EDCTP

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EDCTP Strategic Research Agenda

Version 3 – February 2019

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Contents

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 scope and ranks them in terms of priorities. It aims to help researchers and other partners better understand current EDCTP research priorities, in light of EDCTP's overall mission to accelerate the development of new or improved medical interventions against poverty-related neglected diseases and enhance research capacity.

The priority rankings consider the current importance of a topic and whether EDCTP or other partners are already funding projects addressing it. An asterix is added to a ranking if the topic is considered important but it is not within EDCTP's remit or is already being addressed by EDCTP or other partners. The priority rankings are:

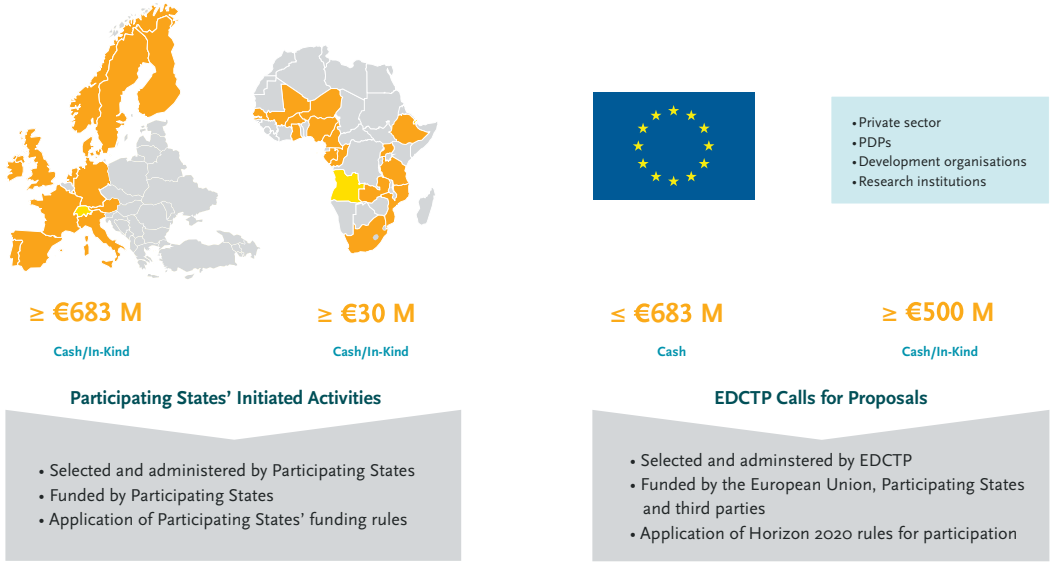
- **Priority A:** Areas of research or research capacity development of utmost importance for the short term
- **Priority B:** Areas of research or research capacity for the medium term
- **Priority C:** Areas of research for the long term
- **Priority D:** Areas of research that do not have to be addressed by EDCTP
- **Priority A/B/C*:** Areas of research that are deemed as priority topics in the field but are currently not a primary priority for EDCTP, either because of good coverage in EDCTP project portfolio or are covered by other partners.

The SRA also indicates how those priorities are being addressed through calls for proposals that are centrally managed by EDCTP (EU-funded actions, supported with the EU contribution to the EDCTP2 programme). The calls for proposals that are centrally managed by EDCTP are implemented using three distinct types of actions:

i. Research & Innovation Actions (RIA),
ii. Coordination & Support Actions (CSA),
iii. Training & Mobility Actions (TMA).

Funding arrangements

EDCTP receives funds from the European Union (EU) through the Horizon 2020 programme. Participating States also make contributions (cash or in-kind) to activities aligned with EDCTP's goals. Third parties, including industry, product development partnerships, development organisations, and research institutions, also make cash or in-kind contributions to EDCTP calls. The table below indicates the type(s) of Horizon 2020 actions that could be used to address a priority.



HIV

Addressing gaps in progress toward the 90-90-90 targets (90% of people living with HIV knowing their status, 90% of HIV-positive people on antiretroviral treatment [ART], and 90% of people on ART virally supressed)[1] will help turn the HIV epidemic around but will require new products and tools and innovative implementation strategies. Current demographic trends in Africa foresee increasing numbers of young people at risk of HIV exposure and increasing numbers of adults living with chronic HIV disease at risk of co-morbidities as they age[2]. Furthermore, challenges with antiretroviral (ARV) drug resistance are ongoing. The 2019 strategic research agenda for HIV focuses primarily on trials of innovative biomedical HIV prevention tools, strategies to reduce ARV drug resistance, and product-focused implementation research. Understanding biological susceptibility and pathogenesis remains paramount. Following on the September 2017 Stakeholder meeting on co-morbidities and co-infections, the 2019 strategic research agenda for HIV includes co-infections with human papilloma virus (HPV), malaria, and neglected infectious diseases as well as research investigating the impact of the vaginal microbiome on product efficacy. Other priorities include treatment optimisation for adults, children, adolescents, and pregnant women; improved diagnostics; and strategies to address the sexual and reproductive health needs of women living with and at risk of HIV.

Topic	Description	Priority	EDCTP2-funded studies (grant code, title of study, acronym)
Pathogen traits	Multi-clade virus	D	
Disease profile	Please see epidemiology (topic 3) and pathogenesis (topic 4) below	D	
Epidemiology	HIV/HPV co-infections, particularly in women	A	TMA2015CDF-1032 The Epidemiology of Human Papillomavirus and Associated Disease in HIV Positive Men in South Africa (TEHSA)
	HIV and malaria co-infection in malaria endemic areas in all age groups	A	
	Description of all-cause mortality associated with HIV	D	
	Other co-infections and co-morbidities in HIV-infected patients	B	TMA2017GSF-1965 The Role of Environmental Enteropathy on HIV-Associated Diabetes (REEHAD)
			TMA2017GSF-1962 Cardiometabolic Diseases Risk Evaluation and Reduction in African People Living with HIV Infection (CaDERAL)
Pathogenesis/ host response / immune response	Improving our understanding of HIV pathogenesis and host immune responses for prevention and treatment.	A	TMA2016CDF-1582 Mucosal type I IFN desensitization and the risk of HIV acquisition (MIDAS)
			TMA2016CDF-1598 Inflammation, T Cell activation and Subclinical atherosclerosis in Treated HIV Infection (Kenya CVHIV)
			TMA2016CDF-1597 Epidemiology, Diagnosis algorithms, and prognostic role of Immunologic and Inflammatory Markers among HIV-2 infected individuals in West Africa (EDIIMark2)
			TMA2015CDF-982 Immunological Selection of Recombinants following HIV-1 Superinfection (ISoReS)

			TMA2017SF-1960 Effect of Pre-Exposure Prophylaxis (PrEP) on immune responses systemically and mucosally in healthy individuals in the CAPRISA 082 study- (PrEP Underlying Mucosal-immunity Before/After PUMBA) (PUMBA)
			TMA2017CDF-1928 Albuminuria Among Virally Suppressed HIV-infected Patients in Botswana: Longitudinal Changes, and Association with Inflammation and ACEI/ARB Use in a Clinical Setting (Albuminuria and ACEI/ARB among HIV-patients)
			TMA2017SF-1955 Identification of Novel HIV Reactivation Agents: Towards Building Translational HIV Cure Research Infrastructure in Ghana (H-CRIS)
			TMA2017CDF-1852 Investigation of the impact of inducible, replication-competent latent HIV-1 as an impediment to HIV/AIDS cure in the context of sustained viral suppression (Latent HIV-1, Viral Suppress and Hope for HIV Cure)
	HIV susceptibility, the vaginal microbiome (inflammatory cytokines, prevotella bivia, gardnerella), and vaginal tissue tenofovir levels	A	
Diagnosis and tracking	Tracking HIV drug resistance to prevent and limit spread of antiretroviral resistance	B	
	The evaluation of novel diagnostic devices used in resource-limited settings	A	
	HIV-associated opportunistic infections and 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)
			TMA2017GSF-1936 Diagnosis and treatment of non-communicable diseases and geriatric syndromes in the HIV aging population in sub-Saharan Africa. (Geriatric HIV cohort Africa)
	ARV drug resistance in children	A	TMA2015SF-1037 Low frequent HIV drug resistant polymorphisms in infants born to HIV seropositive mothers: Implications on response to therapy (HIVDR)
	Improve HIV diagnosis in infants born to HIV-positive mothers	A	RIA2016MC-1615 Neonatal HIV early infant diagnosis (EID) versus standard of care EID – Impact on inFant hEalth: a feasibility study of point-of care testing at birth versus at 6 weeks of age, on the uptake of ART and infant prophylaxis, and on rates of infant survival, morbidity and retention in care. (LIFE study)
	Early detection of HIV infection in pregnancy through point of care (POC) repeat testing at antenatal care (ANC) to reduce MTCT and improve maternal health	A	
	Evaluation of combination tests for syphilis and HIV both in pregnant women at ANC and non-pregnant adults	B	

Treatment	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)
	Treatment optimisation based on PK/PD/PG of ART using existing drugs for the general adult population by sex, age, body weight, presence of co-infections, risk of drug interactions, etc. and for specific sub-populations such as pregnant and breastfeeding women, PWID (people who inject drugs), MSM (men who have sex with men), transgender people (interactions with hormone therapy), and elderly individuals with co-morbidities, etc.	A	TMA2016SF-1508 Pharmacogenomics Research and Clinical Excellence in the Treatment of Infectious Diseases in African Populations (PRACE) 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 (READY-Study) TMA2016CDF-1566 Study of Pharmacogenetics of ARVs treatment outcomes in Mali, West Africa (SPATOMA)
	Treatment of HIV in the context of neglected tropical disease (NTD) co-infections such as urogenital schistosomiasis and leishmaniasis in endemic areas.	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	A	RIA2017MC-2005 BREATHER Plus: A randomised open-label 3-arm, 96-week trial evaluating the efficacy, safety and acceptability of weekends off dolutegravir-based antiretroviral therapy (ART) and monthly long-acting injectable ART compared to daily dolutegravir-based ART in virologically suppressed HIV-infected children and adolescents in sub-Saharan Africa (BREATHER Plus)
	Treatment of opportunistic infections and co-morbidities	B	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)
	Reducing short- and long-term ART-associated complications and toxicities, and their impact on adherence and ARV resistance.	A	TMA2015CDF-1002 Proximal tubular renal dysfunction among HIV patients on Tenofovir versus Tenofovir sparing regimen (TREND study)
	ARVs and anti-tuberculosis drugs and dose optimisation studies to improve HIV-TB co- treatment	B	TMA2017SF-1981 Immune-mediated adverse drug reactions In African TB HIV endemic settings (IMARI-Africa)
	ARVs and anti-malarial drugs and dose optimisation studies to improve HIV-malaria co-treatment	B	
	ARV and other medications during pregnancy and breastfeeding	A	RIA2017MC-2009 Safety and efficacy of Dolutegravir and EFV400 for pregnant and breast-feeding women: a randomized non-inferiority clinical trial (PREGART)
	ARV and anti-cancer drug dose optimization studies to improve treatment of HIV-associated malignancies	B	

Prevention	HIV pre-exposure prophylaxis using long-acting ARV formulated as injectables, implants, and vaginal rings for HIV prevention	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 RIA2016MC-1616 Combined HIV African Prevention Study: On demand Truvada and F/TAF Pre-exposure and Post exposure prophylaxis to protect adolescents from HIV (CHAPS)
	Examining new prevention technologies including combination biomedical prevention and multipurpose prevention technologies to prevent both pregnancy and HIV	B	
	Large-scale trials of HIV vaccines that have demonstrated suitable level of immunogenicity in early phase trials	B	SRIA2015-1066 Globally Relevant AIDS Vaccine Europe-Africa Trials Partnership (GREAT) RIA2016V-1644 A combination efficacy study in Africa of two DNA-MVA- or DNA- Env protein HIV-1 vaccine regimens with pre-exposure prophylaxis (PrEP) (PrEPVacc)
	Studies of passive immunity strategies of antibody-mediated prevention (AMP) using promising broadly neutralizing antibodies as infusions or injections.	A	RIA2017S-2008 CAPRISA 012: Phase I/II trial of Subcutaneous Administration of Monoclonal Broadly-neutralizing Antibodies (CAP012 SAMBA Trial) RIA2017MC-2021 Effectiveness, efficacy and operational feasibility of passive transfer of VRC01-LS antibody to prevent intra-/postpartum HIV mother-to-child transmission during the breastfeeding period in HIV-exposed infants from Tanzania and Mozambique: a prospective, randomized, double-blinded placebo-controlled proof-of-concept trial. (Neo bnAb)
	Effectiveness of option B+: evaluation of adherence and impact	A	
	Prevention strategies for sexually transmitted infections, including vaccine-preventable infections such as HPV infection in HIV-infected women	A	
Product-focused implementation research	Optimising HIV service delivery models, including those to increase uptake of HIV counselling and testing in equitable, sustainable, and ethical ways to reach the first 90 of the 90-90-90 targets[3]	B	EDCTP-CSA-2014-279 Translating Research into Practice (TRIP): Evaluating and Speeding up the adoption of an evidenced based innovative REMSTART package to reduce mortality in advanced stage HIV patients starting antiretroviral therapy in Tanzania (TRIP)
	Optimising integration of HIV/PMTCT and TB services; optimising integration of sexual and reproductive health services with HIV treatment services for women living with HIV (including family planning and cervical cancer screening and treatment); optimising HIV/PMTCT and sexual and reproductive health/family planning to identify HIV-positive women in late pregnancy or while breastfeeding, and to support long-term adherence to lifelong ART for mothers and timely diagnosis of infection in infants and children	B	EDCTP-CSA-2014-273 Improving HIV prevention and sexual and reproductive health care in high risk women in Rwanda using lessons learnt from previous Rinda Ubuzima projects (WISH) TMA2015CDF-1036 Tracing non-retained HIV-positive pregnant women and their babies (sTEPWIse)

			RIA2016MC-1617 Prevention of mother-to-child transmission of HIV-1: program evaluation and innovative rescue intervention integrated in the expanded program of immunization (PROMISE-EPI)
			TMA2017CDF-1906 Effects of preterm birth on HIV acquisition risk and antiretroviral prophylaxis safety in HIV-exposed infants in Botswana (PERHAPS)
			TMA2017CDF-1927 Understanding the determinants of the effectiveness of HIV control strategies targeting HIV-infected pregnant women in Mozambique (Preg_multidrug)
	Implementation research for HIV prevention, treatment, and care and support for adolescents and youth	A	TMA2016CDF-1574 A prospective cohort study to assess the feasibility of enrolling and retaining adolescents at risk of HIV infection from hotspots in Kampala Uganda (FERDAR)
			TMA2017CDF-1923 Feasibility and acceptability of HIV self-testing in adolescents and young people (FAST study)
	Supporting implementation science research to stimulate and sustain declines in population level HIV incidence, including through combination prevention trials that combine behavioural, structural, and biomedical interventions	C	
	Optimising effective linkage to care and adherence to treatment	C	TMA2015CDF-972 Effect of reminder cues and tailored feedback on adherence to antiretroviral drug treatment among HIV-positive individuals in the Kilimanjaro region, Tanzania (REMIND)
			TMA2016CDF-1602 Antiretroviral therapy Outcomes, Barriers and facilitators of Adherence among individuals initiating Treatment following Test and Start guidelines in an urban HIV clinic in Uganda (ABOUT)
			TMA2016CDF-1548 Conditional economic incentives and motivational interviewing to improve adolescents' retention and adherence to antiretroviral therapy in south-east Nigeria: a cluster randomised trial (ARA)
Critical infrastructure & human development needs	Strengthening research capacity to inform HIV control strategies	A	
	Knowledge about sexuality and socio-behavioural and structural determinants of HIV risk to inform prevention strategies	B	

Tuberculosis

Worldwide, TB is one of the top 10 causes of death and the leading cause from a single infectious agent (above HIV/AIDS). In 2017, TB caused an estimated 1.3 million deaths among HIV-negative people[4] and there were an additional 300 000 deaths from TB among HIV-positive people4. TB is one of the main causes of death in African countries south of the Sahara, with HIV infection being one of the main risk factors for TB in Africa. Several clinical presentations of TB are priorities that could benefit from targeted interventions for early diagnosis, treatment, or prevention. These include TB/HIV co-infection, childhood TB, extrapulmonary TB, drug-resistant TB, sub-clinical TB, TB co-morbidity with other communicable diseases (CDs) and non-CDs (NCD), latent TB infection, and TB-related long-term pulmonary functional disability. TB diagnosis is sputum-based, which excludes young children and patients with extra-pulmonary or disseminated forms of disease. There is still no cheap, rapid, and accurate point-of-care (POC) diagnostic test for TB[4]. Ongoing efforts to shorten duration of treatment of both drug-susceptible and drug-resistant-tuberculosis are a priority. Further evaluation of a range of host-directed therapies that can shorten duration of therapy, improve treatment outcomes (reduce mortality and lung damage; prevent long-term functional disability)[5] and act as adjuncts to WHO-recommended standard treatment regimens for drug-sensitive and drug-resistant TB is urgently needed. Potential drug-drug interactions with HIV treatment should be examined, given the high levels of HIV-TB co-infection. Research on both pathogen and host biomarkers for disease activity, response to treatment, relapse and prognosis of TB, are continuing priorities.

Topic	Description	Priority	EDCTP2-funded studies (grant code, title of study, acronym)
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.	C	TMA2017CDF-1885 The role of *Mycobacterium tuberculosis* compensatory mutations in metabolic fitness via the structure and function of mycolic acids (InformaTB)
Disease profile	Evaluation of the sub-clinical TB stage in order to identify potential specific interventions (diagnosis; treatment; prevention)[6]	A	TMA2015CDF-1012 The impact of pulmonary tuberculosis and other lower respiratory tract pathogens on lung function in young South African children (TB-Lung FACT)
Epidemiology	Evaluation of drug-resistant TB in adults and children with and without concomitant HIV infection, focusing on a diagnostic or treatment product/ regimen.	B	TMA2016CDF-1583 *Mycobacterium tuberculosis* Infection Rates Among Health Care Workers in a HIV Care and Treatment Center in Nigeria (M.tb Infection Rates among HCWs in HIV Clinics)
			TMA2017SF-1959 Biostatistical Methods for Longitudinal Analysis of Burden of Lung Health and Tuberculosis in Africa (BioStat-LAB Africa)
			RIA2016S-1632 Tuberculosis Reduction through Expanded Antiretroviral Treatment and Screening for active TB (TREATS)
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[4].	B	TMA2017GSF-1942 Impact of Diabetes on TB disease and Treatment Outcome in Ghana (TB_DM)
			TMA2015SF-1043 Novel biomarkers predictive of susceptibility and treatment response in patients with MDR-TB (DTB)
			TMA2016CDF-1546 Host-directed therapy: Myeloid derived suppressor cell ablation by phosphodiesterase inhibitor (MyTB)
			TMA2016SF-1535 Characterizing the spectrum of TB and Co-infection with HIV – the role of Th22 cells (CaTCH-22)

			TMA2017CDF-1905 NK and B cell determinants of immunity to *Mycobacterium tuberculosis* in humans (BethiNK TB)
			TMA2017SF-1951 Deciphering the immunological signatures of the TB spectrum from infection to disease (TB-SPEC)
			TMA2017CDF-1914 The longitudinal microbiome of South African tuberculosis patients, symptomatic culture-negative controls and healthy household contacts, and its association with treatment outcome (MOSAIC)
			SRIA2015-1065 Using Biomarkers to Predict TB Treatment Duration (Predict TB)
			TMA2015CDF-1052 Biomarker profile predicting unsuccessful treatment response in patients with MDR-TB (BTR-TB)
	Evaluation of diagnostic and prognostic pathogen and host biomarkers for the accurate identification of and differentiation between latent TB infection, sub-clinical disease, and active clinical TB disease (pulmonary TB and extrapulmonary TB), as well as prognostic biomarkers for the accurate prediction of TB risk in individuals with latent TB infection (LTBI) for prophylactic drug treatment[4].	B	DRIA2014-311 Evaluation of host biomarker-based point-of-care tests for targeted screening for active TB (ScreenTB)
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[4,7]	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)
			RIA2016MC-1623 Rapid and accurate diagnosis of paediatric TB (RaPaed TB)
	Evaluating novel interventions using new TB drugs or formulations with new combination regimens to simplify treatment[5].	A	TRIA2015-1102 PanACEA, a drug development programme to shorten and simplify treatment of tuberculosis (PanACEA)
			RIA2017S-2012 Simplified Short Treatment for Tuberculosis (Simplici-TB)
			RIA2017T-2030 Novel Clinical Candidates to Kill TB (CLICK-TB)

	Evaluate treatment regimens using a range of adjunct 'host-directed therapies' to shorten duration of therapy or improve outcomes.	A	
	Improve treatment outcomes in patients with severe forms of TB or comorbidities and prevent long-term pulmonary and extra-pulmonary complications and other co-morbidity in adults and children with drug-sensitive and drug-resistant TB.	A	TMA2016CDF-1576 Evaluating the response to 4 and 6 month treatment of pulmonary tuberculosis by 18F-FDG PET/CT lung imaging (Evaluate 4mTB)
			RIA2017T-2004 Preventing TB relapse and chronic lung disease: A proof-of-concept, double-blind, randomised, placebo-controlled trial to evaluate the safety and efficacy of pravastatin to reduce inflammation after TB treatment completion in HIV-infected and HIV-uninfected adults measured by FDG-PET/CT (PravaTB)
			RIA2017T-2019 Intensified tuberculosis treatment to reduce the high mortality of tuberculous meningitis in HIV-infected and uninfected patients (INTENSE-TBM)
	Pharmacokinetic drug interaction studies to determine optimal drug dosing and safety (especially in pregnancy, among children, and in the context of HIV coinfection).	A	RIA2016MC-1606 Vulnerable populatIon TUberculosis AntiretroviraL (VirTUAL)
			TMA2016CDF-1580 Safety and Efficacy of High Dose Rifampicin in TB-HIV co-infected patients on Efavirenz-based Antiretroviral therapy (SAEFRIF)
			TMA2017CDF-1876 Evaluation of Pharmacokinetics and Safety/Tolerability of Higher Doses of Rifampicin in Children with Newly Diagnosed, Uncomplicated Tuberculosis (HighRif-C)
	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	TMA2015CDF-1018 Optimising linezolid use for drug-resistant tuberculosis in South Africa: the effects of linezolid exposure on toxicity, treatment response, and linezolid resistance (Linezolid for DR-TB in South Africa)
Prevention	Evaluation of new vaccines and new or shorter chemoprophylactic TB drug regimens[6].	A	RIA2016V-1645 A multicenter Phase III double-blind, randomized, controlled study to evaluate the efficacy and safety of VPM1002 in comparison to BCG (priMe)
			RIA2016V-1631 POR TB consortium; Phase 2 trial to determine efficacy of the multistage vaccine H56:IC31 for Prevention Of Recurrent TB disease (POR TB consortium)
			RIA2016V-1637 MTBVAC in Newborns: Phase 2a Dose-Defining Safety and Immunogenicity Study and Capacity Building to Support Vaccine Efficacy Trials in Tuberculosis-Endemic Regions of Sub-Saharan Africa (MTBVAC – Newborns)
			TMA2017CDF-1860 Strategies to optimize the Stability and Bio-activity of a Clinical Tuberculosis Vaccine (ID93-TBVaccine)
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	EDCTP-CSA-2014-283 Tuberculosis: Working to Empower the Nations' Diagnostic Effort (TWENDE)

			CSA2016S-1627 PhArmaco Vigilance Africa (PAVIA)
			RIA2017S-2007 CAP-TB: Close the Gap, Increase Access, Provide Adequate Therapy (CAP-TB)
	Scale up and integration of HIV/TB prevention, contact screening and prevention, treatment, and services; and innovative use of existing and new strategies to prevent, diagnose, and manage TB, MDR-TB and TB/HIV co-infections.	A	TMA2016CDF-1570 An Innovative Collaboration Model Between the National TB Control Program and Informal Healthcare Providers to Detect Additional Cases of TB In Cameroon (ECIP)
			CSA2016S-1608 Translation research into policy and practice: Scaling up Evidence Based Multiple focus Integrated Intensified TB Screening to End TB (EXIT-TB) in the East African region.
	Implementation research to optimize access, uptake and adherence to TB treatment especially among (but not limited to) migrant populations, refugees and humanitarian crises.	A	
Critical infrastructure & human development needs	Development and expansion of TB clinical trials sites.	B	TMA2016SF-1463 Research Capacity Strengthening Programme for Emerging and Re-emerging Infectious Diseases Control in Tanzania (REMODEL-TZ)

Malaria

Sub-Saharan Africa (SSA) continues to be plagued by malaria, despite substantial success in reducing infection and mortality rates in most countries over the past two decades, through improved diagnosis, treatment, and prevention strategies. Since 2010, malaria incidence in WHO's African Region has decreased by 20%, but the decline has stalled since 2014[8]. Ninety one percent of the estimated 445,000 deaths from malaria globally occur in the African Region, with the disease continuing to place an enormous burden on hospital and outpatient facilities, accounting for a high proportion of all presentations[8]. Serious bottlenecks remain in providing full access to preventive interventions, diagnostic testing and treatment. The greatest burden of disease affects children, pregnant women and immune-compromised individuals.

African populations suffer high burdens of other infectious diseases and many patients with malaria harbour other infections, including HIV and TB. Negative interactions between HIV and malaria in the context of co-infection have been described but the full extent of this requires further investigation[9]. Documenting the safety, efficacy, and malaria drug interactions in patients also being treated for HIV and/or TB is a priority. In parts of Africa, malaria elimination strategies underway include radical cure of both *P. falciparum* and *P. vivax* asymptomatic infections in the entire population as the cornerstone. Priority populations include vulnerable people such as children, pregnant women, individuals living with HIV, and those with genetic haemoglobinopathies. Sensitive methods for the rapid diagnosis of asymptomatic malaria infections are required because, increasingly, parasites are being identified with deletion of the histidine-rich proteins leading to false negative results of HRP2 RDTs[10]. A number of antimalarial drugs were developed under the EDCTP1 programme, but the ever-present potential for development of resistance underscores the need for new highly efficacious drugs with adequate safety profiles remains. In addition, new antimalarial drugs with different modes of action are needed for malaria chemoprevention in the most vulnerable populations. Vector control has played a major role in reducing malaria burden over the past two decades, however, it is hampered now by increasing insecticide resistance. Although research on new insecticides and ways to delay the onset of resistance are urgent priorities[11], it falls outside the remit of EDCTP. Although the first malaria vaccine product is now entering pilot implementation studies, its efficacy is modest and relatively short-lasting. The development and evaluation of more effective malaria vaccines that will be key to both improved malaria control and to malaria elimination remain priorities. It is timely to build on the EDCTP1 investments that supported phase II clinical trials of candidate malaria vaccines and enhanced capacity to conduct such trials in order to evaluate the current most promising vaccine candidates, including sporozoite, blood stage, and transmission blocking vaccines and combinations of vaccines.

Topic	Description	Priority	EDCTP2-funded studies (grant code, title of study, acronym)
Pathogen traits	Identification of risk factors for severe disease especially in children and pregnant women, including host, parasite and environmental factors.	D	
Disease profile	Evaluation of the contribution of asymptomatic malaria for disease transmission and as an impediment to elimination.	B	
Epidemiology	Evaluation of simple methodologies for monitoring levels of malaria transmission and for measuring the impact of control strategies on transmission, including focal treatment strategies in relation to malaria elimination.	B	TMA2016SF-1514 Strengthening Malaria Epidemiological, Pathophysiological and Intervention Studies in Highly Endemic Eastern Uganda (MEPIE study)
	Evaluation of simple ways of monitoring of drug resistance and assessing the impact of such resistance on disease burden and transmission.	A	TMA2015CDF-973 Determinants and prevalence of parasite resistance among pregnant women receiving Intermittent Preventive Treatment with Sulphadoxine-Pyrimethamine (IPTp-SP) in a malaria endemic community (IPTp-SP resistance in Nigeria)
	Defining optimal indicators for surveillance of malaria risk and burden, through measures in vectors and human hosts. Establishing surrogate measures of protection for vector control products.	B	

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.	C	TMA2015SF-1001 Harnessing parasite diversity and naturally acquired protective immunity against *Plasmodium falciparum* malaria for the development of highly effective vaccines (SMART)
			TMA2016SF-1513 Determining Correlates of Naturally Acquired Pre-Erythrocytic Immunity to *Plasmodium falciparum* malaria in an Experimental Human Challenge Model (CoNAIPS)
			TMA2017CDF-1892 Understanding the biology of *Plasmodium vivax* and *Plasmodium ovale* for the development of a field-based anti-hypnozoite drug screening model (HypnoBio)
Diagnosis and tracking	Evaluation of novel point of care diagnostic tests, including those for detection of *P. vivax* hypnozoites, and G6PD deficiency.	A	TMA2016CDF-1605 PSOP24-377: An infectious bite marker for sensitive malaria detection and population level surveillance (PSOP24-377)
	Innovative use of new or existing diagnostic technologies for malaria control and elimination efforts.	A	
Treatments	Safety and efficacy testing of new drugs, including single dose treatments and optimisation of schedules for existing drugs, including evaluation of interactions between antimalarials and other drugs, including ARVs and anti-TB drugs (especially amongst children and pregnant women).	A	TMA2016CDF-1555 Single low-dose primaquine efficacy and safety for treatment of uncomplicated *Plasmodium falciparum* malaria based on cytochrome P450 2D6 activity in Bagamoyo district, Tanzania (ESSLDPQ P4502D6)
			RIA2017MC-2022 Clinical evaluation of ArteSunate+Amodiaquine+Atovaquone-Proguanil tri-therapy for malaria treatment in African children (ASAAP)
			RIA2017MC-2025 Efficacy and Safety of a newly registered Artemisinin-Based Combination (Pyronaridine-Artesunate - PYRAMAX®) for the treatment of uncomplicated malaria in African pregnant women (PYRAPREG)
			RIA2017T-2015 Phase III multicenter clinical trial of a Single Dose Regimen of OZ439 (artefenomel) and Ferroquine for the treatment of malaria (SINDOFO)
			RIA2017T-2018 A phase 2 and 3 clinical trial program to assess safety, efficacy and transmission blocking properties of the new anti-malarial KAF156 combined with a new formulation of lumefantrine in children and adults with uncomplicated *Plasmodium* sp. malaria in West and Central Africa (WANECAM - II)
			TMA2017SF-1943 Optimizing Malaria Treatment for HIV-Malaria co-infected Individuals by Addressing Drug Interactions between Artemisinin-based Combination Therapies and Antiretroviral Drugs (OPTIMAL)
			TMA2017CDF-1897 Impact of standard antiretroviral therapy on the pharmacokinetic profile and placental penetration of piperaquine when administered as dihydroartemisinin-piperaquine for intermittent preventive treatment of malaria among pregnant women in Malawi (PENETRATE)

	Evaluation of novel malaria control strategies using drugs and/or vaccines, including Mass Drug Administration (MDA) for malaria elimination or control.	A	
Prevention	Evaluation of novel drugs and strategies for malaria chemoprevention in young children and pregnant women (especially using existing contacts with health services (e.g. vaccination))	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 study)
			TRIA2015-1076 b IPTp with dihydroartemisinin-piperaquine and azithromycin for malaria, sexually transmitted and reproductive tract infections in HIV-infected pregnant women in Kenya and Malawi: a multi-centre 3-arm placebo-controlled trial (IMPROVE-2)
			RIA2016MC-1613 Improving maternal and infant health by reducing malaria risks in African women: evaluation of the safety and efficacy of dihydroartemisinin-piperaquine for intermittent preventive treatment of malaria in HIV-infected pregnant women (MAMAH study)
			TMA2016CDF-1584 Enhancing Training and Research for the Control of Malaria among African Mothers (ETRAM)
	Evaluation of vaccines for prevention, including those targeting different populations such as infants and pregnant women, and of transmission blocking vaccines.	A	RIA2016V-1649 Multi-Stage Malaria Vaccine Consortium: field efficacy testing of a malaria vaccine targeting all four stages of the parasite's life-cycle (MMVC)
Product-focused implementation research	Evaluation of novel implementation approaches for new and existing interventions.	B	EDCTP-CSA-2014-276 Maximising the public health impact of interventions to control malaria in pregnancy through the translation of EDCTP-funded evidence-based global policies to country level policies and plans (IMPP-ACT)
			TMA2017CDF-1903 Impact of RTS,S/AS01 vaccine and insecticide treated bednets on neurobehavioural impairment and school participation in children from rural Kenya (Mal-Brain study)
	Improved strategies for scale-up of access to drugs, vaccines, and diagnostics and for monitoring and evaluation of coverage.	A	EDCTP-CSA-2014-282 Improving the impact of existing Malaria Products – ACTs (IMPACT)
			TMA2017CDF-1878 Monitoring safety of single-low dose primaquine co-administered with AL in routine healthcare practices: addressing potential implementation challenges and policy options for effective roll out (PRIMAQUINE ROLL OUT)
	Evaluation of the feasibility and cost-effectiveness of improved information systems for optimising malaria treatment strategies, including monitoring the coverage of interventions and for the prevention of drug stock-outs.	B	
Critical infrastructure & human development needs	Development of infrastructure for conduct of Phase I to Phase IV trials of malaria interventions and for the evaluation of new vector control tools.	B	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 vector control, diagnostics, drugs and vaccines.	D	

Neglected Infectious Diseases (NIDs)

WHO's list of neglected tropical diseases covers a diverse group of 20 diseases caused by different pathogens that have diverse manifestations, life cycles, and methods of transmission[12]. EDCTPs remit covers the following diseases from this list: Buruli ulcer, dengue and chikungunya, dracunculiasis (guinea-worm disease), echinococcosis, foodborne trematodiases, human African trypanosomiasis (sleeping sickness), leishmaniases, leprosy (Hansen disease), lymphatic filariasis, mycetoma, onchocerciasis (river blindness), rabies, schistosomiasis, soil-transmitted helminthiases, taeniasis/cysticercosis, trachoma, and yaws. One sixth of the world population suffers from one or more NIDs[12] with 50% of those affected living in sub-Saharan Africa. Many of these diseases are avoidable or treatable. More precise tools for diagnosis, better treatment regimens, novel drugs, and enhanced awareness are needed to make progress in the control and elimination of these diseases. A prominent research priority is in the understanding of the consequences of NID co-infection with malaria, TB, or HIV infection and in the context of non-communicable diseases (NCDs). Development of drugs, diagnostics, and vaccines is a priority, along with improved understanding of the consequences of co-infection and co-morbidity. Finally, because many NID persist due to fragile local health systems, programmes to strengthen them by building better infrastructure for good clinical and regulatory practice are required.

Topic	Description	Priority	EDCTP2-funded studies (grant code, title of study, acronym)
Pathogen traits	NIDs include viral, bacterial, fungal, protozoal and helminth infections with diverse manifestations, life cycles and methods of transmission. They include: Buruli ulcer, dengue and chikungunya, dracunculiasis (guinea-worm disease), echinococcosis, foodborne trematodiases, human African trypanosomiasis (sleeping sickness), leishmaniases, leprosy (Hansen disease), lymphatic filariasis, mycetoma, onchocerciasis (river blindness), rabies, schistosomiasis, soil-transmitted helminthiases, taeniasis/cysticercosis, trachoma, and yaws.	C	
Disease profile		D	
Epidemiology		A	
Pathogenesis/host response/ immune response	Diverse mechanisms of pathogenesis and immunity. Epidemiological studies provide a foundation for clinical studies.	B	TMA2017GSF-1956 Contribution of intestinal parasite infections in the risk of developing cardio-metabolic diseases in rural and urban areas of Gabon and Côte d'Ivoire: a pilot study (ParCam) TMA2016CDF-1571 Identification of host regulators of tissue fibroproliferative pathology in schistosomiasis-diseased children in Africa (Maquisard) TMA2016CDF-1561 Impact of secondary bacterial infection in the development of filarial lymphedema among Ghanaian patients (SecBILE)
Diagnosis and tracking	Evaluation of diagnostic/biomarkers, including for treatment response, and 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 (BU-RPA)
			TMA2015CDF-995 Urinary Cytokine ELISA: A tool for Assessing Urinary Tract Pathology in *Schistosoma haematobium* infections (UCE)
			TMA2016SF-1437 Evaluation of the LAMP & db-PCR-NALFIA for the Diagnosis and/or as Test-of-Cure in Patients with Visceral Leishmaniasis in Ethiopia (EvaLAMP & db-NALFIA)
			RIA2016MC-1626 Fast and reliable easy-to-use-diagnostics for eliminating Bilharzia in young children and mothers (FREEBILY)
			TMA2017CDF-1887 Clinical evaluation of novel plasma biomarkers for stage diagnosis among sleeping sickness patients in Uganda (CaNPSTS)
Treatments	Evaluation of novel drugs, drug combinations, immuno-chemotherapy, and formulations for treatment (in particular for Buruli ulcer, dengue, human African trypanosomiasis, mycetoma and the filariases).	A	RIA2016S-1635 Towards an adapted, safe, effective combination treatment for African visceral leishmaniasis (Kala Azar) and improved diagnostic tools (Afri-KA-DIA)
			RIA2016S-1641 Phase III clinical trials and registration of a new praziquantel orally disintegrating tablet formulation suitable for preschool-aged children with schistosomiasis (PZQ4PSAC)
			TMA2016SF-1509 Evaluation of a nitric oxide generating dressing (EDX) to improve management of Buruli ulcer disease (BuruliNox)
			RIA2017NCT-1843 Moxidectin for accelerating onchocerciasis elimination: A paediatric dose-finding study, a phase 3b trial comparing efficacy and safety of annual and biannual moxidectin or ivermectin treatment and mathematical modelling of moxidectin and ivermectin based elimination strategies to support country policy decisions (MoxiMultiDoseMod)
			RIA2017NCT-1845 Towards the interruption of transmission of soil-transmitted helminths: Clinical research development of a fixed-dose co-formulation of ivermectin and albendazole (STOP)
			RIA2017NCT-1846 Towards an arsenic-free oral treatment for human African trypanosomiasis due to Tb rhodesiense as a tool for disease elimination (HAT-R-ACC)
Prevention	Evaluation of safety and efficacy of candidate vaccines (e.g. Buruli ulcer, dengue, leishmaniasis, leprosy, rabies, schistosomiasis, and soil-transmitted helminths (STH).	A	RIA2016V-1640 Clinical development of a therapeutic vaccine for prevention of post kala azar dermal leishmaniasis(PREV_PKDL)

	Strengthen preventive chemotherapy and transmission control, used in MDA (mass drug administration) and MSAT (mass screen and treatment), of STHs, filariases, and trachoma through evaluation of drug combinations, formulations, and treatment regimens.	B	
Product-focused implementation research	Evaluating 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.	A	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 (Twice yearly treatment for the control of LF) RIA2017NIM-1839 Chemoprophylaxis for leprosy: comparing the effectiveness and feasibility of a skin camp intervention to a health centre based intervention. An implementation trial in Mozambique, Ethiopia and Tanzania (PEP4LEP) RIA2017NIM-1842 Impact of increased praziquantel frequency on childhood fibrosis in persistent schistosomiasis morbidity hotspots (FibroScHot) RIA2017NIM-1847 Post ExpOsure Prophylaxis for LEprosy in the Comoros and Madagascar (PEOPLE)
	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 burdens (regional versus localised); and 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 that will require development/strengthening of surveillance and monitoring infrastructure, along with training of staff for pharmacovigilance and recognition of changing patterns of drug susceptibility.	B	

Emerging and re-emerging infectious diseases with epidemic potential

The outbreak of Ebola Virus Disease (EVD) in Guinea, Liberia, and Sierra Leone in 2014 had a devastating effect in those countries, causing over 10,000 deaths from EVD and many more than this through the disruption of health systems for several years. Attempts were made during the epidemic to develop and evaluate vaccines, treatments, and diagnostics for EVD, but these were hampered by weak systems and capacity not in place to carry out these activities on a very rapid timescale[13]. It is vital that capacity be developed to undertake rapid evaluation of interventions in clinical trials when future outbreaks occur of emerging or re-emerging diseases. In parallel, strengthening surveillance systems to detect such outbreaks at an early stage and of laboratory systems to rapidly confirm diagnoses are of high priority. Assembling background data now on diseases, such as Lassa Fever, that are currently prevalent and have epidemic potential, will aid in the planning of clinical trials of new interventions, such as vaccines and treatments, as these are developed.

Topic	Description	Priority	EDCTP2-funded studies (grant code, title of study, acronym)
Pathogen traits	Pathogens with epidemic potential in sub-Saharan Africa: 1. Obtaining baseline data on emerging and re-emerging pathogens, including antimicrobial resistance (incidence, prevalence and trends with time) 2. Creating national and regional databases in existing local surveillance systems for emerging and re-emerging pathogens	A	
Disease profile	No defined priorities. Priorities will be developed when a major outbreak occurs.	-	
Epidemiology	Epidemiological studies of Lassa fever to identify risk factors for infection and areas of high infection incidence/prevalence which might be suitable for Phase 2/3 vaccine trials	A	
	Epidemiological studies of priority pathogens on the WHO list needing urgent R&D attention (not all of which have been identified in sub-Saharan Africa): Arenaviral haemorrhagic fevers (including Lassa Fever); Crimean Congo Haemorrhagic Fever; Filoviral diseases (including Ebola and Marburg), Middle East Respiratory Syndrome Coronavirus (MERS-CoV), other highly pathogenic coronaviral diseases (such as Severe Acute Respiratory Syndrome (SARS)), Nipah, and related henipaviral diseases; Rift Valley Fever, Severe Fever with Thrombocytopenia Syndrome;. Collecting surveillance data on disease burden of these pathogens, where applicable, as a foundation for conducting future trials.	B	TMA2017CDF-1865 Emerging and Reemerging Arboviral Infections in Nairobi, Kenya (ERAIN)
Pathogenesis/host response / immune response	No defined priorities. Priorities will be developed when a major outbreak occurs.		
Diagnosis and tracking	Developing, evaluating, and deploying novel diagnostics and strengthening laboratory systems at country and regional levels, especially at the point-of-care and point-of-need sites for WHO priority pathogens (see above). This is to enable accurate and timely collection and analysis of information, along with laboratory systems capable of safely and accurately detecting all major dangerous pathogens with minimal bio risk.	A	TMA2016CDF-1545 Receiver Operator Characterization of Novel EBOV/MARV-GP Epitopes using 2014-2015 Sierra Leonian Ebola Patient-Samples at the NICD BSL-IV (EBOV-RDT-ROC) RIA2018EF-2081 Biochemical Adjustments of native EBOV Glycoprotein in Patient Sample to Unmask target-Epitopes for Rapid Diagnostic Testing (AdjustEBOVGP-Dx) RIA2018EF-2089 Mobile point of care diagnostic testing for Ebola virus diseasein DRC (MobEBO-DRC)
Treatments	No defined priorities. Several treatments are under development for a range of pathogens. These will require evaluation in the future when outbreaks occur.	C	

Prevention	Vaccines: Lassa Fever, Avian Influenza, Ebola Virus Disease, Yellow Fever.	B	RIA2016V-1633 Non-inferiority of fractional-doses trial for yellow-fever-vaccine (NIFTY) RIA2017S-2014 The Partnership for Research on Ebola Vaccinations-extended follow-UP and clinical research capacity build-UP (PREVAC-UP)
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 identify emerging and re-emerging infectious disease threats through early warning and pro-active surveillance, enabling rapid response to emerging infectious diseases threats.	A	CSA-Ebola-2015-360 Building research capacity in clinical management of infectious diseases at two main adult government hospitals in Freetown, Sierra Leone. (ID-Clinical Capacity) CSA-Ebola-2015-353 Enhancing capacity for Phase 1 clinical trials in Uganda (Capa-CT) CSA-Ebola-2015-337 Enhancing individual and institutional infectious disease outbreaks response capacities of healthcare professionals to mitigate infectious emergencies in the Northern Uganda region (ENDORSE) CSA-Ebola-2015-355 Institutional capacity development for multi-disciplinary health research to support the health system rebuilding phase in Sierra Leone (RECAP-SL) CSA-Ebola-2015-363 Vaccine trials and deployment towards sustainability of Ebola Virus Diseases control (SECC) CSA-Ebola-2015-334 Strengthening laboratory capacities in the St. Joseph's Catholic Hospital (Monrovia) for clinical trials on infectious diseases (SELeCT) RIA2018EF-2082 Epidemic preparedness and risk assessment for Ebola Virus Disease outbreaks in the Republic of Congo (EPIRISK-Ebov)
	Development of regional clinical trial capacity for the rapid conduct of GCP-compliant Phase 1, 2 and 3 trials of new vaccines and other interventions against emerging pathogens, including mobile laboratories.	A	RIA2016E-1612 African coaLition for Epidemic Research, Response and Training (ALERRT) RIA2016E-1609 Pan-African Network For Rapid Research, Response, Relief and Preparedness for Infectious Diseases Epidemics (PANDORA-ID-NET) RIA2018EF-2083 Leveraging capacity for early phase clinical trials for filoviruses in Uganda (CAPA-CTII) RIA2018EF-2087 Prise en charge améliorée de Maladie à Virus Ebola en situation d'urgence en République Démocratique du Congo : du protocole MEURI aux essais randomisés contrôlés (PEAU-EBOV-RDC)

Diarrhoeal diseases

In 2016 diarrhoea was the eighth leading cause of deaths (estimated 1.7 million deaths) globally and the fifth leading cause of death among children younger than five years[14]. Although the number of deaths due to diarrhoea decreased by an estimated 20.3% between 2005 and 2015, disease burden remains high with an estimated 499,000 deaths in children under five and is highest in sub-Saharan Africa and south Asia[15]. Rotavirus is the leading cause of diarrhoeal deaths among children younger than five years, accounting for an estimated 128,515 deaths in this age group in 2016[14]. Global diarrhoea mortality among individuals older than 5 years was dominated by Shigella. *Vibrio cholerae* (cholera) was the third leading cause of diarrhoea mortality among all ages.

New vaccines are urgently needed as are innovative strategies to optimize and deploy available vaccines for the control of these conditions. Notably, the aetiology of severe diarrhoeal diseases in children below five in low-income countries (LICs) corresponds to a limited set of pathogenic microorganisms encompassing rotavirus, Shigella, ST-producing enterotoxic E. coli (ETEC), Cryptosporidium; Campylobacter, and *V. cholerae*. Increasing rollout of the oral rotavirus vaccine has led to a spectacular decrease in diarrhoeal disease incidence in LICs, particularly in sub-Saharan Africa, underscoring the impact that vaccines can have against diarrhoeal disease. Shigella, ETEC, and Cryptosporidium in particular are priority targets for vaccine development. Shigella and ETEC may be considered alone or in the form of a combined vaccine. A candidate Cryptosporidium vaccine is further down the development pipeline, highlighting the need for accelerated development or repurposing of efficient drugs. With several oral and parenteral vaccine candidates against Shigella and ETEC having successfully been evaluated in phase 1 studies in the North, priority should be given to proceeding with phase 2 studies in endemic zones that are well characterised. Expert centres with good epidemiological surveillance of the relevant diseases are needed.

Topic	Description	Priority	EDCTP2-funded studies (grant code, title of study, acronym)
Pathogen traits	Rotavirus, *Shigella*, ETEC (ST and/or LT), Cryptosporidium, and Norovirus.	C	
Intestinal ecology	Microbiome, pathogens, and malnutrition.	D	
Epidemiology	Collecting surveillance data on burden of diarrhoeal diseases and pathogens as a foundation for conducting future vaccine trials (in areas where clinical studies will be conducted).	A	
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 paediatric environmental enteropathy.	B	TMA2016CDF-1550 Immunogenicity to cholera vaccine within a population at risk in Zambia: mapping the kinetics of immune responses over time (ChoVaxim)
	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).	B	
Diagnosis and tracking	Developing point-of-care, multiplexed diagnostic tools allowing quick and reliable detection and diagnostic methods to be used in clinical trials and transferring this knowledge to laboratories in sub-Saharan Africa.	C	
Treatments	Testing of candidate molecules against Cryptosporidiosis, including drug repurposing, as cases occurring in non-immunocompromised patients are on average refractory to current treatments.	A	
Prevention	Testing available vaccine candidates (phase 1 – validated) against the most prevalent diarrhoeal pathogens (i.e. *Shigella*, ETEC, and against *Vibrio cholerae*).		RIA2017S-2024 Field studies of an oral whole cell ETEC vaccine candidate in African toddlers and children: Assess efficacy, and set parameters for pivotal Phase 3 trials (ETEC Vaccine Efficacy)
	Improving effectiveness of existing rotavirus vaccines.		

Product-focused implementation research	Global implementation of current rotavirus vaccines.	A	TMA2016SF-1511 A randomized controlled trial of two versus three doses of Rotarix™ vaccine for boosting and longevity of vaccine immune responses in Zambia (ROVAS-2)
	Evaluating the immunogenicity of currently available enteric vaccine candidates in endemic zones.	A D	RIA2017S-2027 Effect of a novel typhoid conjugate vaccine in Africa: a multicenter study in Ghana and the Democratic Republic of the Congo (THECA)
	Implementation research to explore innovative interventions or strategies to optimize the public health impact of available vaccines against diarrhoeal diseases (especially rotavirus and cholera vaccines).	A	
Critical infrastructure & human development needs	Community programs to reduce child morbidity and mortality through integrated community case management programs where diarrhoeal diseases are treated with zinc.		
	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	
		A	
		D	

Lower Respiratory Tract Infections

Lower respiratory tract infections (LRTIs) caused by a range of pathogens in community or hospital settings are among the top four causes of mortality in children and adults globally. Pneumonia accounts for 16% of all deaths of children under 5 years old, killing 920,136 children in 2015. The incidence of severe pneumonia is higher in the African region (30% of the global burden of severe childhood pneumonia)[16,17,18] and it is the most common reason for adult hospitalisation in sub-Saharan Africa[19]. Co-morbidities (poor nutrition and HIV infection), environmental factors (exposure to indoor air pollution, biomass fuel, smoke exposure) and poor living conditions are among the main risk factors for pneumonia and severe pneumonia[20]. Vaccines against *Streptococcus pneumonia* and *Haemophilus influenzae* type B, the top two causes of LRTI, are highly effective and recommended by WHO to be part of the routine immunization program since 2006. Vaccines against influenza virus are available and recommended in pregnancy but poorly used in LMIC and there is no vaccine against *Respiratory Syncytial Virus*[21]. Further documentation of emerging threats from antibiotic-resistant bacteria in community-acquired or nosocomial LRTI in sub-Saharan African is urgently needed. Key research priorities are the improvement of diagnosis of LRTI through evaluation of optimised clinical algorithms; development of biomarkers to differentiate LRTI from other diagnoses; development of rapid multiplex platforms for diagnosis of bacteria, fungi, and viruses; and design of innovative imaging methods that are suitable to the conditions of health facilities of LMIC. Trials of shorter duration antibiotic treatment for community-acquired LRTI among adults and children (living with HIV and HIV-negative) remain top priority, along with evaluation of adjunct 'host-directed therapies' to improve treatment outcomes. Development of new vaccines, evaluation of the impact of latest vaccines on the aetiology and severity of LRTI, and research on implementation models and on the scale-up of existing vaccines are priorities[20,22].

Topic	Description	Priority	EDCTP2-funded studies (grant code, title of study, acronym)
Pathogen traits	To explore the traits of the following pathogens: • Neonates and children: Group B Streptococcus; Respiratory Syncytial Virus (RSV); pneumococcus; cytomegalovirus; Bordetella pertussis for neonates • Adults: pneumococcus, Haemophilus influenza, Klebsiella pneumoniae • In HIV-infected patients: Pneumocystis jirovecii, fungal infections (e.g. Aspergillus fumigatus). In pregnant women: influenza and para influenza virus.	D	
	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 explore the interaction between respiratory viruses and bacterial infection with regard to child vaccination	C	
Disease profile	To define the severity and outcome of LRTIs in: • Adults with and without HIV infection • Children with and without HIV infection • Neonates • Pregnant women • Elderly persons • Patients with other comorbidities.	B	

Epidemiology	To identify the risk factors of LRTI and severity of LRTI in: • Adults with and without HIV infection • Children with and without HIV infection • Neonates • Pregnant women • Patients with co-morbid diseases, 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*.	D	
	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) and tuberculosis associated pneumonia.	D	
	To estimate the burden of RSV in community deaths[23].	A	
	To develop adequate surveillance programs to better clarify the epidemiology, aetiology, antimicrobial susceptibility patterns, and the effectiveness of preventive and curative strategies in place against paediatric LRTIs.	B	TMA2015CDF-1033 Nasopharyngeal Microbiota in HIV Positive Children Presenting with Respiratory Disease (ALRTI)
	To assess the impact of early ART initiation on the occurrence of LRTI in patients living with HIV.	B	
	To assess the impact of latest vaccines for prevention of LRTIs (type b *Haemophilus influenzae*, *Bordetella pertussis*, *Streptococcus pneumoniae*, RSV, and Influenza) especially in children, pregnant women, and immunosuppressed patients.	C	
Pathogenesis/host response / immune response	To study peripheral blood and lung immune responses in LRTI affecting adults, children (both living with HIV and HIV-negative).	C	
Diagnosis and tracking	To develop and evaluate more accurate clinical diagnostic and management algorithms including severity assessment tools and criteria for early treatment failure for LRTIs according to age groups, comorbidities, and severity[22].	B	
	To evaluate the latest multiplex diagnostic platforms for rapid diagnosis of bacterial, mycobacterial, viral, and fungal causes of LRTIs.	A	
	To develop and evaluate innovative specimen collection methods that are easy to perform at lower level health facilities and well-tolerated to improve the aetiologic diagnosis of LRTI in neonates, children, and adults.	A	
	To evaluate/optimise chest X-ray and new imaging technologies for diagnosis of LRTI (digitalized mobile X-ray, thermal imaging, computerized readers, portable ultrasound).	A	
	To evaluate new or existing host-biomarkers (clinical and laboratory), clinical algorithms and currently available diagnostic tests for determining: 1) severity of illness and prognosis, 2) need for hospitalisation, 3) decision to prescribe antibiotics, and 4) how to improve treatment outcomes and management of co-morbities.	B	
Treatments	To evaluate the efficacy of shorter duration antibiotic treatment regimens for severe and non-severe community acquired LRTI, in children and adults (including those immunocompromised)[24].	A	RIA2017MC-2023 Impact of duration of antibiotic therapy and of oral step-down to amoxicillin or co-amoxiclav on effectiveness, safety and selection of antimicrobial resistance in severe and very severe childhood community-acquired pneumonia (CAP): a randomised controlled trial (PediCAP Trial) (PediCAP)

	To evaluate simplified tools for management of hypoxemia for children with severe LRTI and intravenous fluid in resource limited settings.	A	RIA2016S-1636 Childrens Oxygen Administration Strategies Trial-Nutrition (COAST-Nutrition)
	To evaluate adjunct 'host-directed therapies' to improve treatment outcomes for LRTIs in HIV-infected adults and children, and to prevent long term pulmonary functional disability.	B	
	To evaluate the optimal approach to initiate antimicrobial therapy choices, such as the need to provide early empirical cover for atypical mycobacterial and tuberculosis[22].	A	RIA2017MC-2013 Empirical treatment against cytomegalovirus and tuberculosis in severe pneumonia in HIV-infected infants: a randomized controlled clinical trial EMPIRICAL
	To evaluate upcoming new antiviral drugs against respiratory pathogens[23].	B	
Prevention	Chemoprophylactic prevention of LRTI in adults and children.	A	
	To assess the impact of RSV vaccination of pregnant women on the rates, outcomes, and aetiologies of LRTIs in pregnant women and in their offspring.	A	
	To evaluate novel non-capsular antigen vaccines for pneumococcus.	A	
	To evaluate the impact of conjugated pneumococcal vaccines in adults.	A	
	To evaluate the impact of group B streptococcus targeted vaccines in pregnant women on neonatal mortality and morbidity.	B	
Product-focused implementation research	To optimize delivery and scaling-up of new vaccines (e.g. RSV) for LRTIs in partnership with other funders.	A	
	To support epidemiological and operational research to optimise cost-effective delivery and scaling-up of new diagnostics, drugs, and vaccines for LRTI after they have been tested successfully. This will also include scale-up and integration within acute medical services.	B	
	To assess the integration of LRTI management with HIV/TB/malaria/diarrhoea treatments and services.	A	
Critical infrastructure & human development needs	To support training of local laboratory scientists/staff identified as a critical need, as well as good laboratory collection of baseline data for LRTIs.	A	

Ethics, Regulatory and Pharmacovigilance

Critical infrastructure and human development needs	EDCTP2-funded studies (grant code, title of study, acronym)
ERC grants	CSA2015ERC-880, Renforcement de l'Ethique des Essais Cliniques en Afrique de l'Ouest (REECAO)
	CSA2015ERC-873, Improving ethical review process in Sudan through capacity building of National Regulatory Authorities (Enhancing Ethics in Sudan)
	CSA2015ERC-863, Consortium for clinical research regulation and ethics capacity development in Uganda (CREDU)
	CSA2015ERC-876, East Africa pharmacovigilance initiative (EAPI)
	CSA2015ERC-872, Coast to coast: Transcontinental ethics partnership (C2C-TEP)
	CSA2015ERC-868, Developing LMHRA capacity to effectively exercise its regulatory mandate in clinical trials and health research in Liberia (Lib-Regul-Trials)
	CSA2016ERC-1422, AFRica Ethics Excellence NETwork (AFREENET)
	CSA2016ERC-1420, Improved Governance and Research Capacities in Diagnostics for Infectious Diseases of the Liberian Medicines and Health Products Regulatory Authority (IGORCADIA)
	CSA2016ERC-1418, HATUA - Enabling Compliance And Building Capacity And Community For Clinical Research In Kenya (HATUA – KENYA)
	CSA2016ERC-1423, Strengthening Bioethics Committees in Lusophone African Region (LusoAfro-BioEthics)
	CSA2016ERC-1416, Deepening Research Ethics in Nigeria Project (DREIN)
	CSA2016ERC-1432 Streamlining Ethics review process and Regulatory framework in Tanzania (SMERT)
	CSA2016ERC-1417, Strengthening the Capacity of the National Research and Ethics Review Committee and the National Regulatory Authority for Clinical Trials in Ethiopia (SteRN)
	CSA2016ERC-1414, Biomedical Ethics and Regulatory Capacity Building Partnership for Portuguese-Speaking African Countries (BERC-Luso)
	CSA2017ERC-1857, Strengthening Research Ethics Review and Oversight in Kenya (STReK)
	CSA2017ERC-1904, Building Capacity for Research Ethics and Regulation in Zambia (BUCARERZ)
	CSA2017ERC-1910, Competence-based Fellowship for African Medicines Reviewers and Regulatory Science Professionals (Reg. Science-Fellows)
	CSA2017ERC-1911, Strengthening the regulatory framework to upgrade ethical review of clinical research and drugs safety monitoring in Cameroon (BREEDSAFCA)
	CSA2017ERC-1917, Enhancing Togo's ethical review and regulatory competencies for health research (ERUDIT)
	CSA2017ERC-1924, Strengthening the regulatory oversight of clinical trials in Gabon (S-ROC/Gabon)
	CSA2017ERC-1925, Upgrading National ethics review systems and regulatory bodies in Senegal (SEN-ETHICS)
Other grants	TMA2016CDF-1563, Vaccines and Medicines utilisation and safety monitoring system in a Health and Demographic Surveillance System, Uganda (VXMedSSurv)
	CSA2016S-1618, Pharmacovigilance infrastructure and post-marketing surveillance system capacity building for regional medicine regulatory harmonization in East Africa (PROFORMA)

Grants covering multiple (disease) areas

EDCTP2-funded studies (grant code, title of study, acronym)
TMA2016CDF-1595, Immune responses in rural to urban gradient: identifying geographical footprints of the immune system to improve vaccine development (Geographical differences in the immune response)
RIA2017MC-2029, A cluster randomised trial to evaluate the effectiveness of household alcohol-based handrub for the prevention of sepsis, diarrhoea and pneumonia in Ugandan infants (BabyGel)
EDCTP-RegNet2015-1045, Central Africa clinical research Network (CANTAM2 venture)
EDCTP-RegNet2015-1049, West African Network for TB AIDS and Malaria (WANETAM II)
EDCTP-RegNet2015-1051, Trials of Excellence in Southern Africa II (TESA II)
EDCTP-RegNet-2015-1104, Eastern Africa Consortium for Clinical Research 2 (EACCR II)

Endnotes

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