EDCTP

European & Developing Countries
Clinical Trials Partnership

EDCTP STRATEGIC RESEARCH AGENDA

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Introduction

The EDCTP Executive Secretariat (SEC) – with scientific and strategic advice from the Scientific Advisory Committee (SAC) – prepares a Strategic Research Agenda (SRA). This document is updated annually and provides the basis for the SEC to propose the annual work programme of the following year to the General Assembly for approval. The SRA outlines the key research and capacity gaps for diseases within the EDCTP remit, and ranks them in terms of priorities.

The diseases areas are:

- HIV
- Tuberculosis
- Malaria
- Neglected infectious diseases
- Emerging diseases
- Diarrhoeal diseases
- Lower Respiratory Tract Infections

The priorities are:

A Areas of research or research capacity development of utmost importance for the short term

B Areas of research or research capacity for the medium term

C Areas of research for the long term

D Areas of research that do not have to be addressed by EDCTP

HIV

Topic	Description	Priority	EDCTP2-funded studies (grant code, title of study, Coordinator, EDCTP grant value) relevant to the topic
Pathogen traits	Multi-clade virus	D	
Disease profile			
Epidemiology	HIV co-infections and co-morbidities	A	TMA2015CDF-1032 The Epidemiology of Human Papillomavirus and Associated Disease in HIV Positive Men in South Africa
Pathogenesis/host response / immune response	Improving our understanding of HIV pathogenesis and host immune responses for prevention and treatment	B	TMA2015CDF-982 Immunological Selection of Recombinants following HIV-1 Superinfection
Diagnosis and tracking	Point-of-care diagnosis of: HIV drug resistance to prevent and limit the spread of HIV drug resistance and possible HIV-associated co-morbidities in adults and children	B	DRIA2014-314 Integrating the diagnosis and management of HIV-associated central nervous system (CNS) infections into routine health services in low and middle income countries (LMICs) (DREAMM)
Treatments	Evaluation of new simple and tolerable paediatric ARV formulations as well as dose optimisation studies (based on pharmacokinetics, pharmacodynamics, pharmacogenetics (PK/PD/PG) in infants and children	A	TRIA2015-1078 Children with HIV in Africa – Pharmacokinetics and Acceptability of Simple antiretroviral regimens (CHAPAS-4)
			TMA2015SF-1037 Low frequent HIV drug resistant polymorphisms in infants born to HIV sero-positive mothers: Implications on response to therapy (HIVDR)
	Optimisation (based on pharmacokinetics, pharmacodynamics, pharmacogenetics (PK/PD/PG)) of ART using existing drugs for the general and targeted adult populations, such as pregnant and breastfeeding women (improving PMTCT), MSM, elderly HIV-positive individuals	A	
	Investigating novel therapeutics and novel use of existing therapeutics (ex: long-lasting formulations) to maximise adherence and prevent the evolution and impact of resistance	C	TMA2015CDF-1027 Evaluation of Treatment Response, Drug Resistance and HIV-1 Variability among Adolescents on First- and Second-Line Antiretroviral Therapy in Cameroon: The READY-Study

Treatments	Reducing the short and long-term ART-associated complications and its impact on adherence and ARV resistance, such as long-term toxicities	A	TRIA2015-1092 High Dose AMBISOME on a Fluconazole Backbone for Cryptococcal Meningitis Induction Therapy in sub-Saharan Africa: A Randomised Controlled Non-inferiority Trial (AMBITION-cm)
			TMA2015CDF-1002 Proximal tubular renal dysfunction among HIV patients on Tenofovir versus Tenofovir sparing regimen
			TMA2015CDF-1033 Nasopharyngeal Microbiota in HIV Positive Children Presenting with Respiratory Disease
	Drug interaction studies: • ARVs and antimalarial or anti-tuberculosis drugs and dose optimisation studies to improve HIV-TB and HIV-malaria co-treatment • ARV and other medication during pregnancy and breastfeeding	A	
Prevention	Examining long acting ARVs formulated as injectable and vaginal rings for prevention of HIV and pregnancy. Examining new prevention technologies including combination biomedical prevention and multipurpose prevention technologies – (ex: prevent pregnancy and HIV)	A B	SRIA2015-1061 CAPRISA 018: A randomised controlled trial to assess the safety, acceptability and pharmacokinetics of a sustained-release tenofovir alafenamide sub-dermal implant for HIV prevention in women
	Large-scale trials of HIV vaccines that have demonstrated suitable level of immunogenicity in early phase trials	A B	SRIA2015-1066 Globally Relevant AIDS Vaccine Europe-Africa Trials Partnership
Product-focused implementation research	Examining models of delivery that can increase acceptability to counselling and HIV testing in an equitable, sustainable and ethical way (ex: multi-centre cluster randomized trials to evaluate community-oriented approaches (home-based and out-reach) employing community health care worker or lay counsellors)	A B	
	Optimising the integration of HIV/PMTCT and TB services, HIV/ sexual and reproductive health/family planning and PMTCT programmes in identifying HIV infected women in late pregnancy or while breastfeeding, and in long-term adherence to lifelong ART for the mothers, diagnosis of infection in infants and children	A B	
	Supporting implementation science research to address a decline in population level incidence through combination prevention trials (these include combining behavioural, structural and biomedical interventions to reduce HIV incidence)	A B	

Product-focused implementation research	Optimising effective linkage to care and adherence to treatment	A	TMA2015CDF-972 Effect of reminder cues and tailored feedback on adherence to antiretroviral drug treatment among HIV positive individuals in the Kilimanjaro region, Tanzania
			TMA2015CDF-1036 Tracing non-retained HIV positive pregnant women and their babies
Critical infrastructure & human development needs	Supporting implementation science research to achieve a decline in population level incidence through combination prevention trials.	A	

Tuberculosis

Topic	Description	Priority	EDCTP2-funded studies (grant code, title of study, Coordinator, EDCTP grant value) relevant to the topic
Pathogen traits	Evaluation of *Mycobacterium tuberculosis* strains' genomic differences in the species/lineages of the nine species of *M. tuberculosis* complex (MTBC) and their effect on the efficacy of distinct control tools in certain geographical areas	A	
Disease profile			
Epidemiology	Evaluation of drug resistant TB in both HIV-infected and HIV-uninfected adults and children, with a focus on a diagnostic or treatment product/regimen	A	
Pathogenesis/host response / immune response	Evaluation of specific host response and host signatures (notably immune response and signatures) as predictors of susceptibility, protection, prognosis and response to treatment	B	TMA2015SF-1043 Novel biomarkers predictive of susceptibility and treatment response in patients with MDR-TB (DTB)
			TMA2015CDF-1012 The impact of pulmonary tuberculosis and other lower respiratory tract pathogens on lung function in young South African children
Diagnosis and tracking	Evaluation of point-of-care diagnostic and prognostic products that are sensitive, specific, cheap, easy to use, yield a rapid result, and are applicable for the diagnosis of both drug-sensitive and drug resistant TB. This will include existing and new diagnostics and prognostics in HIV-negative and HIV-positive adults and children	A	DRIA2014-309 A one-stop shop for the same day diagnosis and management of TB and HIV (Stop TB/HIV at One)
			DRIA2014-326 Culture free diagnosis and follow-up of multidrug resistant tuberculosis patients (DIAMA)
			TMA2015SF-1041 What is the feasibility, accuracy, and optimal manner in which next generation tests for tuberculosis can be used in high burden settings? (OPTIMAL DIAGNOSIS)
	Evaluation of diagnostic and prognostic pathogen and host biomarkers for the accurate identification/differentiation between/of latent TB infection, sub-clinical disease, and active clinical TB disease (PTB and EPTB) as well as prognostic biomarkers for the accurate prediction of TB risk in individuals with LTBI for prophylactic drug treatment	B	DRIA2014-311 Evaluation of host biomarker-based point-of-care tests for targeted screening for active TB (ScreenTB)
			TMA2015SF-1043 Novel biomarkers predictive of susceptibility and treatment response in patients with MDR-TB (DTB)

Treatment	Evaluating novel interventions using new TB drugs or formulations with new combination regimens	A	TRIA2015-1102 PanACEA, a drug development programme to shorten and simplify treatment of tuberculosis
			TMA2015CDF-1018 Optimising linezolid use for drug-resistant tuberculosis in South Africa: the effects of linezolid exposure on toxicity, treatment response, and linezolid resistance
	Evaluate treatment regimens using a range of adjunct 'host-directed therapies' to shorten duration of therapy	A	
	Improve treatment outcomes, and prevent long term pulmonary and extra pulmonary complications and other co-morbidity in adults and children with drug-sensitive and drug- resistant TB	B	SRIA2015-1065 Using Biomarkers to Predict TB Treatment Duration (Predict TB)
			TMA2015CDF-1052 Biomarker profile predicting unsuccessful treatment response in patients with MDR-TB
	Pharmacokinetic drug interaction studies to determine optimal drug dosing and safety (especially in pregnancy, children and HIV-coinfection)	A	
	Identify optimal combination of medicines and treatment regimen-design for TB patients (adults and children) with isoniazid resistant, rifampicin-resistant, multidrug-resistant (MDR-TB), and extensively drug-resistant (XDR-TB)	A	
Prevention	Evaluation of new vaccines and chemoprophylactic TB drug regimens	A	
Product-focused implementation research	Delivery methods and research on the use of diagnostics and drugs after they have been tested successfully and in a cost-effective manner	A	
	Scale up and integration of HIV/TB prevention, treatments and services, innovative use of existing and new strategies to prevent, diagnose and manage TB, MDRTB and TB/HIV co-infections	A	
Critical infrastructure & human development needs	Development and expansion of TB clinical trials sites	A	

Malaria

Topic	Description	Priority	EDCTP2-funded studies (grant code, title of study, Coordinator, EDCTP grant value) relevant to the topic
Pathogen traits	Evaluation of parasite determinants for severe disease especially in children and pregnant women	D	
Disease profile	Evaluation of contribution of asymptomatic malaria for disease transmission	B C	
Epidemiology	Evaluation of simple ways of identifying hotspots and monitoring of drug and insecticide resistance and its impact on disease burden and transmission	B C	
	Defining indicators for surveillance: detecting infections and measuring transmission rather than measuring morbidity and mortality to malaria		
Pathogenesis/host response / immune response	Determinants of host-parasite interaction and natural acquisition of immunity and its loss. Evaluation of biomarkers of protection for malaria	B C	TMA2015SF-1001 Harnessing parasite diversity and naturally acquired protective immunity against Plasmodium falciparum malaria for the development of highly effective vaccines (SMART)
			Determinants and prevalence of parasite resistance among pregnant women receiving Intermittent Preventive Treatment with Sulphadoxine-Pyrimethamine (IPTp-SP) in a malaria endemic community
Diagnosis and tracking	Evaluation of novel point of care tests, including those for detection of *P. vivax* hypnozoites, and innovative use of existing technologies for malaria control and elimination efforts.	A	
Treatments	Safety and efficacy testing of new drugs and optimisation of existing drugs, including drug-drug interactions between antimalarials and other drugs such as ARVs (especially amongst children and pregnant women) and anti-TB drugs.	A	
	Evaluation of the role of immunotherapies in malaria control and elimination.		
	Evaluation of approaches of using drugs including Mass Drug Administration (MDA)		

Prevention	Evaluation of novel drugs, immunotherapies and vaccines for prevention targeting different populations such as infants and pregnant women. Taking into account the changing diseases landscape and the declining incidence of malaria, elimination feasibility studies will be given priority	A	TRIA2015-1076 IPTp with dihydroartemisinin-piperaquine and azithromycin for malaria, sexually transmitted and reproductive tract infections in pregnancy in high sulphadoxine-pyrimethamine resistance areas in Kenya, Malawi, and Tanzania (IMPROVE)
Product-focused implementation research	Evaluation of new implementation approaches for new and existing interventions in real life settings	A	
	Monitoring and evaluation of scale-up of access to drugs, vaccines and diagnostics.		
	Evaluation of the feasibility and cost-effectiveness of new information systems		
Critical infrastructure & human development needs	Development of infrastructure for conduct of Phase I to Phase IV trials of malaria interventions	A	TMA2015SF-998 Malaria Research and Capacity building for field trials in Tanzania (MaReCa)
	Development of infrastructure to support epidemiological studies and assessment of transmission reduction potential of new malaria interventions including diagnostics, drug and vaccines	A	

Neglected infectious diseases

Topic	Description	Priority	EDCTP2-funded studies (grant code, title of study, Coordinator, EDCTP grant value) relevant to the topic
Pathogen traits	NIDs include 17 different viral, bacterial, fungal, protozoal and helminth infections with diverse manifestations, life cycles and methods of transmission. They include: dengue/severe dengue; rabies; human African trypanosomiasis (sleeping sickness); leishmaniases; cysticercosis/taeniasis; dracunculiasis (guinea-worm disease); echinococcosise; foodborne trematodiases; lymphatic filariasis; onchocerciasis (river blindness); schistosomiasis; soil-transmitted helminthiases; Buruli ulcer; leprosy (Hansen disease); trachoma; yaws; and mycetoma	A	
Disease profile		D	
Epidemiology		D	
Pathogenesis/host response / immune response	Diverse mechanisms of pathogenesis and immunity. Potential for vaccines for dengue, rabies, leishmaniasis, schistosomiasis, hookworm, provide focus for clinical studies	B C	
Diagnosis and tracking	Evaluation of diagnostic / biomarkers including response products, to be used in population surveillance & monitoring for control, elimination or eradication programmes	A	DRIA2014-308 Evaluation of an antibody detecting point-of-care test for the diagnosis of *Taenia solium* taeniasis and (neuro)cysticercosis in communities and primary care settings of highly endemic, resource-poor areas in Tanzania and Zambia, including training of - and technology transfer to the Regional Reference Laboratory and health centres (SOLID)
			DRIA2014-306 Diagnostic tools for human African trypanosomiasis elimination and clinical trials (DiTECT-HAT)
			TMA2015CDF-979 Rapid detection of *Mycobaterium ulcerans* infection by recombinase polymerase amplification
			TMA2015CDF-995 Urinary Cytokine ELISA: A tool for Assessing Urinary Tract Pathology in *Schistosoma haematobium* infections

Treatments	The evaluation of novel drugs, drug combinations, immuno-chemotherapy, and formulations for treatment (e.g. for human African trypanosomiasis, the leishmaniases , the filariases, schistosomiasis, Buruli ulcer, mycetoma, dengue)	A	
Prevention	Evaluation of safety and efficacy of candidate vaccines (e.g: leishmaniasis, leprosy,, schistosomiasis, soil-transmitted helminths (STH), rabies, dengue)	A	
	Strengthen preventive chemotherapy and transmission control, used in MDA and MSAT (mass screen and treatment), of STHs, filariases, trachoma through evaluation of drug combinations, formulations and treatment regimes	A	
Product-focused implementation research	Evaluating the different approaches to interventions, ranging from novel treatments, MDA, vaccines and diagnostics for both (i) improved treatment, and (ii) disease elimination / control at population level	B	TMA2015CDF-976 Cluster randomized community-based trial of annual versus biannual single-dose Ivermectin plus Albendazole against *Wuchereria bancrofti* infection in human and mosquito populations
	The optimisation and integration of the management of co-endemic NIDs (e.g. co-endemicity of lymphatic filariasis and onchocerciasis with loiasis), evaluation of the different disease burden (regional versus localised), effect of MDA including drug delivery, uptake, compliance and adherence and strategies for accessing treatment especially during the endgame phase for PRDs targeted for elimination	B	
Critical infrastructure & human development needs	MDA in populations across sub-Saharan Africa, for helminth and trachoma infections which will demand (i) development of surveillance and monitoring infrastructure, and (ii) trained staff for (a) changing patterns of drug susceptibility, and (b) pharmacovigilance		

Emerging diseases

Topic	Description	Priority	EDCTP2-funded studies (grant code, title of study, Coordinator, EDCTP grant value) relevant to the topic
Pathogen traits	Pathogens with epidemic potential in sub-Saharan Africa	B	
Disease profile	No defined priorities		
Epidemiology	No defined priorities		
Pathogenesis/host response / immune response	No defined priorities		
Diagnosis and tracking	Developing and deploying novel diagnostics and strengthening laboratory systems at country and regional levels, especially at the point-of-care and point-of-need sites. This is to enable accurate, timely collection and analysis of information, and laboratory systems capable of safely and accurately detecting all major dangerous pathogens with minimal bio risk	A	
Treatments	No priorities currently		
Prevention	No priorities currently		
Product-focused implementation research	No priorities currently		
Critical infrastructure & human development needs	Promotion and development of national, regional and pan-African capacities and monitoring systems that can predict and identify infectious disease threats capacities through early warning and pro-active surveillance, enabling rapid response to emerging infectious diseases threats	A	
	Training and deploying an effective biosurveillance workforce with trained disease and laboratory scientists		

Diarrhoeal diseases

Topic	Description	Priority	EDCTP2-funded studies (grant code, title of study, Coordinator, EDCTP grant value) relevant to the topic
Pathogen traits	Rotavirus, *Shigella*, ETEC (ST and/or LT), Cryptosporidium, Norovirus.	n/a	
Disease profile	Developing standardised clinical severity scores for diseases such as *Shigella* and ETEC infections	n/a	
Epidemiology	Collecting surveillance data on burden of diarrhoeal diseases and pathogens as a foundation for conducting future trials, in particular vaccine trials.	A B	
Pathogenesis/host response / immune response	Understanding oral vaccine effectiveness by examining mechanisms of host susceptibility to vaccine strains: histo /blood group antigens, gut microbiome, effect of chronic/repeated diarrhoeal episodes and pediatric environmental enteropathy	A B	
	Improving immunogenicity of parenteral vaccines in infants and improving the development of good mucosal responses upon parenteral immunisation, Improving /combining routes and modes of immunization and Defining/optimizing immunomonitoring assays and correlates of protection (i.e. B cell memory)	A B	
Diagnosis and tracking	Developing point of care, multiplexed diagnostic tools that may allow quick and reliable detection and diagnostic methods to be used in clinical trials and transfer of this knowledge to SSA laboratories	B	
Treatments	Testing of candidate molecules against Cryptosporidiosis, including drug repurposing, as cases occurring in non-immunocompromised patients are on the average refractory to current treatment	A B	
Prevention	Testing vaccine candidates against the most prevalent diarrheal pathogens (i.e. *Shigella*, ETEC and against Vibrio cholera)	A C *(depending on when they are ready to move to endemic settings)*	
	Improving effectiveness of existing rotavirus vaccines	D	
	Maternal immunization to prevent infant episodes (no candidates exist yet)	D	

Product-focused implementation research	Global implementation of the current rotavirus vaccines	D
	Evaluating the immunogenicity of current *Shigella* & ETEC vaccines in endemic zones	A
	Community programs to reduce child morbidity and mortality through the integrated community case management program where diarrhoeal diseases are treated with zinc	D
Critical infrastructure & human development needs	Selection and capacity strengthening of sites with epidemiological competence and experience in clinical trials	A
	Improved sentinel/surveillance networks for diarrhoeal disease surveillance within and across regions	D
	Training of laboratory personnel in diagnostics and medical staff in prevention and treatment of diarrhoeal diseases (train the trainer model)	D

Lower Respiratory Tract Infections

Topic	Description	Priority	EDCTP2-funded studies (grant code, title of study, Coordinator, EDCTP grant value) relevant to the topic
Pathogen traits	To explore the traits of the following pathogens: • Neonates and children: Group B Streptococcus; ; *Respiratory Syncytial Virus*; pneumococcus; cytomegalovirus; *Bordetella pertussis* for neonates • Adults: pneumococcus; *Haemophilus influenza, Klebsiella pneumoniae* • In HIV-infected patients: *Pneumocystis jirovecii, Fungal infections (eg Aspergillus fumigatus*) • Pregnant women: influenza and para influenza virus	A	
	To document the emerging threats from antibiotic resistant bacteria (extended spectrum beta-lactamase (ESBL)-producing *K. pneumoniae* and methicillin-resistant *S. aureus* (MRSA)	A	
	To assess the incidence of community acquired atypical pneumonia (there is uncertainty about the true incidence of so-called 'atypical infections' in patients with pneumonia in Africa. Infections with organisms such as *C. pneumoniae* and *M. pneumoniae* are cyclical)	A	
Disease profile	To define the burden, severity, etiology, drug resistance and outcome of LRTIs in: • HIV infected and non-infected adults • HIV infected and non-infected children • Neonates • Pregnant women • Elderly • Patients with other comorbidities	A	
	To identify which patients are likely to experience an unusual or prolonged illness course	A	

Epidemiology	To identify the risk factors of LRTI in • HIV infected and non-infected adults • HIV infected and non-infected children • Neonates • Pregnant women • Patients with co-morbid disease, e.g. diabetes mellitus, chronic obstructive pulmonary disease (COPD), and chronic renal and liver failure, who are likely to be infected with Gram-negative organisms such as *Pseudomonas aeruginosa*, *K. pneumoniae* and *Escherichia coli*	A
	To develop adequate surveillance programs to better clarify the epidemiology, aetiology, antimicrobial susceptibility patterns and the effectiveness of the preventives and curatives strategies in place against paediatric LRTIs	C
	To assess the impact of early ART initiation on the occurrence of LRTI in HIV infected patients	A
Pathogenesis/host response / immune response	To explore the adverse immune responses and immunomodulation (host directed therapies and vaccines)	B
Diagnosis and tracking	To evaluate more accurate clinical diagnostic algorithms for LRTIs according to age groups, comorbidities and severity	A
	To evaluate currently available rapid diagnostic platforms for bacterial, viral and fungal causes of LRTIs, including tests for multiple pathogens and point-of-care tests	A
	To evaluate innovative specimen collection methods that are easy to perform at lower level of health facility and well tolerated to improve the etiologic diagnosis of LRTI in neonates, children and adults	A
	To evaluate/optimise the feasibility and reliability of chest X-ray and new imaging technologies for diagnosis of LRTI (digitalized mobile X-ray, thermal imaging, computerized readers, portable ultrasound)	A
	To identify and evaluate new or existing host-response specific tests, including clinical and laboratory indicators of 1) severity of illness, 2) need for hospitalisation and 3) antibiotic treatment options	B

Treatments	To evaluate more accurate clinical management algorithms and criteria for selecting patients requiring antibiotics	A
	To evaluate the efficacy of short duration antibiotic treatment regimens for community acquired LRTI	A
	To evaluate simplified tools for management of hypoxemia for children with severe LRTI in resource limited settings	A
	To evaluate newly antibiotic treatments in the context of co-morbidities and health determinants of sub-Saharan countries	B
	To evaluate adjunct 'host-directed therapies' to improve treatment outcomes for LRTIs and co-morbidities of LRTI with NCDs and to prevent long term pulmonary functional disability	B
Prevention	To assess the impact of available vaccines (type b *Haemophilus influenzae*, *Bordetella pertussis*, *Streptococcus pneumoniae*, and Influenza) on the rates, outcome and aetiologies of LRTIs	A
	To evaluate the role of adjunct 'host-directed therapies' for prevention of LRTIs in children.	C
	To evaluate novel non-capsular antigen vaccines for pneumococcus	A
	To evaluate the role of conjugated pneumococcal vaccines in adults	A
	To assess the impact of RSV vaccination to pregnant women on the rates, outcome and aetiologies of LRTIs in pregnant women	A
	To evaluate interventions targeting mothers for prevention of neonatal disease (increased occurrence of pertussis in mothers highlighted)	A
	To evaluate group B streptococcus targeted vaccines	A
Product-focused implementation research	To optimize delivery and scaling-up of new vaccines (e.g. RSV) for LRTIs in partnership with other funders	B
	To support epidemiological and operational research to optimise delivery and scaling-up of new diagnostics, drugs and vaccines for LRTI after they have been tested successfully and in a cost-effective manner. This will also include the scale up and integration within acute medical services	B
	To assess the integration of LRTI management with HIV/TB/ malaria/diarrhea treatments and services	C
Critical infrastructure & human development needs	To support training of local laboratory scientists/staff identified as a critical need, as well as good laboratories' and collection of baseline data for LRTIs	C