DISCLAIMER: This draft working document reflects the status of current discussions between members of the EDCTP association and the Commission on the content and governance of the Partnership. Several aspects still require further discussion. Therefore, this Proposal has not been formally endorsed either by the Commission or by the EDCTP association.

EDCTP3: EU–Africa Global Health Partnership

European and Developing Countries Clinical Trials Partnership Programme 3

Draft 14 August 2020

About this draft

In autumn 2019 the Commission services asked potential partners to further elaborate proposals for the candidate European Partnerships identified during the strategic planning of Horizon Europe. These proposals have been developed by potential partners based on common guidance and template, taking into account the initial concepts developed by the Commission and feedback received from Member States during early consultation[1]. The Commission Services have guided revisions during drafting to facilitate alignment with the overall EU political ambition and compliance with the criteria for Partnerships.

This document is a stable draft of the partnership proposal, released for the purpose of ensuring transparency of information on the current status of preparation (including on the process for developing the Strategic Research and Innovation Agenda). As such, it aims to contribute to further collaboration, synergies and alignment between partnership candidates, as well as more broadly with related R&I stakeholders in the EU, and beyond where relevant.

This informal document does not reflect the final views of the Commission, nor pre-empt the formal decision-making (comitology or legislative procedure) on the establishment of European Partnerships.

In the next steps of preparations, the Commission Services will further assess these proposals against the selection criteria for European Partnerships. The final decision on launching a Partnership will depend on progress in their preparation (incl. compliance with selection criteria) and the formal decisions on European Partnerships (linked with the adoption of Strategic Plan, work programmes, and legislative procedures, depending on the form). Key precondition is the existence of an agreed Strategic Research and Innovation Agenda / Roadmap. The launch of a Partnership is also conditional

[1] https://www.era-learn.eu/documents/final_report_ms_partnerships.pdf

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to partners signing up to final, commonly agreed objectives and committing the resources and investments needed from their side to achieve them.

The remaining issues will be addressed in the context of the development of the Strategic Research and Innovation Agendas/ Roadmaps, and as part of the overall policy (notably in the respective legal frameworks). In particular, it is important that all Partnerships further develop their framework of objectives. All Partnerships need to have a well-developed logical framework with concrete objectives and targets and with a set of Key Performance Indicators to monitor achievement of objectives and the resources that are invested.

Aspects related to implementation, programme design, monitoring and evaluation system will be streamlined and harmonised at a later stage across initiatives to ensure compliance with the implementation criteria, comparability across initiatives and to simplify the overall landscape.

A Strategic Research and Innovation Agenda (SRIA) is under preparation and its current version can be found in Annex 3 to this document. It is expected that the draft will continue to evolve as more information about the scope of other European programmes and partnerships become available to more precisely delineate the type of activities that should be prioritised in EDCTP3. The SRIA will be adopted at the first meeting of the EDCTP3 Governing Board.

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1 Summary

The EU–Africa Global Health Partnership – the third programme of the European & Developing Countries Clinical Trials Partnership (EDCTP3) – will support international research partnerships accelerating the clinical evaluation of drugs, vaccines and diagnostics for key infectious diseases affecting sub-Saharan Africa, as well as novel approaches for surveillance and control of emerging/re-emerging infections. It will also strengthen clinical research capacity in the region. Building on the two previous EDCTP programmes, the Partnership will ensure that more people gain access to new medical interventions and help to protect regional and global health security.

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2 Context, objectives and expected impacts

2.1 Context and problem definition

2.1.1 Context

Poverty-related infectious diseases remain an important cause of death, disability, and ill-health in sub-Saharan Africa[1] [2]. Despite some recent progress, there is still a dearth of medical products for these diseases. Vulnerable populations, particularly pregnant and breastfeeding women, children, people with additional health conditions (co-infections and co-morbidities) or certain genetic traits affecting drug responses, are slow to benefit from the interventions that are developed.

Furthermore, the nature of infectious disease threats is constantly changing. Emerging and re-emerging infections present major challenges to countries and represent a grave threat to global health security. The rise of antimicrobial resistance is negating the impact of previously effective treatments[3]. The climate crisis is triggering ecological changes that are having a fundamental impact on patterns of disease and altering human activities and population movements in ways that increase the risk of infectious disease outbreaks[4].

Poverty-related infectious diseases are a heterogeneous collection of infections that disproportionately affect the world's poorest and most marginalised populations. More than a billion people, including 400 million children, are affected by these diseases, which cause an estimated 13.7 million deaths each year. As well as deaths, poverty-related infectious diseases are responsible for a high burden of disability, typically measured in DALYs (disability-adjusted life years; one DALY is equivalent to the loss of one year of healthy life). Globally, infectious, maternal, neonatal and nutritional conditions accounted for 29% of DALYs lost in 2016, but for 61% of DALYs in sub-Saharan Africa – more than 410 million DALYs every year. Communicable diseases accounted for 36% of DALYs lost. Importantly, nearly 40% of these DALYs lost are in people aged 15–60 years, when they are at their most economically productive.

Sub-Saharan Africa is disproportionately affected by poverty-related infectious diseases. An estimated 25.7 million people in the region are living with **HIV**, and 1.2 million new cases occur every year[5]. Of the 2.8 million children and adolescents living with HIV globally, nine out of ten live in sub-Saharan Africa[6]. The region accounts for more than two-thirds of the total number of people living with HIV and 61% of HIV-related deaths – 470,000 in 2018[7]. **Malaria** is endemic across much of sub-Saharan Africa, which accounts for 92% of malaria cases and 93% of malaria deaths, mostly of young children[8]. More than 400,000 deaths from malaria occurred in the region in 2017[9].

Tuberculosis (TB) is strongly associated with poverty. An estimated 2.5 million people in sub-Saharan Africa are infected with *Mycobacterium tuberculosis* (Mtb), accounting for 24% of the global burden[10]; 95,000 children and 571,000 people over the age of 14 in the region die of TB every year[11]. More than 25% of TB deaths occur in the African region[12].

Furthermore, Mtb and HIV infections are a deadly combination, with HIV infections increasing the risk and severity of active TB disease, and Mtb infections exacerbating HIV infections. Co-infections also complicate treatment, as several antiretroviral drugs and anti-TB medicines interfere with each other's actions[13] and treatment of HIV/AIDS can trigger a dangerously powerful immune response to Mtb[14]. TB is the leading cause of death among people living with HIV, accounting for around one in three HIV-related deaths. In 2016, 10.4 million people developed TB; of those, 1.2 million were living with HIV[15].

Lower respiratory tract infections remain a major cause of death, particularly among young children and older people. Pneumonia kills more children than any other infectious disease, accounting for the deaths of 800,000 children under 5 years of age every year[16]. Pneumonia is the most common cause of child mortality in sub-Saharan Africa, responsible for 17% of childhood deaths[17]. Multiple bacterial and viral infections can trigger pneumonia in such vulnerable populations.

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Similarly, **diarrhoeal diseases**, again caused by a wide range of pathogens, make a major contribution to the burden of infectious disease among young children in sub-Saharan Africa. Globally, diarrhoeal diseases are the second most common cause of deaths from infections, claiming the lives of 437,000 children under 5 years of age every year[12], including one in ten deaths of young children in sub-Saharan Africa[13].

Furthermore, an estimated one billion people are affected by so-called **neglected infectious diseases**[18] [19] every year, leading to an estimated 200,000 deaths[20]. Nearly 68,000 of these deaths occurred in Africa[15]. Neglected infectious diseases include multiple debilitating parasitic, bacterial and viral diseases that cause severe suffering and stigma; several infections, such as human African trypanosomiasis (sleeping sickness), leishmaniasis and schistosomiasis, disproportionately affect African populations. Neglected infectious diseases again typically affect the poorest and most marginalised populations[21].

Sub-Saharan Africa is also vulnerable to **emerging and re-emerging infections**, including Ebola and other viral haemorrhagic fevers, Lassa fever, yellow fever, and African Rift Valley fever. Humans and animals often live in close proximity, facilitating the spread of infections from animal reservoirs to humans. Such infections often have extremely high mortality rates – for example, 66% for Ebola in the 2018–19 outbreak in the Democratic Republic of the Congo (DRC)[22]. As well as the risk to sub-Saharan Africa, emerging and re-emerging infection have the potential to be disseminated globally, threatening global health security. The current COVID-19 pandemic initially identified in China, illustrates the unpredictability of epidemics, which can arise in any geographic region and spread globally. The capacity of health systems to track the epidemic is crucial for preparedness and response.

Pathogens with animal hosts will be difficult if not impossible to eradicate. The potential for zoonotic transmission will therefore always be present, and surveillance for new human infections is essential to ensure rapid detection of cross-species transfer and the timely launch of outbreak investigation and control responses. Surveillance systems for Ebola in Uganda, for example, have ensured that, while isolated infections do still occur, they have not developed into full-blown outbreaks[23].

Treatment of infections is also being badly affected by the emergence and spread of **antimicrobial resistance**. Resistance to the most commonly used antimalarial medicines, artemisinin-based combination therapies, is spreading across Asia[24], and there are grave concerns that the introduction or emergence of drug-resistant parasites in Africa could compromise treatment[25]. In 2018, molecular markers of resistance to artemisinin were identified in multiple countries, with first-line treatment failure rates exceeding 90% in Thailand[26]. Mutations in genes associated with artemisinin resistance have been found in malaria parasites in Rwanda, but there is no evidence yet that they affect responses to treatment[27].

Despite use of combination therapies to treat HIV/AIDS, resistance to antiretroviral drugs has been rising. In five out of six countries in the region reporting resistance data, resistance rates for the most commonly used first-line treatments exceed 10%; for women, resistance rates exceed 10% in all six countries[28]. Indeed, pre-treatment resistance rates are nearly twice as high for women – a significant finding as women are disproportionately affected by HIV, particularly in sub-Saharan Africa; girls now account for three out of four new infections in young people aged 10–19 years[29].

Treatment of TB requires six months' treatment with multiple antibiotics – a treatment burden exacerbated by the development of multidrug resistance (MDR). Recommended treatment of MDR-TB is based on use of at least four antibiotics over 18 months[30]. An even more challenging threat is presented by extremely drug-resistant TB (XDR-TB), identified in several African countries, with South Africa being particularly badly affected[31].

As well as compromising the treatment of individuals, antimicrobial resistance also facilitates the spread of infections and puts at risk routine medical procedures that rely on effective infection protection and control. Currently, at least 700,000 people die every year due to drug-resistant infections, which could cause 10 million deaths each year by 2050[32].

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Antimicrobial resistance in sub-Saharan Africa is further complicated by the simultaneous over-use of antimicrobials where they are not needed and widespread lack of access to antimicrobials. A significant challenge is presented by the common use of syndromic management, treatment based on symptoms rather than an understanding of the specific causes of infections. There is therefore an urgent need both to enhance access to antimicrobials but also to protect their effectiveness through careful antimicrobial stewardship[33].

The changing nature of infectious disease threats is also exemplified by the influence of **climate change**, which is already having an impact on infectious disease[4]. The changing environment is altering geographic and seasonal patterns of disease, in particular due to impacts on the distribution or survival of vectors such as mosquitoes. Changing weather patterns, such as heavy rainfall and floods, can also create conditions that favour the spread of water-borne diseases such as cholera[34].

These changes are exacerbated by human population movements driven by climate change, accelerating existing trends such as rapid urbanisation – Africa is currently the world's most rapidly urbanising region[35]. Permanent displacement or work-related migration can bring people into contact with new pathogens, and also promote the rapid dissemination of outbreaks. Displaced populations often live in settlements that provide opportunities for the spread of infections. Population movements also present major challenges to the delivery of healthcare services, for example through the creation of high-density informal settlements.

As well as direct impacts on health, infectious diseases have a much wider **socioeconomic impact**[36]. With widespread reliance on out-of-pocket expenses for health care, infectious disease treatments can be a major drain on household resources, contributing to financial hardship. Caregivers must devote time to looking after sick children or relatives, reducing their time spent on economically productive activities. WHO has estimated that the annual indirect cost of illness is US$2.4 trillion, with HIV, TB and malaria accounting for a quarter of this loss[37].

At an individual level, childhood infections can impede growth and development, with long-term impacts on children's earning potential as adults[38]. Furthermore, infections also worsen the impact of malnutrition[39], by damaging and interfering with the function of the gut, and contribute to impaired responses to oral vaccines. Conversely, preventing infections, for example by vaccination, has been shown to benefit health, development and education[40].

Infectious disease outbreaks also have a major economic cost. As well as the direct costs of treatment and outbreak investigation and control, outbreaks can disrupt trade, tourism and other economic activities. Outbreaks can also discourage use of healthcare, indirectly leading to greater morbidity, mortality and financial costs[41]. The financial impact of the 2014–16 West African Ebola outbreak has been estimated to be as high as US$53.2 billion[42]. The social and economic impact of the current COVID-19 pandemic is not yet clear, but is certain to be immense[43].

As well as its benefits to individuals, control of infectious disease is therefore an essential foundation for sustainable national development.

2.1.2 Problem definition

The third EDCTP programme – the EU-Africa Global Health Partnership – will address infectious diseases in sub-Saharan Africa by focusing on two main challenges:

1. Lack of health technologies for tackling infectious diseases in sub-Saharan Africa

Although important strides have been made, limited tools are available to combat infectious diseases. For instance, although the development of antiretroviral therapy in the fight against HIV has been a game changer[44], there is still no effective vaccine to prevent HIV infection[45]. Likewise, while there are numerous treatments for TB, the increasing threat of multidrug-resistant forms of the disease emphasises the need for new vaccines with greater efficacy and broader application, as well as for continued development of new

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(combination) treatments[46]. For diseases such as dengue – a mosquito-borne viral infection affecting around 390 million people annually – there is no effective treatment[47].

Moreover, the progress made in combating infectious diseases is being increasingly challenged by the rising levels of antimicrobial resistance. For instance, while chloroquine has long been used as a malaria treatment, there now is widespread resistance against it in most areas of the world[48]. As a result, new treatments are constantly required.

Detection of infections, including emerging and re-emerging infections, is dependent on reliable diagnostics. There is a shortage of affordable, easy-to-use and rapid diagnostic tests for many infections, limiting the ability to identify cases and track the spread of infection.

2. Insufficient clinical research capacity for tackling infectious diseases in sub-Saharan Africa, and limited knowledge exchange and research collaboration

Sub-Saharan Africa accounts for 10% of the global population but produces only 1.3% of global health research publications[49]. In many disease-endemic countries in the region, there is insufficient capacity for conducting health research and clinical trials[50]. This includes the equipment and tools needed to support trials (e.g. laboratory equipment, IT infrastructure), as well as human resources (e.g. researchers, technicians, health care workers) and the broader enabling research environment (e.g. ethical review boards[51], and national medicines regulatory authorities). Capacity to rapidly identify and respond to infectious disease outbreaks is similarly limited.

Even where suitable health technologies are available, there often is a challenge in getting them to where they are most needed and ensuring that they are used to optimal effect. Most sub-Saharan African countries are faced with weak, under-resourced health systems. As a result, health technologies that have proven efficacious in trial environments may show reduced effectiveness in real-world settings, when they are not used correctly, or if they are used only intermittently as a result of insufficient availability. Implementation research can play a vital role in ensuring that new health technologies are introduced effectively in a timely fashion and made accessible to people in need[52].

2.1.3 Key problem drivers

The dearth of interventions for poverty-related infectious diseases in sub-Saharan Africa reflects several key problem drivers:

- **Lack of medical technologies** to tackle infectious diseases that have successfully navigated all stages of clinical evaluation and reached people in need. This is due in part to insufficient knowledge of the pathogens causing infectious diseases and their capacity to evade immune responses and develop resistance to treatment
- **Insufficient clinical research capacity** for tackling infectious diseases in sub-Saharan Africa, and limited knowledge exchange and research collaboration
- **Lack of investment and fragmentation** of public and private research efforts to tackle infectious diseases affecting sub-Saharan Africa
- **Insufficient capacity to detect, diagnose and monitor emerging and re-emerging infectious diseases** in sub-Saharan Africa

1. Lack of health technologies and insufficient knowledge of the pathogens causing infectious diseases and their capacity to evade immune responses and develop resistance to treatment

The most prevalent pathogens affecting low- and middle-income countries, such as HIV, *Mycobacterium tuberculosis* and *Plasmodium* malaria parasites, have shown tremendous resilience against control measures. One of the main reasons is gaps in our knowledge about host–pathogen interactions and the mechanisms by which they cause disease and escape our immune system. This has slowed development of new vaccines and

treatments. Furthermore, there is a need to conduct clinical trials in many different target populations and settings.

Clinical trials are essential for determining the safety and efficacy of interventions. While valuable safety and efficacy data can be drawn from studies in high-income countries, often studies need to be conducted within sub-Saharan Africa itself. This may be because the infections are found only in this region, or particular strains of pathogen are found in sub-Saharan Africa. In addition, responses to drugs or vaccines may be different in various African populations, because of genetic differences or environmental factors. For example, particular genetic variations found in Africa affect responses to some antiretroviral drugs[53], while responses to rotavirus vaccine are generally lower in sub-Saharan Africa than in high-income countries[54].

Given these challenges, a collaborative approach is required to develop and evaluate vaccines, drugs and other tools needed to control these diseases. Partnerships across a wide range of actors are needed to chaperone new interventions through complex evaluations in disease-endemic settings, regulatory pathways, and implementation into health systems. Collaboration between public and private funders, together with research institutes, product development partnerships and national health authorities, is therefore key to further progress.

Importantly, for later-stage and post registration trials and implementation studies, the nature of local health systems is a crucial factor, central to study design. Given their high degree of local relevance, these studies generally deliver the evidence most useful to national policymakers.

2. Insufficient clinical research capacity for tackling infectious diseases in sub-Saharan Africa, and limited knowledge exchange and research collaboration

Despite the many gains over the last few years, in significant part contributed to by EDCTP funding, sub-Saharan Africa is still faced with a dearth of clinical research infrastructure and established researchers capable of competing for funding and initiating and maintaining major research projects. Many researchers are working in isolation and engaging in activities that may have short term economic advantages that are often not relevant to clinical research.

However, the capacity to undertake high-quality clinical research is generally weak in many sub-Saharan African countries. The region accounts for 10% of the global population but only 1.3% of global health research publications[55]. Clinical studies are governed by stringent international regulations, covering areas such as the conduct of trials, ethical approvals and the quality of laboratory analyses. Studies therefore require sufficient infrastructure and an appropriately trained workforce in order to carry out studies generating data consistent with the standards imposed by national and international regulatory agencies.

Furthermore, as well as shortcomings in institutional and individual capacity, many countries also have limited capabilities to ensure effective oversight and governance of research. This includes the capacity to oversee ethical approvals and ensure compliance with national and international regulatory standards. Without adequate regulatory capacity, it can be difficult to organise trials in countries, application procedures may be unnecessarily slow or not fit for purpose, and the start of trials can be delayed for significant periods.

Over its two programmes, EDCTP has sought to develop a more strategic and integrated approach that maximises the impact of investments and aims to secure a longer-lasting legacy by developing clinical research capacity that endures beyond the duration of EDCTP funding. It has developed a more integrated, systems-oriented approach that addresses all key areas of clinical research capacity development – physical infrastructure, human resources and national regulatory capacity.

Partnership-centred networks are needed to train scientists and build capacity so that more African scientists (and European scientists) gain expertise in clinical research in the diverse African context. With EDCTP2 support, more extensive research partnerships and Networks of Excellence have extended the range of institutions and

countries involved in clinical research, expanded the research capabilities of individuals, institutions and countries, and created sustainable platforms able to host a greater number of research projects that have the potential to be sustainable in the long term.

3. Lack of investment and fragmentation of public and private research efforts to tackle infectious diseases affecting sub-Saharan Africa

Lack of investment: There are few economic incentives for companies to invest in interventions for diseases that predominantly affect low-resource settings. Development of vaccines and drugs is both costly and high risk, and the lack of financial resources in countries in sub-Saharan Africa inevitably makes them an unattractive market for commercial organisations. Companies may also be reluctant to invest in studies that would enable the use of products to be extended to specific subpopulations, such as children or pregnant women and those with additional health conditions, who are typically excluded from pivotal clinical trials. As a result, most support is provided through public sources, which are limited in the sub-Saharan African region. Moreover, this lack of investment hinders the development of the scientific leadership of African researchers.

For devices such as diagnostics, a further challenge is the need for products that are affordable, reliable, easy to use, and robust enough for challenging environmental settings. This demanding set of criteria deters investment when the potential to achieve a reasonable return on investment is highly uncertain.

As a result, the product development pipeline for infectious diseases is poorly stocked, and progress has been slow. In 2019, there were only 129 active clinical studies/trials on poverty-related neglected diseases, compared to 3,499 oncology studies/trials[56]. The 2018 Access to Medicines Index[57] showed that, out of 1,314 R&D projects in the pipelines of the 20 largest pharmaceutical companies, only 298 targeted priority products for infectious diseases[58] [59] [60] [61] [62].

Fragmentation of responses: Development of new interventions for resource-poor settings such as sub-Saharan Africa remains a neglected area, emphasising the importance of maximising investments. Europe has a long history of supporting medical research in sub-Saharan Africa, but this has often been based on informal contacts between researchers and institutions, and bilateral arrangements that reflect long-standing geopolitical legacies.

While excellent research has been carried out, this non-strategic approach is less appropriate for the systematic clinical evaluation of interventions. This requires systematic investment in infrastructure, generally across multiple countries, which can be challenging to achieve through bilateral or project-based initiatives. Clinical research capacity in sub-Saharan Africa still typically resides in isolated pockets of excellence, and maintaining and extending capacity through individual project funding is challenging and unsustainable.

Tackling infectious diseases affecting sub-Saharan Africa therefore requires long-term commitments from a large set of actors. These range from academic researchers to international development agencies, philanthropies and pharmaceutical companies. As all these actors have their own priorities and focus areas[63], one of the main challenges is uniting such diverse actors around a common strategic agenda and roadmaps, in order to use resources effectively and efficiently.

Although EU Member States have shown willingness to align and coordinate their national programmes for infectious disease R&D around a common strategic research agenda, these efforts are hindered by diverging national political priorities for international cooperation and development. EDCTP has provided an important mechanism for aligning activities around a shared scientific and developmental agenda.

4. Insufficient capacity of national health systems to detect, diagnose and monitor emerging and re-emerging infectious diseases in sub-Saharan Africa

As mentioned above, due to increased globalisation and migration, with overpopulated urban environments, climate change and close contact with wild animals in certain settings, the potential for infectious diseases to rapidly spread around the world has increased.

Early detection and diagnosis are vital to responding and limiting the number of new infections in case of an outbreak. This can be particularly challenging in sub-Saharan Africa where systems for detection, diagnosis and monitoring may be inadequate. In its first annual report, *A World at Risk*, published in September 2019[64], the Global Preparedness Monitoring Board concluded that the world is poorly prepared to respond to new global threats. It suggested that global actions were still dominated by responses to outbreaks, with too little investment in preparedness. This is well illustrated by the current COVID-19 outbreak[65].

Compared to many other geographical areas, health systems in many sub-Saharan African countries have limited research and innovation capacity. One possible consequence of such limited capacity is a slower response to emerging infectious disease threats and preparedness for epidemics. This leads to less than optimal control of outbreaks, and the potential for further spread to populations at risk and international dissemination.

In summary, the high burden and the emergence and re-emergence of infectious diseases in sub-Saharan Africa are due, to a large extent, to the lack of robust health technologies, insufficient clinical research capacity in the region, the lack of investment and fragmentation of research efforts, and the insufficient capacity of several sub-Saharan African national health systems to control emerging infectious disease outbreaks. As well as impacts on population, these factors undermine economic development in the region and increase the risk of global dissemination of novel pathogens (Figure 1).

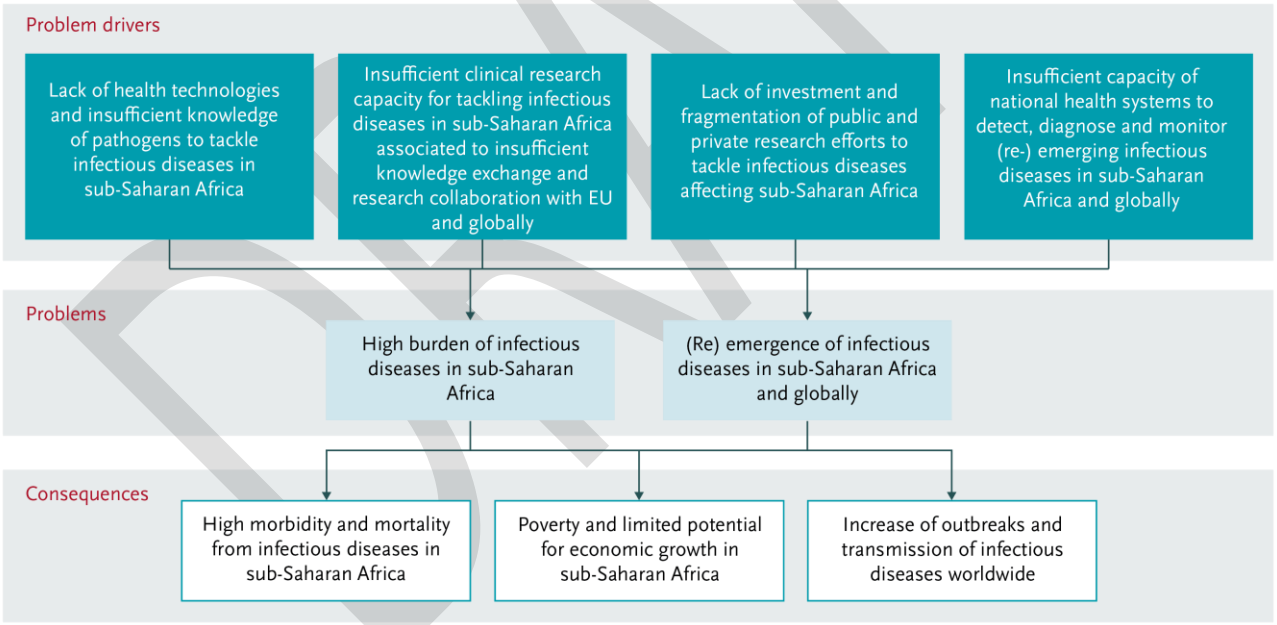

Figure 1: *Problem tree underpinning the research and innovation agenda of the EDCTP3/EU–Africa Global Health Partnership*

2.1.4 How will the problems evolve?

Drug resistance: Infectious diseases present an ever-moving target. Because of natural selection, the use of therapeutics inevitably selects for resistant organisms. **Antimicrobial resistance** is now recognised as one of the gravest threats to the health of people globally[66]. Responses must include not just the development of new therapeutics, but also strategies for more careful use of existing agents, better identification of organisms causing infections, as well as additional preventive measures such as vaccines and better infection prevention and control.

Diagnostics have been highlighted as crucial tools in the battle against antimicrobial resistance, supporting targeted use of antimicrobials, and enabling clinicians to select treatments to which pathogens are known to be susceptible. Diagnostics are also of wider public health value, their use in surveillance providing insights into the prevalence and spread of drug-resistant strains nationally, regionally and globally. However, as well as technical challenges, diagnostic development also faces practical implementation barriers, given the need to adapt clinical pathways and introduce new technologies and ways of working[67].

Vaccines preventing bacterial infections can reduce the need for antibiotics, but even vaccines against viruses can reduce unnecessary antibiotic use[68].

Outbreaks and epidemics: The current COVID-19 pandemic is a global health crisis unlike any in the last 75 years, killing people, spreading human suffering, and disrupting people's lives[69]. However, it is just the latest in a long list of outbreaks of emerging infections, following on from SARS in 2002–2003, H1N1 influenza in 2009, MERS in 2014, Zika in 2016, and Ebola in 2014 and 2018. Further infectious disease outbreaks with pandemic potential are inevitable.

The 2014–16 West African Ebola epidemic, which claimed the lives of at least 11,000 people, focused the world's attention on **global health security**. With extensive population movements and intercontinental travel, the potential now exists for new infections to be rapidly disseminated globally. Sub-Saharan Africa is at risk of outbreaks of a wide range of native pathogens, including Ebola and other viral haemorrhagic fevers, Lassa fever and yellow fever, and of importation of infections from other regions. The global establishment of HIV, which to date has killed more than 32 million people[70], illustrates the impact that an emerging infection can have when it is not successfully contained.

The emphasis now is on **preparedness**, including systems to rapidly detect and respond to infectious disease outbreaks. One important aim is to ensure that systems are in place to evaluate new interventions as rapidly as possible when outbreaks occur, generating evidence that can enhance responses to both the immediate and any future outbreak. Preparedness is fundamentally dependent on pre-existing international research partnerships and established local research capacity.

Preparedness and effective responses, including clinical evaluation of interventions, benefit countries, limiting the human and economic impact of infectious disease outbreaks. But they also establish processes and create the tools needed to ensure that the world more generally is a safer place.

Climate change: Another factor contributing to global volatility is the **climate crisis**. The changing dynamics of pathogen, vector and human behaviours driven by changing weather patterns and environmental impacts are creating a new set of disease risks. An important challenge is to understand these changing dynamics and to predict their likely impacts on human health, including infection risk, to underpin mitigation measures and appropriate focusing of prevention and control activities.

Uptake capabilities: Even when interventions are shown to be safe and efficacious, there is no guarantee that they will be taken up by health systems. The implementation gap is now widely recognised as an important translational bottleneck limiting the access of populations in need to new medical interventions.

Many factors may underlie the implementation gap. The immediate cost of interventions may be an obstacle to their introduction, an issue that can be addressed by cost-effectiveness studies. Often policymakers may require local evidence of effectiveness. Frequently, however, implementation may reflect an institutional inertia, which can be addressed through practical implementation or operational research to identify the barriers to and enablers of the introduction of new interventions and ways of working[71].

At a national level, it is also important that the operations of regulatory authorities do not impose unnecessary obstacles to the introduction of new interventions.

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2.1.5 The current R&D/innovation landscape

Recent years have seen significant progress made in the development of new interventions for poverty-related infectious diseases. Although funding investments still do not reflect disease burdens[72], product pipelines are in general in a healthier state than they were a decade ago. In large part, this reflects the work of academic groups involved in early-stage drug discovery, innovative non-profit agencies and large global public–private product development partnerships (PDPs).

The global health security agenda has also accelerated new product development, for example through the creation of the Coalition for Epidemic Preparedness and Innovations (CEPI). Under the umbrella of WHO's global R&D Blueprint[73], CEPI is supporting the development of vaccines for prioritised emerging and re-emerging infections. The licensing by the European Medicines Agency (EMA) of the Ebola vaccine rVSV-ZEBOV-GP in November 2019[74] was a major milestone in the development of interventions against emerging infections.

Nevertheless, global funding remains inadequate and a limited number of products are in development[46]. It remains essential to advance the development of multiple products in pipelines given the continuing risk of failure during clinical trials, the development of resistance, and the need for alternative treatments with different characteristics to meet different needs.

Furthermore, while early stages of clinical evaluation of interventions for poverty-related infectious diseases are now better supported, later stages have emerged as important bottlenecks in the translational pathway. These include expensive large-scale phase III trials, pragmatic effectiveness studies, and post-licensing implementation studies. In particular, certain populations are generally excluded from clinical trials, such as children, pregnant and breastfeeding women, and people with additional health conditions. Specific clinical trials may be needed to ensure that products can be safely used in such people.

In addition, new formulations may be needed for groups such as infants and children, and specific studies may be needed to evaluate the impact of co-administration of medications, for example in those taking antiretroviral, anti-TB or antimalarial drugs. Treatments may also need to be adapted for those with genetic variants found in the region that affect responses to drug therapies.

This is also a period of great innovation in **clinical trial design**. Increasingly, trials are evaluating multiple treatment options (such as drug combinations, different doses and/or different durations of treatment) in a single study. Adaptive trial designs are also being used so that use of less-effective treatments can be halted mid-way through trials. Such studies are being aided by work on novel biomarkers and endpoints that provide early indications, before clinical responses are apparent, of the efficacy of treatments. These kinds of approaches are having a major impact on the efficiency of trials and promise to further accelerate the clinical evaluation of new products.

Greater use of **implementation and operational research** has the potential to accelerate the introduction of new evidence-based interventions. Such highly practical studies are generally designed and implemented with input from local policymakers and generate the evidence of impact to support both their local sustainability and promote their uptake elsewhere. Implementation research is a relatively new field[75], and there is a need to enhance the capacity for such research in sub-Saharan Africa. Understanding local country contexts is key to identifying the reduced efficacy that has been seen with several new and improved highly efficacious medical interventions, when deployed on a large scale, after evaluation under highly controlled settings.

Additional opportunities for innovation arise from the increasing use of **digital technologies**. On the one hand, these are providing novel tools for collection of research data in the field and in health facilities, but they are also providing opportunities to improve the quality of care and patient engagement. Carefully designed studies are required to evaluate these innovative new approaches and to develop a pathway for their scale-up and wider introduction, as many innovations currently do not progress beyond piloting.

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These examples illustrate important potential synergies between the EDCTP3/EU–Africa Global Health Partnership and the broader agenda of primary health care, health systems strengthening and universal health coverage. As illustrated by the Astana Declaration[76], primary health care has re-emerged as a critical aspect of people-centred care and the drive towards **universal health coverage**[77]. Product-focused implementation research has the potential to make important contributions to health systems strengthening in primary health care, and in enhancing access of all populations to innovative new interventions.

A further important piece of the jigsaw is the role of **national regulatory agencies**. Clinical research is only feasible if national regulatory agencies function effectively and efficiently. They are also key gatekeepers to the introduction of new medical interventions. Further work is needed to develop the capacity of national regulatory agencies, particularly in light of the great speed of innovation in clinical trial design.

Simplification of processes, without loss of rigour, can reduce administrative burdens, improve the efficiency of intervention development, and accelerate the introduction of new products. Harmonisation of processes across countries, and coordination with other regulatory agencies, such as the EMA and the US Food and Drug Administration (FDA), can also deliver further efficiencies – as illustrated by the coordinated regulatory appraisal of the Ebola vaccine rVSV-ZEBOV-GP by countries at risk of Ebola outbreaks[78].

A further key trend in regulatory affairs is the drive towards great **openness in access to clinical trial data**. Since July 2018, the EMA has been publishing data on all medicines authorised in the European Economic Area. Marketing authorisation holders must submit and maintain this information in accordance with EU legislation.

Ongoing dialogue with the EMA is required to ensure adherence to EMA standards, including any new initiatives associated with access to clinical trial data, and to promote alignment between EMA processes and guidelines and those adopted by national regulatory authorities in countries in sub-Saharan Africa.

2.1.6 Evolution of EDCTP

The EDCTP3/EU–Africa Global Health Partnership will build on the foundation laid by the highly successful EDCTP programmes, based on a partnership between institutions mandated by the governments of 14 European and 16 African countries. Since 2003, the two EDCTP programmes have carried out pioneering work by supporting clinical trials carried out collaboratively by groups in Europe and sub-Saharan Africa. EDCTP2 extended the first EDCTP programme, establishing a governance structure that allowed equal partnership status to African States, increasing the number of Participating States and the number of focus diseases. The EDCTP2 programme was launched in 2014 and is due to run until 2024.

The programmes have generated evidence that has had a significant impact on national and international policy and practice – and on people's access to medicines. Furthermore, the programmes have had a strong focus on capacity building, nurturing African scientific leadership, building technical capacity and research skills, and strengthening the ethics and regulatory capacities of countries in sub-Saharan Africa. EDCTP-supported work has strengthened national health research systems, underpinning long-term sustainability.

2.1.7 EDCTP2 funding inputs

Since its launch in 2014, the EDCTP2 programme has committed €608.6m funding (as at November 2019) (Annex 1). The number of countries participating in EDCTP-funded activities has risen to 65 – of which 37 are from Africa, 20 from Europe and eight from elsewhere. A total of 217 clinical studies have been funded, including 130 clinical trials, 130 African researchers supported through fellowships, and more than 7500 have benefited from training opportunities and workshops on key topics such as study protocols, specimen collection, research administration, Good Clinical Practice and epidemic preparedness. Ethics and regulatory projects have been funded in 27 African countries.

Moreover, since 2014 EDCTP has integrated Participating States Initiated Activities in EDCTP2 annual work plans, helping to align the global health research efforts of European countries. A total of 400 Participating

States Initiated Activities have been included in EDCTP2 annual work plans (2014 -2019), equivalent to an additional investment of €1.06 billion in support of EDCTP2 objectives.

EDCTP2 has so far leveraged an additional €300m funding from third parties, including global funders such as the US National Institutes of Health (NIH), philanthropic donors such as the President's Emergency Fund for AIDS Relief (PEPFAR) and the US Agency for International Development (USAID), global funders such as the Bill and Melinda Gates Foundation, PDPs such as the TB Alliance and Medicines for Malaria Venture, and pharmaceutical companies.

Joint initiatives have been launched with WHO/TDR, Fundacion Mundo Sano-Espana, African Research Excellence Fund and GlaxoSmithKline. Further joint initiatives are planned with the Coalition for Epidemic Preparedness Innovations (CEPI), the Novartis Foundation, Fondation Botnar, and the Africa Centres for Disease Control and Prevention.

2.1.8 EDCTP and EDCTP2 impacts

Since 2003, EDCTP has delivered more than 800 scientific peer-reviewed publications, built ethical review panels and regulatory capacity, launched international networks of scientists, and generated data with a significant impact on global and national health policy and practice. A summary of the EDCTP2 portfolio and a selection of major impacts can be found in Annex 1.

Direct impacts:

- **Delivering on EU commitments to tackle global challenges**. EDCTP-funded studies have made vital contributions to the development of HIV antiretroviral drug formulations tailored to children. It has also supported the evaluation of the Xpert MTB/RIF diagnostic technology for the detection of drug-resistant TB bacteria, now recommended by WHO and implemented globally. EDCTP-funded studies have generated key evidence on malaria treatments for pregnant women, who are particularly susceptible to malaria. In addition, the PredART trial provided the first evidence of a strategy to reduce the risk of fatal complication when HIV-infected patients begin antiretroviral treatment while being treated with TB therapy. The TB-NEAT consortium generated evidence on new TB diagnostics.

- **Boosting scientific excellence and Europe's global competitiveness in research and innovation**. Between 2003 and 2011, over 90% of publications from EDCTP-funded projects were published in high-impact journals[79]. Moreover, papers from Europe-wide or Europe–sub-Saharan Africa collaborations typically have higher citation rates and greater research impact, compared to studies without international collaboration[80].

- **Developing the evidence base for national and international health policy-making (bridging the gap between science and policy for health**). EDCTP-funded projects have generated data that have led to changes in health policy. For example, the WANECAM (West African Network for Antimalarial Drugs) study demonstrated the safety and efficacy of an antimalarial formulation for children, paving the way for its approval by the European Medicines Agency and recommendation by WHO. EDCTP-UK funded studies contributed to Paediatric European Network for Treatment of AIDS (PENTA) guidelines. EDCTP established the Pan-African Clinical Trials Registry (PACTR), which is the only WHO-endorsed primary registry in Africa, with >1,000 clinical trials registered. EDCTP is a member of the African Medicines Regulatory Harmonisation Partnership Platform, which aims to improve coordination of regulatory systems strengthening and harmonisation activities in Africa. EDCTP also has a long-term working relationship with the WHO Regional Office for Africa (WHO-AFRO), which hosts the African Vaccine Regulatory Forum (AVAREF). In order to boost country ownership and alignment with specific national health research needs in sub-Saharan Africa, EDCTP has been collaborating with WHO-AFRO on a National Health Research Systems (NHRS) survey project for the assessment of NHRS capacity, informing progress towards the achievement of universal health coverage.

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- **Providing mechanisms to prepare for and respond to public health emergencies in Africa and Europe.** EDCTP is supporting preparedness to respond to infectious disease outbreaks in sub-Saharan African countries, including two large multidisciplinary consortia, ALERRT (African coaLition for Epidemic Research, Response and Training) and PANDORA-ID-NET (Pan-African Network for Rapid Response and Preparedness for Infectious Diseases Epidemics), involving 22 institutions in 18 sub-Saharan African countries and 16 institutions in six European countries, respectively. Each consortium has actively responded to disease outbreaks in the region (Lassa fever, Ebola, plague, monkeypox), and rapidly reoriented their research to address the COVID-19 pandemic in sub-Saharan Africa. In addition, they have jointly enhanced the capacity of African regions to carry out clinical research in emergency situations. In response to the COVID-19 crisis, EDCTP rapidly launched an emergency call, supporting 20 new projects focused on improving disease surveillance capabilities, evaluating point-of-care diagnostic tests, trials of promising therapeutics and diagnostics, establishing biobanks, and validating and adapting serological tests, which have strengthened national and local research capacity. Joint calls with WHO have developed capacity in responding to Ebola outbreaks, clinical research and implementation research.

- **Creating and retaining a new generation of African scientists.** A comprehensive EDCTP fellowship programme focused on the career development of individual African researchers has already supported 130 individual researchers. Most EDCTP-funded clinical studies include a capacity-building work package that supports short- and long-term training, including PhDs and master's degrees, in addition to improving site infrastructure and equipment. Nearly 7,500 people have participated in EDCTP project-related training and workshops on topics such as study protocols, specimen collection, research and administration, Good Clinical Practice and epidemic preparedness. EDCTP is also developing innovative fellowship approaches, such as 'tandem fellowships', whereby senior fellows oversee trainee fellows at a separate institution with a less well-established track record in research. Since its inception in 2003, EDCTP has supported more than 500 African researchers, including fellows and MSc/PhD candidates, with 90% continuing their research career in Africa.

- **Supporting integrated capacity building for health research in Africa**. EDCTP has supported the creation of four Networks of Excellence spanning 42 institutions in 25 sub-Saharan African countries, in Central Africa (CANTAM), Western Africa (WANETAM), Southern Africa (TESA) and Eastern Africa (EACCR), to address disparities between countries in terms of clinical research capacity. In each Network, strong institutions work with institutions in countries with less well-developed health research systems to build capacity. In addition, two major international networks – ALERRT and PANDORA-ID-NET – are strengthening capacity in epidemic preparedness and response. EDCTP is also supporting 57 projects to strengthen the enabling environment for clinical trials and research in sub-Saharan Africa, including health research systems strengthening, pharmacovigilance activities, and the translation of research results into policy and practice. Furthermore, EDCTP is contributing to the strengthening of national health research systems in sub-Saharan Africa, by supporting the strengthening of functional regulatory systems and capacities for ethical review of clinical research.

- **Enhancing research administration.** EDCTP offers grant-writing workshops in different languages (English, French and Portuguese) as well as project and financial management training. It is also supporting the development of a standardised Financial Management Assessment Tool for assessing the financial capacity of beneficiaries and the international standard for Good Financial Grant Practice for better financial governance.

- **Enhancing coordination and cooperation.** EDCTP integrates Participating States' Initiated Activities and centrally managed activities in order to optimise investments in infectious diseases R&D and maximise the impact of limited financial resources. This has played a key role in aligning European funding around a common strategic agenda.

- **Promoting good practice and data access.** EDCTP has encouraged adoption of good practice in clinical research registration and dissemination of data. As well as supporting the establishment of

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PACTR, EDCTP has also collaborated with the Global Health Network to develop online tools to facilitate open-source clinical trials and data sharing. This includes a data management tool for better clinical data management; a Clinical Trial Protocol builder for open source development of clinical trial protocols; and a one-stop data-sharing portal called EDCTP Knowledge Hub to provide free access to a virtual research community.

Indirect impacts:

- **Contributing to the achievement of the SDGs and African Union Agenda**. By accelerating the development, evaluation and implementation of new health technologies, EDCTP contributes to health-related Sustainable Development Goals (SDG), particularly SDG3. Furthermore, by enhancing population health, its activities will contribute to the achievement of multiple other SDGs. EDCTP's work aligns with the African Union's Agenda 2063 and the Science, Technology and Innovation Strategy for Africa 2024 (STISA-2024).

- **Contributing to a stronger African research and innovation base**. EDCTP is helping to build human scientific capital in sub-Saharan Africa. This is a national asset, providing expertise to guide national health policymaking and helping to build local innovation capacity and high-value enterprises.

- **Strengthening public trust**: Through its capacity-strengthening work in ethical review and regulatory oversight, and in pharmacovigilance, EDCTP is ensuring that the interests of research participants and populations are protected. This will help to build public confidence in clinical research and in health systems.

Thus, EDCTP is already a global health initiative with high brand recognition that has made vital contributions to the development of treatments against diseases such as HIV/AIDS, TB, malaria and neglected infectious diseases. It has strengthened capacity in sub-Saharan Africa and fostered strong research collaboration between the EU and Africa.

2.1.9 Lessons learned from EDCTP programmes

The EDCTP programmes have undergone several independent evaluations[81] and impact assessments[82] [83]. The independent interim evaluation of the EDCTP2 programme concluded that EDCTP had "made important inroads in strengthening cooperation and partnership between European and sub-Saharan African countries and developing clinical trial capacity and scientific career development in Africa"[65]. It also noted that, because of the long timescales associated with new healthcare product development and implementation, achieving EDCTP's ambitious goals will require long-term commitment and investment.

The evaluation panel made a number of recommendations to improve the efficiency and effectiveness of EDCTP, including a strengthening of links to policymakers in African Participating States, an additional emphasis on strategic alliances, and a strong focus on developing African scientific leadership. It also highlighted programme management challenges imposed by EDCTP2's legal status within the Horizon 2020 programme and suggested that planning begin on a successor programme to maintain continuity across programmes.

To guide the development of the EDCTP3 programme, a SWOT (strengths, weaknesses, opportunities, threats) analysis of the first two EDCTP programmes has been carried out (Annex 2), drawing on the independent evaluations and impact assessments, as well as the insights of Scientific Advisory Committee members and other key stakeholders. In summary, this analysis suggested that EDCTP has established itself as an important contributor to health research in sub-Saharan Africa, with a distinct niche in the funding landscape – particularly through its progressive commitment to later-stage trials and to under-served groups with unmet medical needs. Its integration of capacity-building activities into projects, as well as dedicated capacity-building funding, was also seen as a notable feature of its work.

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A range of scientific opportunities were identified to accelerate the development and implementation of new interventions against poverty-related infectious diseases. Opportunities exist to increase the size and general visibility of the partnership, and to extend the range of partners, for example through collaborations with private funders and pharmaceutical companies in related areas such as antimicrobial resistance and global health security. Moreover, incentives are required to involve more Participating States, to leverage additional financial resources and to better align national strategies.

It will also be important to create a more flexible funding model, to facilitate partnerships with a wider range of funders, and to promote synergy and complementarity with other funders with common interests, especially through rigorous and transparent funding mechanisms for costly late-stage trials.

2.2 Common vision, objectives and expected impacts

International partnerships are critical to achieve the critical mass, blend of interdisciplinary expertise and coordination required to deliver large-scale clinical trials in a complex global environment. By working together, partners in the global North and South, across the public and private sectors, can maximise the impact of their investments and deliver new medical interventions to populations in need.

2.2.1 Vision, mission and objectives

The EDCTP3/EU–Africa Global Health Partnership, running from 2021 to 2031, will maintain the focus on poverty-related infectious diseases and successful approaches established in the EDCTP programmes, with some shifts in emphasis to reflect changing global, regional, and national contexts. Full details are provided in the associated Strategic Research and Innovation Agenda (SRIA).

Vision
To reduce the individual, social, and economic burden of poverty-related infectious diseases in sub-Saharan Africa

Mission
To support global collaborative research, capacity strengthening, and international partnerships to accelerate the development, evaluation, and implementation of medical interventions to prevent, identify, and treat infectious diseases and emerging/re-emerging infections in sub-Saharan Africa with the overriding goal to reduce mortality and morbidity.

Goals
Through its activities, the EDCTP3/EU–Africa Global Health Partnership will:

- Reduce the individual, social, and economic burdens of infectious diseases in sub-Saharan Africa, promoting the development and uptake of new or improved interventions by supporting clinical trials in sub-Saharan Africa;

- Increase health security in sub-Saharan Africa and globally, in particular in the context of environmental change and the climate crisis, by enhancing national and regional capacity to address antimicrobial resistance and to prepare for and respond to infectious disease outbreaks.

Specific objectives

The EDCTP3/EU–Africa Global Health Partnership will have four specific objectives:

1. **Advance the development and use of new or improved health technologies for tackling infectious diseases in sub-Saharan Africa**

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The EDCTP3/EU–Africa Global Health Partnership will support clinical studies on medical products and interventions designed to prevent, detect, and treat priority diseases, and on technological innovations that facilitate research or access to care. These will include diagnostics, vaccines, novel drug treatments and formulations, and new therapeutic regimens.

Clinical trials and other intervention studies will make up the bulk of the Partnership's portfolio. It will have a greater emphasis on phase III and IV pharmacovigilance and post-licensing effectiveness studies (pragmatic trials and product-focused implementation research). This will include scope for a wide variety of studies to inform national decision-making, including modelling studies and pharmaco-economic analyses.

The EDCTP3/EU–Africa Global Health Partnership will also support preparatory studies essential for the design, conduct, and evaluation of trials. These could include epidemiological studies to generate baseline data on disease burdens, as well as observational studies and social/behavioural/ethics research on health systems and health-seeking behaviours to inform intervention design and implementation.

The Partnership's scope will encompass innovative and rigorous clinical trials of interventions based on herbal medicines and will consider other study designs on a case-by-case basis.

Clinical studies will be required to pay explicit attention to overall impact on health and wellbeing, sex and gender, community engagement, the contribution of social sciences, and ethics.

Key targets:

- To progress to licensing at least two new or improved health technologies
- To generate evidence included in at least 30 guidelines for improved or extended use of existing health technologies
- To progress the clinical development of approximately 30 candidate health technologies.

2. Strengthen research and innovation capacity and national health research systems in sub-Saharan Africa for tackling infectious diseases

The EDCTP3/EU–Africa Global Health Partnership will strengthen clinical research capacity and health systems in sub-Saharan Africa and accelerate the development and application of innovative technologies in healthcare. It will do this by (1) building indigenous intellectual capital, (2) enhancing local infrastructure, and (3) developing supportive regional and national science governance systems (including strengthening of national health research support systems, ethics oversight, and the regulatory environment for clinical research).

This will be achieved through a combination of specific funding for capacity development at individual, institutional, and national and regional levels (e.g. through fellowship schemes and investigator awards, institutional infrastructural development, and regional networks), integration of healthcare and research capacity-building activities in projects, support for international networking (North–South and South–South), and staff exchange and mentorship programmes.

The Partnership will carefully balance the need to promote research excellence while also paying special attention to the challenges of gender balance and regional equity. The importance of local co-funding of clinical trials for maintaining gains made in the conduct of clinical trials will be highlighted with policymakers and the public to raise awareness of the importance of investing in science.

The Partnership will place high priority on strengthening the capacity of countries in sub-Saharan Africa to conduct high-quality clinical trials and implementation research consistent with fundamental ethical principles and recognised international regulatory standards and good participatory practices. The objective of capacity building is to develop individuals, organisations, and societies (individually and collectively) to perform research effectively, efficiently, and in a sustainable manner. Projects should leave a tangible legacy and reduce dependency on external resources. Fulfilling capacity-building objectives in a partnership is key to ensuring

that research for health responds to local health needs and prioritises the safety and health of all affected populations.

To achieve this objective, the Partnership will invest in both people and institutions in sub-Saharan Africa, and promote the exchange of ideas, information, and people between institutions in Europe and those in Africa. To accomplish research goals and translate them into mass-scale innovations, human capital is a prerequisite. Personal support schemes will play a key role in developing the next generation of African scientific leaders. The capacity development part of the Partnership will have a strong focus on research training (master's and PhD) and a comprehensive range of postdoctoral and fellowship schemes, as well as on needs-driven short-term training, mentoring, and exchange. In addition to supporting training in practical research techniques, study design, and research conduct, the Partnership will develop expertise in laboratory and research institution management. It will also develop researchers' skills in other key areas of scientific practice, including biostatistics, applying for grants, preparation of manuscripts, and other aspects of scientific communication.

The Partnership will support and track the career progression and retention of scientists in Africa, and actively intervene to increase awareness and provide a supportive environment for the advancement of talented women in global health research. It will develop mechanisms to increase the competitiveness of researchers from French- and Portuguese-speaking countries.

The Partnership will fund upgrades to clinical and laboratory facilities to support high-quality clinical research, but not entirely new facilities. To increase sustainability of local research capacities arising from its support, it will be open to strengthening the capacities of national health research authorities to continue supporting researchers and research institutions after the end of Partnership funding, including through co-funding mechanisms.

Key targets: Funding for at least 50 specific capacity-building projects and at least 250 fellowships, reinforcing the environment for conducting clinical trials in sub-Saharan countries in compliance with fundamental ethical principles and relevant national, regional and international legislation.

3. Facilitate better alignment around a common strategic research and innovation agenda to increase the cost-effectiveness of European public investment and other global health research funding

The EDCTP3/EU–Africa Global Health Partnership aims to coordinate, align, and, where appropriate, integrate national research and development programmes to add value to European investments in health research on poverty-related infectious diseases. Impact will be increased through collaborations with other EU initiatives, particularly those related to development assistance.

It will promote North–North coordination and pooling of resources, by encouraging European Participating States to jointly develop calls for proposals with other European and sub-Saharan African countries and/or with other partners, facilitated by the EDCTP3 framework.

The Partnership will broker productive and sustainable partnerships – promoting North–South and South–South networking and building relationships with multiple private- and public-sector organisations. It will support established and successful networking and partnering activities with a range of objectives:

- Fostering productive relationships between European and African individuals, groups and institutions.
- Concentrating efforts, promoting efficiency, and avoiding duplication by facilitating coordination and where possible alignment of the strategies of European and African funders, institutions, and authorities.
- Attracting additional investment through global strategic partnerships involving partners in the private, public, and charitable sectors.

North–South collaboration: bidirectional benefits

The programme will promote North–South networking to strengthen project and institutional collaborations by raising awareness of common interests and facilitating collaboration between institutions and research groups with shared goals. Through calls for proposals, the programme will help to establish new North–South collaborations to conduct multi-country, multi-site studies in sub-Saharan Africa. In addition, a regular international conference (the EDCTP3/EU–Africa Global Health Partnership Forum) will provide a platform for scientists from Europe, Africa, and elsewhere to share findings and ideas, and to establish collaborative links.

North–South networks will also benefit European researchers, for example through interactions with experienced African clinicians/researchers with first-hand experience of infectious disease in the African setting, as well the possibility for developing collaborative arrangements that provide access to samples and cases, in an equitable fashion governed by clear and fair material transfer agreements. Furthermore, with the growing research and innovation capacity in the global South, there is often the potential to introduce into Northern countries innovations first developed in/for the global South – so-called 'reverse innovation'[84]. Innovative processes and use of technology to maximise use of scarce resources can provide a source of inspiration for Northern health systems facing financial pressures[85].

South–South collaboration: sharing expertise and good practices

The Partnership will support in-country and regional networking, and promote international cooperation to share good practices, expand capacity, and build platforms for multi-centre trials. South–South networking will build on existing EDCTP regional Networks of Excellence[86] to allow for consolidation during this phase of the collaboration. The Networks provide a mechanism for sharing of resources, knowledge, and expertise, enabling less well-established institutions to participate in multi-centre clinical trials. They also support mentoring and training of early-career researchers. The Networks conduct epidemiological and demographic studies to facilitate the planning of future trials and to enable countries to address new scientific challenges and take advantage of emerging research technologies. The Networks of Excellence will be encouraged to foster excellence within all its members, so that at the end of the Partnership several institutions would have become well-established institutions that can participate as equal partners in multi-centre clinical trials.

The Partnership will promote wider use of the EDCTP Alumni Network and online platform[87] to encourage collaboration and increased dialogue among EDCTP fellows and regional Networks of Excellence. Four disease-specific working groups established within the Alumni Network – on HIV, TB, malaria, and neglected infectious diseases and emerging infections – will further galvanise South–South collaboration. Additional disease-specific working groups could be considered.

Building partnerships and strategic alliances

The EDCTP3/EU–Africa Global Health Partnership will consolidate its investment in late-stage product development, using more flexible and long-term approaches to establish strategic alliances with product developers, including small- and medium-sized enterprises (SMEs), large pharmaceutical companies, and PDPs.

Global health is a large, complex domain. Multiple agencies – including global multilateral agencies, the private sector, charitable foundations, non-profit organisations, and public–private partnerships – work across a variety of sectors, including research capacity strengthening, implementation research, outbreak preparedness, health research for development, and regulatory system capacity building. Sustained progress in global health is costly and most effectively achieved when bodies that support clinical research work together rather than in isolation. The EDCTP3/EU–Africa Global Health Partnership aims to work with a broad range of public and private partners to attract additional investment, exploit opportunities for high-quality clinical research, and maximise the impact of integrated approaches to research.

Strengthening EU cooperation

The EDCTP3/EU–Africa Global Health Partnership aims to increase interactions with other EU initiatives and partners, including those linked to development cooperation, thereby enabling the Partnership and development partners to achieve synergies and greater impact than they would by working independently. Collaboration with development cooperation initiatives will take advantage of the renewed momentum to

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develop more effective and equitable primary health care systems in resource-poor settings, to drive forward progress towards universal health coverage.

Key targets: Launch of joint actions with other public and private funders, with an increased budget of at least €500 million compared with €300 million under EDCTP2.

4. Strengthen capacity in sub-Saharan Africa for epidemic preparedness through effective and rapid research response to develop essential diagnostics, vaccines and therapeutics for early detection and control of emerging diseases of epidemic potential

Early detection and diagnosis are vital to responding and limiting the number of new infections in case of an outbreak. This can be particularly challenging in some countries in sub-Saharan Africa where systems for detection, diagnosis and monitoring are inadequate.

Furthermore, mechanisms are required to ensure that research studies can be launched in a timely fashion, and integrated within public health responses, so that evidence can rapidly be generated on new interventions – drug treatments, vaccines, diagnostics and other public health measures. Such evidence can inform immediate responses to an outbreak and also enhance preparedness for future outbreaks.

The global spread of COVID-19, a pandemic of unprecedented global scale, occurred despite existing knowledge about other coronaviruses responsible for earlier epidemics. EDCTP2 networks have rapidly pivoted to generate data on COVID-19 and to support control activities. The EDCTP3/EU–Africa Global Health Partnership will have a more explicit role in research preparedness and response to emerging epidemics and in coordinating research and innovation support with other funders.

A related challenge is the spread of antimicrobial resistance, which requires ongoing surveillance and coordinated responses to prevent wider dissemination. Moreover, the climate crisis will drive changes in pathogen epidemiology and human behaviour that will significantly increase the risk of infectious disease outbreaks and emergence of novel human pathogens.

In recognition of the importance of related infectious disease threats and the opportunities for synergistic investments, as part of the Strategic Research and Innovation Agenda the Partnership will expand its interests in the following priority areas:

- **Emerging and re-emerging diseases**: Building partnerships to enhance countries' capacity to detect, prevent and respond to emerging and re-emerging infections, including the evaluation of new interventions during outbreaks.
- **Climate crisis-related infectious disease**: The programme will work with other global health partners and national counterparts to determine how best to strengthen response capacities and minimise the health impacts provoked by climate crisis-related increases in the incidence of infectious diseases.
- **Antimicrobial resistance**: Accelerating the development of alternative treatments, vaccines and other preventive interventions, and diagnostics to promote enhanced antimicrobial stewardship.
- **Co-infections and co-morbidities:** Co-infections and interactions of infectious diseases with non-communicable diseases.

Key targets: Twinning of 50 established and 50 upcoming research institutes in at least 30 sub-Saharan countries for an effective and rapid research response to develop essential diagnostics, vaccines and therapeutics to tackle emerging epidemics in accordance with international health regulations.

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2.2.2 Additionality

The EDCTP3/EU–Africa Global Health Partnership is founded on the principle that partners can achieve more by pooling resources and acting together than they can by acting alone. Intervention development for poverty-related diseases is a long, complex and inherently risky process. It requires the expertise of multiple parties, from multiple sectors, spanning academia, industry (SMEs and pharmaceutical companies), the technology sector, the regulatory sector, the global and national health policy sector and others. Furthermore, given the lack of market incentives, traditional models of competition do not apply, and more coordinated and collaborative approaches are essential.

Pooling of resources enables major funding to be awarded to projects that would be out of the scope of many national funders. It also enables large-scale networks to be set up, creating an infrastructure that can support multiple projects. It also enables dedicated capacity-building grants to be awarded, enhancing national health research systems.

The EDCTP3/EU–Africa Global Health Partnership will also help to ensure resources are not wasted through duplication of efforts. Priority setting, for example, is best undertaken strategically and systematically at a regional scale, encompassing the full range of infectious diseases affecting sub-Saharan Africa, all populations, and all geographic settings. The strong participation of African countries in the Partnership will ensure that priorities accurately reflect unmet regional needs.

The Partnership will be strategically important for the EU in ensuring that efforts of partners and EU goals are aligned with agreed objectives and expected inputs as described in detail in the Scientific Research and Innovation Agenda. By creating an appropriate critical mass of partnerships, the Partnership will also be able to maintain relationships with all key stakeholders, including global agencies such as WHO and regional and national regulatory agencies, which again might be beyond the scope of individual countries. The Partnership will enable academic groups and SMEs to gain and build relationships with international networks, global resources and expertise to which they might not otherwise have access.

At the same time, by maintaining the focus on excellence through open calls for proposals, the Partnership can focus its resources on projects and programmes targeting the areas of highest unmet need and with the greatest chance of success.

With the active involvement of European and African countries and inclusion of Participating States activities in its portfolio, the Partnership will enable countries to make strategic decisions about their allocation of resources. As well as being better able to target their funding in areas not covered by the programme, countries will be able to align research with Partnership projects and identify opportunities to support projects taking advantage of research platforms by the Partnership.

2.2.3 Directionality and links to other programmes and initiatives

The EDCTP3/EU–Africa Global Health Partnership directly contributes to SDG3, 'Ensure healthy lives and promote well-being for all at all ages'. By protecting health, it also contributes indirectly to multiple other SDGs, including SDG8 ('Decent work and economic growth'), SDG1 ('No poverty') and SDG10 ('Reduced inequalities'). The Partnership will explore opportunities for collaboration with other EU initiatives with interests in infectious disease control, capacity building, education, health security and emergency responses, and health and development. In several of these areas, discussions will build on links already established in previous EDCTP programmes. The goal is to develop mutually beneficial arrangements that enable both parties to better achieve their aims through aligned activities and joint initiatives (Figure 2).

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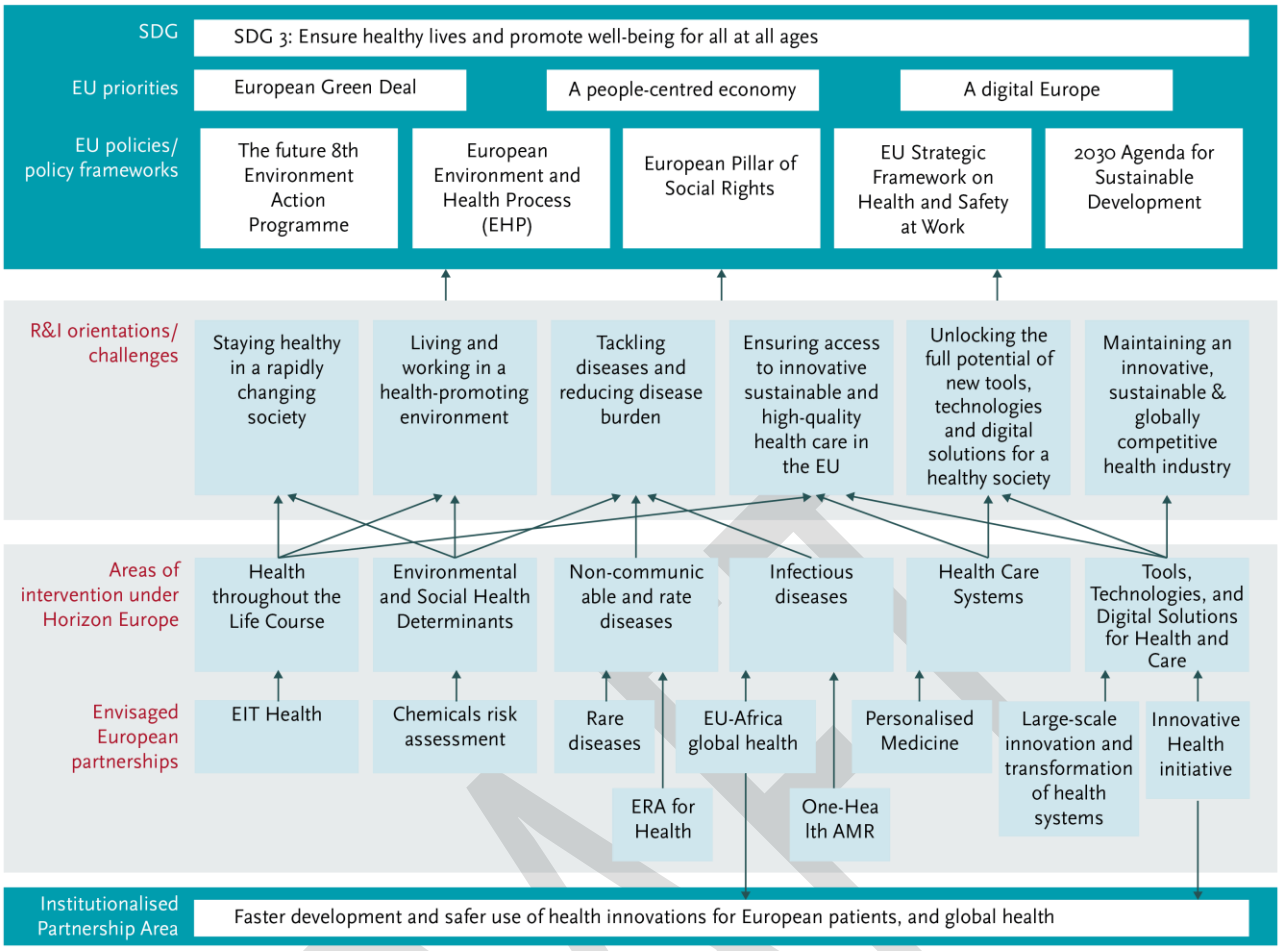

Figure 2: *EU policies and priorities related to SDG3*

Due to its versatility and cross-sectoral integration, the EDCTP3/EU-Africa Global Health Partnership will need to be managed through close collaboration with other programmes and initiatives to create synergies and limit duplications. Administrative mechanisms will be designed to address these synergies and complementarities.

The Partnership will have some areas of common interest with Horizon Europe work programmes and other EU initiatives or programmes with shared objectives to enable effective prevention, diagnosis and treatment of diseases and to facilitate the uptake of new interventions in the field of infectious diseases. Health is one of the six Horizon Europe clusters under the Pillar II addressing global challenges and industrial competitiveness through targeted funding of collaborative research and innovation projects. Cross-cluster research on antimicrobial resistance will be facilitated by the Joint Programming Initiative on Antimicrobial Resistance (JPAMR), the global initiative providing opportunities for collaboration to reduce reliance on antimicrobials, and with the future partnership on One Health Antimicrobial Resistance, focused on the environment and animal health and their interaction with human health. In addition, the Innovative Health Initiative is expected to advance the development and uptake of health care technologies and innovations to help transform health systems, mainly in Europe. Another instrument with shared interests in infectious diseases is the InnovFinID and the future EuropeInvest of the European Investment Bank, which foresee support through loans in the infectious diseases area.

Figure 3 shows potential initiatives in the Health cluster, where complementarities and interconnections are expected, in terms of both research topics covered and stakeholders involved.

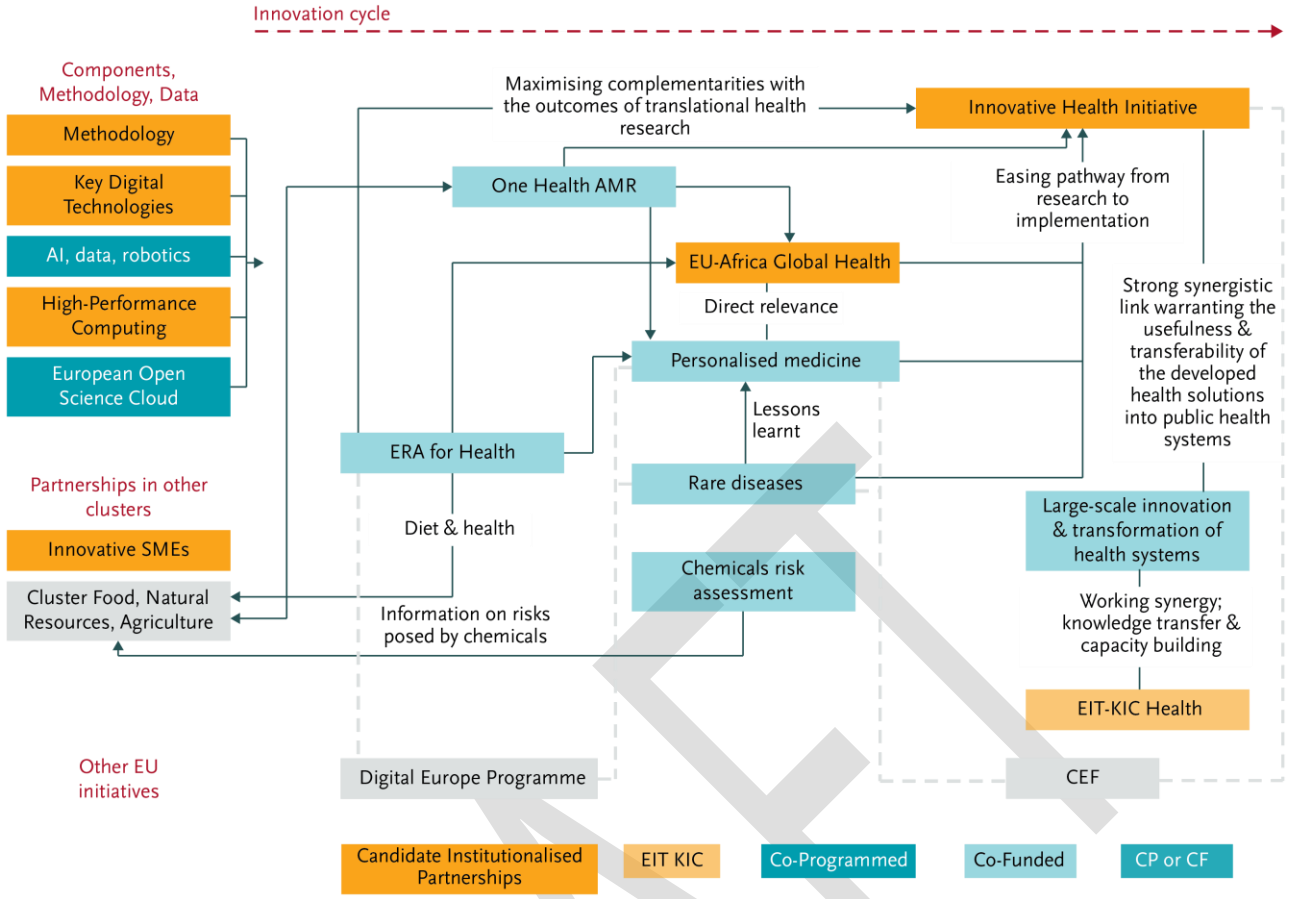

Figure 3: *EU partnerships and initiatives related to the EDCTP3/EU–Africa Global Health Partnership*

The problems that the EDCTP3/EU-Africa Global Health Partnership will address are highly complex and are set in the context of weak health systems and institutions for the delivery of health care. Health systems are particularly vulnerable during outbreaks, as illustrated during the devastating 2014–2016 Ebola virus epidemic in West Africa, which had a major impact on the delivery of health services.

Health research is challenging to conduct in weak health systems. Health research investments therefore deliver collateral benefits by strengthening health system infrastructure. The Partnership will seek synergies with the EU programmes and initiatives that aim to build resilient and responsive health systems and advance progress towards universal health coverage, so that health innovations are accessible to the widest range of populations. Support for epidemic preparedness will contribute to efforts to enhance implementation of International Health Regulations in the region, offering further opportunities for partnerships and synergies with development agencies.

Development assistance is provided through the EU instruments of the Development Cooperation and External Action, the future European Neighbourhood, Development and International Cooperation Instrument, the Universal Health Coverage Partnership and other initiatives, with the support to global initiatives such as the Global Fund, Gavi, the Vaccine Alliance, and the Global Financing Facility.

These instruments also support health systems during public health emergencies by promoting mechanisms to expedite product approval and subsidising the delivery of new health technologies, strengthening regional health security organisations and supporting epidemiological surveillance. The EU Emergency Trust Fund for Africa provides emergency medical assistance and support in basic health services to irregular migration and displaced persons in Africa.

The Partnership will engage with both the European Centre for Disease Prevention and Control (ECDC) and the Africa Centre for Disease Control and Prevention (ACDC), in the areas of human capital and physical

infrastructure, to ensure strategic alignment and coordinated implementation of activities. In the area of outbreaks, the initiative will also contribute to and take into account the recommendations of the Global Research Collaboration for Infectious Disease Preparedness (GloPID-R), an international network of research funding organisations, to facilitate a rapid and effective research response in outbreak settings.

While development of new health technologies is essential, they will not benefit populations unless they are authorised for use where they are needed. Regulatory capacity in Africa for assessment and approval of medicines, as well as the infrastructure for post-authorisation pharmacovigilance, is still weak. Here, the recently established African Medicines Agency (AMA) will have an important role to play. The EDCTP3/EU-Africa Global Health Partnership will contribute to regulatory capacity building and work closely with the AMA. It will also engage with other agencies, such as the European Medicines Agency (EMA) and the US Food and Drug Administration (US FDA), to prepare for future registration of new or improved medicinal products, especially for use in groups with major unmet medical needs (such as children).

The EDCTP3/EU-Africa Global Health Partnership will seek to identify synergies with programmes falling under the remit of the following DGs:

- Directorate-General for Research and Innovation (DG RTD), as the leading DG;
- Directorate-General for International Cooperation and Development (DEVCO) for implementation research and capacity development of national health research systems, as well as increasing programme visibility in African countries with EU country offices;
- Directorate-General for Education, Youth, Sports and Culture (EAC) for collaboration on fellowship programmes, especially involving social sciences and medical studies, for example through Marie Sklodowska Curie Actions and Erasmus Mundus;
- Directorate-General for Communications Networks, Content and Technology (CNECT): for collaboration on future activities involving research and innovation on digital technologies and e-health for use in clinical trials-related activities (DG CNECT is already working with a number of ministries of science and technology in Africa).
- Directorate-General Health and Food Safety (SANTE): Potential cooperation on cross-border preparedness for infectious diseases with epidemic potential, where European countries are involved in preparedness consortia.

The EDCTP3/EU-Africa Global Health Partnership will also look for synergies with the European Investment Bank in relation to the future Europe Invest and with the current InnovFin Infectious Diseases and EU Malaria Fund, an initiative focusing on innovative financial instruments (e.g. loans) to support malaria control initiatives, potentially offering opportunities for complementary funding of late-stage clinical trials.

2.2.4 Preferred partnership model

Based on the comprehensive analysis of the available data in the Impact Assessment of the EDCTP3/EU-Africa Global Health Partnership candidate, the preferred option is that of an Institutionalised Partnership under Article 187 of the Treaty of Functioning of the European Union. The main added value of this option is that the contributions of sub-Saharan African countries, and those of philanthropies, industry and third countries, can count towards the EU's matching contribution, which was not the case under the EDCTP2 programme, based on Article 185.

A partnership under Article 187 will attract the widest range of actors, leveraging and pooling resources. The value of this approach has been illustrated in the response to the COVID-19 pandemic, which has seen the public sector, industry/private sector and philanthropies work together to address the problem.

This new approach recognises the political and operational importance of African countries in the partnership. In addition, Article 187 provides a framework within which philanthropies, industry and other third countries can also join and contribute to the Partnership, allowing the EU to collaborate with a wider range of key global health players.

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Moreover, under an Article 187 arrangement, the EU, represented by the European Commission, is a full partner in and co-owner of the endeavour. This means that the Commission is an active actor in the policy dialogue and the governance mechanism of the partnership and not only an observer, as is the case in the current EDCTP2.

In the EDCTP3/EU-Africa Global Health Partnership, the EU would become a full partner, alongside the EDCTP Association, which would represent its members (EU Member States, countries associated to Horizon Europe, third countries from sub-Saharan Africa and any other third country). The Partnership would also maintain and strengthen inclusive governance with African countries, through the EDCTP Association, a model that has been proven to work effectively in the EDCTP2 programme. Any third party could participate as an 'associated partner' on an ad hoc basis. This option would allow the EU to match contributions from the EDCTP Association and its members as well as from the other associated partners. In turn, it would leverage additional budgetary commitments and promote coordination.

An Article 187 arrangement would therefore leverage substantial and sustainable funding around a common agenda, offer the greatest potential for alignment of partners around shared strategic objectives, and be the option most likely to deliver the identified impacts. It would position the Partnership as a stronger global player, increasing the likelihood of achieving greater impact. With its broader multi-stakeholder partnership, an Article 187 arrangement would be a powerful actor to address global health. It would be able to deliver at the necessary speed and scale, with the Commission having a clear role in its governance to ensure that public interests remain at the core of the Partnership.

The COVID-19 crisis also illustrates the appropriateness of the proposed mechanism. An Article 187 arrangement provides the greatest capacity to coordinate and generate impact in research preparedness and response research, to provide an evidence base to increase individual and community resilience, to facilitate operational readiness, and to improve decision-making during emergency responses.

2.2.5 Expected impacts

Intervention logic: The four objectives of the EDCTP3/EU-Africa Global Health Partnership are designed to address the four problem drivers detailed below (Figure 4).

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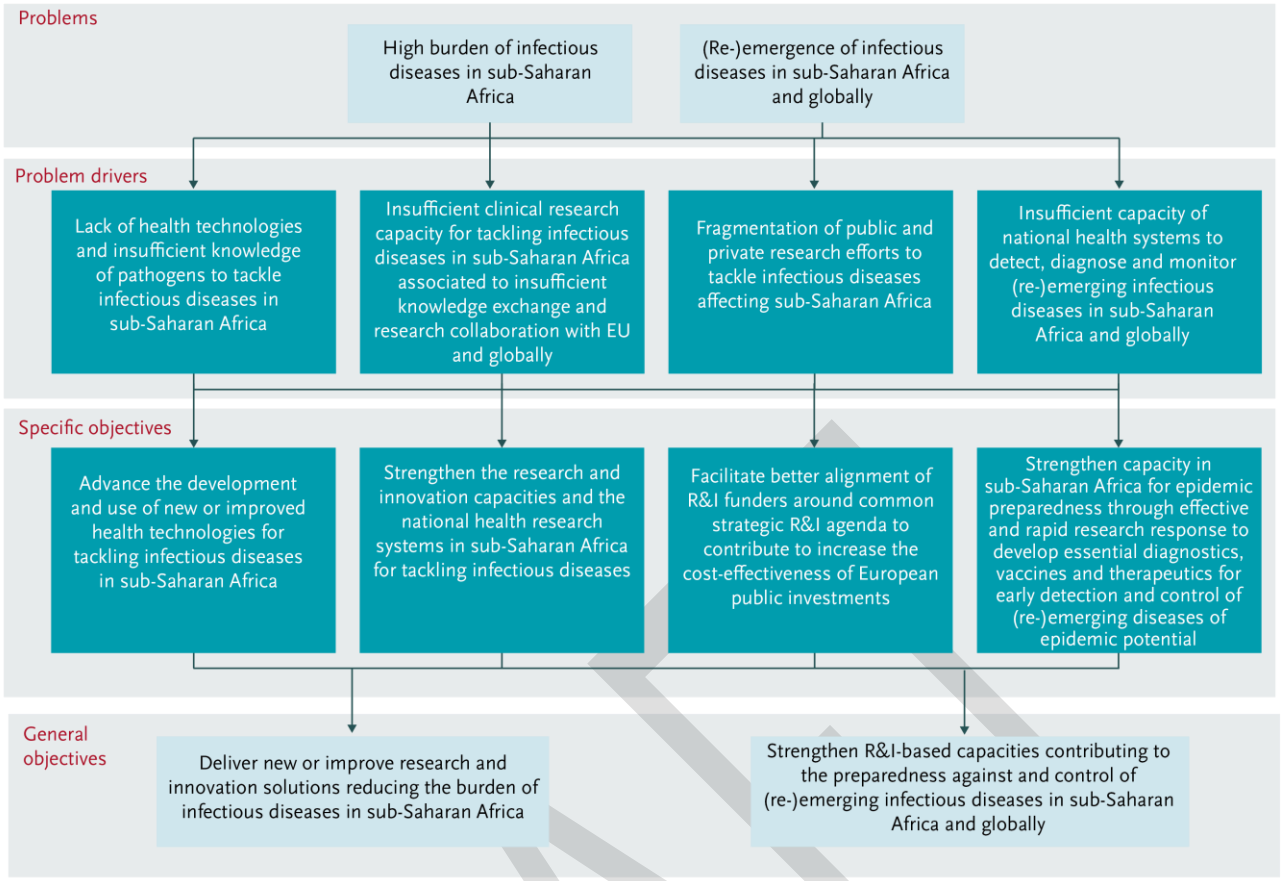

Figure 4: *Intervention logic for the EDCTP3/EU–Africa Global Health Partnership*

By achieving its specific objectives, the EDCTP3/EU-Africa Global Health Partnership would deliver the following impacts:

Scientific knowledge and capacity impacts:

- Deeper understanding of poverty-related infectious diseases and of the safety and efficacy of new medical interventions against them.
- Strengthened EU scientific excellence in clinical research for infectious diseases;
- Increased scientific leadership of sub-Saharan Africa in the infectious diseases field;
- Increased research response capacity to control emerging and re-emerging infections in sub-Saharan Africa;
- Increased evidence base for national and international health policy-making (bridging the gap between science and policy for health).
- Increased critical mass of researchers: Providing the conditions for scientific talents working in sub-Saharan Africa to flourish, collaborate internationally and contribute to training young African talent.

Economic/technological impacts:

- Increased research capacity of institutions in sub-Saharan Africa to design, conduct and manage infectious disease research projects;
- Greater capacity of research institutions to attract funding;
- Increased industry participation in research projects in sub-Saharan Africa;
- Increased number of researchers employed in sub-Saharan Africa;
- Strengthened EU innovation sector in infectious disease field.

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Societal impacts:

- Increased uptake of new or improved health technologies benefiting populations at risk of poverty-related infectious diseases;
- Increased gender equality as tropical diseases can disproportionally affect and disadvantage women[88].
- Greater economic security due to protection against infection/disease.

Global health research is a large and complex field, with multiple actors. The EDCTP3/EU-Africa Global Health Partnership will therefore focus its efforts where it can make greatest impact. Academic groups and PDPs have had a significant impact on early-stage drug discovery and development for poverty-related infectious diseases. While some funding may be required in this area, the Partnership will prioritise later-stage evaluation, including phase III and phase IV studies, including pragmatic effectiveness trials, product-focused implementation research, and research designed to enhance access of underserved populations such as infants, children, pregnant and breastfeeding women, and people with additional health conditions to newly licensed products.

The focus on product-focused implementation research is a distinctive feature, and reflects the significant 'know-do' gap in global health research, whereby regulatory approval of a medical product or successful piloting of an intervention often fails to lead to its widespread use or unnecessary delays in its introduction. As well as addressing and further understanding this bottleneck, the Partnership's research will also build capacity in the area of cross-disciplinary research.

The Partnership will also have a major impact on the capacity of more sub-Saharan African countries to conduct robust clinical research and clinical trials. The impact will be visible in the form of improved infrastructure for clinical trials and in an increased number of African scientists who will receive training through the Partnership and knowledge transfer with Europe. The concepts of ownership and sustainability are important elements of this training, and take many years to build. The EDCTP3/EU-Africa Global Health Partnership can build on the achievements of EDCTP and EDCTP2, and is thus in a good position to further advance these developments.

2.2.6 Monitoring achievement and evaluation of programme implementation

In line with internationally recognised principles of results-based management and Key Impact Pathways Indicators set centrally in the Regulation of Horizon Europe, the EDCTP3/EU-Africa Global Health Partnership will be systematically monitored and evaluated. These activities will help to report on its performance and results, and ensure that the Partnership functions effectively and achieves its objectives while maintaining its commitment to transparency.

Monitoring and evaluation will draw on a 'theory of change' model (Figure 5) that maps out the route through which the Partnership's funding is anticipated to generate outputs (such as the published results from clinical trials), outcomes (such as changes in health policy and practice) and impact (improvements in health and wellbeing and economic gain).

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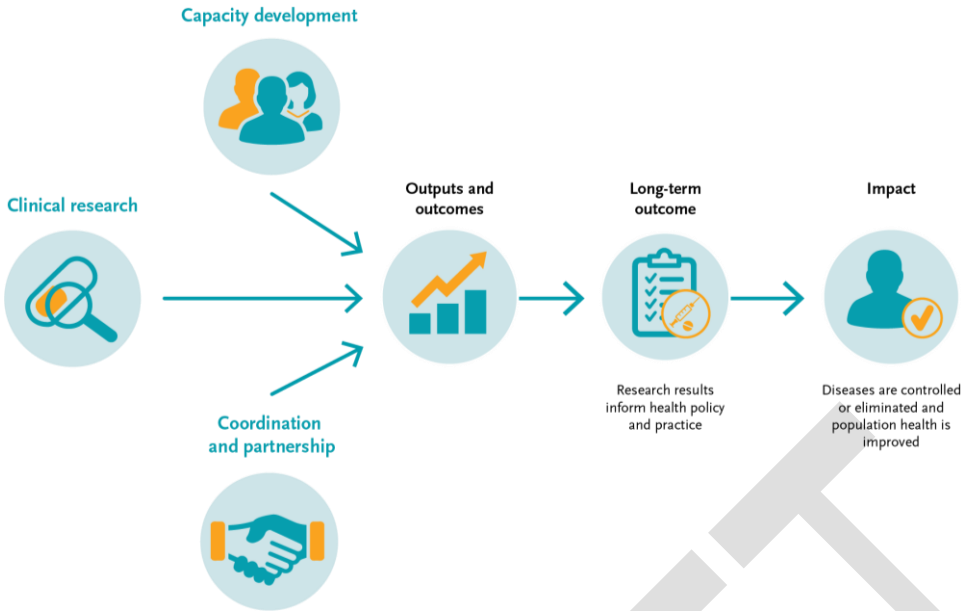

Figure 5: *The EDCTP3/EU–Africa Global Health Partnership theory of change for tracking progress towards impact on health.*

Monitoring

The Partnership will be monitored based on the programme-wide monitoring and evaluation framework developed initially under the first two EDCTP programmes. The performance of individual projects will be monitored to ensure that they achieve their specific objectives and deliverables.

To ensure efficient **operational performance**, implementation of the EDCTP3 programme will be monitored on a regular basis using Key Performance Indicators set out in Table 1, in addition to the Key Impact Pathways indicators set centrally in the Regulation of Horizon Europe. The additional EDCTP3 monitoring indicators have been identified to enable the tracking of progress of the Partnership towards its objectives. Whenever possible, these indicators will be reported in relation to an initial country-level baseline.

Table 1: Monitoring indicators additional to the Horizon Europe key impact pathway indicators

	Short-term (typically as of year 1+)	**Medium-term (typically as of year 3+)**	**Long-term (typically as of year 5+)**
Scientific impacts	**Launching calls to pursue EDCTP3/EU-Africa Global Health Partnership** (# of calls launched, and projects funded in each scheme, and € invested. **Engaging stakeholders to promote generation of high quality scientific knowledge of relevance to EU-Africa global health priorities** (outcomes of stakeholders' consultative meetings; # of topics informing future calls for proposals**)**	**Generating high-quality scientific knowledge of relevance to EU-Africa global health priorities** (# of peer-reviewed international publications generated by projects; citation index of publications) **Building South-South and North-South networks to facilitate (rapid) decisions, actions and information exchange for making (urgently needed) clinical resources and products available** (# of countries and institutions participating in Regional Networks, # of countries and institutions participating in projects addressing epidemic preparedness; # of clinical resources and products on track to gather information for regulatory approval)	**Advancing development of diagnostic kits, candidate vaccines and treatment products for addressing infectious disease-related challenges of relevance to the EU and Africa** (# of new or improved health technologies progressed to licence; # of new or improved health technologies (diagnostics, vaccines, drug candidates, etc.) having progressed through key milestones **Improving R&D preparedness for diseases that might lead to epidemics (surveillance, response and health capacity) and readiness to promptly conduct R&D during an emergency** (# of projects resulting in, e.g. guidance and good practices, response mechanisms and other tools facilitating a coordinated response in case of epidemics, # of projects with activities/deliverables oriented towards "twinning" between stronger and weaker regions/sites, # of robust early warning systems in place; effectiveness of investments in building preparedness capacity as judged by independent evaluations)

	Short-term (typically as of year 1+)	Medium-term (typically as of year 3+)	Long-term (typically as of year 5+)
Economic/ technological impacts	**Supporting studies into cost-effectiveness and economic benefits of products** (# of projects addressing improved efficiency of healthcare resources) **Facilitating participation of industry and private foundations to accelerate R&I** (# of projects with participation of industry and/or private foundations)	**Leveraging investments in R&I and developing partnerships to support joint working and minimising duplication (#€** leveraged though partnerships with other public and private funders, # of public–private publications) **Improving coordination of national Participating States' investments** (Participating States' budget in centrally funded activities and in joint activities with other Participating States)	**Driving forward advancements in global health R&I through innovative public–private collaborations (**# of new or improved health technologies (diagnostics, vaccines, drug candidates) submitted to standardisation or regulatory approval, or in use in at least one country, having progressed through key milestones)
Societal impacts (incl. environmental / sustainability impact)	**Supporting human capital in R&I through training and mobility schemes** (# of calls launched, # of projects supported by gender) **Supporting enabling environment for conducting clinical studies in sub-Saharan countries, compliance with fundamental ethical principles and relevant national, EU and international legislation** (# of projects funded)	**Addressing through research specific needs of more vulnerable groups** (# of clinical studies targeting vulnerable populations: women, children, adolescents, etc.) **Building and sustaining engagement and co-ownership of EDCTP3/EU-Africa Global Health Partnership** (# of sub-Saharan Africa and European institutions and countries participating in partnership projects, # of sub-Saharan African and European countries participating in EDCTP both through ongoing activities, and contributing financially to the programme (cash and in-kind). **Encouraging uptake of new or improved health technologies** (# of calls and projects addressing uptake of research results into policy and practice)	**Pursing effective and sustainable investments into human capital in R&I** (# of trainees retained, disaggregated by gender, career advancement and professional recognition of researchers following funding) **Training and Mobility Actions and Coordination and Support Actions** (# of projects completed -- categorised by gender, country and regional representation) **Improving policy research uptake** (# of policy changes to which Partnership research contributed; e.g. citations in clinical reviews, clinical guidelines, systematic reviews or other policy documents issued by national, regional or international policy-making bodies)

In the medical sector, the timelines for development are long; it takes up to 12-15 years on average to develop a new drug and approximately 2-8 years to develop a new medical device. Regulatory approval and implementation can add an additional 5 years. Therefore, some of the Partnership's objectives would not be fully achieved until long after projects have finished.

Monitoring would be a continuous process and would support results-based evaluation. Programme monitoring will be compatible with the European Commission's common data model, to enable timely reporting of programme activities.

Evaluation

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Evaluation of the EDCTP3/EU-Africa Global Health Partnership will be done in full accordance with the provisions laid out in Horizon Europe Regulation Article 47 and Annex III, with external interim and ex-post evaluations feeding into overall Horizon Europe evaluations. As set out in the criteria for European Partnerships, evaluations will include an assessment of the most effective policy intervention mode for any future action and the positioning of any possible renewal of the Partnership in the overall European Partnerships landscape and its policy priorities. In the absence of renewal, appropriate measures will be developed to ensure phasing out of Framework Programme funding according to conditions and a timeline agreed beforehand with legally committed partners.

Risk management

The EDCTP3/EU-Africa Global Health Partnership will include a strategy for risk management and mitigation. Risk is considered to be any threat that might prevent the programme from achieving its objectives. While risk cannot be eliminated entirely, it can be anticipated, and mechanisms put in place to reduce risk exposures and to manage risk effectively. Risk management is already integral to EDCTP programme management. EDCTP has an overarching responsibility to promote a culture of risk management within the organisation. Implementation of the corporate risk management strategy is the responsibility of the Risk Management Committee. The Committee maintains a risk register that identifies the key risks facing EDCTP, their likelihood and potential impact, and how they are to be managed (including individual responsibility for each risk). Risks are categorised as either financial, strategic, operational or reputational. This model would form the basis of the EDCTP3/EU-Africa Global Health Partnership's risk management strategy.

The Partnership would also adopt the procedures established by EDCTP to ensure grant-holder compliance with guidelines on financial management and other key aspects of project management (such as ethical and regulatory approvals and data protection).

2.2.7 Exit strategy

The monitoring and evaluation system to be implemented will ensure that progress is analysed in the wider context of Horizon Europe objectives and EU priorities. The programme evaluation will be the basis of the exit strategy from Framework Programme funding. This approach is underpinned by the principles of openness, coherence and EU added value.

Infectious diseases present an ongoing challenge to sub-Saharan Africa, requiring a continuing supply of new interventions to support disease control. The timescales of new product development also require a long-term perspective. By building on the already established work on clinical research capacity within sub-Saharan African countries, the EDCTP3/EU-Africa Global Health Partnership will also help to establish a sustainable infrastructure to enable countries to continue planning and running high-quality clinical research studies. By engaging closely with national governments, the Partnership will ensure that capacity is fully embedded within national infrastructure, ensuring country ownership and long-term sustainability.

In practical terms, the Partnership will consist of an implementation phase (2021–27) followed by a phasing out and conclusion of grant management processes (2027–31) (Figure 6). The programme would formally end in 2031. By the time of finalisation of the programme, sub-Saharan countries should have significant trials capacity to ensure a sustainable infrastructure for infectious disease control and clinical research, providing a solid foundation for future studies and further development of capacity.

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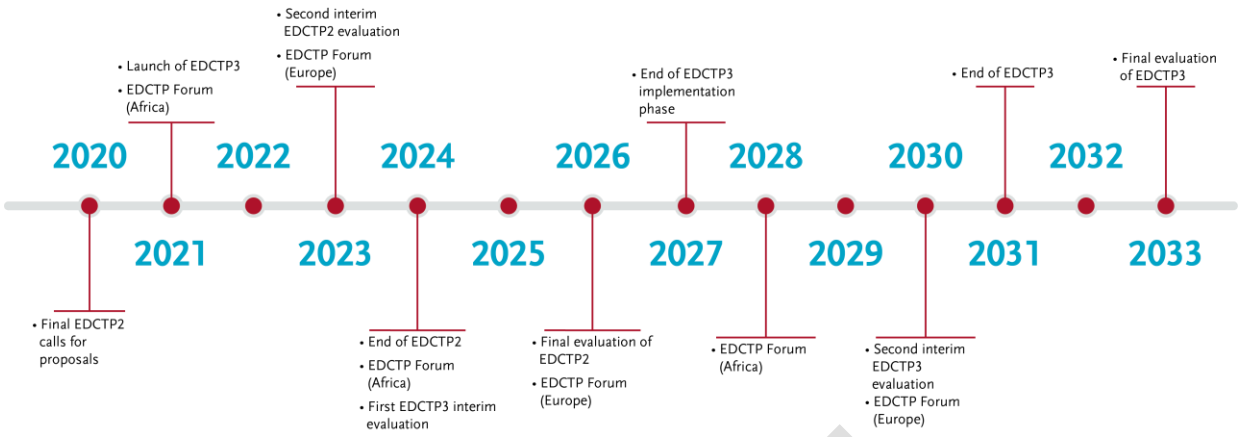

Figure 6: *Proposed EDCTP3 EU–Africa Global Health Partnership timeline and integration with the conclusion of the EDCTP2 programme.*

2.2.8 Strategic Research and Innovation Agenda

To ensure its relevance to stakeholders in both Europe and sub-Saharan Africa, and to inform the development of its Strategic Research and Innovation Agenda (SRIA) and governance model, a potential EDCTP3 programme has been discussed at multiple consultations with stakeholders in Europe and sub-Saharan Africa.

The draft EDCTP3/EU-Africa Global Health Partnership SRIA has been developed by the EDCTP Scientific Advisory Committee, and has included input from the research community and partners represented by European universities and global health institutes, PDPs, WHO, and EDCTP constituencies. It has taken into account the various perspectives stated by EDCTP stakeholders in position papers, voicing broad and strong support for a third EDCTP programme. Consultations have included formal meetings of EDCTP's Scientific Advisory Committee and General Assembly, discussions with representatives of Participating States, and informal contacts with other key stakeholders.

A first consultation process took place during the Ninth EDCTP Forum and was followed by a series of high-level meetings held on 9-10 July 2018 in Ghana, 30 August 2018 in Senegal, and 17 September 2018 in Portugal. Further input was received during 2018—2019 from the EDCTP Scientific Advisory Committee and the EDCTP General Assembly. Additional perspectives were gained from EDCTP member states at high-level dialogue events held in Africa and Europe to gather input from political leaders and the public health, academic, health policy, regulatory, and partner communities.

The SWOT (strengths, weaknesses, opportunities, threats) analysis of the two EDCTP programmes has guided the development of the SRIA (Annex 3). The analysis revealed that EDCTP has established a presence and visibility in sub-Saharan Africa, covering key knowledge gaps by focusing on end-to-end R&D, especially large late-stage clinical trials. The integration of highly collaborative R&D investments with multi-faceted capacity building (individual, institutional, systems, national, and regional) has been an important strength of the programmes, yielding high-impact research results. EDCTP has established a well-defined niche in global health, with a clear focus on later stages of clinical evaluation and adaptation of interventions for underserved groups, including women, children, and those with co-morbidities and co-infections, generating findings that have had a significant impact on national and global policy and practice.

The SWOT analysis suggested that covering a broad range of pathogens resulted in limited funding per disease category, particularly for the neglected infectious diseases. It also revealed that little research had been conducted to date on the impact of the climate crisis and how to mitigate rising levels of antimicrobial resistance. The analysis also identified difficulties in aligning funding strategies of European Participating States, limited progress in advancing women in global health research, and lack of support to enable researchers from some French- and Portuguese-speaking African countries with weaker research systems to

submit high-quality applications. In terms of threats, major disease outbreaks could overwhelm country response capacity and undermine research efforts on priority diseases, while rising antimicrobial resistance is already compromising use of therapeutics. The climate crisis is also likely to significantly increase exposures to pathogens.

The main topics described in the SRIA include:

- The scope of the programme
- Guiding principles
- Criteria for setting priorities
- Infectious diseases covered by the programme (HIV, TB, malaria, neglected infectious diseases, diarrhoeal diseases, lower respiratory tract infections, emerging and re-emerging infectious diseases, climate crisis-related infectious diseases, antimicrobial resistance and non-communicable disease co-morbidities)
- Mechanisms of support
- Expected outcomes and impact.

2.3 Necessity for a European partnership

2.3.1 Strategic importance to the EU

Launched in 2003 and renewed in 2014 with funding through to 2024, EDCTP has been the focal point of EU support for global health research in Africa, and a visible sign of the EU's commitment first to the Millennium Development Goals and then to the SDGs. Through its evolution, EDCTP has been driven by the infectious disease priorities of sub-Saharan Africa and the need to develop African countries' capacity to collectively address these priorities into the future. Driven by the needs of the South, and operating as a genuine 'partnership of equals', EDCTP has been committed to supporting high-quality clinical research that accelerates the development and implementation of novel and improved interventions – making a real difference to the lives of millions of people across sub-Saharan Africa.

EDCTP was the first initiative based on Article 185 of the Treaty on the Functioning of the EU (ex-Art. 169), which allows the EU's participation in research programmes undertaken by EU and Associated Member States.

The EU is a major contributor to international health development assistance and to research. In 2010, the European Commission Communication and Council Conclusions on the role of Europe in global health established a conceptual framework, with emphasis on strengthening national health systems, maternal and child health, and the fight against HIV, TB, and malaria. Further, at their Berlin meeting in 2015, G7 Ministers of Science expressed their resolve to support the fight against "poverty-related infectious diseases and neglected tropical diseases", with EDCTP recognised as one of the mechanisms to be built upon.

The 2007 EU Programme for Action and its 2009 Progress Report highlighted the key role of EDCTP in its own right and as a model for other programmes aiming at coordinated international collaboration. This aspect of EDCTP has also been emphasised in multiple policy declarations, programmes and reports. The Africa–EU Strategic Partnership, emanating from the 2007 Lisbon Declaration and re-emphasised in the Europe 2020 Strategy, identifies EDCTP as an important body in its first Action Plan for implementation of this Strategic Partnership.

The EDCTP programme contributes to the European Commission flagship 'Innovation Union' initiative and to the vision of a European Research Area. EDCTP2 was the key mechanism for EU support for global health research under the Horizon 2020 umbrella. The EDCTP3/EU-Africa Global Health Partnership would be similarly pivotal to the Horizon Europe Programme.

EDCTP is contributing to the EU commitment to the United Nations 2030 Agenda for Sustainable Development and its associated SDGs, most directly to SDG3 ('Ensure healthy lives and promote well-being for all at all ages') but also indirectly to others, including SDG1 ('End poverty in all its forms everywhere'). The Commission

reflection paper 'Towards a Sustainable Europe by 2030', adopted in January 2019, emphasises the continuous need to face persisting or novel challenges in science, society and policy for achieving a sustainable Europe by 2030. In this context, health research and related innovation actions play a significant role in improving productivity, health care systems and the functioning of its industries[89].

The proposed initiative is also fully in line with the 'EU-Africa Alliance for Sustainable Investments and Jobs'[90] of September 2018, through which the EU is committed to increase access to quality education, skills, research, innovation, health and social rights, and to reinforce Africa as a partner in trade, in foreign investment and in development, and to tackle together the green and digital transformations, as well as promoting sustainable investments and jobs.

Moreover, the EDCTP3/EU-Africa Global Health Partnership will also contribute to the Commission's 'Towards a comprehensive Strategy with Africa'[91], adopted in March 2020, and to the recent Communication on the 'Global EU response to COVID-19'[92], which calls for 'Stepping up the preparation with EU Member States and third countries of the Global Health Partnership'.

The Partnership will make a major contribution to the fifth EU policy priority identified by the President, 'A stronger Europe in the world'[93]. This priority emphasises the need for international partnerships and multilateral initiatives to tackle global challenges, including threats to global health. It envisages strengthened scientific and technological links with key partners, as well as multilateral alliances to tackle issues such as antimicrobial resistance, emerging and re-emerging infectious diseases, and epidemic outbreaks. It also acknowledges the importance of ensuring common high standards in areas such as research ethics. All these ideas are core to the objectives of the EDCTP3/EU-Africa Global Health Partnership.

Through its emphasis on global health security, the Partnership will also contribute to priority 4, 'Protecting our European way of life'. In addition, the emphasis on new product development and use will contribute to priority 2, 'An economy that works for people'.

2.3.2 Benefits to Europe

The ultimate beneficiaries of the EDCTP3/EU-Africa Global Health Partnership will be people in sub-Saharan Africa who gain access to potentially life-saving interventions. However, the Partnership will also directly and indirectly deliver benefits to the EU in multiple ways:

Global leadership: The Partnership will be a demonstration of the EU's commitment to the health and well-being of disadvantaged populations in sub-Saharan Africa, and its pursuit of the SDGs. The Global Action Plan for Healthy Lives and Well-being for All[94], launched at the UN General Assembly in September 2019, noted that extra efforts would be required if health-related SDGs were to be met by 2030. It identified R&D as a key accelerator of progress and emphasised the importance of global collaboration and alignment.

Health security: By addressing key global threats to health such as antimicrobial resistance and emerging and re-emerging infections, the Partnership will help to ensure the health security of the EU as well as in sub-Saharan Africa. In the modern world, infectious diseases can rapidly spread between countries and regions, driven by multiple factors[95]. Better control of infectious diseases and antimicrobial resistance in sub-Saharan Africa will reduce the risk of their spread to the EU and protect EU citizens travelling to the region.

Global influence: The Partnership will enable the EU to undertake activities beyond the capacity of individual countries. It will provide a powerful voice for Europe in global health research, as well as an important mechanism to promote European objectives and values, including open access to research findings.

Industrial competitiveness: The EU has long been a supporter of global health research and has a strong life sciences sector. By sharing the risks of new product development with companies and PDPs, it is helping to create sustainable markets for products and safeguarding a strategically important industrial sector in the EU.

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Scientific competitiveness: International networking will benefit researchers in Europe. Networking will provide additional opportunities for collaboration, exchange of knowledge and development of new skills. Early-career researchers in particular will have greater potential to develop their skills and knowledge of infectious diseases in their natural settings. By strengthening ties with sub-Sahara Africa, networks will also enable European researchers to focus their research on priority questions and achieve greater impact.

Innovation from Sub-Saharan Africa: The Partnership will explore innovative uses of technology to expand access to interventions and improve the quality of integrated and people-centred health care services in sub-Sahara Africa. These innovations may also be applicable to the health systems of high-income countries, improving the quality and cost-effectiveness of services in the EU.

2.4 Partner composition and target group

Given the lack of market incentives for new product development for poverty-related infectious diseases, traditional models of product development do not apply. Instead, there is a strong emphasis on collaboration between partners in different sectors to advance a limited number of products meeting clearly defined unmet medical needs. The EDCTP3/EU-Africa Global Health Partnership will be an active participant in this collaborative ecosystem, working with product developers in the public and private sector, other funding agencies (including global foundations), and other important stakeholders (including countries and WHO) to advance the clinical development of products addressing unmet needs. This will extend to the clinicians and policymakers with responsibility for introducing innovations into routine practice.

2.4.1 Partners

The EDCTP3/EU-Africa Global Health Partnership will build on the EDCTP's existing partnerships between 14 European and 16 African countries (Figure 7). As a sign of their commitment, up to 2019, EDCTP2 Partner States have committed €1.04bn to the EDCTP2 programme (and third-party contributions have amounted to €185.57m). Active efforts will be undertaken to increase the numbers of Participating States from the EU and sub-Saharan Africa, particularly Eastern European EU states. It will seek to minimise the barriers that might deter countries from joining the Partnership. Unlike EDCTP2, where only EU Member States and Associated States were partners, the new structure based on Article 187 will broaden potential participation to third countries, foundations and industry.

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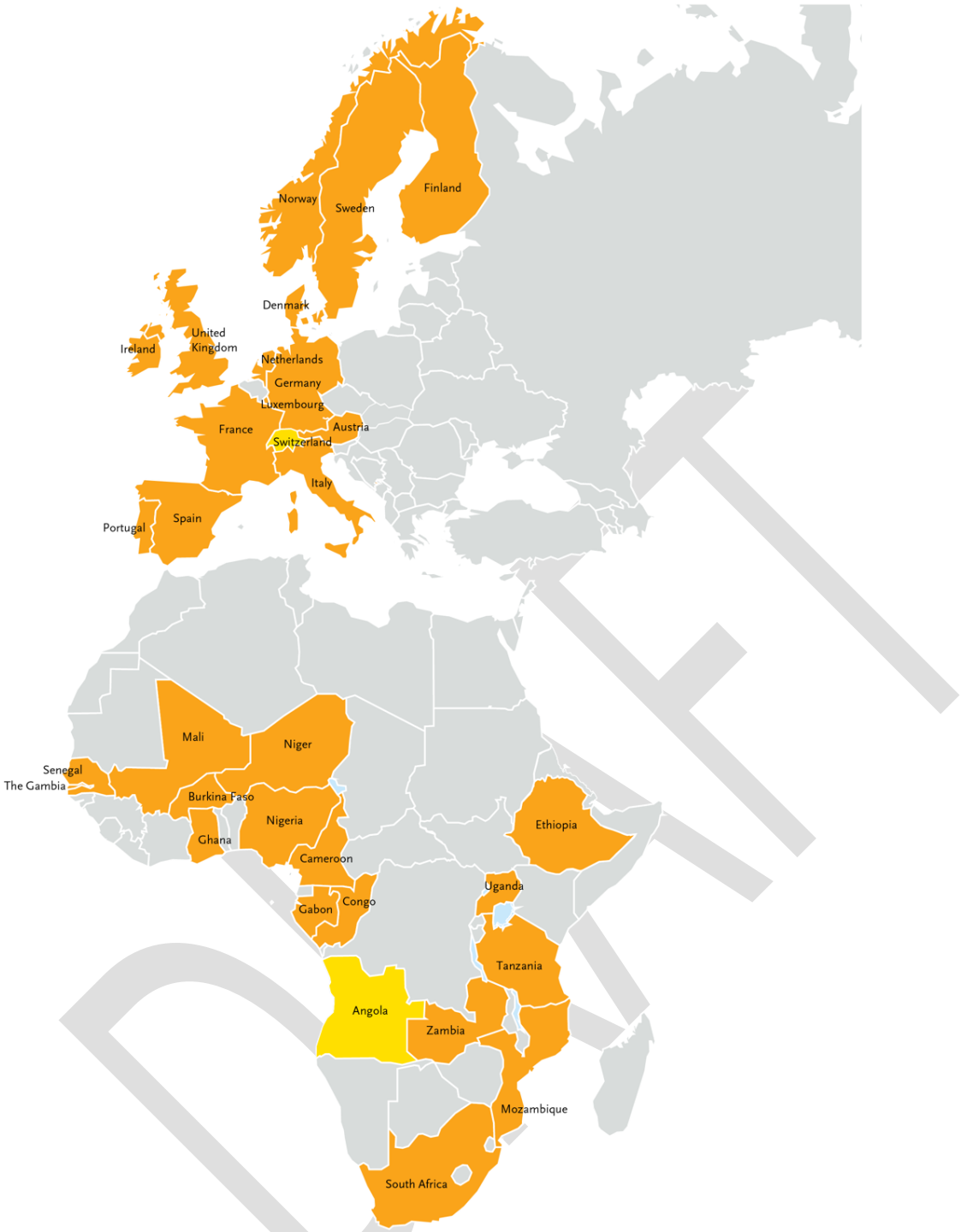

Figure 7: *Current EDCTP2 Participating States.*

As well as activities centrally managed by EDCTP, the Partnership's annual work programmes will also include Participating States activities. However, as in EDCTP2, these must be aligned with activities of other Participating States, to promote coordination and, where appropriate, integration of national programmes and activities. New approaches will be developed to enhance alignment of Participating States managed activities.

The Partnership will harness the investments of the EU, EU Member States and Associated States to the Framework Programme and sub-Saharan Africa States. In addition, for specific trials or diseases, other third countries, philanthropies and industry can join and contribute to the Partnership.

The EDCTP3 will establish meaningful collaborations between partners (the EU represented by the Commission and Participating States represented by the EDCTP Association) in the Governing Board deciding on the

programme implementation, but also with the research community through advisory bodies such as the Scientific Advisory Committee and Stakeholders Group.

The motivation for EU, European and African countries to join the Partnership comes mainly from the successes of the EDCTP and EDCTP2 partnerships. These partnerships have shown that European and African governments can join forces with the EU around common objectives, creating an environment within which results were achieved that individual countries or the EU research framework programme alone would not have been able to obtain. The governance of EDCTP2 is based on an EDCTP Association, which provides meaningful participation and involvement of sub-Saharan African countries in decision making, essential for tackling the burden of diseases in sub-Saharan African countries.

In addition, to further leverage larger and sustained funding and to play a stronger global health leadership role than the current EDCTP2, the EDCTP3/EU-Africa Global Health Partnership will address emerging infectious diseases threats, exemplified by the COVID-19 pandemic, and the ever-increasing problem of antimicrobial resistance and non-communicable disease co-morbidities. This will require coordination with other funders and acceleration of research by harnessing different investments. Therefore, the Partnership will engage with other international research funders, such as philanthropies and industry, which will be able to contribute to the Partnership on an ad hoc basis.

Philanthropies, such as the Bill and Melinda Gates Foundation or Wellcome Trust, are looking for opportunities to share the costs of late-stage clinical trials for the development of medicines or vaccines for poverty-related diseases. They are therefore seeking partners to join forces with. These philanthropies are flexible in their investments and can act speedily, when new developments emerge or in the case of a public health emergency.

The Ebola epidemics in West Africa and the Democratic Republic of Congo have encouraged the **pharmaceutical industry** and **vaccine manufacturers** to invest in infectious diseases threats affecting Africa. Also, some companies see investment in research relevant to Africa as part of their corporate social responsibility (such as Johnson & Johnson, GSK and Novartis). Industry partners bring important expertise in clinical trial management, product registration, manufacturing and distribution. Industry is increasingly open to partnering to advance development of products even in the absence of strong commercial drivers.

While industry has participated in some EDCTP2 projects, this has generally been on an ad hoc basis, with no overarching strategy to advance products through clinical evaluation stages, regulatory pathways and to ensure access. The Partnership will continue the approach developed in EDCTP2 to coordinate activities across partners to map out pathways through to implementation in settings of unmet medical need.

Potential industry partners are those that have a research agenda relevant to infectious diseases in low- and middle-income countries.

The COVID-19 pandemic and the EU-led Coronavirus Global Response pledge illustrate the need for the public sector, philanthropies and industry to join forces to combat infectious threats. All these organisations are aligned around the same strategic research agenda and are seeking partners for cooperation so that they jointly can support larger clinical trials and fund research capacity building more efficiently, therefore achieving greater impact.

Through the Article 187 structure, institutions mandated by Participating States' governments can contribute to the Partnership's governance mechanisms (see below). It is anticipated that other partners, such as global health foundations and other funders, third countries and pharmaceutical companies, which are also involved in the development of new interventions for poverty-related infectious diseases, would bring to the Partnership their special expertise and skills.

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2.4.2 Additional stakeholders

The EDCTP3/EU-Africa Global Health Partnership will engage with other organisations with shared interests in control of poverty-related infectious disease and health research system strengthening in the region. The aim will be to develop strategic alliances and explore opportunities for synergy and complementarity to maximise impact.

The Partnership will develop strong links with a range of stakeholder organisations and communities, again building on the relationships established by the first two EDCTP programmes. These include researchers, scientific leaders and clinical product development experts, and product development partnerships that have often been crucial for ensuring the final development of products and their delivery to the market.

The programme will also liaise with national and international institutions focused on infectious disease research, such as the WHO Regional Office for Africa, which could be involved in joint projects, consultation workshops and/or in assessments of national health research capacities across the region.

The programme will also retain its strong links to the regulatory community, particularly the European Medicines Agency (EMA) in Europe and national regulatory authorities and the bodies that represent them in the African region, including the African Vaccine Regulatory Forum (AVAREF), the African Medicines Regulatory Harmonization Initiative, and the African Medicines Agency. Through these and other routes, the EDCTP3 programme will work closely with the African Union's Regional Economic Communities, such as the East African Community (EAC), the Southern Africa Development Community (SADC) and the Economic Community of West African States (ECOWAS), as well as the African Union Development Agency (AUDA, formally NEPAD).

The programme will also maintain strong ties with regional scientific and public health bodies, in particular the African Academy of Sciences, which has a shared interest in research capacity building, and the Africa Centres for Disease Control and Prevention.

Regional and national health policymakers in sub-Saharan Africa will be a key audience, to promote political commitment to the Partnership and to health research more generally, and to ensure that research address questions of regional and national importance. These links will be strengthened through the appointment of a High Representative for Africa, based in sub-Saharan Africa. A High Representative for Europe, based in Europe, will play a similar role in raising awareness of the Partnership across EU states and encouraging additional commitment to the Partnership.

The Partnership will have a particular aim to extend the geographical range of contributors and partners. It will seek to develop new relationships with organisations from North America, Japan and elsewhere working in global health research to bring in additional expertise and resources, and to secure closer global alignment of activities across a wider range of partners.

2.4.3 Priority populations

The vision of the EDCTP3/EU-Africa Global Health Partnership is to reduce the individual, social, and economic burden of poverty-related infectious diseases in sub-Saharan Africa. The Partnership will therefore have a particular focus on the development and uptake of new or improved health technologies to benefit vulnerable populations in sub-Saharan Africa. It will have a stronger focus on accelerating access to new health technologies by people in need, and on strengthening project engagement with beneficiaries and communities.

The Partnership will have a particular focus on disadvantaged groups that are often excluded from pivotal clinical trials and may therefore be slow to be given access to and benefit from newly developed or improved health technologies. These include infants, young children, pregnant women, and people with co-infections or other co-morbid health conditions.

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Furthermore, the efficacy and safety of new health technologies are increasingly recognised to be highly dependent on local contexts, because of genetic factors, local environmental exposures, nutritional status, and other factors. This will call for increasingly fine-grained evaluation of interventions in different settings.

This strong focus on individual benefits calls for an enhanced emphasis on community engagement, social science involvement, and good participatory practice. Beyond helping to create public support for clinical research, this provides opportunities for communities to inform research study design, trial conduct, and interpretation of findings. The Partnership will follow the principles for good participatory practice developed by WHO for use in emergency outbreak settings[96] [97] and specifically for COVID-19-related clinical studies[98].

3 Planned implementation

3.1 Activities

A set of six operational objectives have been developed to guide implementation of the EDCTP3/EU-Africa Global Health Partnership:

1. To support clinical trials on new or improved health technologies for infectious diseases affecting sub-Saharan Africa, generating relevant and high-quality research evidence, and to promote dissemination of research results
2. To support research on the uptake and effective use of new or improved health technologies
3. To identify and support opportunities for increased coordination of research and innovation efforts, promote synergies and joint strategic programming, and the dissemination of research results
4. To strengthen the capacity of institutions in sub-Saharan Africa to design, conduct and manage clinical trials in infectious diseases
5. To strengthen an enabling environment for infectious disease research in sub-Saharan Africa
6. To strengthen networks and institutions involved in infectious disease detection and control in sub-Saharan Africa.

Figure 8 shows the links between actions, operational objectives, and the specific and general objectives of the Partnership.

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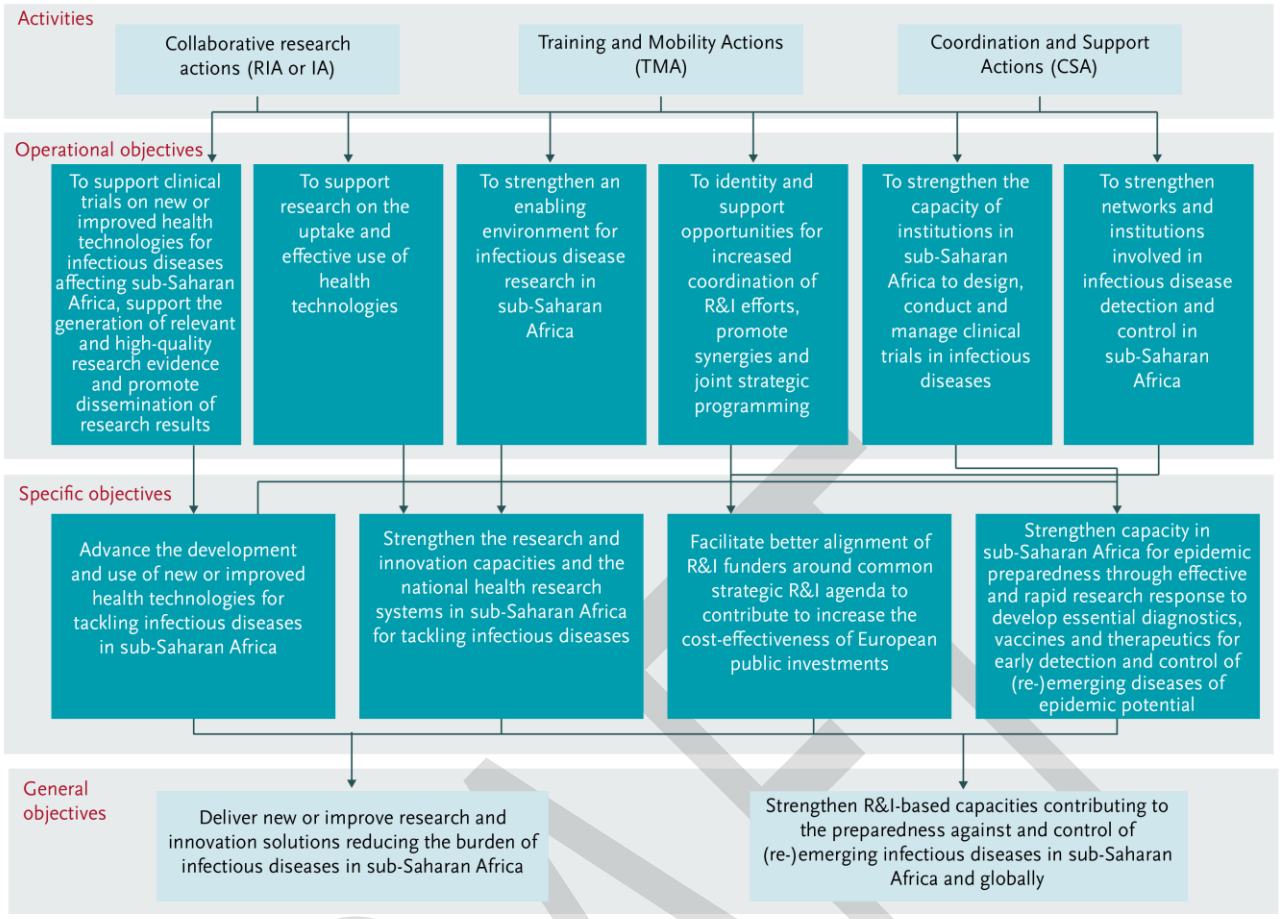

Figure 8: *Operational objectives of the Partnership in relation to the specific and general objectives*

This list of actions and activities to be carried out reflects the definition of European Partnerships in the Horizon Europe regulation as initiatives where the EU and its partners "commit to jointly support the development and implementation of a programme of research and innovation activities, including those related to market, regulatory or policy uptake".

3.1.1 Portfolio of activities

The mechanisms of funding will reflect the nature of the Partnership's objectives. The bulk of its funding will be devoted to support for **multicentre clinical trials** in sub-Saharan Africa carried out by international partnerships. Other research studies may be embedded within a trial. Project funding will also include integrated support for capacity development of researchers, institutions and sites in sub-Saharan Africa as well as for networking activities.

Specific funding schemes will be set up to **build the capacity** of institutions and countries to conduct high-quality clinical research. These schemes will aim to (1) strengthen clinical research capacities in sub-Saharan Africa, (2) promote networking and collaboration both between European and African researchers and among African researchers, institutions and sites, and (3) foster collaboration with public and private funders. In particular, these funding schemes will enable sub-Saharan African countries to develop robust ethical and regulatory frameworks for conducting clinical trials.

The Partnership will also organise **personal support schemes** to build individual research capacity. These schemes will promote the career development of junior and senior researchers from sub-Saharan Africa, training and mentorship, and the mobility of individual researchers and research staff. The availability of personal support will also help to retain proven scientific leaders in the region, around whom centres of research excellence can be developed and nurtured, helping to further embed research capacity in institutions.

The Partnership will maintain flexibility in its approach to funding. This will enable it to work more closely with a wider range of funding partners and organise more joint funding initiatives.

Calls for proposals in priority areas will be made each year according to an annual work programme developed by a Scientific Committee (see the SRIA for further details, Annex 3).

Participating States activities represent national efforts towards the Partnership's objectives and are an essential component of the EDCTP portfolio. They are activities that fall within the scope of the Partnership, while being funded and implemented by one or more Participating States. They can also cover clinical studies, capacity building and training programmes in sub-Saharan Africa in the areas within the scope of the Partnership. As such, they will be included in the annual work programmes. Before these activities are included in annual work programme, a discussion between two or more Participating States should have taken place to look for potential synergies to ensure alignment of national activities and to avoid duplication of efforts.

Other third countries, such as Switzerland and the UK, with long global health traditions, have expressed interest in contributing to a common strategic agenda. They can ask the Joint Undertaking to join on an ad hoc basis once their association agreement to Horizon Europe has been signed.

3.1.2 Complementarity of activities

The EDCTP3/EU-Africa Global Health Partnership will proactively monitor Horizon Europe funding decisions to identify potential opportunities for collaboration or coordination of activities. As detailed in section 2.2.3 above, it will also explore potential synergies and opportunities for alignment with other European initiatives in health, education and international development. This will include promotion of international coherence through the inclusion of Participating States activities in the annual work programmes. Further efforts will be made to enhance alignment of centrally managed and Participating States activities to achieve additional synergies and greater impact.

3.2 Resources

3.2.1 Joint financing as a prerequisite for a joint programme

To be able to set up the partnership and reach the expected impact, it is desired to reach a level of financing at least similar to the one under the current EDCTP2.

In principle, the maximum budget depends on the contributions (cash or in-kind) from Participating States, third countries, foundations and industry, which the EU will be matching at a mandatory 50/50 ratio.

Through the commitment to pool resources from all partners, the partnership will ensure the necessary leverage to be able to successfully tackle its objectives and deliver on its impacts.

The Partnership's proposed additional focus on emerging and re-emerging infectious diseases is extremely relevant given the COVID-19 pandemic and the inevitability of further epidemics. Given the economic impact of the COVID-19 pandemic, there is some uncertainty surrounding the capacity of Member States and African countries, philanthropies, and industry to commit sizeable amounts. Should fewer resources be available, strategic prioritisation would be necessary. This would happen at the level of the Strategic Research and Innovation Agenda to be co-developed with stakeholders.

3.2.2 Types of Participating States contributions

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Only new research and capacity development activities[2] can be included in annual work programmes. Due to the fact that on-going activities may continue beyond the end of the EDCTP2 programme, a procedure to avoid double counting will be put in place to screen and consider new activities that are submitted to new annual work programmes under the EDCTP3/EU-Africa Global Health Partnership.

The Partnership will continue the co-labelling requirement used in EDCTP2 for eligibility of in-kind contributions. If an activity is included in the annual work programme, it is considered part of the Partnership, and it should be co-labelled accordingly. All Participating States in-kind activities should have similar reporting requirements so that the various contributions can be easily tracked and matched by the EU contribution.

The following types of **Participating States contributions** can be matched by the EU:

1. **Scheme 1:** Financial contributions to projects resulting from centralised calls[3] for proposals managed by the Joint Undertaking, with compulsory additional funding from EDCTP3 Participating States. Other funders, such as foundations, industry and other third countries, can also contribute to these calls. All financial contributions must be transferred to the Joint Undertaking for central management, without exception. The involvement of Participating States, in terms of number of countries and proportion of the budget, may vary on a call-by-call basis. This includes central evaluation of proposals and **centralised project management, according to Horizon Europe funding rules**. Selected projects will be funded from the common pot, according to the rules of participation of the JU based on Horizon Europe,

2. **Scheme 2:** Contributions in the form of funding provided to projects resulting from aligned and coordinated calls[4] for proposals organised by Participating States at trans-national or national level and that fit within the Partnership's strategic research and innovation agenda, but which are independently managed (**de-centralised project management)**. This type of funding can be open to legal entities in all EU Member States, Associated States and sub-Saharan States, or restricted to certain legal entities in organising countries and in sub-Saharan African countries, depending on the applicable national funding rules. Other funders, such as foundations, industry and other third countries, can also contribute to these aligned calls.

   These in-kind contributions must fall within the scope of the Partnership's Scientific Research and Innovation Agenda (SRIA) and it must be made clear that the Partnership is needed to implement them. When activities are planned, the organisers must seek to identify synergies with the activities of other partners before they are submitted for inclusion in the Partnership's annual work programmes and the synergies identified should be included in the descriptions of activities. Common evaluation activities are desirable, such as shared expert evaluators. While all activities of the Partnership must be planned and approved in advance by the Joint Undertaking, part of them may be organised and run by Participating States. They will have to be foreseen in the approved annual work programme and their costs will have to be auditable.

   This type of call can be launched separately by two or more Participating States. Calls can also take the form of joint calls, like what is the established standard in current Horizon 2020 ERA-NET actions[5]. Each Participating State will independently manage the selected projects or national part of the transnational project, according to national funding rules. The costs related to the aligned calls will be considered as in-kind contributions to additional activities.

[2] Discussions on how best to include high-budget, portfolio-based, and long-term activities (e.g. PDPs, contribution to multilateral organisations) are ongoing.

[3] Centralised calls: call that are co-developed by the members of the EDCTP Association and the EU (represented by the European Commission) and that are managed by the Joint Undertaking

[4] Aligned and coordinated calls: Calls that are aligned to the SRIA and coordinated between concerned Participating States but that are not managed by the Joint Undertaking

[5] ERA-NET Cofund under Horizon 2020 is a type of programme co-fund action designed to support public-public partnerships (P2Ps). https://ec.europa.eu/programmes/horizon2020/en/h2020-section/era-net

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3. **Scheme 3:** Contributions in the form of activities implemented by sub-Saharan Africa governmental research organisations and aligned with the EU-Africa Global Health Partnership Strategic Research and Innovation Agenda. The governmental funding towards these activities will be considered as in-kind contributions.

Financial contributions to the administrative costs of the Joint Undertaking are mandatory and must cover 50% of the Joint Undertaking's administrative costs. The contributions from the Participating States to the Joint Undertaking should be one single contribution from the EDCTP Association.

In addition, and independent of the contributions to the Joint Undertaking, the Participating States should also provide the contributions **to maintain the EDCTP Association** and its activities through financial and/or in-kind contributions (e.g. staff secondment). These contributions to the Association cannot be matched by the EU.

3.2.3
The EDCTP Association

The management of the EDCTP Association is **not part** of the Joint Undertaking governance. The EDCTP Association tasks are distinct from those of the Joint Undertaking. The EDCTP Association tasks, carried out in the European Office and the African Office, are as follows:

- Coordinating the participation of the members of the EDCTP Association, including their contributions to the Partnership and shaping their common position in the Joint Undertaking
- Conducting advocacy and networking activities
- Managing the legacy of the EDCTP2 programme.

As the statutes of the EDCTP Association related to the EDCTP3 programme will need to be drawn up by its members, the minimum criteria for participation will be open to discussion. Meetings of the Association and the administration of the Association's affairs would require secretariat support. This could be, a stand-alone administrative office. The costs of this administrative support would have to be shared between the members of the Association and would not be covered by the European Commission. However, the basis for sharing costs is something that would have to be agreed by members.

The minimum contribution to the EDCTP Association by the Participating States is to be assessed at the collective level by the Association partners. The way it will be provided by individual partners within the EDCTP Association is generally the decision of Participating States.

3.3 Governance and management structures

Under Article 187, the EDCTP3/EU-Africa Global Health Partnership Joint Undertaking is a partnership between two entities – the **European Commission, representing** the European Union, and the European and Developing Countries Clinical Trials Association (**EDCTP Association**), representing the governments of European and sub-Saharan African countries participating in the partnership (Participating States).

The coordination tasks necessary to establish a collective position of Participating States is the EDCTP Association's responsibility and it is the Participating States that need to cover the costs of the functioning of the Association. It will also be up to the EDCTP Association to decide the representation and voting rights of the Participating States internally within the EDCTP Association.

The Joint Undertaking **governance structure** (Figure 9) includes the following:

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- The **Governing Board** will have overall responsibility for the strategic orientation and the operations of the Joint Undertaking and supervise the implementation of its activities. It is composed of representatives from the two founding members – the European Commission and the EDCTP Association. The Executive Director of the initiative will attend and participate in the meetings but will not be permitted to formally vote on matters submitted for a vote. The Governing Board members may invite observers to its meetings, such as e.g. representatives of organisations participating to the initiative's activities as Associated Partners or representatives of other relevant European Partnerships, on an ad hoc basis and dependent on the scope of discussions taking place. The Governing Board will focus on strategic matters and take decisions regarding the most important issues pertaining to the JU, such as Annual Work Plans, funding decisions, membership and appointment of the Executive Director.

  On the Governing Board, the European Commission has a vote equalling 50% and the Participating States the other 50%.

- The **Executive Director** will be in charge of the daily operations of the EDCTP3 Office. Based on provisions of the regulation or by delegation of the Governing Board, s/he will be empowered to take decisions such as appointment of staff, sign the grant agreements or represent the initiative, etc. The Executive Director will be supported by Joint Undertaking staff, who will act as a secretariat to the Joint Undertaking and to the EDCTP Association.

The EDCTP Association would elect from among its members a Chair, two Vice-Chairs and two to five additional members. These persons would form an Executive Committee (the size of the Executive Committee would need to be agreed by members when drawing up the Articles of Association and with the European Commission). The Executive Committee would be mandated to represent the Association at meetings with the European Commission on the Governing Board of the Joint Undertaking. Meetings of members of the EDCTP Association (the General Assembly) would be informed by reports from minutes of meetings of the Joint Undertaking and other consultations. The General Assembly would agree the position that the Executive Committee would adopt in negotiating annual work programmes and calls, and other relevant matters with the European Commission. The Executive Committee would not be able to agree to proposals at the board that had not been approved by the General Assembly.

The Joint Undertaking can have **advisory bodies**:

- The **Scientific Committee** is made up of scientific experts from diverse fields and continents and provides high-level recommendations on priorities and strategic needs regarding clinical research. It advises the Joint Undertaking on the content, scope and dimension of the draft annual work programme and reviews the scientific and technical aspects of implementing the programme. The annual work programmes must be approved by the Governing Board prior to implementation.

- The **Stakeholders Group** consists of representatives of groups such as philanthropies, industry, product development partnerships, international organisations such as WHO, Africa CDC, research organisations, researchers, regulators and policymakers, who represent the global health community in theme-linked meetings and consultations. It provides opinions on scientific, administrative and financial matters.

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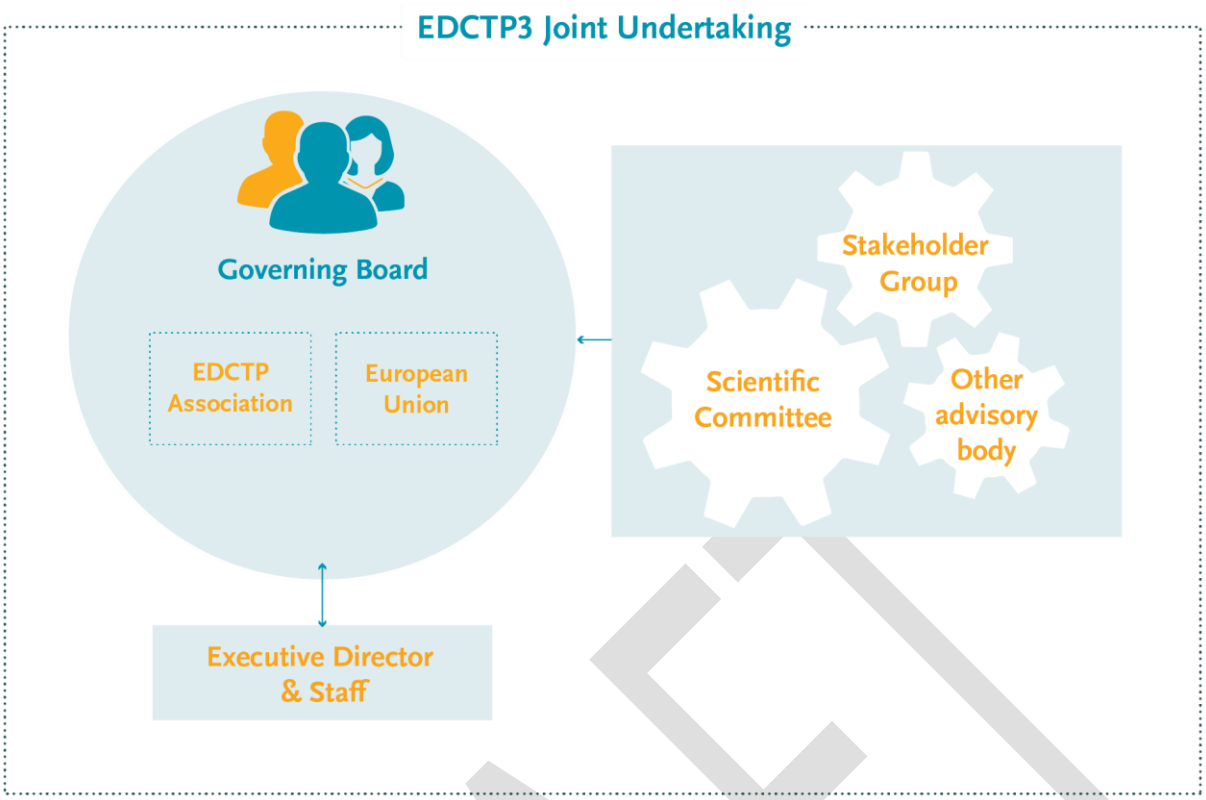

Figure 9: *Joint Undertaking governance structure.*

The Joint Undertaking can also have **Associated Partners** not involved in Joint Undertaking governance:

- **Associated Partners** are global health players committed to public health, such as philanthropic organisations, pharmaceutical industries and other third countries running their own health research programmes related to global health, clinical research studies and uptake of health technologies in sub-Saharan Africa. Such bodies could apply to become Associated Partners of the Joint Undertaking on an *ad hoc* basis. Associated Partners financially contribute to a call for proposal and participate in the development of the call topic (Figure 10).

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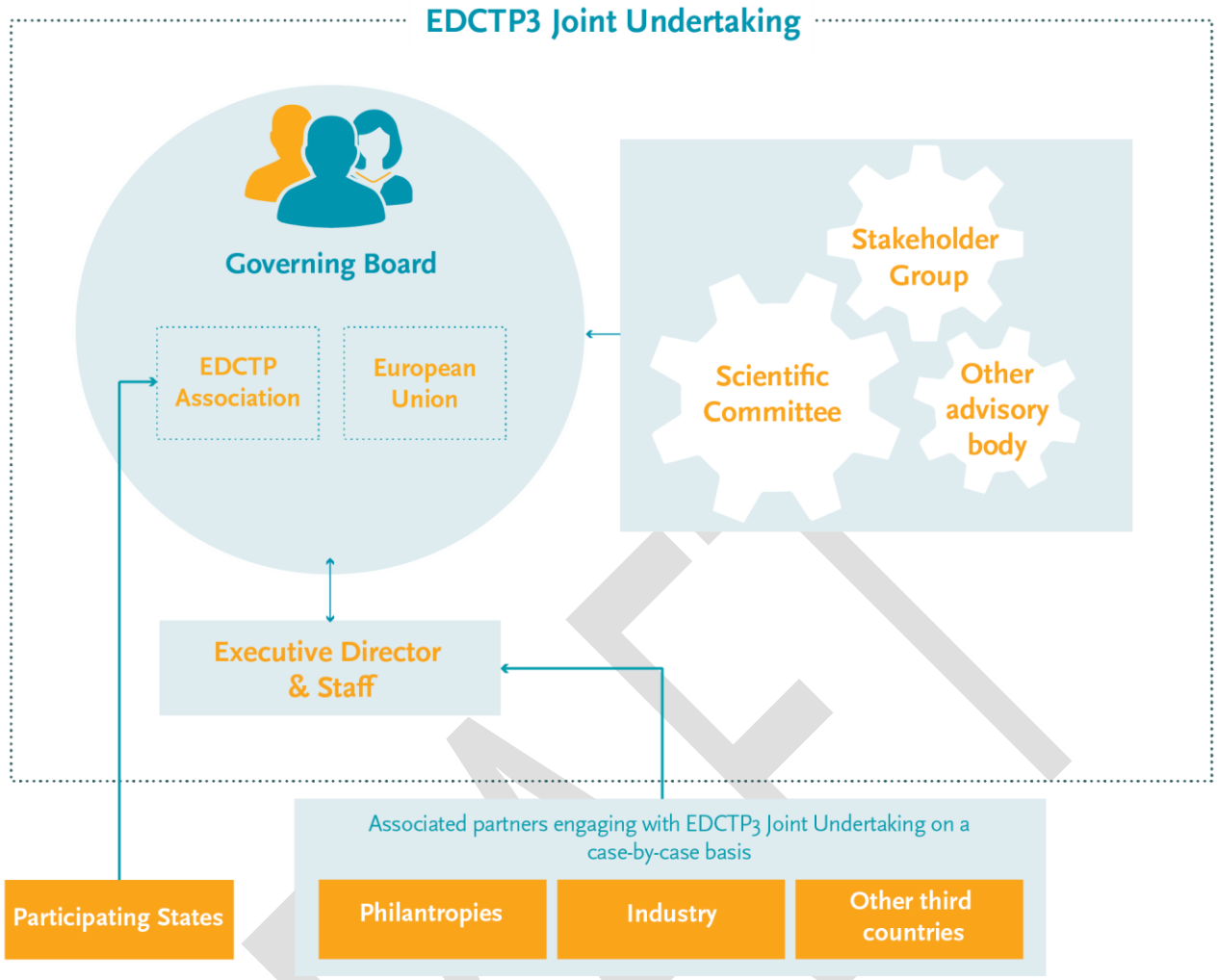

Figure 10: *How to generate priority thematic topics to addressed by the Partnership*

The Commission will be fully involved in the preparation of the EDCTP3/EU-Africa Global Health Partnership together with the EDCTP Association and in the submission of the Partnership's proposal to the Council and European Parliament.

3.4 Openness and transparency

3.4.1 Participation

High-level consultative meetings have been organised to capture input from a range of stakeholders on a future EDCTP programme. Meetings were held in July 2018 in Ghana and at the WHO African Regional Committee meeting in Dakar, Senegal, in August 2018, which brought together political leaders, regional bodies, policymakers and strategic partners to discuss international cooperation to achieve strengthening of national health research systems. The Dakar meeting emphasised the need for African countries to make the necessary political and financial commitments to grow their clinical research and regulatory capacities, and to create environments that promote use of research evidence to shape health policy and enhance access to effective interventions. Development of research capacity was seen as critical, including maximising the contribution of female health researchers, as was the need for highly policy-relevant research studies (such as effectiveness and implementation studies) to provide 'actionable evidence' for national policymakers.

A further high-level meeting was held in Lisbon, Portugal, in September 2018, providing opportunities for political leaders, policymakers, academics and other stakeholders from both Europe and Africa, as well as representatives from other stakeholder organisations, to discuss the achievements of the EDCTP2 programme

and possible revisions for a successor programme. The core features of the EDCTP approach were widely endorsed. Implementation plus scaling up of interventions was again identified as a major challenge, and the potential role of social science in implementation and uptake studies was highlighted. Building on EDCTP2's successes, it was suggested that new models of engagement could be explored with a wider range of potential partners.

In addition, Working Groups have consulted on four specific areas: African involvement, Participating States' contributions, Governance and Science. The African involvement Working Group has identified the needs of sub-Saharan African countries. The Participating States' contributions Working Group has suggested ways to improve the current EDCTP2 Participating States' contributions. The Governance Working Group has identified a model based on Article 187 of the Treaty on the Functioning of the EU as the most appropriate for a successor programme and has developed a suggested governance model. The Science Working Group has taken the lead in developing the Partnership's SRIA.

Participation in the governance of the EDCTP3 programme is open to any country in the EU and sub-Saharan Africa, and to countries outside these groupings (third countries). Active efforts will be made to extend the membership of the EDCTP3 Association beyond the 14 European and 16 African countries that are currently members of the EDCTP Association. Particular efforts will be made to engage with newly joined members of the EU, especially those in Eastern Europe, and French- and Portuguese-speaking countries in sub-Saharan Africa. The activities of High Representatives for Europe and Africa will include efforts to encourage additional participation of countries in the programme and fundraising.

3.4.2 Access to information

The EDCTP3/EU-Africa Global Health Partnership will maintain EDCTP's commitment to openness and transparency. It will make available information on successful grant applications in a timely fashion and maintain a website and undertake other communications activities to keep stakeholder communities aware of its activities. It will continue the online EDCTP Alumni Network platform[69], which provides details of EDCTP-funded fellows and their work, promoting networking across the continent.

The Partnership will require clinical trials to be registered, for example in the Pan-African Clinical Trials Registry[99], a free open access platform established with EDCTP funding. Clinical trial results will be published in line with the guidelines of the International Committee of Medical Journal Editors[100]. Projects will be required to publish results in open access publications, in line with Horizon Europe's Open Access policy[101] and the 'Plan S' initiative[102]. The programme will also explore opportunities to incorporate other aspects of open science[103] into its work.

The Partnership will liaise closely with the EMA to ensure it complies with good practice in access to clinical data.

3.4.3 Work programmes

Based on the Strategic Research and Innovation Agenda, the EDCTP Association can suggest topics for the annual work programme for acceptance by the Governing Board. In parallel, the Executive Director starts consultations with advisory bodies and stakeholders, including organising the EDCTP Forum and thematic stakeholder meetings.

The procedure for the development of annual work programmes is described in the Partnership's SRIA (Annex 3). In brief, a set of criteria have been developed to inform priority setting, ranging from the state of the product development landscape to disease burdens and translational bottlenecks.

Extensive consultations will lead to a set of priorities across disease areas, outlined in the SRIA, which will form the basis of more specific three-year plans and annual work plans. Three-year plans, put together by a Scientific Committee with input from thematic stakeholder meetings, will outline medium-term priorities. Annual work

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programmes will include details of the specific calls for proposals for the following year. All calls for proposals will be actively promoted to the relevant communities.

Criteria for setting priorities

As indicated in the SRIA, in setting priorities the Partnership will follow these criteria:

- State of the product development landscape: For each disease area, the current state of clinical development of interventions for prevention, diagnosis, and treatment will be analysed.
- Priority infections: Priority setting will be informed by analyses of disease burdens, changing patterns of disease, an inventory of unmet medical needs, and potential impact on a disease as a public health problem.
- Disease burden and treatment/prevention priorities: These analyses will identify key knowledge gaps and need for new evidence.
- Emerging opportunities of translational bottlenecks: EDCTP3 will focus on points in the translational and implementation pathway that delay the clinical development and uptake of novel interventions, supporting effectiveness studies, pharmacovigilance, and product-focused implementation research as required.
- Strategic engagement: Committed to early engagement with WHO and other strategically important international and African partners, the Partnership will ensure global alignment of its policies and priorities and promote coordinated responses to evidence gaps and capacity-building needs.
- Strategic portfolio: the Partnership will aim to develop and sustain a strategic portfolio across disease areas, types of intervention, and types of study. It will balance short-term and long-term priorities and funding across targeted diseases, with a view to supporting intervention research that is most likely to produce significant reductions in disease burden and overall mortality. In some areas, a portfolio approach will be used in prioritising and selecting different intervention candidates for funding.

The Partnership will adhere to the principles of international peer review in decision making. Applicants will be provided with feedback on proposals and given an opportunity to respond to peer review comments. Applicants whose proposals are rejected will have the right to appeal.

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Annex 1: EDCTP2 funding and portfolio of grants 2014-2019

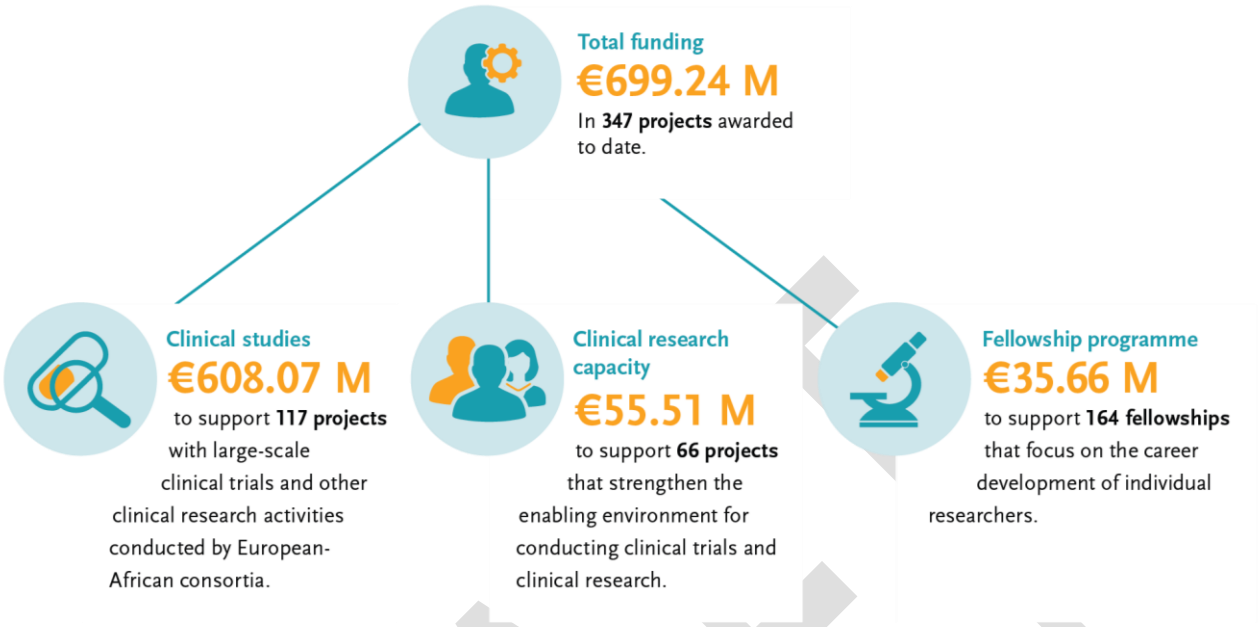

Figure 11: *A summary of EDCTP2 funding up to July 2020.*

EDCTP2 funding has been well spread across priority disease areas, with the greatest number of grants and funding going towards TB projects (Figure 12).

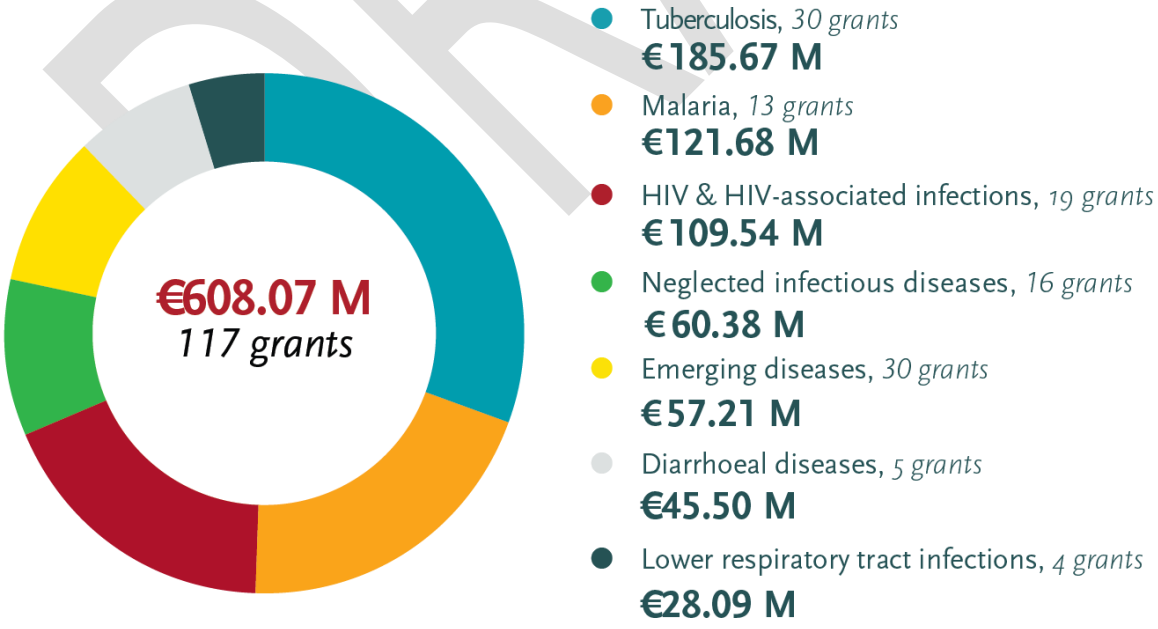

Figure 12: *Allocation of EDCTP2 funding up to July 2020.*

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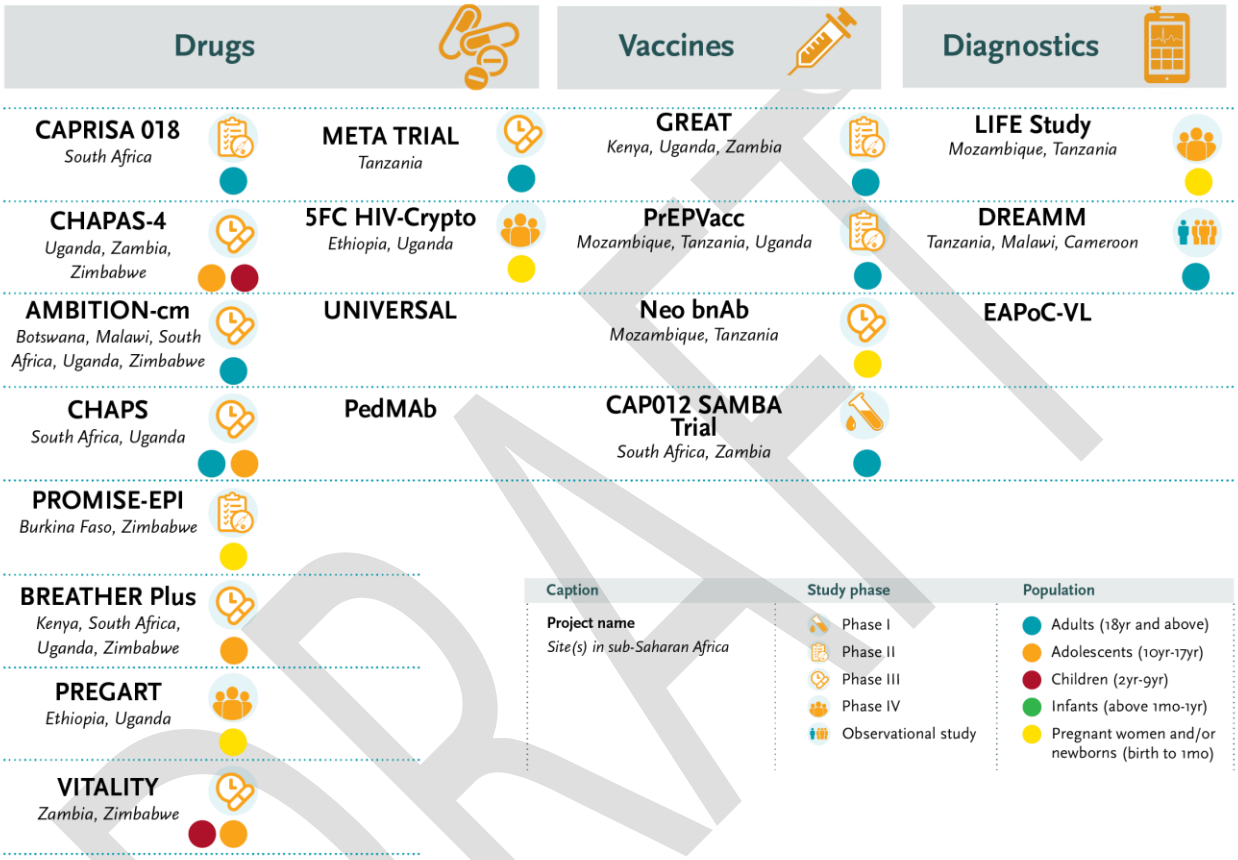
Of the clinical trials funded, 58% are phase II and III studies of drugs and vaccines, providing key data on safety and efficacy; 16% are phase IV post-licensing studies designed to inform policymaking and practice.

In terms of priority populations, 14% of projects focus on pregnant women and new-born babies, 35% involve children, and 43% adolescents.

HIV & HIV-associated infections



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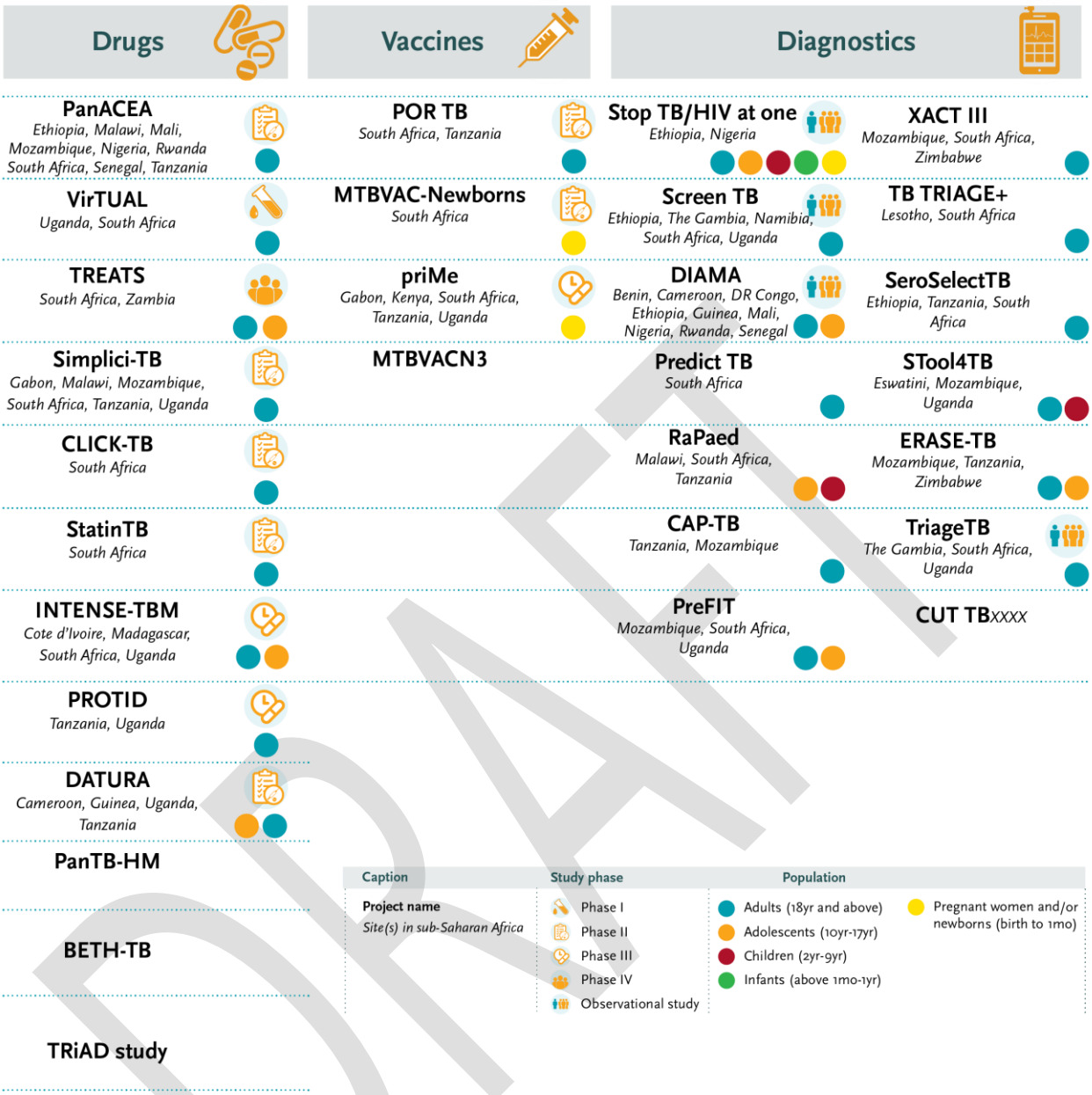
Tuberculosis



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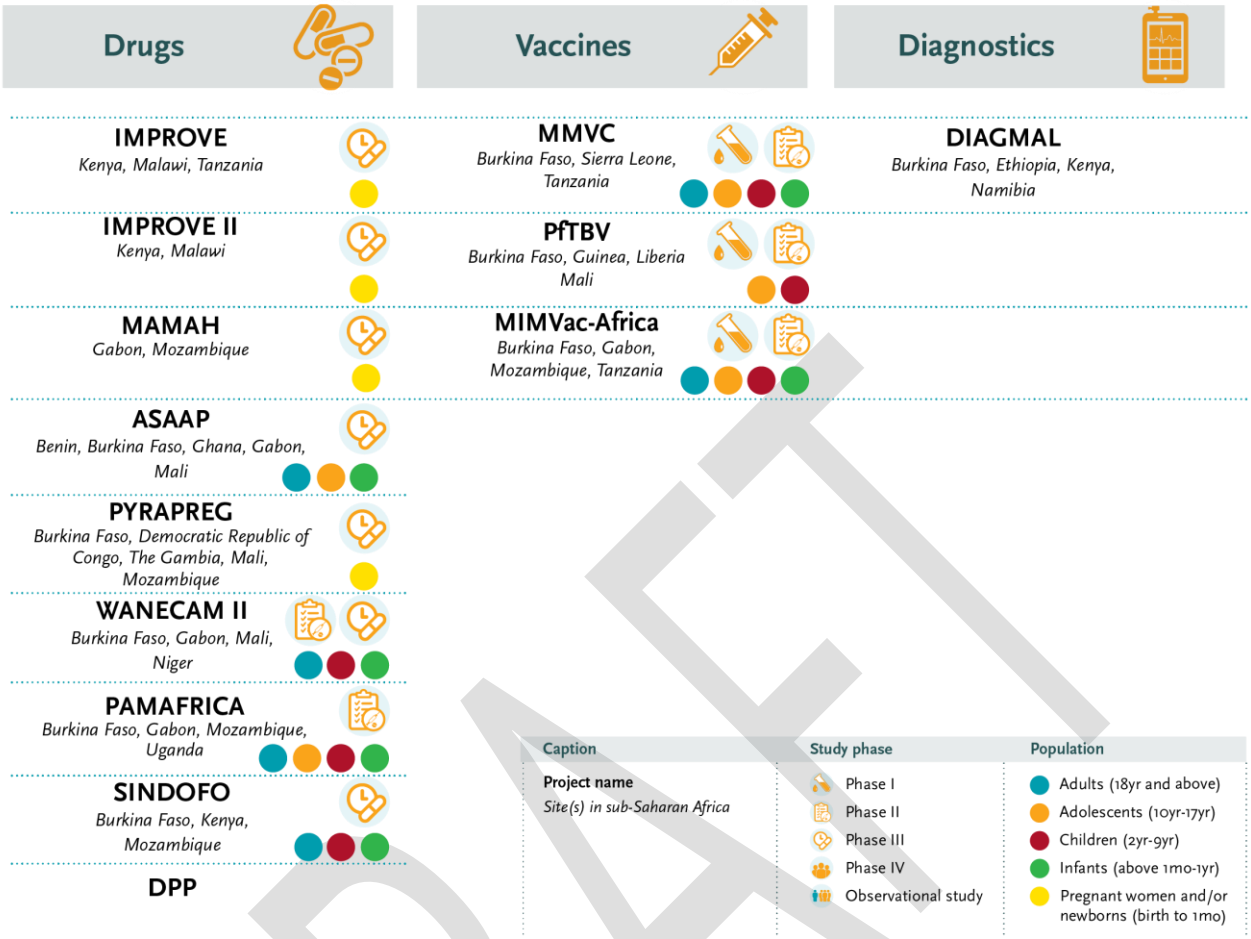
Malaria



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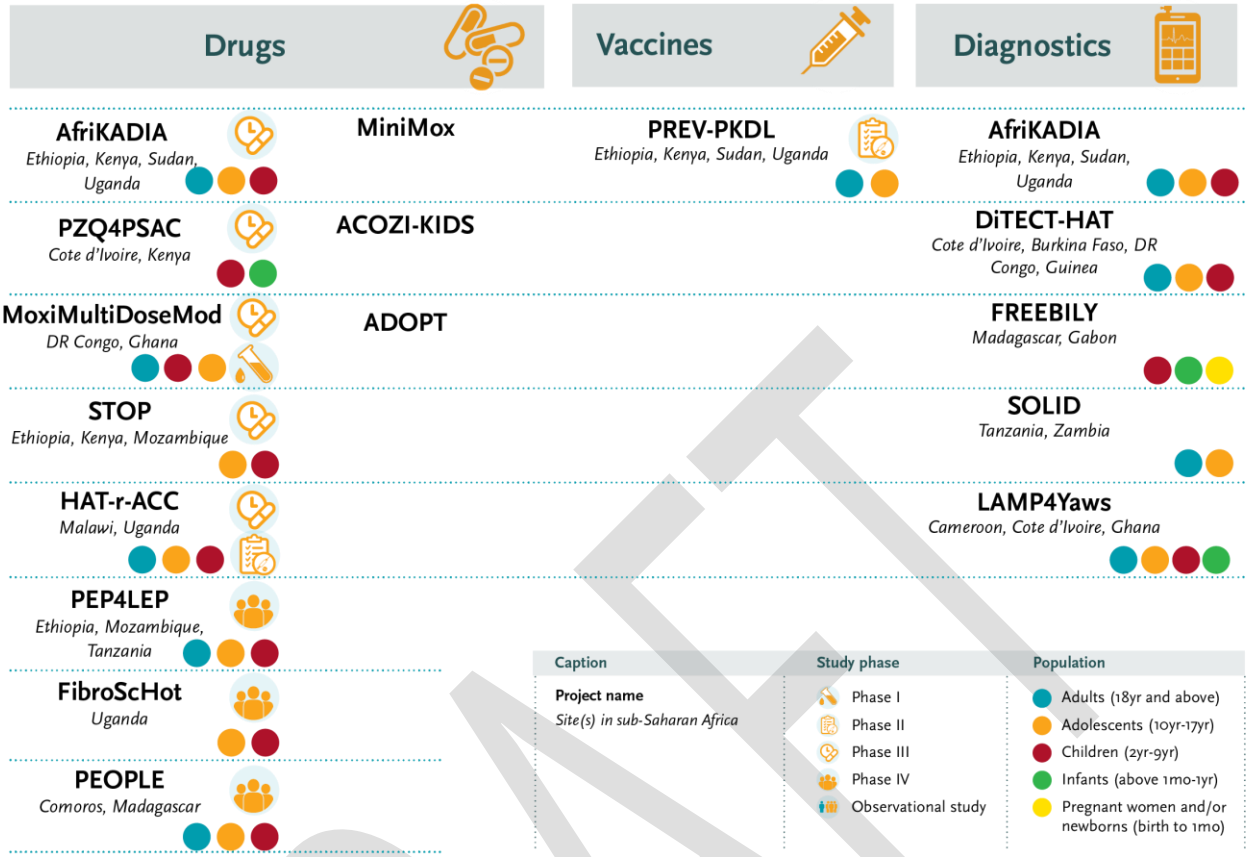
NIDs


Drugs
Vaccines
Diagnostics
AfriKADIA
Ethiopia, Kenya, Sudan, Uganda
MiniMox
PREV-PKDL
Ethiopia, Kenya, Sudan, Uganda
AfriKADIA
Ethiopia, Kenya, Sudan, Uganda
PZQ4PSAC
Cote d'Ivoire, Kenya
ACOZI-KIDS
DiTECT-HAT
Cote d'Ivoire, Burkina Faso, DR Congo, Guinea
MoxiMultiDoseMod
DR Congo, Ghana
ADOPT
FREEBILY
Madagascar, Gabon
STOP
Ethiopia, Kenya, Mozambique
SOLID
Tanzania, Zambia
HAT-r-ACC
Malawi, Uganda
LAMP4Yaws
Cameroon, Cote d'Ivoire, Ghana
PEP4LEP
Ethiopia, Mozambique, Tanzania
FibroScHot
Uganda
PEOPLE
Comoros, Madagascar
Caption
Project name
Site(s) in sub-Saharan Africa
Study phase
Phase I
Phase II
Phase III
Phase IV
Observational study
Population
Adults (18yr and above)
Adolescents (10yr-17yr)
Children (2yr-9yr)
Infants (above 1mo-1yr)
Pregnant women and/or newborns (birth to 1mo)

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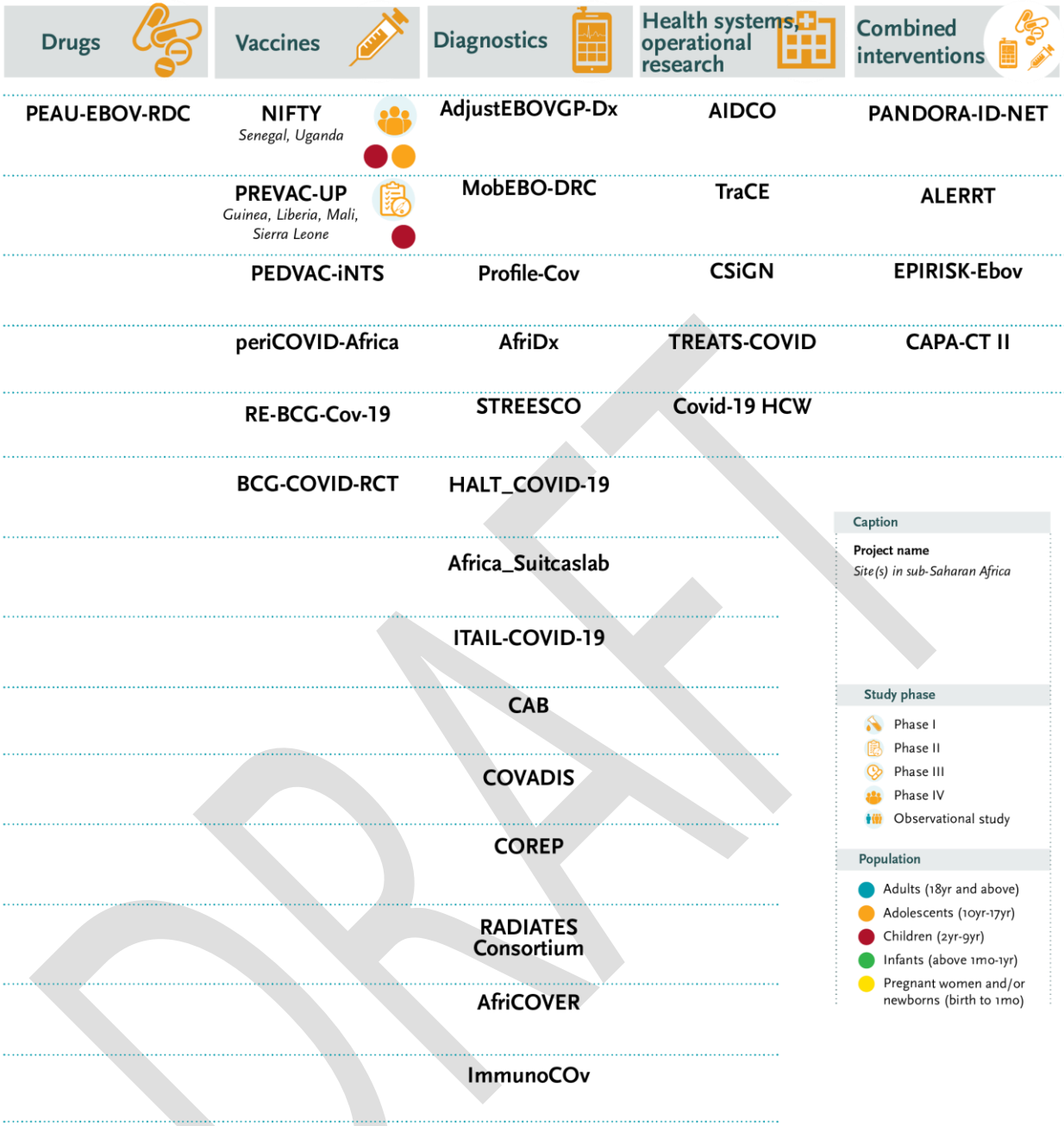
Emerging diseases



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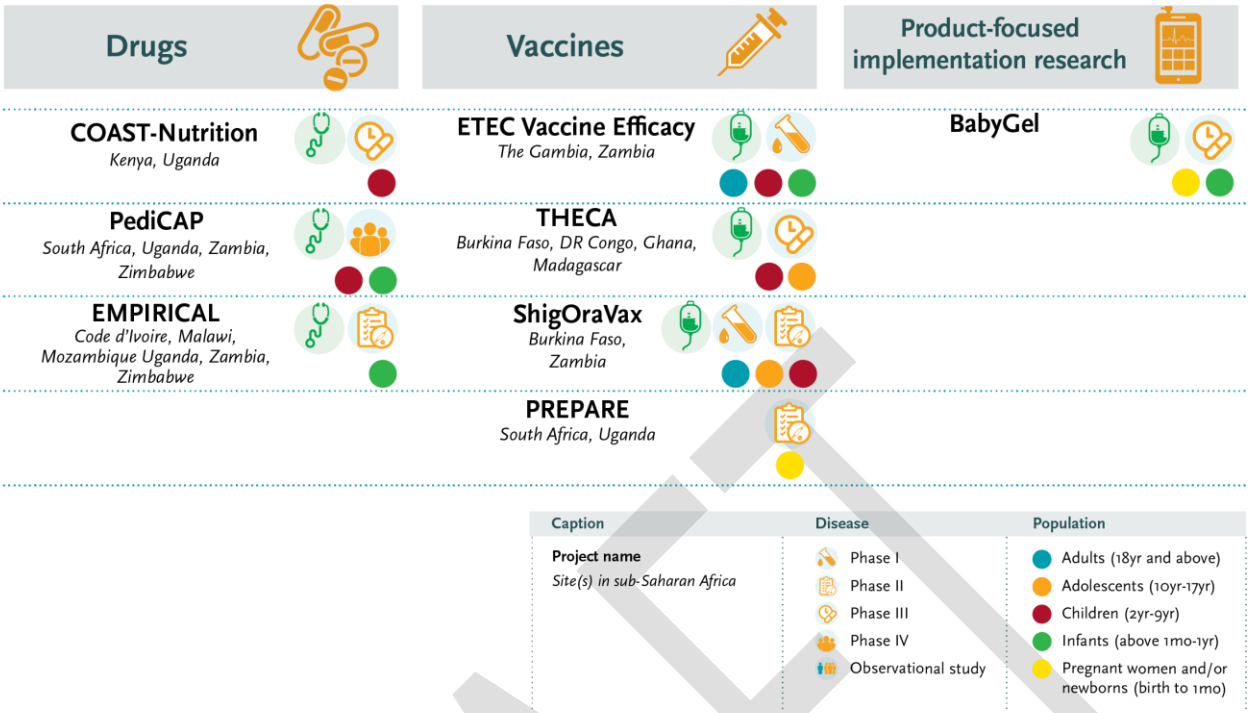
Diarrhoeal diseases and lower respiratory tract infections



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EDCTP1 and EDCTP2 Success stories

- **HIV in children**: The CHAPAS series of trials generated key data on the most appropriate choice and doses of antiretroviral therapy for children living with HIV[104] [105].
- **HIV management**: The REMSTART trial showed that a new approach to HIV management incorporating community support and early screening for cryptococcal meningitis reduced deaths by 28%[106].
- **Drug treatments for TB**: As well as identifying possible ways to shorten TB treatment regimes, the PanACEA consortium pioneered innovative trial designs to accelerate the evaluation of new TB drugs and novel formulations[107].
- **Antimalarials for mothers**: A comparison of four artemisinin-based combination therapies in the PREGACT trial identified the most suitable for treatment of uncomplicated malaria in pregnant women[108].
- **TB-IRIS prevention**: The PredART trial found that a readily available drug, prednisone, significantly reduced the risk of a potentially lethal inflammatory response (TB-IRIS) in patients being treated for TB who were starting antiretroviral therapy[109].
- **Mother-to-child transmission**: The Kesho Bora study found that triple antiretroviral therapy was highly effective at reducing the risk of mother-to-child transmission of HIV[110], informing the revision of WHO guidelines and highlighting the potential feasibility of elimination of mother-to-child transmission, now a key global goal.
- **TB diagnosis**: Professor Mark Nicol's Senior Fellowship research provided key evidence on real-world use of the Xpert MTB/RIF TB diagnosis technology in resource-poor settings[111], informing WHO endorsement of Xpert MTB/RIF.
- **Antimalarials for children**: The WANECAM (West African Network for Clinical Trials of Antimalarial Drugs) trial[112] and 4ABC study[113] generated data on new drug combinations and formulations suitable for use in children, feeding in to EMA approvals.

In the area of capacity development, EDCTP has supported the development of an enabling environment for clinical research in several ways. EDCTP has so far invested in 182 postgraduate fellowships, supporting the career development of current and aspiring African scientific leaders. The profiles of current and former EDCTP fellows are available on the EDCTP Alumni Network platform, which was launched in 2017, including how EDCTP has strengthened national and regional regulatory and ethical review capacities – with 27 African countries from all regions benefiting. In addition, four EDCTP Regional Networks are developing as centres of excellence for clinical trials, three grants are supporting national pharmacovigilance activities, and additional projects are building capacity to use research evidence in policymaking. The Sida cash co-funding through the common pot that is managed centrally has been instrumental in providing flexibility to support several projects in all categories of capacity development.

EDCTP was also part of the TRUST ethics consortium. Its main deliverable was the Global Code of Conduct for Research in Resource-Poor Settings, which was presented at the European Parliament in June 2018. Adopted as a resource, it is available to applicants and grant-holders via the Horizon 2020 Online Manual. Regarding regulatory affairs, EDCTP is now a fully recognised member of the African Medicines Harmonisation Partnership Platform coordinated by the African Union.

Anticipated outcomes

EDCTP2 has funded several trials that will deliver pivotal evidence to inform policymaking and practice. Examples include:

- **Schistosomiasis control in young children**: The **PZQ4PSAC** trial[114] is evaluating a new more palatable formulation of praziquantel to treat schistosomiasis in pre-school-age children. The new formulation will

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enable younger children to benefit from a highly effective drug for treatment and mass prevention. (Trial co-funded by the Global Health Innovative Technology Fund and sponsored by Merck.)

- **Better tools for control of parasitic worm infections**: The STOP study is developing a convenient fixed-dose pill that combines ivermectin and albendazole to improve control of parasitic worm infections in Africa.
- **Better detection of sleeping sickness**: The DiTECT-HAT study is evaluating a range of tools that will make it easier to detect, treat and ultimately eradicate sleeping sickness. By evaluating different tools and pathways of analysis, DiTECT-HAT will identify how diagnostic tools could be deployed most effectively to treat infection in routine care, to support eradication campaigns, and to facilitate the development of new drugs.
- **Fungal infections**: The **AMBITION-cm** project[115] is evaluating a novel liposome-based formulation of amphotericin B, which could transform treatment of cryptococcal meningitis, responsible for up to one in five HIV-related deaths in Africa.
- **Novel vaccines**: The **THECA study** will provide additional data on Typbar-TCV, a typhoid conjugate vaccine that has been recommended for use despite limited data on its efficacy. The study will also provide data on protection when the vaccine is used within routine public health systems. The **PREVAC-UP** project will enable an additional four years' data to be collected on the safety and efficacy of the two leading Ebola vaccines, rVSV-ZEBOV-GP and Ad26.ZEBOV, including data on vaccine use in children, building on the work of the existing PREVAC Consortium.
- **Pneumonia in children**: The **PediCAP** project is aiming to identify an optimal treatment for severe pneumonia in children, including an earlier switch from injected to oral antibiotics.
- **River blindness**: The **MoxiMultiDoseMod** project is extending use of moxidectin, the first new treatment for river blindness (onchocerciasis) approved in 20 years. The project is evaluating repeat use of moxidectin in children, which will be necessary for its application in mass drug administration campaigns.
- **A portfolio of novel antimalarial drugs**: The WANECAM II study is accelerating the development of a new class of antimalarial drug that may have significant advantages over existing treatments; and the PAMAFRICA portfolio grant is advancing the development of a suite of novel drugs to address unmet needs in malaria treatment.

In addition to these examples, the EDCTP2 programme is also generating important clinical data on a range of innovative interventions for poverty-related infectious diseases. These include studies of broadly neutralising antibodies, including their use to prevent mother-to-child transmission of HIV, innovative multistage and transmission-blocking malaria vaccines, and novel genetically tailored vaccines for TB. Such products could have a transformative impact on global health.

The current EDCTP2 portfolio includes projects across all target diseases and all stages of clinical development (see above). More than 60% of the products under clinical evaluation originate from the European Research Area.

Participating States-Initiated Activities success stories

Participating States-Initiated Activities (PSIAs) represent an important component of the EDCTP portfolio. PSIAs are activities that fall within the scope of the EDCTP2 programme (and the EDCTP3 programme), while being implemented or funded by one or more Participating States. Inclusion of PSIAs in the EDCTP portfolio helps to ensure alignment with national activities and avoids duplication of efforts.

By the end of 2018, the total value of PSIAs amounted to €556.3m. A total of 61 countries have participated in PSIAs, 20 from Europe and 41 from Africa.

As of August 2019, 378 PSIAs have been submitted for inclusion in the EDCTP2 portfolio (European and African Participating States, as presented in the 2014-2019 work plans), of which 184 have been completed. These

PSIAs include at least 144 clinical studies as well as other activities that fall within the remit of EDCTP2, including support for capacity development, ethics and regulatory activities, operational and implementation research, and health systems strengthening.

More than 465 publications have been reported as resulting from PSIA-funded research. Moreover, Participating States have reported that PSIAs have resulted in significant policy change and positive influence on national or international guidelines. Examples of key results from PSIAs include:

- **TB diagnosis**

Through studies funded by Denmark, a novel *Mycobacterium tuberculosis* test to detect latent TB infection has been developed, the C-tb skin test[116]. It has been shown to have higher sensitivity than other tests and has proven to be safe, with no significant adverse events.

UK-funded research on a novel diagnostic biosignature has influenced policy in The Gambia. A project led by the MRC Unit in The Gambia achieved a doubling of the notification of cases of childhood TB in the country and contributed to a new case classification for research in childhood TB[117].

Spain has funded influential research on the incidence and epidemiology of TB in Mozambican children[118]. The objective of the study was to determine the incidence, clinical characteristics, and consequences of TB in children under three years of age. The results showed that the incidence of TB is high in the study area and provided initial estimates of TB incidence for this age group in Mozambique.

- **HIV diagnosis and treatment**

In the area of HIV treatment in children, the UK contributed to the registration of a new formulation for an existing medical intervention. The CHAPAS-3 trial, which was also funded centrally by EDCTP, was the first randomised controlled trial conducting a head-to-head comparison of the three most relevant nucleoside reverse transcriptase inhibitors (NRTIs) for paediatric treatment. The trial confirmed the effectiveness of fixed-dose combinations, providing further impetus to the rollout of antiretrovirals to children. Its evidence on abacavir informed the WHO recommendation of abacavir-containing combinations for first-line therapy in children.

UK-funded research contributed to an update to the Paediatric European Network for Treatment of AIDS (PENTA) guidelines in 2016. Moreover, research fellows supported by the UK MRC have contributed to the establishment of a referral system for improved linkage of diagnosed HIV-infected patients with HIV care and treatment services in rural Tanzania.

In adults, routine cotrimoxazole prophylactic therapy (CPT) has been recommended for all HIV-infected patients since 2000. Research funded by the UK has shown that it can be safe to stop CPT once HIV-infected patients have regained their immune competence due to antiretroviral therapy[119]. This has impacted policy through a change in Guidelines for the Prevention and Treatment of HIV and AIDS in Uganda.

Regarding mobile and digital solutions, the UK funded the development of a smartphone app looking at HIV drug interactions (HIV iChart) and an HIV drug interaction website[120], which is now established as a decision support tool in around 30 guidelines from over 16 countries worldwide, as well as in WHO and European treatment guidelines.

France, through the ANRS (National Agency for AIDS Research) Research Grants, funded a number of clinical trials on HIV drugs, including studies comparing the WHO standard antiretroviral therapy regimens with new combinations as a way to provide further evidence for the choice of regimen in resource-limited settings.

Italy has supported research addressing low retention in care of HIV patients in Ethiopia. The study observed attrition differences in antiretroviral therapy retention that are expected to contribute to antiretroviral therapy programmes and strategies to address patient retention and care[121].

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Portugal supported the development and validation of a sensitive and cheap PCR-based assay for early infant diagnosis in HIV-1-exposed infants using dried blood spot samples. The new assay enables early and accurate early infant diagnosis. The simplicity and low cost of the assay make it suitable for generalised implementation in Angola and other resource-constrained countries[122].

- **Malaria prevention and treatment**

The UK funded the first randomised controlled trial showing that PBO-treated long-lasting insecticidal nets (containing the synergist piperonyl butoxide, PBO) were more effective than standard pyrethroid-treated long-lasting insecticidal nets against malaria infection and transmission. As a direct consequence of this trial, WHO revised its policy on long-lasting insecticidal nets in September 2017, gave interim endorsement to pyrethroid-PBO nets as a new WHO class of vector control product, and recommended that PBO nets be deployed for prevention of malaria where vectors are resistant to pyrethroids if vector control coverage is not compromised[123].

Spain has supported research in Mozambique related to the RTS,S vaccine, the world's first licensed malaria vaccine. One of the studies funded showed that RTS,S continues to protect young children and new born babies against clinical malaria for up to 18 months after vaccination.

In relation to malaria treatment, studies funded by Spain on the antimalarials artemether–lumefantrine and artesunate–amodiaquine found very high efficacy for both treatments, confirming their position as the first- and second-line treatments for malaria, respectively.

- **Diarrhoeal diseases prevention and treatment**

Spain co-funded the Global Enteric Multi-Center Study (GEMS), which has provided important information that can serve as a basis for the development of strategies for the prevention and control of diarrhoeal diseases in Mozambique. The data were used by the Ministry of Health to support the implementation of rotavirus vaccination in the country.

- **Emerging and re-emerging infections**

Participating States have also contributed to tackling emerging and re-emerging infections in sub-Saharan Africa, particularly through the funding of the Coalition for Epidemic Preparedness Innovations (CEPI) and Ebola vaccine research. Through the GLOBVAC programme, Norway is funding an Ebola vaccine trial in Guinea, and Germany supported the clinical evaluation of the Ebola vaccine VSV-ZEBOV-GP through a phase I study.

PSIAs have also demonstrated the commitment of Participating States to institutional capacity building in sub-Saharan Africa. Examples include: the creation of the Benin Clinical Research Institute (IRCB) funded by France; institutional support to the Armauer Hansen Research Institute (AHRI) in Ethiopia by Sweden and Norway; and support given by Spain to research activities conducted by the Manhiça Health Research Centre (CISM) in Mozambique for malaria vaccine research. In addition, core funding has been given to 11 PDPs and Sweden has provided unearmarked programmatic funding to the WHO-based Special Programme for Research and Training in Tropical Diseases (TDR), including the activities of ESSENCE on Health Research[124].

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Annex 2: A SWOT analysis of the EDCTP programmes

Strengths	Weaknesses
ORGANISATION • Established a presence and visibility in sub-Saharan Africa • Covered a key gap in the funding landscape; few other private and public bodies fund large late-stage clinical trials in sub-Saharan Africa • Supported scientific excellence, with projects generating major publications in high-profile publications • Focused research activity on underserved populations, addressing key market failures • Integrated capacity-building into grants • Developed African scientific leadership • Established new African networks • Strengthened the regulatory and ethics review capabilities of multiple African countries • Expanded the range of African countries with capacity to carry out clinical research • Facilitated formation of enduring global partnerships **PORTFOLIO** • Impactful HIV studies, particularly prevention of mother-to-child transmission, paediatric HIV treatment • Influential trials on HIV co-infections, particularly HIV–TB and HIV–malaria co-infections and opportunistic infections (e.g. Cryptococcus) • Significant advances in TB diagnostics • Major studies in TB drug development and vaccine evaluation, with globally important collaborations and innovative trial methodologies • Landmark studies on malaria treatment during pregnancy, in children, and in co-infected patients • Capacity developed in malaria vaccine evaluation • Advances in diagnostics for neglected infectious diseases	**ORGANISATION** • Relatively small player, in terms of funds available per pathogen, compared with some funders in global health research • General lack of visibility/awareness • Fewer funding partners than initially envisaged, especially with pharmaceutical companies • Lack of flexibility in funding approach can be an obstacle to joint initiatives with other funders • Challenges leveraging additional cash funding from PSs • Lack of incentives to join EDCTP Association • Challenges aligning funding strategies of EU PSs • Lack of support to enable researchers from French- and Portuguese-speaking countries with weaker research systems to submit high-quality applications. **PORTFOLIO** • Disappointing results in early microbicide and HIV vaccine trials • Large range of pathogens covered resulted in limited funding per disease category in EDCTP2 thus far, particularly for the newly incorporated diseases
Opportunities	**Threats**
ORGANISATION • Enhanced global networking and engaged new partners • Additional engagement with newer EU 'EU13' Member States • Alignment with other global health agendas (e.g. outbreak preparedness, antimicrobial resistance, universal health coverage and design of people-centred health systems) • Alignment with other EU initiatives (e.g. other Horizon Europe initiatives, Joint Programming Initiative on Antimicrobial Resistance, Innovative Medicines Initiative). • Increased synergies and better coordination of the PSs' own contributions to research activities within EDCTP's scope (PSIAs). • Additional joint funding initiatives and co-funding schemes	**ORGANISATION** • Insufficient funds to support all highly ranked projects • Expanded scope to include non-communicable diseases or other bigger thematic areas could spread resources too thinly • Ineffective global collaboration could lead to both duplication of efforts and missed opportunities • Inappropriate use of funds by recipients could damage confidence and cause reputational harm to EDCTP • Insufficient funding to support activities of the growing EDCTP Alumni Network and its integration with the EDCTP Regional Networks **PORTFOLIO** • Major disease outbreaks could overwhelm country response capacity and undermine research efforts on priority diseases • Rising antimicrobial resistance could compromise use

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- Increased proportion of projects led by African and female researchers
- Increased collaboration among emerging research leaders funded by EDCTP

PORTFOLIO

- Improved pipelines offer more scope for later-phase studies and head-to-head comparisons
- Scope for additional implementation studies and synergy with health system strengthening in pursuit of universal health coverage
- Co-infections and co-morbidities associated with longer survival
- Maternal vaccination
- Drug repurposing
- Multiplex diagnostic platforms
- New digital and other technologies, to enhance diagnosis, delivery of interventions and design of people-centred care
- Opportunities for greater multi-disciplinary input, e.g. from social and behavioural sciences, anthropology
- Repurposing of platforms/infrastructure to address new threats, including emerging infectious disease threats and antimicrobial resistance
- Innovative trial designs for faster and more flexible clinical evaluation

of therapeutics

- Civil unrest and conflict could compromise countries' ability to conduct clinical research
- Public rejection of research or experimental interventions could threaten research and implementation
- Major adverse reactions to a new intervention could trigger negative public attitudes to clinical research
- Significant global funding gaps could compromise achievement of challenging global targets
- Insufficient local investment could threaten sustainability of newly developed research capacity

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Annex 3: Strategic Research and Innovation Agenda

EU-Africa Global Health Partnership (GHP)
Strategic Research and Innovation Agenda

(28 July 2020)

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1 Executive summary

The EU–Africa Global Health Partnership (GHP) – the third programme of the European & Developing Countries Clinical Trials Partnership (EDCTP3) – Strategic Research and Innovation Agenda will support international collaborations accelerating the clinical evaluation and implementation of interventions against poverty-related infectious diseases affecting sub-Saharan Africa. By building research capacity, it will also enhance the ability of sub-Saharan African countries to identify and respond to key infectious disease health challenges.

Infectious diseases remain a major cause of death, disability, and ill-health in sub-Saharan Africa. Diseases such as HIV, malaria, tuberculosis (TB), respiratory infections, diarrhoeal disease, and a panoply of neglected infectious diseases have a devastating impact on individuals and communities, and delay national economic development.

Sub-Saharan African is also at risk of emerging and re-emerging infections, such as Ebola, Lassa fever, and yellow fever, which also imperil global health security. The alarming rise of antimicrobial resistance is compromising the few treatments that are available and undermining multiple branches of medicine that rely on effective infection control. These challenges are being exacerbated by changing patterns of disease driven by the climate crisis and environmental degradation.

Combating infectious disease will therefore be central to achieving Sustainable Development Goal 3 (SDG3), to ensure healthy lives and promote well-being for all at all ages. Furthermore, preventing infections will support progress towards multiple other SDGs, by reducing the economic burden on countries, enhancing child development, and ensuring that healthier populations contribute to greater productivity and national prosperity.

However, despite some progress, the Global Action Plan for Healthy Lives and Well-being for All, launched at the UN General Assembly in September 2019, noted that extra efforts would be required if health-related SDGs were to be met by 2030. It identified research and development (R&D) as a key accelerator of progress and emphasised the importance of global collaboration and alignment.

For infectious diseases predominantly affecting low- and middle-income countries (LMICs), few commercial incentives exist to encourage the substantial investment required to develop and evaluate new vaccines, diagnostics, and treatments. Innovative models of collaboration are therefore required across public and private sectors, national governments, and regional and global agencies.

Set up in 2003, the European and Developing Countries Clinical Trials Partnership (EDCTP) has established itself as the focal point of cooperation between the EU and sub-Saharan Africa in infectious disease research. Through its support of EU–sub-Saharan Africa research partnerships, two EDCTP programmes have made major contributions to the development of vaccines, diagnostics, and treatments for the most important infectious diseases affecting sub-Saharan Africa and enhanced the capacity of countries in sub-Saharan Africa to carry out clinical research of the highest standard. The GHP programme will build on and extend the platform created by EDCTP.

Scope of the GHP programme

The GHP programme will focus on the major infectious disease threats facing sub-Saharan Africa – HIV, TB, malaria, lower respiratory tract infections, and diarrhoeal disease – as well as emerging and re-emerging infections, antimicrobial resistance, and the infectious disease impacts of the climate crisis. Priority evidence gaps have been identified in these areas, but the programme will maintain the flexibility to respond to emerging challenges and opportunities through annual reassessments.

The GHP programme will focus on all stages of clinical evaluation, particularly later-stage (phase III and phase IV) studies, including product-focused implementation studies, in recognition of their growing importance as bottlenecks in intervention development. It will have a particular focus on populations that are typically

excluded from clinical trials, such as children, adolescents, pregnant and lactating women, and people with co-morbidities (including non-communicable conditions), and who may therefore not initially benefit when new interventions become available.

Capacity building will be an integral part of GHP-funded clinical trials. In addition, specific funding will be provided to improve the technical infrastructure of countries in sub-Saharan Africa, and to build intellectual capacity in the region – including the development of the next generation of African scientific leaders. International networking – North–South and South–South – will be encouraged to promote the exchange of knowledge and expertise.

Intended impact of the GHP programme

The GHP programme will generate high-quality data on the safety and efficacy of new diagnostics, preventive tools, and treatments, accelerating their progression through clinical evaluation pathways and providing policymakers with key evidence to inform their decision-making to reduce the disease burden. The aim is that all populations would benefit from the GHP activities.

The GHP programme will also ensure that countries in sub-Saharan Africa are better able to plan, lead, and conduct the clinical studies required to counter the infectious disease threats that they face. They will be better prepared to prevent and manage outbreaks of emerging and re-emerging infections and drug-resistant infections, safeguarding national and global health security, and to anticipate key health impacts of the climate crisis.

The programme will focus and align European efforts, maximising the impact of European investments. Strategic alliances and partnerships with other global bodies will further promote coordination, integration, and complementarity of activities.

Through these efforts, the GHP programme will catalyse progress towards the infectious disease-related objectives of SDG3, and ultimately ensure that significantly more people in sub-Saharan Africa live longer, healthier, and more productive lives.

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2 Introduction

Despite much progress, infections such as HIV, tuberculosis (TB), malaria, respiratory infections, diarrhoeal disease, and other poverty-related and neglected infectious diseases are still responsible for a huge burden of disease in sub-Saharan Africa. As well as their impact on individuals, infectious diseases impose a high economic burden on countries, impeding on national development. Achieving most if not all Sustainable Development Goals will depend on effective control of infectious diseases.

Control of infectious diseases requires effective interventions for prevention, detection, and treatment. However, little economic incentive exists for commercial organisations to invest in intervention development for infections predominantly affecting low- and middle-income countries (LMICs). Innovative models are required to advance the development of new interventions, particularly global partnerships between governments, academia, funders, and the private sector.

Over the last decade, significant progress has been made in the development of new diagnostics, drugs, vaccines, and other interventions against poverty-related diseases. While product pipelines still require strengthening, there is also a need to conduct later-stage clinical evaluation, including phase III and phase IV trials, effectiveness studies, and product-focused implementation studies. Such studies generate the most 'policy-relevant' information to support national health policymaking. They aim to ensure that products can reach neglected or vulnerable priority populations – such as children or pregnant women, or those with additional health conditions – and that they have the anticipated beneficial impact on overall health.

This Strategic Research and Innovation Agenda (SRIA) is founded on lessons learnt from the highly successful European and Developing Countries Clinical Trials Partnership (EDCTP) programmes. Since 2003, the two EDCTP programmes have carried out pioneering work by supporting clinical trials carried out collaboratively by groups in Europe and sub-Saharan Africa. The programmes have generated evidence that has had a significant impact on national and international policy and practice – and on people's access to medicines. Furthermore, the programmes have had a strong emphasis on capacity building, nurturing African scientific leadership, building technical capacity and research skills, and strengthening the ethics and regulatory capacities of countries in sub-Saharan Africa. EDCTP-supported work has strengthened national health research systems, underpinning long-term sustainability.

This SRIA is anchored in the important niche that has been carved out by EDCTP in global health research. Its focus on phase III and phase IV studies complements the work of product development partnerships primarily engaged in drug, vaccine, and diagnostic test discovery and in earlier stages of clinical evaluation. Its approach addresses key bottlenecks and maintains momentum through later stages of the translational pathway. Its additional emphasis on pragmatic effectiveness trials and on product-focused implementation studies that have overall health as the key outcome meets important evidence needs of national health decision-makers.

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3 Vision, mission, and objectives

The EU–Africa Global Health Partnership (GHP) – the third programme of the European & Developing Countries Clinical Trials Partnership (EDCTP3) – programme, running from 2021 to 2031, will maintain the focus on poverty-related infectious diseases and successful approaches established in the EDCTP1 and EDCTP2 programmes, with some shifts in emphasis to reflect changing global, regional, and national contexts.

Vision
To reduce the individual, social, and economic burden of poverty-related infectious diseases in sub-Saharan Africa.

Mission
To support global collaborative research, capacity strengthening, and international initiatives to accelerate the development, evaluation, and implementation of medical interventions to prevent, identify, and treat infectious diseases and emerging/re-emerging infections in sub-Saharan Africa with the overriding goal to reduce overall mortality and morbidity.

Overall objectives
The GHP aims to (1) reduce the individual, social, and economic burdens of infectious diseases in sub-Saharan Africa through the development and uptake of new or improved interventions, and (2) increase health security in sub-Saharan Africa and globally, in particular in the context of environmental change and the climate crisis, by reducing the risk of outbreaks and pandemics, and enhancing national and regional capacity to address antimicrobial resistance. These objectives are in line with the objectives outlined in the document on *orientations towards the first strategic plan for Horizon Europe*, which is an important part of the co-design process of the Horizon Europe Strategic Plan [1].

Specific objectives
The GHP programme will have six specific objectives:

1. Advance biomedical interventions towards improved overall health
GHP will support clinical studies on medicinal products and interventions designed to prevent, detect, and treat priority diseases, and on technological innovations that facilitate research or access to care. These will include diagnostics, vaccines, novel drug treatments and formulations, and new therapeutic regimens. GHP's scope will encompass innovative and rigorous clinical trials of interventions based on traditional medicines and will consider other study designs on a case-by-case basis.

Clinical trials and other intervention studies will make up the bulk of the GHP portfolio (Figure 1). GHP will have an emphasis on phase III and IV pharmacovigilance and post-licensing effectiveness studies (pragmatic trials and product-focused implementation research[6]). This will include scope for a wide variety of studies to inform national decision-making to reduce mortality and morbidity, including modelling studies and pharmaco-economic analyses.

GHP will also support preparatory studies essential for the design, conduct, and evaluation of trials. These could include epidemiological studies to generate baseline data on disease burdens, as well as observational studies and social/behavioural/ethics research on health systems and health-seeking behaviours to inform decision making on intervention design and implementation.

Special effort will be required for the design of clinical studies so that explicit attention is given to overall health effects, sex and gender, community engagement, the contribution of social sciences, and ethics.

[6] "Implementation research is the scientific study of methods to promote the systematic uptake of proven clinical treatments, practices, organizational, and management interventions into routine practice, and hence to improve health." In this context, it includes "the study of influences on patient, healthcare professional, and organizational behaviour in either healthcare or population settings." This definition from the journal *Implementation Science* can be found at https://implementationscience.biomedcentral.com/about.

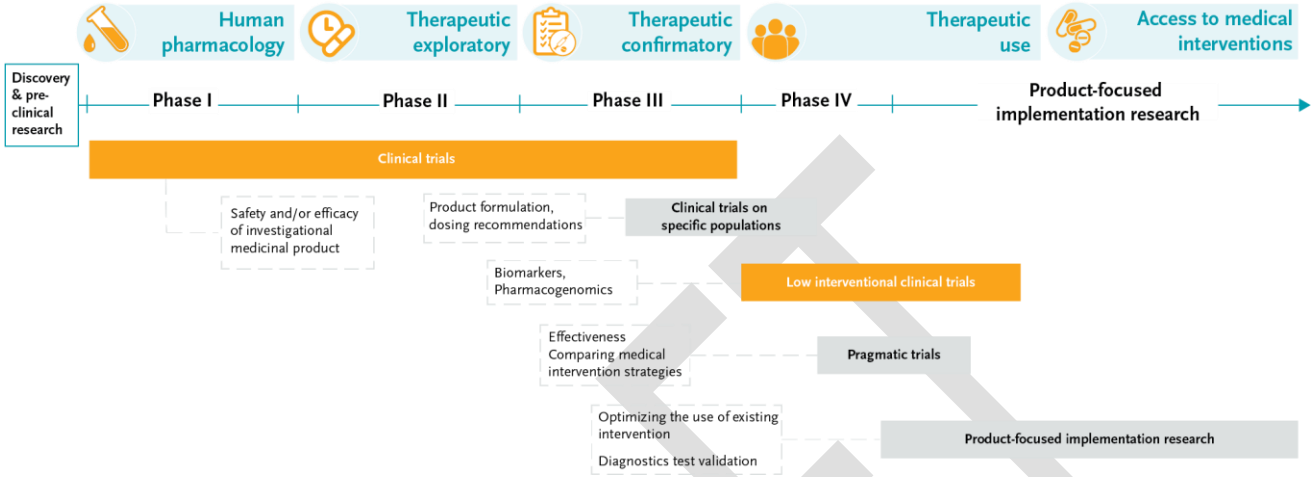

Figure 1: *Types of clinical studies supported by GHP*

2. Collaboration and research capacity development

GHP will strengthen clinical research capacity in sub-Saharan Africa and accelerate the development and application of innovative technologies in healthcare. It will do this by building indigenous intellectual capital, enhancing local infrastructure, and by developing supportive regional and national science governance systems (including strengthening of national research support systems, ethics oversight, and the regulatory environment for clinical research). This will be achieved through a combination of specific funding for capacity development at individual, institutional, and societal (national and regional) levels (e.g. through fellowship schemes, institutional infrastructural development, and regional networks), integration of healthcare and research capacity-building activities in projects, support for international networking (North–South and South–South), and staff exchange and mentorship programmes. GHP will ensure achieving a careful balance on promoting research excellence and paying special attention to the challenges of gender balance and regional equity. Moreover, communication with policy makers and the public to raise awareness of the importance of investing in science will be promoted.

GHP will place high priority on strengthening the capacity of countries in sub-Saharan Africa to conduct high-quality clinical trials and implementation research consistent with fundamental ethical principles and recognised international regulatory standards and good participatory practices. The objective of capacity building is to develop individuals, organisations, and societies (individually and collectively) to perform research effectively, efficiently, and in a sustainable manner. Projects should leave a tangible legacy and reduce dependency on external resources. Fulfilling capacity building objectives in a partnership is key to ensuring that health research responds to local health needs and prioritises the safety and health of all affected populations.

To achieve this objective, GHP will invest in both people and institutions in sub-Saharan Africa, and promote the exchange of ideas, information, and people between institutions in Europe and those in Africa. To accomplish research goals and translate them into mass-scale innovations, human capital is a prerequisite. Personal support schemes will play a key role in developing the next generation of African scientific leaders. GHP will have a strong focus on research training (Master's and PhD) and a comprehensive scope of postdoctoral and fellowship schemes, as well as on needs-driven short-term training, mentoring, and

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exchange. As well as supporting training in practical research techniques, study design, and research conduct, GHP will also develop expertise in laboratory and research institution management.

GHP will support and track the career progression and retention of scientists in Africa, and actively intervene to increase awareness and advance women in global health research [2]. GHP will develop mechanisms to increase the capacity of researchers from French- and Portuguese-speaking countries to develop high-quality research proposals.

GHP will fund upgrades to clinical and laboratory facilities, but not entirely new facilities, to support high-quality clinical research. To increase sustainability of local research capacities arising from its support, GHP will build the capacities of national health research authorities to continue supporting researchers and research institutions after GHP funding.

3. Enhanced European coordination

GHP aims to coordinate, align, and, where appropriate, integrate national research and development programmes to add value to European investments in health research on poverty-related infectious diseases. Impact will be increased through collaborations with other EU initiatives, particularly those related to development assistance.

GHP will promote North—North coordination and pooling of resources, by encouraging European Participating States to develop calls for proposals together and with countries in sub-Saharan Africa and/or with other partners, facilitated by the GHP framework.

GHP will broker productive and sustainable partnerships – promoting networking and building relationships with multiple private- and public-sector organisations. GHP will support established and successful networking and partnering activities with a range of objectives:

- Fostering productive relationships between European and African individuals and institutions.
- Concentrating efforts, promoting efficiency, and avoiding duplication by aligning the strategies of European and African funders, institutions, and authorities.
- Attracting additional investment through global strategic partnerships involving partners in the private, public, and charitable sectors.

GHP will promote North–South networking to strengthen project and institutional collaborations by raising awareness of common interests and facilitating collaboration between institutions and research groups with shared goals. Through calls for proposals and Participating States activities, GHP will help to establish new North–South collaborations to conduct multi-country, multi-site studies in sub-Saharan Africa. In addition, a regular international conference (the GHP Forum) will provide a platform for scientists from Europe, Africa, and elsewhere to share findings and ideas, and to establish collaborative links.

4. South–South collaboration: sharing expertise and good practices

GHP aims to support in-country and regional networking, and promote international cooperation to share good practices, expand capacity, and build platforms for multi-centre trials. South–South networking will build on existing regional Networks of Excellence. The Networks provide a mechanism for sharing of resources, knowledge, and expertise, enabling less well-established institutions to participate in multi-centre clinical trials. They also support mentoring and training of early-career researchers. The Networks conduct epidemiological and demographic studies to facilitate the planning of future trials and to enable countries to address new scientific challenges and take advantage of emerging research technologies.

GHP will promote wider use of the EDCTP Alumni Network and online platform to encourage collaboration and increased dialogue among EDCTP fellows and regional Networks of Excellence. Four disease-specific working groups established within the Alumni Network – HIV, TB, malaria, and NIDs and emerging infections – will further galvanise South–South collaboration. Additional working groups could be considered.

5. Building partnerships and strategic alliances

Global health is a large, complex domain. Multiple agencies – including global multilateral agencies, the private sector, charitable foundations, non-profit organisations, and public–private partnerships – work in LMICs across a variety of sectors, including research capacity development, implementation research, outbreak preparedness, health research for development, and regulatory system capacity building. Sustained progress in global health is costly and most effectively achieved when bodies that support clinical research work together rather than in isolation. GHP aims to work with a broad range of public and private partners to attract additional investment, exploit opportunities for high-quality clinical research, and maximise the impact of integrated approaches to research.

GHP will consolidate its investment in late-stage product development, using more flexible and long-term approaches to establish strategic alliances with product developers, including both small- and medium-sized enterprises, large pharmaceutical companies, and product development partnerships.

6. Strengthening EU cooperation

GHP aims to increase interactions with other EU initiatives and partnerships, including those linked to development assistance, thereby enabling the programme and development partnerships to achieve synergies and greater impact than they would by working independently.

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4 Development of the Strategic Research and Innovation Agenda

The GHP SRIA will concentrate research efforts on the poverty-related infectious diseases that are still responsible for a huge disease burden in sub-Saharan Africa. Its studies will generate evidence on the effectiveness of new drugs, vaccines, and other interventions, accelerating their introduction into routine use.

This SRIA has been developed in collaboration with the participating states, research communities, and partners represented by European and African universities and global health institutes, product development partnerships, the World Health Organization (WHO), and EDCTP constituencies. A first consultation process took place during the Ninth EDCTP Forum and was followed by a series of high-level meetings held on 9-10 July 2018 in Ghana, 30 August 2018 in Senegal, and 17 September 2018 in Portugal. Further input was received during 2018—2019 from the EDCTP Scientific Advisory Committee and the EDCTP General Assembly. Additional perspectives were gained from EDCTP member states at high-level dialogue events held in Africa and Europe to gather input from political leaders and the public health, academic, health policy, regulatory, and partner communities. This SRIA has taken into account the various perspectives stated by EDCTP stakeholders in position papers, voicing broad and strong support for a future programme.

The SWOT (strengths, weaknesses, opportunities, threats) analysis of the two EDCTP programmes has guided the development of the SRIA. The analysis revealed that EDCTP has established a presence and visibility in sub-Saharan Africa, covering key knowledge gaps by focusing on end-to-end research and development (R&D), especially large late-stage clinical trials. The integration of highly collaborative R&D investments with multi-faceted capacity building (individual, institutional, systems, national, and regional) is among the important strengths of the programmes, yielding high-impact research results [3] [4]. EDCTP has established a well-defined niche in global health, with its clear focus on later stages of clinical evaluation and adaptation of interventions for underserved groups, including women, children, and those with co-morbidities and co-infections, generating findings that have had a significant impact on national and global policy and practice.

The SWOT analysis suggested that covering a broad range of pathogens resulted in limited funding per disease category, particularly for the neglected infectious diseases. It also found out that little research had been conducted to date on the impact of the climate crisis and how to mitigate rising levels of antimicrobial resistance. The analysis also revealed difficulties in aligning funding strategies of European Participating States, limited progress in advancing women in global health research, and lack of support to enable researchers from some French- and Portuguese-speaking African countries that have weaker research systems, to submit high-quality applications. In terms of threats, major disease outbreaks could overwhelm country response capacity and undermine research efforts on priority diseases, while rising antimicrobial resistance is already compromising use of therapeutics. The climate crisis is also likely to significantly increase exposures to pathogens.

This SRIA will tackle these issues. It will focus on priority populations to ensure that interventions are adapted for those in greatest need, including children and pregnant women. Its support for clinical research in Africa is essential for identifying environmental and genetic factors that affect the effectiveness of interventions and their impact on overall health. It will also contribute to strengthening national health research systems, to ensure that countries in sub-Saharan Africa are able to develop and lead the health research agendas needed to address their infectious disease health challenges. EDCTP's strong commitment to capacity building integrated within R&D will continue to be one of the most important distinguishing features of the SRIA.

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5 Guiding principles

In developing its activities, GHP will incorporate and extend the principles that have successfully guided the implementation and day-to-day activities of the EDCTP programmes.

Leveraging its role as an established focal point: EDCTP established itself as a key contributor to the Africa–EU Strategic Partnership and a focal point for European research activities, promoting coordinated action to maximise impact on poverty-related infectious diseases. GHP will leverage this visibility to strengthen international cooperation and achieve even greater synergies in global health research and capacity development.

Operating as a partnership of equals: GHP will operate as a true partnership of equals between North and South. African partners will be involved at all levels, including priority setting, strategy development, implementation of plans, and leadership. This co-ownership will foster political and financial commitments, and make an important contribution to longer-term sustainability.

Working together to achieve more: The partnership will provide a means of reducing fragmentation and achieving jointly what no single funding agency could accomplish alone. By facilitating greater coordination of funding and research activities within and between countries, it will focus resources on key questions and maximise impact. Rarely can a single national programme cover all aspects addressed by GHP, so by collectively contributing to a joint programme that is greater than the sum of its parts, GHP participating states can align and strengthen actions to achieve an agreed common vision and set of priorities.

Ensuring relevance to societal challenges: The partnership will seek input from multiple stakeholders to identify key infectious disease health challenges. This will ensure that GHP has a strong focus on the highest priority diseases and populations most in need, anticipating the potential impact of societal challenges such as the climate crisis, antimicrobial resistance, urbanisation, global health security, and the emerging challenges in the "end game" of disease elimination.

Focusing on excluded populations: Equity of access will be a key driver of GHP's work. This encompasses populations often excluded from clinical studies but with major unmet medical needs – including pregnant and lactating women, new-borns, children, adolescents, other vulnerable and neglected populations, and people with co-infections and co-morbidities.

Promoting people-centred approaches: GHP will have a strong interest in ensuring that interventions are implementable within people-centred universal health systems.

Supporting product-focused implementation research: GHP will include implementation research in its portfolio, providing opportunities for partnerships with disease programmes, as well as development organisations working on health systems, to optimise and integrate health services, and promote universal health coverage.

Promoting local innovation: GHP will provide opportunities to advance the local development and adaption of technological innovations to solve health challenges by facilitating the generation of data on effectiveness and implementation into people-centred universal health systems.

Maintaining a commitment to excellence: By adhering to the principles of international peer review and open calls for proposals, as well as conducting extensive project monitoring and evaluation, GHP will ensure that it funds only high-quality studies that adhere to international and local ethics and regulatory standards and norms. It aims at excellent study completion rates and its projects will generate multiple landmark papers in high-profile journals.

Ensuring flexibility: GHP will be adaptable in its approach to funding, to ensure its schemes meet the needs of those conducting research and to facilitate productive relationships with strategic partners.

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Promoting transparency and openness: GHP will strive to be open and transparent in its work and to support the principles of open access to research findings, including clinical data, with appropriate safeguards.

Improving the design of clinical trials: GHP will promote innovation in clinical trial design to optimise testing of infectious disease interventions. GHP will place importance on trial designs that adapt to developments in the field, respond to the evolving regulatory environment, and incorporate ethical considerations, sex and gender specificities, meaningful community engagement, and the contribution of social sciences.

Utilisation of digital technologies: Following the cross-cutting priorities of Horizon Europe, GHP will place significance on the digitalisation of the health sector, including health technologies, medical devices, key enabling technologies, and decision-support systems, especially in sub-Saharan Africa where the use of digital technologies is rapidly growing. Application of digital technologies in clinical research and implementation science will be encouraged.

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6 GHP research & innovation priorities

To maximise the impact of the partnership, strategically important areas of unmet medical need have been identified within the GHP priority disease areas. The GHP programme will support all the elements required to develop and evaluate medical interventions against the key infectious diseases affecting Africa, through clinical science, research capacity development, and networking (national and international).

Target diseases: GHP will support research on HIV, TB, malaria, neglected infectious diseases (see footnote[7]), diarrhoeal diseases, lower respiratory tract infections, and emerging/re-emerging infections affecting sub-Saharan Africa. GHP's scope will also include antimicrobial resistance, climate-crisis-provoked changes in infectious disease incidence, and co-infections and co-morbidities (including co-morbid non-communicable conditions) associated with target diseases or their treatment.

6.1 Criteria for setting priorities

To maximise the impact of the partnership, the GHP SRIA will focus on strategically critical areas of unmet medical need. Mechanisms will be established to identify emerging priorities and opportunities. GHP will issue annual calls for proposals that reflect specific current research needs for target diseases and research capacity development.

Prioritisation will take account of the following criteria:

State of the product development landscape: For each disease area, the current state of clinical development of interventions for prevention, diagnosis, and treatment will be analysed.

Priority infections: Priority setting will be informed by analyses of disease burdens, changing patterns of disease, an inventory of unmet medical needs, and potential impact on a disease as a public health problem.

Disease burden and treatment/prevention priorities: These analyses will identify key knowledge gaps and need for new evidence.

Emerging opportunities of translational bottlenecks: GHP will focus on points in the translational and implementation pathway that delay the clinical development and uptake of novel interventions, supporting effectiveness studies, pharmacovigilance, and product-focused implementation research as required.

Strategic engagement: Committed to early engagement with WHO and other strategically important international and African partners, GHP will ensure global alignment of its policies and priorities and promote coordinated responses to evidence gaps and capacity-building needs.

Strategic portfolio: GHP will aim to develop and sustain a strategic portfolio across disease areas, types of intervention, and types of study. It will balance short-term and long-term priorities and funding across targeted diseases, with a view to supporting intervention research that is most likely to produce significant reductions in disease burden and overall mortality. In some areas, a portfolio approach will be used in prioritising and selecting different intervention candidates for funding.

Priority setting aims to balance the need for an over-arching framework to guide GHP's work with the flexibility to respond to emerging opportunities and health challenges. The priorities for targeted disease areas provided in this SRIA are not intended to be definitive or comprehensive and are likely to evolve throughout the programme as circumstances change. Therefore, an annual mechanism will be developed for

[7] 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. GHP's remit will cover 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. GHP's remit will not cover chromoblastomycosis and other deep mycoses, scabies and other ectoparasites, and snakebite envenoming.

reviewing and updating the research and associated research – capacity priorities.

The broad priorities outlined in this SRIA will form the basis of more specific three-year plans and annual work plans (Figure 2). Three-year plans, put together by a Scientific Advisory Committee with input from thematic stakeholder meetings, will outline medium-term priorities. Annual plans will include details of the specific calls for proposals for the following year.

Figure 2: *GHP Priority-setting mechanisms*

6.2 HIV

The key aim is to support research that helps sub-Saharan African countries to achieve, and ideally surpass, the 2030 UNAIDS 95-95-95 target – 95% of people with HIV know their HIV status, 95% of people with diagnosed HIV infection receive antiretroviral therapy, and 95% of people receiving antiretroviral therapy have effective viral suppression [5]. This would result in 86% of all people living with HIV in sub-Saharan Africa achieving effective viral load suppression, which provides clinical benefits for individuals and reduces HIV transmission at a population level. 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 [6] at risk of co-morbidities as they age.

Achieving these 95-95-95 targets will depend on people-centred and community-oriented approaches that facilitate timely diagnosis, ensure long-term retention in care, and achieve effective integration with other

services. There is considerable scope for novel approaches and the harnessing of innovative technologies to improve engagement with populations.

To enhance coverage and effective viral suppression, special attention will need to be paid to priority populations, such as infants, children, and pregnant and lactating women, and to all those who face stigma, discrimination, marginalisation, criminalisation, and other barriers to access to care. Long-term HIV management will also require an increasing focus on co-infections and co-morbidities, both of which will be associated with polypharmacy, which in turn will present a serious risk for drug—drug interactions. Furthermore, challenges with antiretroviral drug resistance are ongoing. The need for accessible and affordable methods to provide HIV drug resistance testing will be critical for the achievement of the third 95% of the triple 95 target for HIV.

Ultimately, control of the HIV pandemic will depend on reducing the numbers of new infections. GHP will emphasise the urgent need to assess novel delivery mechanisms for innovative biomedical methods of prevention, including antiretroviral-based interventions, broadly neutralising antibodies, and HIV vaccines. Effective implementation of such innovations will require innovative people-centred and community-oriented approaches. While studies of biological susceptibility remain important, understanding human behaviour, including uptake and adherence of novel HIV prevention methods, is paramount [7] [8].

6.3 Tuberculosis

In line with the Sustainable Development Goal to end the TB epidemic by 2030, GHP's key aim is to support research that will enable countries in sub-Saharan Africa to achieve WHO's End TB Strategy targets – by 2035 to reduce the number of TB-related deaths by 95%, to reduce the TB incidence rate by 90%, and to ensure that no families face catastrophic costs due to TB [9].

Achieving these ambitious targets will depend on greatly enhanced detection, treatment, prevention, and tracking of infection. Immediate goals include the development and evaluation of novel approaches for early diagnosis of active TB, shortening the duration of therapy, improving treatments for both drug-sensitive and drug-resistant TB, preventing relapse, reducing drug resistance, preventing long-term lung damage, and preventing latent TB infection progressing to active TB.

Ultimately, TB control will require affordable, short, effective, and well-tolerated treatments for all forms of TB (latent TB infection, drug-susceptible and drug-resistant TB disease, childhood TB, extra-pulmonary TB, sub-clinical TB, TB co-morbidity with other communicable diseases and non- communicable diseases, 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. Cheap, rapid, and accurate point-of-care diagnostic tests able to characterise drug resistance are urgently needed, as are effective vaccines.

Host-directed therapies that can shorten duration of therapy, improve treatment outcomes (reduce mortality and lung damage, prevent long-term functional disability), and act as adjuncts to WHO-recommended standard treatment regimens for drug-sensitive and drug-resistant TB are a high priority. Potential drug—drug interactions with HIV treatment should be examined, given high levels of HIV—TB co-infection. Research is needed on both pathogen and host biomarkers for disease activity, response to treatment, relapse, and prognosis [10] [11] [12].

GHP will support the evaluation of new TB treatment regimens for both drug-sensitive and drug-resistant TB, as well as adjunct host-directed therapies based on repurposed drugs, cellular therapies, and other immunomodulators. Given the relatively well-stocked pipelines for TB diagnostics and vaccines, increasingly there are opportunities for head-to-head comparisons and for adaptive and other innovative trial designs to evaluate these interventions.

Product-focused implementation research will be required to support the introduction of evidence-based interventions into policy and practice, including for integrated delivery of TB and HIV care. GHP will explore

the potential for partnerships with global initiatives supporting TB vaccine research, TB drug discovery, and early clinical development.

6.4 Malaria

In line with the Sustainable Development Goal to end the malaria epidemic by 2030, GHP aims to support research to enable countries in sub-Saharan Africa to achieve the targets of the WHO's Global Technical Strategy for Malaria 2016–2030 – to reduce malaria incidence and mortality rates by 90%, to eliminate malaria from at least 35 countries, and to prevent re-establishment of malaria in countries declared malaria-free [13].

Serious bottlenecks remain in providing full access to preventive interventions, diagnostic testing, and treatment. The greatest burden of disease affects children and pregnant women [14]. In addition, malaria constitutes one of the most important preventable causes of morbidity and mortality among adolescents living in high-transmission regions in Africa. Priority populations for malaria interventions include people with genetic haemoglobinopathies, immune-compromised individuals, migrants, and mobile populations. The safety, efficacy, and malaria drug interactions in patients also being treated for HIV and/or TB is a priority for study. Novel tools for the treatment and prevention of malaria in early pregnancy are missing.

In parts of Africa, malaria elimination strategies underway include the aim of radical cure of both *Plasmodium falciparum and Plasmodium vivax* asymptomatic infections in the entire population. However, current diagnostic tools are insufficient to differentiate these infections, and sensitive methods for the rapid diagnosis of asymptomatic malaria infections are urgently required.

Vector control has played a key role in reducing malaria burden over the past two decades; however, it is now hampered by increasing insecticide resistance. GHP will support studies on vector control, including novel and improved biomedical technologies for vector control, as well as use of combination disease control interventions and product-focused implementation and operational research.

GHP will support the evaluation of new drugs and drug combinations, for the prevention and treatment of both uncomplicated and severe malaria, with particular attention paid to children and pregnant and lactating women. Novel highly efficacious drugs with adequate safety profiles are needed to address resistance, and new antimalarial drugs with different modes of action are needed for malaria chemoprevention in the most vulnerable populations. As many symptomatic and asymptomatic individuals living in malaria-endemic areas also have infections other than malaria, it is increasingly important to understand interactions between antimalarial drugs and other treatments, such as antiretroviral and anti-TB drugs.

Field-testing of diagnostics to identify low-level infections and resistance mutations will be a key focus. The development and evaluation of new and improved malaria vaccine candidates, in partnership with other players in vaccine R&D, will be key to both improved malaria control and to malaria elimination, with the most promising vaccine candidates including sporozoite, blood stage, and transmission-blocking vaccines and combinations of vaccines.

GHP will support the evaluation of strategies for enhancing access to malaria diagnostics and drugs, and vaccines as they become available, as well as malaria elimination strategies, potentially incorporating improved methods of monitoring and surveillance and novel vector control interventions [15] [16] [17].

As the burden of malaria decreases in some countries, clinical studies that explore approaches to the syndromic treatment of acute febrile illnesses will be necessary, involving combined evaluation of new diagnostics and treatments adapted to the emerging profile of causal agents.

6.5 Neglected infectious diseases

The Sustainable Development Goals include a commitment to end the epidemic of neglected infectious diseases (NIDs). In 2015 alone, a billion people globally were treated for at least one of these diseases. Consistent with the principle that 'no one must be left behind', GHP will support research that leads to

progress in eliminating NIDs and ensuring that the delivery of health services meets the needs of those affected by such diseases [18] [19].

The state of disease control varies markedly among the NIDs. Dracunculiasis (guinea-worm disease) is close to eradication, while the number of cases of human African trypanosomiasis has fallen by more than 90%. However, diseases such as schistosomiasis, onchocerciasis, and other NIDs continue to affect hundreds of millions of people, generally society's poorest, 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 understanding the consequences of NID co-infection with malaria, TB, or HIV infection and in the context of non-communicable diseases. Methods of disease control vary, but there is a strong emphasis on preventive chemotherapy, effective disease management, and vector control. The efficacy and affordability of chemotherapeutics varies widely between diseases.

Where effective treatments already exist, the main priorities will be clinical trials of combination therapies against multiple diseases and implementation research to identify the most effective ways to deliver treatments and preventive chemotherapy in specific settings, including integration with other health services in people-centred universal health systems. For infections where treatments are inadequate or lacking entirely, early phase clinical trials will be required in the development of new and improved interventions.

Development of drugs, diagnostics, and vaccines will be a priority, along with improved understanding of the consequences of co-infection and co-morbidity. For vector-borne NIDs, GHP will also support studies on vector control and integrated disease control strategies. Finally, many NIDs persist due to fragile local health systems, which can be strengthened by programmes building better infrastructure for good clinical and regulatory practice.

6.6 Diarrhoeal diseases

The key aim is to support research that leads to the reduction of the burden of diarrhoeal disease in sub-Saharan Africa [20], thereby making a major contribution to the Sustainable Development Goal to end the preventable deaths of children under 5 years of age.

Epidemiological studies have provided a clearer picture of the microbiological causes of diarrhoeal disease in sub-Saharan Africa. Mortality has fallen without a corresponding fall in morbidity, reflecting a shift from severe life-threatening diarrhoeal episodes towards recurrent disease. The wider introduction of rotavirus vaccines has been responsible for some, but not all, of this shift. Persistent enteric infections contribute to abnormalities in gut function (enteropathy), affecting nutrient uptake and response to oral vaccines, thereby creating a vicious circle of diarrhoea and malnutrition leading to stunting and delayed development [21] [22].

New vaccines are urgently needed as cost-effective ways to control diarrhoeal diseases, as are innovative strategies to optimise and deploy available vaccines for the control of these conditions. Vaccines against other viral and bacterial pathogens are now entering clinical trials. GHP will prioritise the following diarrhoeal disease-causing pathogens for which vaccines are either available or are in advanced stages of development: rotavirus, *Shigella*, cholera, enterotoxigenic *E. coli, Cryptosporidium*, and norovirus. GHP will aim to advance the clinical pipeline of vaccines against these diarrhoeal diseases.

There also remains a significant need for point-of-care diagnostics for diarrhoeal pathogens and for enhanced laboratory capacity for the characterisation of infections.

6.7 Lower respiratory tract infections

The key aim is to support research on interventions that will reduce the burden of lower respiratory tract infections in sub-Saharan Africa, contributing to the Sustainable Development Goal to end preventable deaths among new-borns and children under 5 years of age, as well as to enhance the survival of older people and immunocompromised individuals [23].

The incidence of severe pneumonia is higher in the African region (30% of the global burden of severe childhood pneumonia) and it is the most common reason for adult hospitalisation in sub-Saharan Africa [24]. Co-morbidities (poor nutrition and HIV infection), environmental factors (exposure to indoor air pollution, biomass fuel, and smoke), and poor living conditions are among the main risk factors for pneumonia and severe pneumonia. There is a dearth of information about specific causes of lower respiratory tract infections in many settings.

One of the important priorities is the need for new point-of-care diagnostics, including simple methods to identify patients requiring antibiotics. Evidence on effective antibiotic regimens is sparse and antibiotic resistance is a major and growing problem. Key research priorities are the improvement of diagnosis of lower respiratory tract infections through evaluation of optimised clinical algorithms; development of biomarkers to differentiate lower respiratory tract infections from other diagnoses; evaluation of rapid multiplex platforms for diagnosis of bacterial, fungal, and viral infections; and design of innovative imaging methods that are suitable for use in LMIC health facilities.

Trials of shorter duration antibiotic treatment for community-acquired lower respiratory tract infections among adults and children (living with HIV and HIV-negative) remain a top priority, along with evaluation of host-directed therapies to strengthen host immunity and to improve treatment outcomes. Low-cost methods for oxygen delivery to treat children with hypoxaemia (low blood oxygen levels) are required. Vaccines, including maternal vaccines, will remain central to disease control and prevention. Development of these vaccines, evaluation of the impact of recently introduced routine vaccines on the aetiology and severity of lower respiratory tract infections, and research on implementation models and on the scale-up of existing vaccines will also be priorities for GHP [25].

Priority populations for intervention development and evaluation will include children, immunocompromised people living with HIV, older people, those hospitalised with lower respiratory tract infections, and people living in hard-to-reach communities who need treatment options. Priority pathogens, for which vaccines either exist or are in advanced development and affect particular population groups include: group B streptococci, respiratory syncytial virus (RSV), and pneumococcus in neonates; RSV, pneumococcus, and cytomegalovirus in children; and pneumococcus in adults.

6.8 Emerging/re-emerging infectious diseases

GHP's key aim is to enable countries in sub-Saharan Africa to prepare for, prevent, and effectively manage infectious disease outbreaks. GHP will continue the EDCTP Emergency Funding Mechanism that has allowed rapid mobilisation of research funding without a call for proposals in exceptional and duly substantiated public health emergencies that are unforeseen and present a serious and immediate risk to human health. Emerging and re-emerging infectious diseases with epidemic potential are a persistent threat to global health security, as well as to public health in many African countries [26], and to socioeconomic development. Although infections such as Ebola, Lassa fever, plague, and yellow fever are native to sub-Saharan Africa, other infectious disease threats with epidemic potential can be imported from other continents, as the COVID-19 pandemic has underscored.

It is vital to strengthen capacity for preparedness during peace time to address emerging/re-emerging infectious disease and to undertake rapid evaluation of interventions in clinical trials when future outbreaks occur and treatments are inadequate or lacking entirely [27]. Increasingly fine-grained evaluation in different settings of the safety and efficacy of new health technologies is needed to address genetic factors, local environmental exposures, nutritional status, and other contextual factors. In parallel, strengthening surveillance capabilities and systems to detect such outbreaks at an early stage and strengthening laboratory systems to rapidly confirm diagnoses are of high priority. GHP implementation of competitive fellowships for epidemiologists, statisticians, clinical researchers, and disease modellers to assemble and analyse real-time data on zoonoses, and other diseases that have epidemic potential, will inform critical public health responses and aid in the planning of clinical trials of vaccines and treatments, as well as novel diagnostics and prognostics. Partnering with CDC-Africa, WHO, national public health institutes, and others, GHP aims to

contribute to the development of a tailored sub-Saharan Africa public health approach to emerging/re-emerging infectious disease that addresses health care systems capacity and resilience, technology supports for home-based self-care, impact on the health care workforce, and displaced health care delivery for GHP priority infectious diseases.

Given GHP's focus on the development and uptake of new or improved health technologies, including vaccines, to benefit vulnerable populations in sub-Saharan Africa, it will strengthen project engagement with beneficiaries and communities. To ensure that disadvantaged groups that are often excluded from pivotal clinical trials, with resultant delayed access to beneficial newly developed health technologies, the GHP will have an enhanced emphasis on community engagement, social science involvement, and good participatory practice. To strengthen the science, communities will have opportunities to inform research study design, trial conduct, and interpretation of findings. The Partnership will follow the principles for good participatory practice developed by WHO for use in emergency outbreak settings [28] [29] and specifically for COVID-19-related clinical studies [30].

6.9 Climate crisis-related infectious disease

GHP will work with other global health partners and national counterparts to determine how best to strengthen response capacities and minimise the health impacts provoked by climate crisis-related increases in the incidence of infectious diseases.

The climate crisis is affecting the distribution and severity of infectious disease, with growing evidence of associations between climatic conditions and infectious diseases. The changing climate is affecting the range of pathogen vectors and leading to population movements, increasing the risks of disease transmission. Worldwide, the combined impacts of rapid demographic, environmental, social, technological, and other changes are contributing to increases in the prevalence of many infectious diseases, including some newly circulating ones.

Research has a critical role to play in identifying likely future impacts and evaluating public health responses. Many adaptive measures responding to the climate crisis have additional benefits, with rebuilding and maintaining public health infrastructure often viewed as the most important, cost-effective, and urgently needed adaptation strategy. This includes public health training, more effective surveillance and emergency response systems, and sustainable prevention and control programmes, including those targeting vector control [31].

6.10 Antimicrobial resistance

Antimicrobial resistance is already having a major impact in sub-Saharan Africa, compromising the use of multiple antibiotics and antimalarial, antiviral, and antifungal therapeutics [32] [33].

GHP will address antimicrobial resistance in sub-Saharan Africa, taking into consideration the specific environmental and epidemiological factors that influence the spread of antimicrobial resistance in this region. Special emphasis will be put on those poverty-related- and neglected infectious diseases most affected by antimicrobial resistance and posing the greatest health security risks.

Novel treatments for diseases within GHP's scope will help to combat antimicrobial resistance. Also key is the development of better diagnostic tools, ideally point-of-care diagnostics, to determine susceptibility/resistance to antibiotics and to distinguish bacterial and viral infections so that unnecessary use of antibiotics can be avoided. Antibiotic stewardship and promoting the use of new e-health technologies will help reduce antibiotic consumption.

Development of new vaccines and optimised and other host immune interventions, and optimisation of existing ones will reduce the burden of diseases treated with antibiotics but may also drive changes in disease aetiology. Studies will be required to support updating of treatment guidelines, in light of evolving burdens of disease and changing patterns of antibiotic susceptibility.

6.11 Non-communicable diseases

Although this SRIA does not include a separate programme specific to non-communicable diseases, it will support co-morbidity studies that contribute to WHO's vision of a world free of the avoidable burden of non-communicable diseases, as outlined in the WHO Action Plan for the Prevention and Control of Non-communicable Diseases [34].

To ensure it does not spread its resources too thinly to achieve impact, GHP will retain a core focus on infectious disease, while acknowledging that infectious and non-communicable diseases cannot be considered in isolation. Infections may increase the risk of chronic conditions (or vice versa) and co-morbidities and their associated therapies may influence the effectiveness or safety of treatments for infectious diseases.

GHP will therefore support studies on interventions to prevent or treat non-communicable diseases in patients with infectious disease (or vice versa). Infections that have a direct causal link to non-communicable diseases, including co-morbidities associated with infectious diseases, will be within the GHP scope.

Recognising the importance of patient-centred approaches to healthcare, GHP will also support studies examining how prevention or treatment of non-communicable diseases can be integrated into models of care established for the management and treatment of infectious diseases.

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7 Mechanisms of support

The GHP programme will use a range of funding mechanisms as necessary to achieve its objectives.

Support for trials and related studies: Support will be provided for clinical research activities and clinical trials, as well as other epidemiological or observational studies. Funding will also cover additional research studies embedded within a trial as well as integrated support for capacity development of researchers, institutions, and sites in sub-Saharan Africa, and networking activities.

Support for research capacity building and networking: Specific funding will be provided to (1) strengthen clinical research capacities in sub-Saharan Africa; (2) promote networking and collaboration both between European and African researchers and among African researchers, institutions, and sites (including support for regional Networks of Excellence in sub-Saharan Africa); (3) foster collaboration with public and private funders; and (4) promote communication with policy makers and the public to create awareness of the importance of research to reduce poverty and attain the SDGs. Support will be provided to enable sub-Saharan African countries to develop robust research governance (including research support structures, ethical and regulatory frameworks) for conducting clinical trials with long-term sustainability.

Personal support: Funding will be provided to support activities promoting the career development of junior and senior researchers from sub-Saharan Africa, training and mentorship, and mobility of individual researchers and research staff.

GHP's integrated approach to clinical research funding and implementation will ensure that all the targeted diseases are tackled with optimal tools and through collaborative research networks (Figure 3).

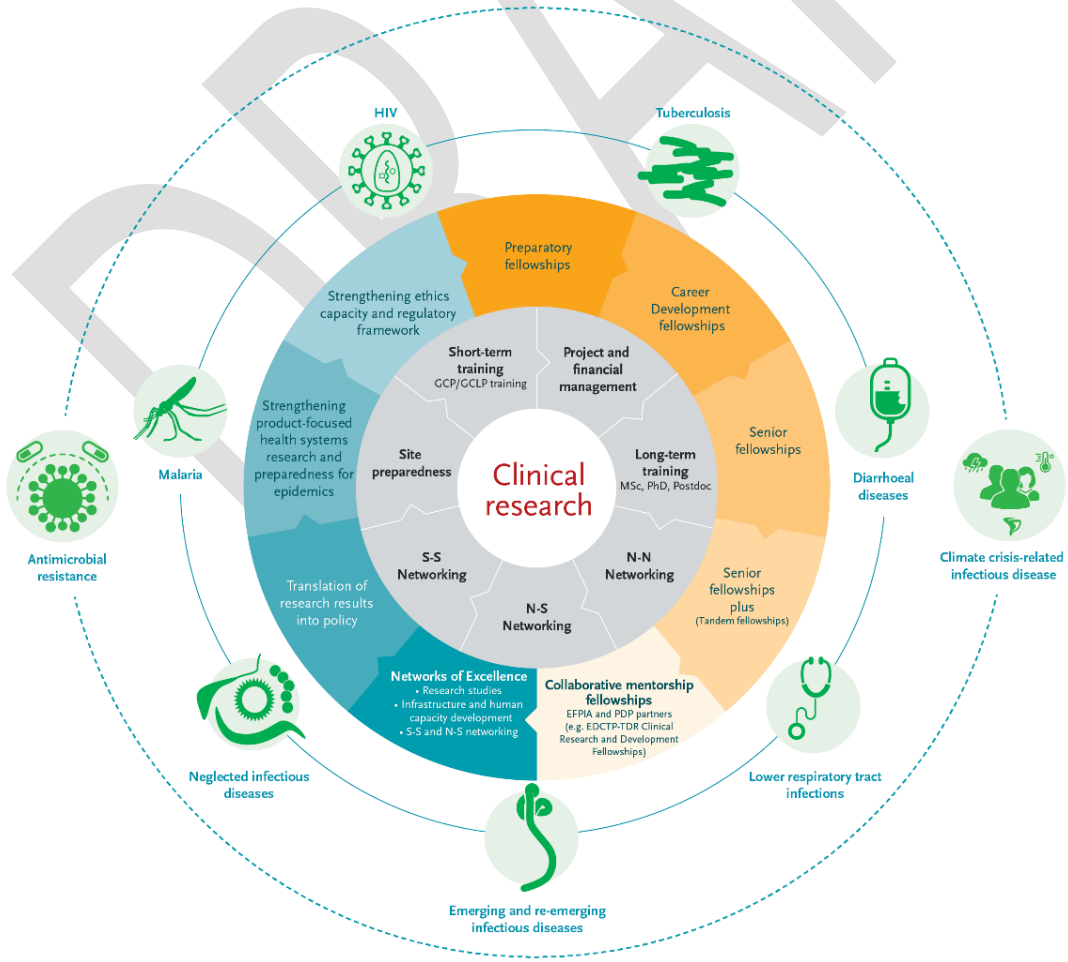

Figure 3: *GHP's integrated approach.*

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8 Expected outcomes and impact

Through its support of international collaborations conducting high-quality clinical trials and research capacity building, GHP will make significant contributions to the reduction of the individual, social, and economic burden of poverty-related infectious diseases in sub-Saharan Africa.

GHP will support research to accelerate the development and implementation of interventions to prevent, identify, treat, and track poverty-related diseases affecting sub-Saharan Africa, including HIV, TB, malaria, diarrhoeal diseases, respiratory infections, neglected infectious diseases, emerging and re-emerging disease, antimicrobial resistance, and increases in the incidence of climate crisis-related infectious disease. Ultimately, all populations stand to benefit, but GHP will have a disproportionately positive impact on the health of women, new-borns, children, and adolescents through expanding their access to proven biomedical interventions. In the longer term, healthier populations will be important drivers of economic growth and national prosperity.

The programme will enhance the research base in both Europe and sub-Saharan Africa. European science will benefit from a more coordinated and integrated approach, uniting groups with common interests in infectious disease and ensuring research is more tightly coupled to national needs in sub-Saharan Africa. Research in sub-Saharan Africa will benefit from links to globally leading researchers and access to the most up-to-date knowledge, research tools, and methodologies.

GHP's primary output will be evidence that has the potential to influence international and national health policy and practice. However, its impact will extend beyond generation of data to inform policy.

Evidence: GHP will generate high-quality research data relating to the safety, efficacy, and impact on overall health of new and improved medical products/interventions, and on how they can be implemented most effectively in sub-Saharan Africa.

Research capabilities: By developing clinical research capacity, ethics review, and regulatory and legal capacities in sub-Saharan Africa countries, GHP will enhance the ability of such countries to design, conduct, and analyse the results from clinical research studies, including multi-site and multi-country studies.

African collaboration: By catalysing regional collaboration, GHP will ensure more coordinated and effective responses to infectious diseases across borders, maximising the impact of local investments.

Coordinated responses: By encouraging greater coordination and alignment of national research efforts, GHP will seek to maximise the impact of European investments in global health research.

Global synergies: Partnerships with public and private organisations (both for-profit and non-profit) will ensure that best use is made of the clinical research capacity established in sub-Saharan Africa to accelerate the evaluation of new medical interventions.

Strengthened health systems: Through partnerships with development agencies and related organisations, GHP will contribute to strengthened universal healthcare systems delivering more integrated people-centred care and contributing to universal health coverage.

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GHP objectives and expected outcomes

Objectives	Outcomes
Health interventions Evaluate new or improved health interventions against poverty-related infectious diseases and their interaction with non-communicable diseases	• Advanced clinical evaluation of vaccines, diagnostics, and treatments • Focus on overall health in addition to other intermediate outcomes • Influence on national and international policy guidelines • Enhanced implementation of evidence-based interventions.
Collaboration and capacity development Increase EU–Africa collaboration to build capacity to conduct clinical trials and implementation research according to ethical principles and regulatory standards	• Strengthened infrastructure for clinical research and implementation in sub-Saharan Africa • Increased clinical research capacity and scientific leadership, including advancement of women scientists • Enhanced ethics and regulatory capacities.
European coordination Improve coordination, alignment, and integration of European national research programmes	• More closely aligned national research programmes and activities on poverty-related diseases, at scientific, management, and financial levels. • Increased number of co-funding programs in Europe.
South–South collaboration Enhance scientific collaboration and international cooperation across sub-Saharan Africa	• New and strengthened international networks sharing good practice, extending capacity, and creating platforms for multicentre trials • More closely aligned national research programmes and activities on poverty-related diseases • More closely aligned regulatory mechanisms across countries, with increased common regulatory reviews of new products.
Partnership building Increase international cooperation with public and private partners	• Aligned strategy with key global players • Increased cooperation and additional joint actions with other public and private funders, including WHO initiatives.

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EU cooperation Increase interaction with other EU initiatives, including those linked to development assistance	• Increased cooperation and additional joint actions with development partners • Increased awareness, endorsement, and acknowledgement of GHP.

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