP Project Code:	NW.2005.10501.003
EDCTP Project Start Date:	30 Oct 2006
EDCTP Project End Date:	25 May 2007
Site Principal Investigator(s):	Not applicable
Collaborators:	Benoit Marquis (Uganda) Elise Arrive, Francois Dabuis (France) Matthias Egger (Switzerland) Mary Kieffer (USA)
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.
Key Publications	

9.1.4 Sheena McCormack

EDCTP Project Coordinator:	Sheena McCormack
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
Objectives:	<p>To:</p> <ul style="list-style-type: none"> • 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 • Identify and develop the materials and tools to meet these learning needs in African settings • Strengthen the collaboration between European/African clinical trial networks on poverty-related diseases
EDCTP Project Code:	NW.2005.10501.002
EDCTP Project Start Date:	10 Oct 2006
EDCTP Project End Date:	24 January 2008
Site Principal Investigator(s):	Not applicable
Collaborators:	Eeva Kaarina Koskelo (South Africa), Kathryn Maitland (Kenya), Veronica Mulenga (Zambia), Chifumbe Chintu (Zambia), Mary Edwards (South Africa), Delany Moretlwe (South Africa), Jocelyn Moyes (South Africa), Helen Rees (South Africa), Gita Ramjee (South Africa), Phillipa Musoke (Uganda), Peter Mugenyi (Uganda), Hermione Lyall (Italy), Carlo Giaquinto (Italy), Janneke van de Wiggert (Netherlands), Nneka Nwokolo (UK), Mark Nelson (UK), Brian Gazzard (UK), Jean-Pierre Kraehenbuhl (Switzerland), Lynda Harper (UK), Mary Rauchenberger (UK), Julie Bakobaki, Nicola Kaganson (UK), Andrew Nunn (UK), Sarah Meredith (UK), Diana Gibb (UK)
Results and Outcomes:	This networking grant contributed to the Development of a networking that is string in applications for HIV microbicide trials. Delany Moretlwe has recently been awarded a Senior Fellowship grant by EDCTP
Key Publications	

9.1.5 Amina Jindani

EDCTP Project Coordinator:	Amina Jindani
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
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.
EDCTP Project Code:	NW.2005.10501.001
EDCTP Project Start Date:	10 October 2006
EDCTP Project End Date:	13 November 2007
Site Principal Investigator(s):	Not applicable
Collaborators:	Martin Boeree (Netherlands), Thomas Kenyok (WHO), Thomas Harrison (UK), Roxana Rustomjee (South Africa) and Andrew Nunn (UK)
Results and Outcomes:	This network is conducting clinical trials of Rifapentine in simplification of TB drug regimen (Rifaquin trial) and also part of PanACEA
Key Publications	

9.1.6 Abraham Aseffa

EDCTP Project Coordinator:	Abraham Aseffa
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
Objectives:	To advise professionals involved in TB control in identifying research needs and the conduct of research that contributes to the control of TB in Ethiopia
EDCTP Project Code:	NW.2005.20103.001
EDCTP Project Start Date:	30 Oct 2006
EDCTP Project End Date:	4 March 2008
Site Principal Investigator(s):	Not applicable
Collaborators:	Tsehainesh Messele, Yemane Teklai, Zerihun Tadesse and Getachew Aderaye (all from Ethiopia)
Results and Outcomes:	Dr Aseffa has lead an EDCTP funded TB vaccine trial to a successful completion. He still coordinates the activities of PABIN. He has collaborated with Professor Petros Beyene in training ethics committees in Ethiopia
Key Publications	

9.1.7 Jenny Hill

EDCTP Project Coordinator:	Jenny Hill
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
Objectives:	To conduct a last in a series of three meetings convened by the group which aim to: 1) develop a global MiP research strategy and 2) to develop and initiate studies that contribute to the evidence base for best practices to prevent and control malaria in pregnancy
EDCTP Project Code:	NW.2005.10401.001
EDCTP Project Start Date:	3 April 2006
EDCTP Project End Date:	14 January 2008
Site Principal Investigator(s):	Not applicable
Collaborators:	Clara Menendez (Spain), Theonest Mutabingwa (Tanzania) and Ayo Palmer (Gambia)
Results and Outcomes:	The network is very active in this research area has received a malaria treatment grant from EDCTP through Professor Feiko ter Kuile
Key Publications	

9.1.8 Jane Navia

EDCTP Project Coordinator:	Jane Navia
EDCTP Call Title:	Coordination and Networking of research activities in Africa
EDCTP Project Title:	Ifakara-Lambarene-Manhiça Partnership
Objectives:	To develop guidelines and standardize procedures and other matters concerning Malaria vaccine trials among 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
EDCTP Project Code:	NW.2005.10400.002
EDCTP Project Start Date:	30 November 2006
EDCTP Project End Date:	12 August 2008
Site Principal Investigator(s):	Not applicable
Collaborators:	Bertrand Lell (Germany), Hassan Mshinda (Tanzania), Salim Abdallah (Tanzania), Marcel Tanner (Switzerland), Issoufou Saadou (Gabon), Jahit Sacarlal (Mozambique), John Aponte (Spain)
Results and Outcomes:	The three sites are currently in many EDCTP funded grants
Key Publications	

9.1.9 Concepta Merry

EDCTP Project Coordinator:	Concepta Merry
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
Objectives:	To conduct a meeting to i) review the questions surrounding research in the African continent, with a particular focus on the pharmacology of antiretroviral drugs; ii) shape and discuss initiatives in the area of pharmacology research capacity strengthening; iii) develop a strategy for future research applications.
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 (South Africa), 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)
Results and Outcomes:	Dr Merry coordinates network of pharmacologists in the African region that was a product of this grant. She also provides her expertise as a collaborator of other EDCTP approved grants in Uganda. A number of collaborators of this networking meeting are also holders of EDCTP grants
Key Publications	

9.1.10 Diana Elbourne

EDCTP Project Coordinator:	Diana Elbourne
EDCTP Call Title:	Development of an MSc course in clinical trials methodology
EDCTP Project Title:	EDCTP Grant to support at least 21 Studentships for distance learning Master-course in clinical trials offered by LSHTM
Objectives:	Through this grant, EDCTP has funded 21 MSc students to follow the distance learning MSc in Clinical Trials course of the London School of Hygiene and Tropical Medicine
EDCTP Project Code:	NW.2005.10403.005
EDCTP Project Start Date:	9 August 2007
EDCTP Project End Date:	9 August 2010 (in process of applying NCE to 2013)
Site Principal Investigator(s):	Not applicable
Collaborators:	
Results and Outcomes:	<p>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:</p> <ul style="list-style-type: none"> • 6 have already completed their MSc • 13 had been awarded their postgraduate diploma and had started working on their advanced modules • 1 is still working on core modules and one has been withdrawn after failing core modules twice. <p>The withdrawal follows the policy of London School of Hygiene and tropical medicine</p>
Key Publications	

9.1.11 Andy Hall

EDCTP Project Coordinator:	Andy Hall
EDCTP Call Title:	Development of an MSc course in clinical trials methodology
EDCTP Project Title:	Masters courses in clinical trials for sub-Saharan Africa
Objectives:	To modify a course initially funded by BMGF at the LSHTM to satisfy the EDCTP call in three ways: First the course will be translated into French with the assistance of a French partner. Second a module on field methods in Africa will be developed as an option for the course. Third an African partners in Ghana and Burkina Faso will offer practical field training in clinical trials
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)
Site Principal Investigator(s):	Not applicable
Collaborators:	Phillippe van de Perre (France), Fred Binka (Ghana), Nicolas Meda (Burkina Faso), Paul Milligan (UK), Shabar Jaffar (UK)
Results and Outcomes:	The grant has resulted in establishment of MSc clinical trial course in English at University of Ghana and University of Witwatersrand and in French at Bobo-Dioulasso in Burkina Faso
Key Publications	

10 Joint Programme Activities

Table 10-1: Summary table of Joint Programme Activities projects

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

10.1.1 TriMSID

EDCTP Project Coordinator:	Kalanda Gertrude
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:	06-Apr-09
EDCTP Project End Date:	06-Apr-12
Site Principal Investigator(s):	Not applicable
Clinical Trial/Study Sponsor:	Not applicable
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.
Secondary Objective(s):	-
Clinical Trial/Study site(s):	Not applicable
Collaborating site(s):	1) College of Medicine, Malawi 2) Liverpool School of Hygiene and Tropical Medicine, UK 3) Vienna School of Clinical Research, Austria
Study design:	Not applicable
Product(s):	Not applicable
Manufacturer/Developer:	Not applicable
Cofunders:	None
Trial Registration number(s):	Not applicable
Sub-studies:	-
Status:	Ongoing
Results and Outcomes:	-
Total number of subjects (clinical trials only):	Not applicable
Total number of subjects (cohort/epidemiological/other studies):	20 participants are being trained in clinical trial management
PhD study-1	Not applicable
PhD study-2	Not applicable
MSc study-1	Not applicable
MSc study-2	Not applicable
Other/Sub-studies:	Not applicable
Key Publications:	None

10.1.2 PFRGIT

EDCTP Project Coordinator:	Benjamin Mordmüller
EDCTP Call Title:	Call for Identification and Strengthening of Joint Programme Activities
EDCTP Project Title:	Implementation and standardization of <i>in vitro Plasmodium falciparum</i> culture for resistance phenotyping and immune-mediated growth inhibition testing
EDCTP Project Code:	JP.2008.10800.004
EDCTP Project Start Date:	31-Mar-09
EDCTP Project End Date:	31-Mar-12
Site Principal Investigator(s):	Not applicable
Clinical Trial/Study Sponsor:	The Medical Research Unit of the Albert Schweitzer Hospital in Lambaréné (MRU), Gabon
Trial/Study title:	<i>In vitro</i> resistance phenotyping and immune-mediated growth inhibition of <i>Plasmodium falciparum</i> 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 <i>P. falciparum</i> culture.
Primary Objective(s):	<ol style="list-style-type: none"> 1) To implement continuous culture of <i>P. falciparum</i> 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):	<ol style="list-style-type: none"> 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, and 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):	<ol style="list-style-type: none"> 1) The Department of Parasitology of the University of Tübingen (UKT), Germany, 2) The Medical Research Unit of the Albert Schweitzer Hospital in Lambaréné (MRU), Gabon, 3) The Medical Research Center of the province Ngounie in Fougamou (CRMN), Gabon, 4) The Leiden University Medical Center (LUMC), the Netherlands. 5) 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 6) Other partners: Members of the CANTAM Project
Study design:	The study is laboratory and epidemiological
Product(s):	<p>Drugs: Artemisinin derivatives; Quinolines; Antimalarial antibiotics (clindamycin, tetracycline derivatives); Atovaquone; Antimetabolites; Natural compounds; Exploratory compounds</p> <p>Vaccines: Pre-erythrocytic vaccines (e.g. RTS,S); Blood stage vaccines (e.g. GMZ2); Naturally acquired antibodies</p>
Manufacturer/Developer:	not applicable
Cofunders:	None
Trial Registration number(s):	Not applicable
Sub-studies:	None
Status:	Ongoing
Results and Outcomes:	<i>Plasmodium falciparum in vitro</i> culture implemented
Total number of subjects (clinical trials only):	Not applicable
Total number of subjects (cohort/epidemiological/other studies):	Up to 2995
PhD study-1	Not applicable
PhD study-2	Not applicable
MSc study-1	Not applicable

MSc study-2	Not applicable
Other/Sub-studies:	Other training: Anne-Marie Nkoma received additional training in parasite culture at the University of Tübingen.
Key Publications:	None

10.1.3 IMPDIAGNOST

EDCTP Project Coordinator:	Thomas Schön
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-Apr-10
EDCTP Project End Date:	27-Apr-13
Site Principal Investigator(s):	Thomas Schön (Ethiopia), Christian Wejse (Guinea Bissau)
Clinical Trial/Study Sponsor:	Not applicable
Trial/Study title:	Immunonutrition and Deworming Against Tuberculosis
Goal:	Our goal is 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):	<ol style="list-style-type: none"> 1) To evaluate and develop a recently published <u>clinical scoring system</u> 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 <u>methodology for drug susceptibility testing</u> of the first and second line drugs against <i>Mycobacterium tuberculosis</i> 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 <u>new scoring system for chest x-ray</u> 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 <u>biomarker soluble urokinase plasminogen activator receptor (suPAR)</u> as an early prognostic marker of mortality in TB suspects in combination with the TB-score. 5) To describe <u>the role of adjuvant deworming in patients with smear positive TB</u> 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):	Gondar University, Ethiopia; Armauer Hansen Research Institute (AHRI), Ethiopia; Bandim Health Project, Guinea-Bissau; Linköping University, Sweden; Karolinska Institutet, Sweden; Kalmar County Hospital, Sweden; University of Aarhus, Denmark; institut de recherche, Denmark
Study designs:	Objective 4: Prospective observational clinical study Objective 5: A placebo controlled randomised prospective study
Product(s):	Albendazole
Manufacturer/Developer:	Not applicable
Cofunders:	Swedish Heart and Lung Foundation, Swedish Association of Medicine, DANIDA, SIDA
Trial Registration number(s):	Objective 4: PREDINAM study: PCTR (ATMR2009110001673419). Objective 5: www.clinicaltrials.gov (NCT00857116)
Sub-studies:	NA
Status:	All studies in the described objectives are active and have started data collection and/or inclusion
Results and Outcomes:	Partly presented during the EDCTP-meeting in Addis Abeba 2011 (Objective 1, 2 and 5).
Total number of subjects (clinical trials only):	Objective 4: Aiming for 300 patients Objective 5: Aiming for 400 patients
Total number of subjects	Objective 1: Aiming for 500 patients

(cohort/epidemiological/other studies):	Objective 2: Aiming for 200 patient isolates Objective 3: Aiming for 200 patients
PhD study-1	Objective 5: Deworming against tuberculosis. Ebba Abate, Gondar University and Linköping University.
PhD study-2	Objective 4: suPAR as an early prognostic marker in TB and TB suspects. Frauke Rudolf, Bandim Health Project and Aarhus University
MSc study-1	Objective 2: A new strategy for second line drug susceptibility against tuberculosis. Wassihun Wedajo, Armauer Hansen Research Institute. Addis Abeba, Ethiopia.
MSc study-2	Cidia Camara, Bandim Health project
Other/Sub-studies:	NA
Key Publications:	None

10.1.4 ITAFR

EDCTP Project Coordinator:	Anders Sonnerborg
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-10
EDCTP Project End Date:	26-May-13
Site Principal Investigator(s):	Not applicable
Clinical Trial/Study Sponsor:	Not applicable
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):	<ol style="list-style-type: none"> 1) To conduct integrated training activities in order to improve expertise and Good Clinical Practice for surveillance and management of drug resistance 2) To upgrade on-site IT infrastructure and to conduct integrated training activities in order to improve IT data management 3) To improve capacity to conduct clinical trials
Secondary Objective(s):	-
Clinical Trial/Study site(s):	Not applicable
Collaborating site(s):	<ol style="list-style-type: none"> 1) University of Addis Ababa, Ethiopia 2) Neema Mamy Hospital, Kenya 3) Muhimbili University College of Health Sciences, Tanzania 4) Karolinska Institutet, Sweden 5) Area Vasta Toscana Sud-Est, Italy 6) University of Siena, Italy
Study design:	Not applicable
Product(s):	Not applicable
Manufacturer/Developer:	Not applicable
Cofunders:	Karolinska Institutet, Tuscany Area Vasta Sud-Est, EuResist Network
Status:	Ongoing
Results and Outcomes:	-
Trial Registration number(s):	Not applicable
Total number of subjects (clinical trials only):	Not applicable
Total number of subjects (cohort/epidemiological/other studies):	800
PhD study-1	Drug resistance in minor quasispecies (Halime Ekici)
PhD study-2	Developing and Evaluating a Monitoring Algorithm for Antiretroviral Treatment Efficacy and HIV-1 Drug Resistance Mutations among Failing Patients in Ethiopia (Nigus Fikrie)
PhD study-3	Genotypic analysis of HIV-I drug resistance associated mutations from plasma of antiretroviral drug naive patients, Co-receptor tropism, and impact of transmitted drug resistance on Virological and immunological response to HAART in Ethiopia (Amare Worku)
Other/Sub-studies:	Not applicable
Key Publications:	None

11 Information Management

Table11-1: Summary table of information management project(s)

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

11.1 Pan African Clinical Trial Registry (PACTR)

EDCTP Project Coordinator:	Jimmy Volmink
EDCTP Call Title:	Coordination and Networking of research activities in Africa
EDCTP Project Title:	AIDS, TB and Malaria (ATM) Register
Objectives:	To increase the prospective registration of clinical trials in Africa
EDCTP Project Code:	CT.2004.70100.001
EDCTP Project Start Date:	10 June 2006
EDCTP Project End Date:	17 July 2010
Site Principal Investigator(s):	Not applicable
Collaborators:	Nandi Siegfried (South Africa), Amber Abrahams (South Africa)
Results and Outcomes:	<ul style="list-style-type: none"> • It has been a positive response to a request from WHO and AVAREF for registration of all randomised controlled and controlled clinical trials regardless of disease type conducted in Africa, thus the ATM Clinical Trials Registry was transformed to a 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 online registration facility at the standards required of the WHO International Clinical Trials Platform (ICTRP) and its status as a Primary Registry was renewed in 2010 • By January 2010 the registry applications had doubled since the official launch. By the end of 2010, the registry had received 67 applications, of which 36 eligible trials were registered • By April 2011 the submission for application 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.
Key Publications	<ul style="list-style-type: none"> • Abrams, A. and 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. <i>The Journal of Evidence-Based Medicine</i>, 2010, 3. Pp.195 – 200 • Baleta, A. African Trials Registry Launches Child Strategy. <i>The Lancet</i>, 2010, 375. pp. 1423 • Abrams, A and Siegfried, N. "A Pan-African Clinical Trials Registry for the specific needs of triallists on the continent". <i>South African Medical Journal</i>, 2010, 100(5): 294 -95 • Abrams, A. and Siegfried, N. "Compliance with the WHO minimum data-set in the first Pan African WHO-endorsed Primary Registry." <i>Comments, trialsjournal.com</i>, 1 October 2009 • Abrams A, Siegfried N. Guest Editorial: Maximising the effectiveness of trial registries in resource-constrained settings, <i>BMJ Clinical Evidence</i>, 13 July 2009 • Lutje, V. Siegfried, N and Gerritsen, A. Randomized controlled trials of malaria intervention trials in Africa, 1948 to 2007: a descriptive analysis <i>Malaria Journal</i> 2011, 10:61.

12 Regulatory Authorities

Table7-1: Summary table of projects on capacity strengthening for regulatory authorities and environment

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

12.1.1 WHO-National Regulatory first phase

EDCTP Project Coordinator:	WHO
EDCTP Call Title:	Coordination and Networking of research activities in Africa
EDCTP Project Title:	AIDS, TB and Malaria (ATM) Register
Objectives:	To increase the prospective registration of clinical trials in Africa
EDCTP Project Code:	CB.2005.20900.001
EDCTP Project Start Date:	9 June 2006
EDCTP Project End Date:	15 August 2008
Site Principal Investigator(s):	Not applicable
Collaborators:	Not applicable
Results and Outcomes:	<ul style="list-style-type: none"> • 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.
Key Publications	

12.1.2 WHO-National Regulatory second phase

EDCTP Project Coordinator:	WHO
EDCTP Call Title:	Coordination and Networking of research activities in Africa
EDCTP Project Title:	AIDS, TB and Malaria (ATM) Register
Objectives:	To increase the prospective registration of clinical trials in Africa
EDCTP Project Code:	CB.2005.20900.002
EDCTP Project Start Date:	20 August 2008
EDCTP Project End Date:	31 March 2010
Site Principal Investigator(s):	Not applicable
Collaborators:	Not applicable
Results and Outcomes:	<ul style="list-style-type: none"> • 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.
Key Publications	

13 List of key publications

13.1 HIV

List of key publications from funded project HIV projects

No.	EDCTP Project Acronym	EDCTP Project Coordinator	Full details of publication
1	CHAPAS-1	Chifumbe Chintu	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. <i>Limited Sampling Models to Predict the Pharmacokinetics of Nevirapine, Stavudine, and Lamivudine in HIV-Infected Children Treated With Pediatric Fixed-Dose Combination Tablets</i> . Therapeutic Drug Monitoring 2010;32:369-372
2	Kesho Bora	Marie Louise Newell	Mephams S, Zondi Z, Mbyazi A, Mkhawanazi N, Gaillard P, Newell ML. <i>Challenges in PMTCT antiretroviral adherence in northern KwaZulu-Natal</i> . AIDS Care 2010 (<i>in press</i>)
3	Kesho Bora	Marie Louise Newell	The Kesho Bora Study Group. <i>Eighteen-Month Follow-Up of HIV-1-Infected Mothers and Their Children Enrolled in the Kesho Bora Study Observational Cohorts</i> . J Acquir Immune Defic Syndr (JAIDS) 2010; 54(5): 533-541
4	Kesho Bora	Marie Louise Newell	The Kesho Bora Study Group. <i>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</i> . Contemporary Clinical Trials 2010 (<i>in press</i>)
5	ComTru	Terese Katzenstein	Arreskov A, Minja E, Theilgaard Z, Mandara C, Gerstoft J, Lemnge M, Katzenstein TL. <i>Follow-up rates among HIV-infected women and HIV-exposed children referred for monitoring and treatment in Tanga, Tanzania</i> . International Health 2010 E-pub. 10.1016/j.inhe.2009.12.
6	TaMoVac	Muhammad Bakari	Said About, Charlotta Nilsson, Katarina Karlen, et al. <i>Genes Virus Ankara Expressing HIV-1 Recombinant Modified Vaccinia Vaccine and Boosted with Immunized with an HIV-1 DNA Responses in Healthy Individuals T-Lymphocyte Proliferative</i> . Clinical and Vaccine Immunology, July 2010;17(7):1124-1131.
7		Muhammad Bakari	Patricia J. Munseri, Muhammad Bakari , Kisali Pallangyo & Eric Sandstrom. <i>Tuberculosis in HIV voluntary counselling and testing centres in Dar es Salaam, Tanzania</i> . Scandinavian Journal of Infectious Diseases, 30 June 2010; Early Online, 1-8.
8		Muhammad Bakari	Edith A.M. Tarimo, Anna Thorson, Muhammad Bakari , Joachim Mwami, Eric Sandstrom and Asli Kulane. <i>Willingness to volunteer in a Phase I/II HIV vaccine trial: a study among police officers in Dar es Salaam, Tanzania</i> . Global Health Action 2009. Aug 7;2. DOI: 10.3402/gha.v2i0.1953.
9		Muhammad Bakari	Edith AM Tarimo, Anna Thorson, Thecla W Kohi, Joachim Mwami, Muhammad Bakari , Eric Sandström and Asli Kulane. <i>Balancing collective responsibility, individual opportunities and risks: a qualitative study on how police officers reason around volunteering in an HIV vaccine trial in Dar es Salaam, Tanzania</i> . BMC Public Health 2010, 10:292.
10	AfrEVacc	Jonathan Weber	S. Fuller, J. Imrie, G. Hart, M-L Newell. <i>Using social science to improve young men's engagement, recruitment and retention in biomedical research: the Impilo Yamadoda - Men's Health HIV Vaccine Preparedness Study in KwaZulu-Natal, South Africa</i> . Abstract submitted to the Journal of

			the International AIDS Society Special Issue: Bridging the Social and the Biomedical: Engaging the Social and Political Sciences in HIV Research: call for abstracts
11	van de Wijgert - HIV Mic	Wijgert, Janneke van de	High HIV incidence in a cohort of Rwandan female sex workers. Sarah L. Braunstein, Chantal M. Ingabire, Evelyne Kestelyn, Aline Umutoni Uwizera, Lambert Mwamarangwe, Justin Ntirushwa, Denis Nash, Nienke J. Veldhuijzen, Annalene Nel, Joseph Vyankandondera, Janneke H.H.M. van de Wijgert. <i>Sexually Transmitted Infections 2011;Volume 38 (5): 385-394</i>
12			High burden of prevalent and recently acquired HIV among female sex workers and female HIV voluntary testing center clients in Kigali, Rwanda. Sarah L Braunstein, Chantal M Ingabire, Joseph Vyankandondera, Marie-Michèle Umulisa, Elysée Gahiro, Mireille Uwineza, Eveline Geubbels, Coosje J Tuijn, Denis Nash, Janneke HHM van de Wijgert <i>Submitted</i>
13			A dual testing algorithm of BED-CEIA and AxSYM Avidity Index assays performs best in identifying recent HIV infection in a sample of Rwandan female sex workers. Sarah L Braunstein, Denis Nash, Andrea A Kim, Ken Ford, Lambert Mwambarangwe, Chantal M Ingabire, Joseph Vyankandondera, Janneke HHM van de Wijgert <i>PLoS ONE April 12, 2011; 6(4)</i>
14			Risk factor detection as a metric of STARHS Performance among Female Sex Workers in Kigali, Rwanda. Sarah L. Braunstein, Janneke H.H.M. van de Wijgert, Joseph Vyankandondera, Evelyne Kestelyn, Justin Ntirushwa, Denis Nash. <i>Submitted</i>
15			The epidemiology of human papillomavirus infection in HIV-positive and HIV-negative high-risk women in Kigali, Rwanda Nienke J. Veldhuijzen, Sarah Braunstein, Chantal Ingabire, Justin Ntirushwa, Evelyne Kestelyn, Coosje Tuijn, Ferdinand W. Wit, Aline Umutoni, Mireille Uwineza, Tania Crucitti, Joseph Vyankandondera, Janneke H.H.M. van de Wijgert <i>Submitted</i>
16			HIV acquisition is associated with prior high-risk human papillomavirus infection among high-risk women in Kigali, Rwanda. Nienke Veldhuijzen, Joseph Vyankandondera, Janneke van de Wijgert <i>AIDS 2010;10;24(14):2289-92</i>
17			HIV diagnosis, linkage to HIV care, and HIV risk behaviors among newly diagnosed HIV positive female sex workers in Kigali, Rwanda Sarah L. Braunstein, Marie-Michèle Umulisa, Nienke J. Veldhuijzen, Evelyne Kestelyn, Chantal M. Ingabire, Jeanine Nyinawabega, Janneke van de Wijgert, Denis Nash <i>Journal of Acquired Immunodeficiency Syndrome, March 2011, Epub ahead of print</i>
18			Anal intercourse among female sex workers in East Africa is associated with other high-risk behaviours for HIV Nienke J. Veldhuijzen, Chantal Ingabire, Stanley Luchters, Wilkister Bosire, Sarah Braunstein, Matthew Chersich, Janneke van de Wijgert <i>Sexual Health – in press</i>
19			HIV is the most important risk factor for high-risk HPV prevalence and concordance in heterosexual couples in

			Kigali, Rwanda. Nienke J. Veldhuijzen, Nathalie Dhont, Joseph Vyankandondera, Ammiel Gasarabw, Rosetta Busasa, Tania Crucitti, Janneke H.H.M. van de Wijgert <i>Submitted</i>
20			HIV infection and sexual behaviour in primary and secondary infertile relationships: a case-control study in Kigali, Rwanda Nathalie Dhont, Claude Muvunyi, Stanley Luchters, Joseph Vyankandondera, Ludwig De Naeyer, Marleen Temmerman, Janneke van de Wijgert <i>Sex Transm Infect. 2011 Feb;87(1):28-34.</i>
21			Results of infertility investigations and follow-up among 312 infertile women and their partners in Kigali, Rwanda. Dhont N, van de Wijgert J, Vyankandondera J, Busasa R, Gasarabwe A, Temmerman M. <i>Trop Doct. 2011 Apr;41(2):96-101</i>
22			'Mama and papa nothing': living with infertility among an urban population in Kigali, Rwanda. Dhont N, van de Wijgert J, Coene G, Gasarabwe A, Temmerman M. <i>Hum Reprod. 2011 Mar;26(3):623-9.</i>
23			Sexual violence, HSV-2 and HIV are important predictors for infertility in Rwanda. Dhont N, van de Wijgert J, Luchters S, Muvunyi C, Vyankandondera J, Temmerman M. <i>Hum Reprod. 2010 Oct;25(10):2507-15.</i>
24			Gender differences and factors associated with treatment-seeking behaviour for infertility in Rwanda. Dhont N, Luchters S, Ombelet W, Vyankandondera J, Gasarabwe A, van de Wijgert J, Temmerman M. <i>Hum Reprod. 2010 Aug;25(8):2024-30.</i>
25			The risk profile of women with secondary infertility: an unmatched case-control study in Kigali, Rwanda. Nathalie Dhont, Stanley Luchters, Claude Muvunyi, Joseph Vyankandondera, Ludwig De Naeyer, Marleen Temmerman, Janneke van de Wijgert . <i>Accepted for publication in BMC Women's Health</i>

13.2 Malaria

List of key publications from funded Malaria projects

No.	EDCTP Project Acronym	EDCTP Project Coordinator	Full details of publication
1	Imoukhuede-MVVC-Mal Vac	Imoukhuede	'Malaria Vectored Vaccines Consortium (MVVC)'. Sharmila Bakshi and Babatunde Imoukhuede. <i>Human Vaccines</i> 6:6, 4-5; June 2010
2	Ejigu (Noor/Chilengi)	Ejigu	B. Mordmüller et al. . Safety and immunogenicity of the malaria vaccine candidate GM22 in malaria-exposed, adult individuals from Lambaréné, Gabon. <i>Vaccine</i> 28 (2010) 6698–6703

13.3TB

List of key publications from funded TB projects

No.	EDCTP Project Acronym	EDCTP Project Coordinator	Full details of publication
-	PanACEA - HIGHTRIF	Boeree	Not yet applicable
-	PanACEA - REMox	Gillespie	Not yet applicable
-	PanACEA - SQ109	Hoelscher	Not yet applicable
1	TB Vac	Musoke	[Draft submitted for publication] - Knowledge, Attitudes, Practices towards TB and Willingness to Participate in TB Vaccine Trials in Uganda Buregyeya Esther, Kulane Asli, Kiguli Juliet, Mitchell Ellen M.H., Wajja Anne, Nabongo Patrick, Musoke Philippa, Mayanja-Kizza Harriet
2	TB SurMark (diagnosis)	van Helden	Hanne Veenstra, Ralf Baumann, Pauline T. Lukey, Nulda Beyers, Paul D. van Helden and Gerhard Walzl. <i>High levels of intracellular IL-4 are expressed in circulating apoptotic T cells in patients with tuberculosis and in community controls.</i> Tuberculosis 2008;88:21-30.
3	TB SurMark (diagnosis)	van Helden	Joel Fleury Djoba Siawaya, Nchinya Benedict Bapela, Katharina Ronacher, Hanne Veenstra, Martin Kidd, Robert Gie, Nulda Beyers, Paul van Helden and Gerhard Walzl. <i>Immune parameters as markers of tuberculosis extent of disease and early prediction of anti-tuberculosis chemotherapy response.</i> Journal of Infection 2008;56:340-347.
4	TB SurMark (diagnosis)	van Helden	Joel Fleury Djoba Siawaya, Nchinya Benedict Bapela, Katharina Ronacher, Nulda Beyers, Paul van Helden, and Gerhard Walzl. <i>Differential expression of interleukin-4 (IL-4) and IL-4 delta 2 mRNA, but not transforming growth factor beta (TGF-beta), TGF-beta RII, Foxp3, gamma interferon, T-bet, or GATA-3 mRNA, in patients with fast and slow responses to antituberculosis treatment.</i> Clinical and Vaccine Immunology, Aug 2008;15(8):1165-1170.
5	TB SurMark (diagnosis)	van Helden	Joel Fleury Djoba Siawaya, Nulda Beyers, Paul van Helden and Gerhard Walzl. <i>Differential Cytokine Secretion and Early Treatment Response in Patients with Pulmonary Tuberculosis.</i> Experimental Immunology 2008; article accepted.
6	TB SurMark (diagnosis)	van Helden	N.M. Carroll, P. Uys, A. Hesselning, K. Lawrence, C. Pfeiffer, F. Salker, K. Duncan, N. Beyers and P.D. van Helden. <i>Prediction of delayed treatment response in pulmonary tuberculosis: Use of time to positivity values of Bactec cultures.</i> Tuberculosis, November 2008;88(6):624-630.
7	TB SurMark (diagnosis)	van Helden	Djoba Siawaya JF, Roberts T, Babb C, Black G, Golakai HJ, Stanley K, Bapela NB, Hoal E, Parida S, van Helden PD and Walzl G. <i>An evaluation of commercial fluorescent bead-based Luminex cytokine assays.</i> Plos One. 2008;3(7):e2535.
8	TB SurMark (diagnosis)	van Helden	Pfeiffer C, Carroll NM, Beyers N, Donald P, Duncan K, Uys P and van Helden P. <i>Time to detection of Mycobacterium tuberculosis in BACTEC systems as a viable alternative to colony counting.</i> Int J Tuberc Lung Dis. 2008;12(7):792-798.
9	TB SurMark (diagnosis)	van Helden	Gerhard Walzl, Katharina Ronacher, Joel Fleury Djoba Siawaya and Hazel M. Dockrell. <i>Biomarkers for TB treatment response: Challenges and future strategies.</i> Journal of Infection 2008;57:103-109.
10	TB SurMark (diagnosis)	van Helden	Chegou NN, Black GF, Kidd M, van Helden PD and Walzl G. <i>Host markers in Quantiferon supernatants differentiate active TB from latent TB infection: preliminary report.</i> BMC Pulmonary Medicine, 2009;9:21-56.

11	TB SurMark (diagnosis)	van Helden	Mathebula, N, Pillay, J, Toschi, G, Verschoor, JA & Ozoemena, KI. <i>Recognition of anti-mycolic acid antibody at self-assembled mycolic acid antigens on gold electrode: A potential impedimetric immunosensing platform for active tuberculosis</i> . Chemical Communications, 2009. 3345-3347.
12	TB SurMark (diagnosis)	van Helden	Lemmer, Y, Thanyani, ST, Vrey, PJ, Driver, CHS, Venter, L, Van Wyngaardt, S, Ten Bokum, AMC, Ozoemena, K, Pilcher, LA, Fernig, DG, Stoltz, AC, Swai, HS, Verschoor, JA. <i>Detection of anti-mycolic acid antibodies by liposomal biosensors</i> . Methods in Enzymology, 2009. (Accepted)
13	TB SurMark (diagnosis)	van Helden	Kenneth I. Ozoemena,* Nsovo S. Mathebula, Jeseelan Pillay, Gianna Toschi and Jan A. Verschoor. <i>Electron Q1 transfer dynamics across self-assembled N-(2-mercaptoethyl) octadecanamide/mycolic acid layers: impedimetric insights into the structural integrity and interaction with anti-mycolic acid antibodies</i> .
14	TB SurMark (diagnosis)	van Helden	Y. Lemmer, S. T. Thanyani, P. J. Vrey, C. H. S. Driver, L. Venter, S. van Wyngaardt, A. M. C. ten Bokum, K. I. Ozoemena, L. A. Pilcher, D. G. Fernig, A. C. Stoltz, H. S. Swai, and J. A. Verschoor. <i>Detection of Antimycolic Acid Antibodies by Liposomal Biosensors</i> .
15	TB – Short Treatment	Merry	Helen McIlleron, Graeme Meintjes, William J. Burman, and Gary Maartens. <i>Complications of Antiretroviral Therapy in Patients with Tuberculosis: Drug Interactions, Toxicity, and Immune Reconstitution Inflammatory Syndrome</i> . The Journal of Infectious Diseases 2007;196:S63-75.
16	TB – Short Treatment	Merry	Mohammed Lamorde, Pauline Byakika-Kibwikaa and Concepta Merry. <i>Antiretroviral therapy in developing countries: pharmacologic considerations</i> . Current Opinion in HIV and AIDS 2008;3:252-257.
17	TB – Short Treatment	Merry	Yuan Ren, James J. C. Nuttall, Claire Egbers, Brian S. Eley, Tammy M. Meyers, Peter J. Smith, Gary Maartens, and Helen M. McIlleron. <i>High Prevalence of Subtherapeutic Plasma Concentrations of Efavirenz in Children</i> . J Acquir Immune Defic Syndr 2007.
18	TB – Short Treatment	Merry	Yuan Ren, James J. C. Nuttall, Claire Egbers, Brian S. Eley, Tammy M. Meyers, Peter J. Smith, Gary Maartens, and Helen M. McIlleron. <i>Effect of Rifampicin on Lopinavir Pharmacokinetics in HIV-Infected Children With Tuberculosis</i> . J Acquir Immune Defic Syndr 2008;47(5):566-569.
19	TB – Short Treatment	Merry	Karen Cohen, Gilles van Cutsem, Andrew Boulle, Helen McIlleron, Eric Goemaere, Peter J. Smith and Gary Maartens. <i>Effect of rifampicin-based antitubercular therapy on nevirapine plasma concentrations in South African adults with HIV-associated tuberculosis</i> . Journal of Antimicrobial Chemotherapy 2008;61:389-393.
20	TB – Short Treatment	Merry	Ren Y, Nuttall JJC, Egbers C, Eley BS, Meyers TM, Smith PJ, Maartens G, McIlleron HM. <i>Effect of Rifampicin on Efavirenz Pharmacokinetics in HIV-infected Children with Tuberculosis</i> .
21	TB – Short Treatment	Merry	D Elsherbiny D, Ren Y, McIlleron H, Maartens G, Simonsson USH. <i>Population Pharmacokinetics of Lopinavir in Combination with Rifampicin-based Antitubercular Treatment in HIV-Infected South African Children</i>
22	REMOx I	Gillespie	Andrew J. Nunn, Patrick P.J. Phillips, Stephen H. Gillespie. <i>Design issues in pivotal drug trials for drug sensitive tuberculosis (TB)</i> . Tuberculosis 2008;88(1):S85-92.
23	REMOx I	Gillespie	Andrew J Nunn, Sarah K Meredith, Melvin K Spigelman, Ann M Ginsberg, Stephen H Gillespie. <i>The ethics of non-infectiority trials</i> . The Lancet 2008;371:895.

24	TBHIV drugs combi	Bertilsson	KP Kanebratt, U Diczfalusy, T Bäckström, E Sparve, E Bredberg, Y Böttiger, TB Andersson and L Bertilsson. <i>Cytochrome P450 Induction by Rifampicin in Healthy Subjects: Determination Using the Karolinska Cocktail and the Endogenous CYP3A4 Marker 4β-Hydroxycholesterol</i> . <i>Clinical Pharmacology & Therapeutics</i> , Nov 2008;84(5):589-594.
25	TBHIV drugs combi	Bertilsson	Eleni Aklillu, Collet Dandara, Leif Bertilsson and Collen Masimirembwa. <i>Pharmacogenetics of cytochrome p450s in African populations: Clinical and molecular evolutionary implications</i> . (http://eurekah.Com/chapter/3164); in Suarez-Kurtz G (ed <i>Pharmacogenomics in admixed populations</i> . Rio de Janeiro, Brasil, 2006.
26	TBHIV drugs combi	Bertilsson	Ulf Diczfalusy, Jun Miura, Hyung-Keun Roh, Rajaa A. Mirghani, Jane Sayi, Hanna Larsson, Karl G. Bodin, Annika Allqvist, Mary Jande, Jong-Wook Kim, Eleni Aklillu, Lars L. Gustafsson and Leif Bertilsson. <i>4beta-Hydroxycholesterol is a new endogenous CYP3A marker: relationship to CYP3A5 genotype, quinine 3-hydroxylation and sex in Koreans, Swedes and Tanzanians</i> . <i>Pharmacokinetics and Genomics</i> 2008;18:201-208.
27	TBHIV drugs combi	Bertilsson	F. Josephson, L. Bertilsson, Y. Böttiger, L. Flamholc, M. Gisslén, V. Ormaasen, A. Sönnnerborg and U. Diczfalusy. <i>CYP3A induction and inhibition by different antiretroviral regimens reflected by changes in plasma 4beta-hydroxycholesterol levels</i> . <i>Eur J Clin Pharmacol</i> 2008;64:775-781.
28	TBHIV drugs combi	Bertilsson	Mukonzo JK, Röshammar D, Waako P, Andersson M, Fukasawa T, Milani L, Svensson JO, Ogwal-Okeng J, Gustafsson LL, Aklillu E. <i>A novel polymorphism in MDR1 gene, CYP2B6*6 and sex predict single dose efavirenz population pharmacokinetics in Ugandans</i> . Submitted to: <i>Br J Clin Pharm</i> 2009 (MP-00003-09-AC)

14 Template tables

14.1 Clinical Trials and Integrated Projects

EDCTP Project Coordinator:	
EDCTP Call Title:	
EDCTP Project Title:	
EDCTP Project Code:	
EDCTP Project Start Date:	
EDCTP Project End Date:	
Trial 1	
Site Principal Investigator(s):	
Clinical Trial/Study Sponsor:	
Trial/Study title:	
Goal:	
Primary Objective(s):	
Secondary Objective(s):	
Clinical Trial/Study site(s):	
Collaborating site(s):	
Study design:	
Number of subjects:	
Product(s):	
Manufacturer/Developer:	
Cofunders:	
Sub studies:	
Status:	
Results and Outcomes:	
Trial 2	
Site Principal Investigator(s):	
Clinical Trial/Study Sponsor:	
Trial/Study title:	
Goal:	
Primary Objective(s):	
Secondary Objective(s):	
Clinical Trial/Study site(s):	
Collaborating site(s):	
Study design:	
Product(s):	
Manufacturer/Developer:	
Cofunders:	
Trial registration number(s):	
Status:	Not yet Recruiting/Ongoing/Completed plus comments
Results and Outcomes:	
Trial Registration number(s):	
Total number of subjects (clinical trials only):	
Total number of subjects (cohort/epidemiological/other studies):	
PhD study-1	(Study title) (Name of candidate) (Study title) (Name of candidate)
PhD study-2	(Study title) (Name of candidate) (Study title) (Name of candidate)
MSc study-1	(Study title) (Name of candidate) (Study title) (Name of candidate)
MSc study-2	(Study title) (Name of candidate) (Study title) (Name of candidate)
Other/Sub-studies:	(Study title)
Key Publications:	

14.2 Networking, Networks of Excellence, JPA other projects

EDCTP Project Coordinator:	
EDCTP Call Title:	
EDCTP Project Title:	
Objectives:	
EDCTP Project Code:	
EDCTP Project Start Date:	
EDCTP Project End Date:	
Collaborators:	5) Name (country) 6) Name (country)
Results and Outcomes:	
Key Publications	