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Global Health
EDCTP3

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Strategic Research and Innovation Agenda

Global Health EDCTP3 Joint Undertaking

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1. Executive summary

The Global Health European & Developing Countries Clinical Trials Partnership (EDCTP)3 Joint Undertaking (Global Health EDCTP3), which is the European Union (EU)–Africa global health partnership, represents the third programme of the EDCTP. Its Strategic Research and Innovation Agenda will support international collaborations accelerating the clinical evaluation and implementation of interventions against poverty-related infectious diseases including the neglected ones 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, with equity of access as a key driver of Global Health EDCTP3's work.

Infectious diseases remain a major cause of death, disability, and ill health in sub-Saharan Africa. Diseases such as human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), 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 Africa is also at risk of emerging and re-emerging infections, such as Ebola, Marburg, Lassa fever, yellow fever and, most recently, SARS-CoV-2, which imperil global health security. The alarming rise of antimicrobial resistance is compromising available treatments and undermining multiple branches of medicine that rely on effective therapies for infection control. Changing patterns of disease driven by the climate crisis and environmental degradation exacerbate these challenges.

Combating infectious disease will be central to achieving Sustainable Development Goal 3 (SDG3), to ensure healthy lives and promote well-being for all at all ages. Furthermore, preventing and treating 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.

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 to develop and evaluate new products are therefore required across public and private sectors, national governments, and regional and global agencies.

Initially set up in 2003, EDCTP has established itself as the focal point of cooperation between the EU and sub-Saharan Africa in research on the control of infectious diseases and the development of new interventions. Through its support of EU-sub-Saharan Africa research partnerships, the consecutive EDCTP programmes (EDCTP1 and EDCTP2) 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 Global Health EDCTP3 programme will build on and extend the platforms created by EDCTP, including through secondary analysis of data collected under the previous programmes.

Scope of the Global Health EDCTP3 programme

The Global Health EDCTP3 programme will focus on the major infectious diseases and linked co-morbidities threats facing sub-Saharan Africa – HIV, TB, malaria, lower respiratory tract infections, diarrhoeal disease and the neglected, emerging and re-emerging infections, with special reference to antimicrobial resistance, and the impact of the climate crisis on infectious diseases. Priority evidence gaps have been identified, and the programme will maintain the flexibility to respond to emerging challenges and opportunities through annual reassessments.

The Global Health EDCTP3 programme will focus on all stages of clinical evaluation, but particularly later-stage (phase III and phase IV) studies, including product-focused implementation studies, in recognition of their growing importance as bottlenecks in application of interventions. It will have a particular focus on equity through the inclusion of vulnerable population groups, including children, adolescents, pregnant and lactating women, older persons, and people with co-morbidities (including non-communicable conditions). Currently, these groups are often excluded from clinical trials of new products and therefore do not benefit initially when new interventions become available. It will also put emphasis on ensuring efficient links between funded activities and Ministries of Health in the countries where research takes place and to regulatory bodies and regional international organisations, including Africa Centres for Disease Control and Prevention (Africa CDC) and the WHO regional office for Africa, to further facilitate rapid translation from research to policy.

Capacity building will be an integral part of Global Health EDCTP3-funded studies. In addition, specific funding will be provided to improve the technical infrastructure for health research of countries in sub-Saharan Africa, and to utilise the intellectual capacity in the region to develop the next generation of African scientific leaders. International networking, North–South, South–South and North-North, will be promoted to foster the exchange of knowledge and expertise.

The involvement of cross-cutting themes and diverse actors in collaborative efforts across sectors, as part of the Global EDCTP3 programme, will be instrumental in safeguarding public health in sub-Saharan Africa. It will help in addressing critical health challenges, including the emergence of infectious diseases and combating antimicrobial resistance, among others.

Intended impact of the Global Health EDCTP3 programme

The Global Health EDCTP3 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 through implementation research providing policymakers with key evidence to inform their decision-making to reduce the disease burden. The aim is that all populations in sub-Saharan Africa benefit from the Global Health EDCTP3 activities.

The Global Health EDCTP3 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 on research on poverty-related diseases in sub-Saharan Africa. Strategic alliances and partnerships with other global bodies will further promote coordination, integration, and complementarity of activities. The programme will also play a pivotal role in promoting alignment of research activities in sub-Saharan African countries, notably through the activities of the EDCTP Africa office.

Through these efforts, the Global Health EDCTP3 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. Though not the main purpose of the Global Health EDCTP3 programme, lessons learned during this process may also inform public health in Europe.

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 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. Innovative models are required to advance the development of new interventions against diseases predominantly affecting LMICs, 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 relevant products can reach neglected or vulnerable priority populations – such as children, pregnant women, and 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 & Developing Countries Clinical Trials Partnership (EDCTP) programmes. Since 2003, the two consecutive EDCTP programmes have carried out pioneering work by supporting clinical trials conducted collaboratively by research 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 clinical trials, and especially phase III and phase IV studies without excluding early stage trials, 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 of products 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. It will also encompass partnerships with adjacent sectors and stakeholders to collaborate on mitigating the specific burdens associated with each disease and as an opportunity to identify and tackle social determinants of health. Finally, this SRIA will also consider important advances

and lessons learnt for clinical research studies and related technology platforms in the response to the COVID-19 pandemic and Mpox.

3. Vision, mission, and objectives

The EU-Africa Global Health EDCTP3 Joint Undertaking (Global Health EDCTP3) – the third programme of the European & Developing Countries Clinical Trials Partnership (EDCTP) – 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, including the neglected, emerging, and re-emerging 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 interventions to prevent, identify, and treat infectious diseases and emerging/re-emerging infections in sub-Saharan Africa, with the overarching goal to reduce overall mortality and morbidity.

Overall objectives

The Global Health EDCTP3 programme 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 Global Health EDCTP3 programme has five specific objectives:

(1) Advance biomedical interventions towards improved overall health

Global Health EDCTP3 will support clinical studies on products and interventions designed to prevent, detect, and treat priority diseases, and on technological innovations that facilitate disease control, research or access to care. These will include diagnostics, vaccines, novel drug treatments and formulations, and new or improved therapeutic regimens. Global Health EDCTP3's scope will encompass rigorous clinical trials of interventions and innovative study designs, as appropriate.

Clinical trials and other intervention studies will make up the bulk of the Global Health EDCTP3 portfolio (Figure 1). Global Health EDCTP3 will put emphasis on phase III and phase IV pharmacovigilance and post-licensing pragmatic effectiveness trials and product-focused implementation research[1]. This will include scope for a wide variety of studies to inform national decision-making to reduce overall mortality and morbidity, including modelling studies and pharmaco-economic analyses. Further attention will also be given to the implementation of large-scale, multi-centre clinical trials that are set up under efficient trial designs such as adaptive platform trials and common protocols.

Global Health EDCTP3 will also support preparatory studies essential for the design and conduct of trials. These could include epidemiological studies to generate baseline data on disease incidence or burden, 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. This also includes aspects relating to the identifying of social determinants of health.

A focus in the design of clinical studies will be that explicit attention is given to overall health effects, sex and gender, wider community engagement and empowerment the contribution of social sciences, and ethical considerations, including strict processes to ensure patient safety in line with the Global Patient Safety Action Plan.

[1] "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.

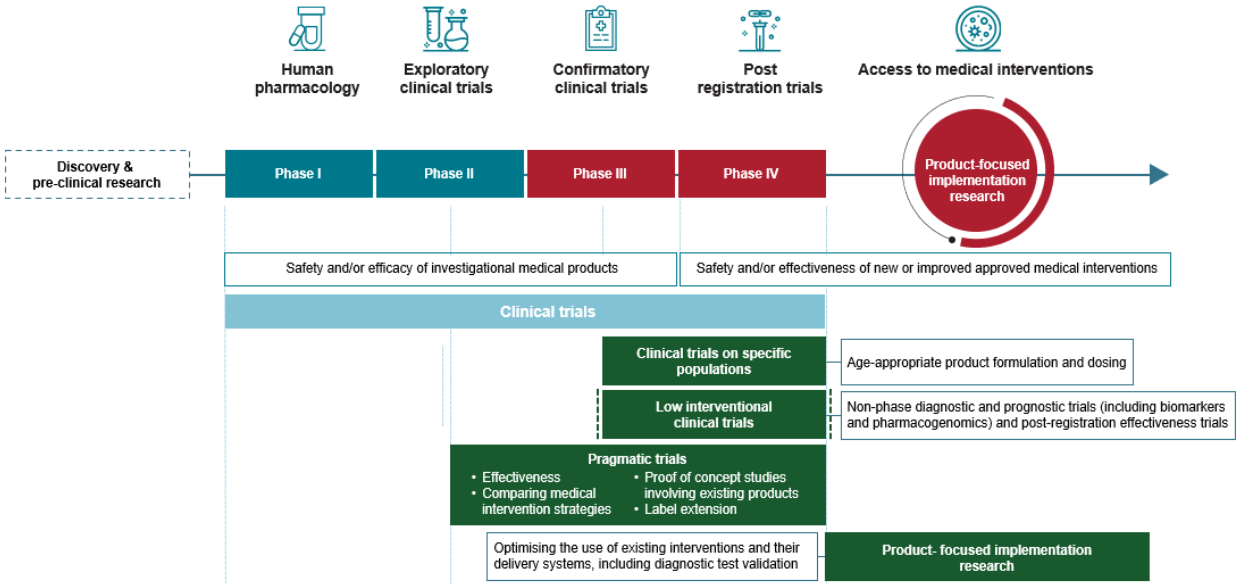


Figure 1 Types of clinical studies to be supported by Global Health EDCTP3.

(2) Research capacity development

Global Health EDCTP3 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 on 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 all career steps fellowship and grant 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), building on the achievements of the existing EDCTP Regional Networks of Excellence and long-term trial site development (e.g. for vaccines) and staff exchange and mentorship programmes. Global Health EDCTP3 will ensure 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 will be conducted to raise awareness of the importance of investing in science. Communication with the public will be promoted to ensure involvement in and understanding of the value of research studies.

Global Health EDCTP3 will place high priority on strengthening the capacity of investigators in 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 will be to develop individuals, institutions, 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 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, Global Health EDCTP3 will invest in both people and research 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 large-scale implementation, human capital is a prerequisite. Personal support schemes will play a key role in developing the next generation of African scientific leaders. Global Health EDCTP3 will have a strong focus on early and mid-career research training (Master's and PhD, MD) and a comprehensive scope of postdoctoral and follow-on career grants for senior fellowship schemes, as well as on needs-driven short-term training, mentoring, and exchange. As well as supporting training in practical research techniques, study design, and research conduct, Global Health EDCTP3 will also develop expertise in laboratory and research institution management.

Global Health EDCTP3 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) Global Health EDCTP3 will develop mechanisms to increase the capacity of researchers from French- and Portuguese-speaking countries to develop high-quality research proposals.

Global Health EDCTP3 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, Global Health EDCTP3 will build the capacities of national health research authorities to continue supporting researchers and research institutions after Global Health EDCTP3 funding.

(3) Enhanced coordination

Global Health EDCTP3 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.

Global Health EDCTP3 will promote *North—North coordination* and collaboration 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 Global Health EDCTP3 framework.

Global Health EDCTP3 will broker productive and sustainable partnerships – promoting networking and building relationships with multiple private- and public-sector organisations. Global Health EDCTP3 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.

Global Health EDCTP3 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, Global Health EDCTP3 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 Global Health EDCTP3 Forum) will provide a platform for scientists from Europe, Africa, and elsewhere to share findings and ideas, and to establish collaborative links.

Global Health EDCTP3 will promote *South-South coordination and collaboration* through networking, joint projects, and pooling of resources. Countries will be encouraged to develop calls for proposals together and with European Participating States, facilitated by the Global Health EDCTP3 framework.

Global Health EDCTP3 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.

At the global level, Global Health EDCTP3 is committed to aligning with the Lusaka Agenda's key shifts by:

i) Making a stronger contribution to primary health care (PHC) by effectively strengthening systems for health, through the design of annual work plans and calls in such a way that RIAs and CSAs stimulate integrated delivery of services, e.g. by focusing on cross-platform technologies, community-level solutions and integration of new technologies in countries' health systems.

ii) Playing a catalytic role towards sustainable, domestically-financed health services and public health functions, by supporting the transition of balance and focus of external vs domestic resource mobilisation financing relevant to R&D. Global Health EDCTP3 will consider aligning funding calls with other GHIs (e.g. with Global Fund country and regional grants) and further stimulate African member countries to co-invest in domestic (capacity for) health R&D.

iii) Strengthening joint approaches for achieving equity in health outcomes, particularly with regard to equitable access to new and necessary products. Beyond clinical trials, Global Health EDCTP3 further consideration will be given to delivery with a strong focus on the most vulnerable and marginalised, as well as support integrated services for unreached communities where relevant, and require that grant applications to show how they actively engage local stakeholders. In addition, Global Health EDCTP3 will adopt a systematic end-to-end approach that includes namely: a. Contributions to closing the gaps on prevention and treatment options for underserved populations, such as infants, children, pregnant and lactating women, elderly

people and marginalized and hard-to-reach populations, as a prerequisite for strengthening the clinical development of new or improved health technologies for poverty-related and neglected infectious diseases. b. Support to information systems enabling countries to move from undifferentiated treatment and control strategies to approaches that are tailored to each region, district, or even neighbourhood based on factors such as incidence, access to care, and seasonality of disease. c. Promotion of technology transfers and capacity building to enable regional and local manufacturers to position on the market of quality-assured pharmaceuticals products so as to promote supply security.

iv) Achieving strategic and operational coherence by aligning where possible (administrative) processes and resulting demands on country actors with those of other Global Health Initiatives (e.g. more integrated approaches to allocative decisions across health; reduction of transaction costs harmonising reporting with national plan metrics, putting funding on-budget etc), as well as through the requirement that grant applications show how they respond to those plans in the countries where activities are proposed to take place and potentially beyond. Furthermore, transitioning the balance and focus of external vs DRM financing is relevant in the R&D space. However, it was noted that the "public good" elements/network effects of research and knowledge generation also presents benefits from linking across international, regional and national R&D efforts. Various R&D, clinical networks and information platforms are being established, with a risk of continued fragmentation and missed opportunities for interoperability and more sustainable infrastructure. Global Health EDCTP3 aims to align with investors in R&D/clinical trials and to collectively support stronger regional leadership (including domestic financing), improve inter-network collaboration and better linking of up and downstream activities.

v) Coordinate approaches to products, research and development and regional manufacturing to address market and policy failures in global health by increased coordination around the R&D ecosystem, within and beyond Global Health EDCTP3; by putting more emphasis on regional R&D and not just manufacturing, as there is a need for developing a regional innovation ecosystem, capable to create IP. Furthermore, coordinated tracks or portfolios will be developed together with countries, GHIs and other stakeholders for addressing key health problems within Global Health EDCTP3's mandate in which subsequent phases such as product development, clinical trials, post-marketing research and implementation are planned with joint funding (e.g. PDPs upstream of Global Health EDCTP3 funding, Gavi or Unitaid downstream of Global Health EDCTP3 funding) and in which reaching a predefined milestone triggers funding for the next phase.

(4) Strengthen capacity for epidemic preparedness

Global Health EDCTP3 aims to strengthen capacity in sub-Saharan Africa for epidemic preparedness. This requires an effective and rapid research response to develop and evaluate essential diagnostics, vaccines and therapeutics for early detection and control of emerging diseases of epidemic potential. For this, surveillance and laboratory capabilities are essential. Also, appropriately designed cohorts can play a key role in surveillance.

Clinical trial networks, which will be supported through Global Health EDCTP3, will allow testing interventions fighting an infectious disease outbreak of epidemic potential or that has evolved into an epidemic. In recent years, adaptive platform trials have emerged as a promising approach to quickly evaluate a range of interventions, which may be particularly relevant in an epidemic situation.

The Covid-19 pandemic has demonstrated how important it is to rapidly share data and to have data available according to the FAIR principles: findable, accessible, interoperable, and reusable. Global Health EDCTP3 will also provide support to dedicated data platforms.

In addition to the support for facilities and structures supporting epidemic preparedness research, Global Health EDCTP3 will invest in specific training, such as for epidemiologists. The above-mentioned support for alignment of the ethics and regulatory capabilities of sub-Saharan African countries facilitates smooth implementation of essential clinical studies, which are needed especially during an epidemic outbreak.

When a specific outbreak occurs, Global Health EDCTP3 will resort to emergency funding mechanisms, to make financing rapidly available.

(5) Networking, 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, universities, research institutions, 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. Global Health EDCTP3 aims to work with a broad range of public and private partners to attract additional investment, maintain, when deemed relevant by experts, the assessment of a potential beneficiary as essential (essentiality status of partners not yet part of the EDCTP Association or Horizon Europe) to exploit opportunities for high-quality clinical research, and maximise the impact and cost-effectiveness of integrated approaches to research.

Global Health EDCTP3 will consolidate its investment in late-stage product development, whilst not excluding early-stage evaluations, 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, as per the Global Health EDCTP3 contributing partners guidelines.

Global Health EDCTP3 aims to support in-country and regional networking, and promote international cooperation to share good practices, expand capacity, build platforms for multi-centre trials and create synergies between local researchers. South–South networking will build on existing regional Networks of Excellence and consortia for epidemic preparedness. 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.

Global Health EDCTP3 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 neglected infectious diseases (NIDs) and emerging infections – will further galvanise South–South collaboration. Additional working groups could be considered.

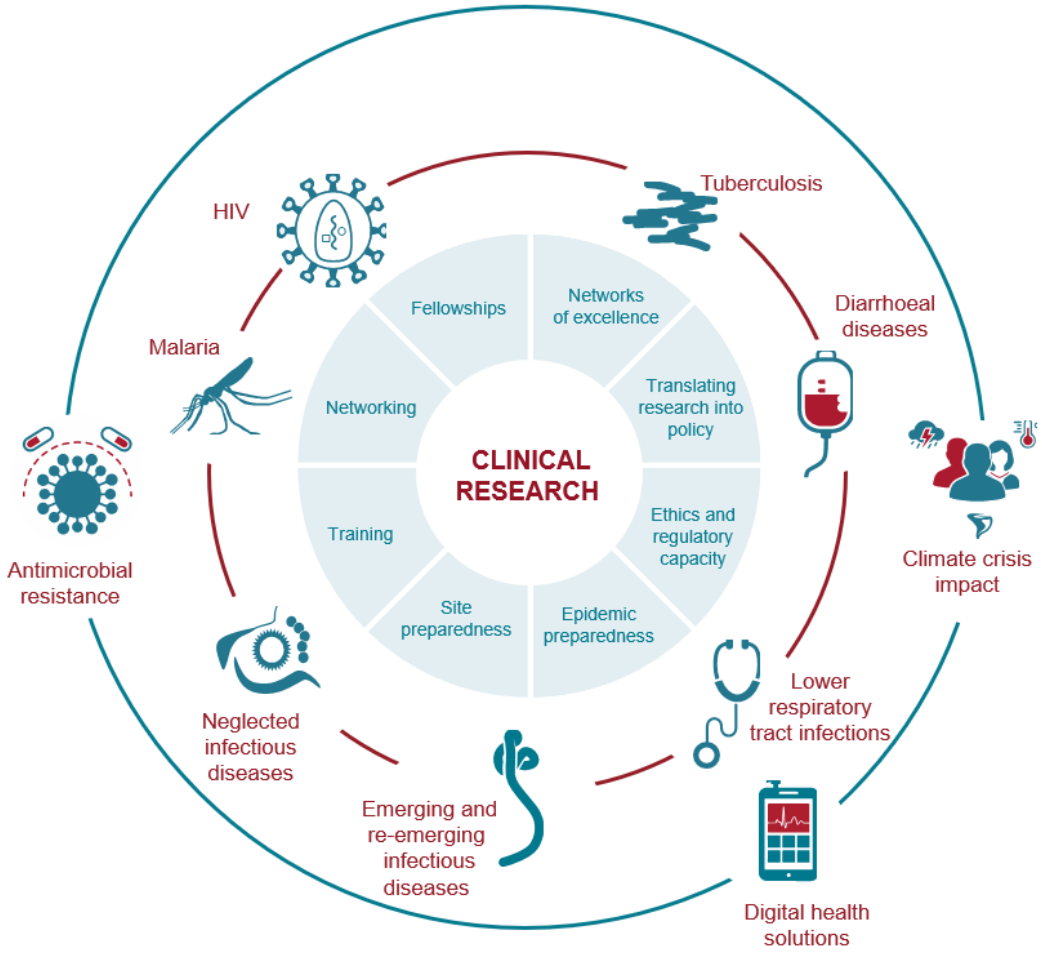


Figure 2 Global Health EDCTP3's integrated approach.

4. Expected outcomes and impact

Through its support of international collaborations conducting high-quality clinical research and intervention studies (Figure 2) and building research capacity, Global Health EDCTP3 will make significant contributions to the reduction of the individual, social, and economic burden of poverty-related infectious diseases, including neglected infectious diseases in sub-Saharan Africa.

Global Health EDCTP3 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 diseases, antimicrobial resistance, and increases in the incidence of climate crisis-related infectious diseases. Ultimately, all populations stand to benefit, but Global Health EDCTP3 will have a disproportionately positive impact on the health of women, newborns, 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.

Global Health EDCTP3'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 the generation of data to inform policy.

Evidence: Global Health EDCTP3 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 African countries, Global Health EDCTP3 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, Global Health EDCTP3 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, Global Health EDCTP3 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, Global Health EDCTP3 will contribute to strengthened universal healthcare systems delivering more integrated people-centred care and contributing to universal health coverage.

Global Health EDCTP3 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 • Registration of new health interventions • Focus on overall health in addition to other intermediate outcomes • Focus on sex and gender differences in responses to existing and new interventions • 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 programmes in Europe • Increased North-North collaboration around global health-related research.
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.
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 Global Health EDCTP3.

5. Development of the Strategic Research and Innovation Agenda

The Global Health EDCTP3 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 (without the exclusion of early-stage clinical trials) 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 exposure to pathogens.

This SRIA will address these issues, describing approaches to tackle them. 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 contributing to

identifying environmental and genetic factors that affect the effectiveness of interventions and their impact on overall health. It will also assist in 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.

Based on input from the Global Health EDCTP3 Stakeholders' Group and Scientific Committee, the Governing Board will decide on an update of the SRIA.

6. Guiding principles

In developing its activities, Global Health EDCTP3 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. Global Health EDCTP3 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: Global Health EDCTP3 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 Global Health EDCTP3, so by collectively contributing to a joint programme that is greater than the sum of its parts, Global Health EDCTP3 participating states can align and strengthen actions to achieve an agreed common vision and set of priorities. In addition, a more sustainable funding structure could be explored with participating states, with possible domestic resource mobilisation and strengthening of domestic funding structures and agencies.

Ensuring relevance to societal challenges: The partnership will seek input from multiple stakeholders to identify key infectious disease health challenges. This will ensure that Global Health EDCTP3 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 Global Health EDCTP3's work. This encompasses populations often excluded from clinical studies but with major unmet medical needs – including pregnant and lactating women, newborns, children, adolescents, other vulnerable and neglected populations, and people with co-infections and co-morbidities.

Promoting people-centred approaches: Global Health EDCTP3 will have a strong interest in ensuring that interventions are implementable within people-centred universal health systems.

Engaging and empowering communities: Projects funded by Global Health EDCTP3 will support meaningful community engagement throughout the research life cycle, considering the co-design of the research, determining together the key questions that should be addressed,

the best ways of answering them and sharing results from the research with community participants.

Supporting product-focused implementation research: Global Health EDCTP3 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 while also continuing to monitor the real-life effect on overall health of newly implemented health interventions.

Promoting local innovation: Global Health EDCTP3 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, Global Health EDCTP3 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. The ultimate goal is knowledge translation of trial findings into policy and practice to improve the health of populations.

Ensuring flexibility: Global Health EDCTP3 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. Where possible and relevant, longer-term (co-)funding in product development through portfolio funding would be considered. In addition, horizontal topics could benefit from a fixed percentage of funding applied in all relevant grants.

Promoting transparency and openness: Global Health EDCTP3 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. Emphasis will be placed on improving data sharing across sub-Saharan Africa to inform decision making and open avenues for research, while leveraging the experience of the national data hubs established under the European COVID-19 Data Platform.

Improving the design of clinical trials: Global Health EDCTP3 will promote innovation in clinical trial design to optimise testing of infectious disease interventions. Global Health EDCTP3 will place importance on trial designs that adapt to developments in the field, respond to emergence on novel trial designs, the evolving regulatory environment, and incorporate ethical considerations, sex and gender specificities, meaningful community engagement and empowerment, and the contribution of social sciences.

Utilisation of digital technologies: Following the crosscutting priorities of Horizon Europe, Global Health EDCTP3 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 and the implementation of existing technologies supported.

Framework of fundamental questions to assess proposed new areas:

When assessing the value adding of novel thematic priorities to the Global Health EDCTP3 remit and globally strategic areas, the following questions are to be considered:

1. Does this disease disproportionately affect people in sub-Saharan Africa?

2. Is there a need for new or improved medical products (drugs, vaccines, or diagnostics)?

3. Is there an insufficient commercial market to attract R&D by private industry?

4. Considering the current global products landscape, preclinical and translational research, are there potential medical products worth considering for progression in clinical development?

5. Are other funders better placed and already investing 'sufficiently' in these priority R&D areas?

6. Based on what we know, is there sufficient justification for Global Health EDCTP3 to prioritise this disease?

7. Global Health EDCTP3 research & innovation priorities

To maximise the impact of the partnership, strategically important areas of unmet medical need have been identified within the Global Health EDCTP3 priority disease areas. The Global Health EDCTP3 programme will support all the elements required to develop and evaluate medical interventions against the key infectious diseases affecting sub-Saharan Africa, through clinical science, research capacity development, and networking (national and international).

Target diseases: Global Health EDCTP3 will support research on HIV, TB, malaria, neglected infectious diseases[2], diarrhoeal diseases, lower respiratory tract infections, and emerging/re-emerging infections affecting sub-Saharan Africa. Global Health EDCTP3'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.

7.1 Criteria for setting priorities

To maximise the impact of the partnership, the Global Health EDCTP3 SRIA will focus on strategically critical areas of unmet medical need. Mechanisms will be established to identify emerging priorities and opportunities. Global Health EDCTP3 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 (including vaccination), diagnosis, and treatment will be analysed.

Priority infections: Priority setting will be informed by analyses of disease burdens, changing patterns of disease, contribution of a weakened immune system, extent of unmet medical needs, and the potential impact on a disease as a public health problem.

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

Emerging opportunities of translational bottlenecks: Global Health EDCTP3 will focus on points in the translational and implementation pathway that delay the clinical development and

[2] 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. Global Health EDCTP'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. Global Health EDCTP's remit will not cover chromoblastomycosis and other deep mycoses, scabies and other ectoparasites, and snakebite envenoming.

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, Global Health EDCTP3 will ensure global alignment of its policies and priorities and promote coordinated responses to evidence gaps and capacity-building needs.

Strategic portfolio: Global Health EDCTP3 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 overarching framework to guide the work of Global Health EDCTP3 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.

The broad priorities outlined in this SRIA will form the basis for the annual work plans. Annual plans will include details of the specific calls for proposals for the following year. The prioritisation is based on the above-mentioned criteria, structured around the five specific objectives of the Strategic Research and Innovation Agenda (SRIA) and populated with the outputs of i) comprehensive literature reviews of the SRIA identified targeted diseases allowing to outline the key research and capacity gaps, ii) current policy developments, iii) ongoing and upcoming funding from countries, donors, and other public and private entities, iv) previous Global Health EDCTP3 work programmes and funding.

7.2 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. Global Health EDCTP3 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)

Adjacent sectors to be encompassed as part of the HIV calls when possible: health education (fellowship programmes, training…), public-private partnerships (product development for diagnostics/drugs/vaccines, policy and advocacy), digital health and AI, regulatory capacity and pharmacovigilance, local manufacturing and sustainability, education and training, migration, community trust, transparency, health financing, drug resistance, nutrition, cancer and mental health.

Stakeholders to be considered for possible partnership for HIV projects: researchers, academia, patient representatives, organisations and family, disease networks, stakeholders from affected communities, communities marginalised, civil society, industry (big pharma, biotech, SMEs), Regulatory agencies (EMA, AMA), National Ethics Committees, public bodies, public-private partnerships organisations, NGOs and philanthropic foundations, international (e.g., WHO) and national organisations (EDCTP), national health programmes per disease, community health workers and clinicians, pharmacists and associations, military, beneficiaries of former EU-funded projects, insurance companies, African regional centres of excellence (e.g., IEC).

7.3 Tuberculosis

In line with the Sustainable Development Goal to end the TB epidemic, Global Health EDCTP3'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 greatly on 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 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. (10–12)

Global Health EDCTP3 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 efficiently 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. Global Health EDCTP3 will explore the potential for partnerships with global initiatives supporting TB vaccine research, TB drug discovery, and early clinical development.

Adjacent sectors to be encompassed as part of the TB calls when possible: health education (fellowship programmes, training…), public-private partnerships (product development for diagnostics/drugs/vaccines, policy and advocacy), digital health and AI, regulatory capacity and pharmacovigilance, local manufacturing and sustainability, education and training, migration, community trust, transparency, health financing, agriculture and food programs, antimicrobial resistance (AMR), disaster response, urbanisation and mobility, veterinary products (potential candidates for medicinal products human use), nutrition, cancer and mental health.

Stakeholders to be considered for possible partnership for TB projects: researchers, academia, patient representatives, organisations and family, disease networks, stakeholders from affected communities, communities marginalised, civil society, industry (big pharma, biotech, SMEs), regulatory agencies (EMA, AMA), National Ethics Committees, public bodies, public-private partnerships organisations, NGOs and philanthropic foundations, international (e.g., WHO) and national organisations (EDCTP), national health programmes per disease, community health workers and clinicians, pharmacists and associations, military, beneficiaries of former EU-funded projects, insurance companies, African regional centres of excellence (e.g., IEC).

7.4 Malaria

In line with the Sustainable Development Goal to end the malaria epidemic by 2030, Global Health EDCTP3 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 (Malaria in adolescence: burden of disease, consequences, and opportunities for intervention - The Lancet Infectious Diseases). Priority populations for malaria interventions include children, adolescents and pregnant women living in high-transmission regions, 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. The development of novel tools for the treatment and prevention of malaria in early pregnancy is a priority.

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. The growing impact of non-falciparum malaria in elimination settings requires assessment of improved diagnostics and management of these neglected forms of malaria.

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. Global Health EDCTP3 will support studies on vector control, to improve clinically relevant outcomes, including research on novel and improved technologies for vector control, as well as use of combination disease control interventions and product-focused implementation and operational research.

Global Health EDCTP3 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, adolescents, and pregnant and lactating women. Novel highly efficacious, especially single dose and fewer dose 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. Global Health EDCTP 3 will also contribute to improved access to malaria interventions through the support of studies informing the rational and efficient use of drugs and diagnostics.

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.

Global Health EDCTP3 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 (15–17). 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.

Adjacent sectors to be encompassed as part of the malaria calls when possible: health education (fellowship programmes, training…), public-private partnerships (product development for diagnostics/drugs/vaccines, policy and advocacy), digital health and AI, regulatory capacity and pharmacovigilance, local manufacturing and sustainability, education and training, migration, community trust, transparency, health financing, AMR, climate change, disaster response, urbanisation & mobility, WASH (Water, Hygiene and Sanitation Programs) and vector control.

Stakeholders to be considered for possible partnership for malaria projects: researchers, academia, patient representatives, organisations and family, disease networks, stakeholders from affected communities, communities marginalised, civil society, industry (big pharma, biotech, SMEs), regulatory agencies (EMA, AMA), National Ethics Committees, public bodies, public-private partnerships organisations, NGOs and philanthropic foundations, international (e.g., WHO) and national organisations (EDCTP), national health programmes per disease, community health workers and clinicians, pharmacists and associations, military, beneficiaries of former EU-funded projects, insurance companies, African regional centres of excellence (e.g., IEC).

7.5 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’, Global Health EDCTP3 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 and the number of cases of human African trypanosomiasis has significantly decreased with the disease now targeted for elimination by 2030. However, diseases such as schistosomiasis, onchocerciasis, and other NIDs continue to affect hundreds of millions of people who are most often 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 prevention, diagnostic tools, effective disease management, and vector control. The efficacy and affordability of chemotherapeutics vary 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. The latter is critical for diseases scheduled for elimination because failures in integration will inevitably lead to resurgence. 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, Global Health EDCTP3 will also support studies on vector control and integrated disease control strategies. Finally, many NIDs persist due to fragile local health systems. Programmes building better infrastructure for good clinical and regulatory practice can contribute to strengthening local health systems.

Adjacent sectors to be encompassed as part of the NTDs calls when possible: health education (fellowship programmes, training…), public-private partnerships (product development for diagnostics/drugs/vaccines, policy and advocacy), digital health and AI, regulatory capacity and pharmacovigilance, local manufacturing and sustainability, education and training, migration, community trust, transparency, health financing, agriculture and food programs, AMR, climate change, disaster response, urbanisation and mobility, veterinary products (potential candidates for medicinal products human use), WASH, vector control, nutrition, cancer and mental health.

Stakeholders to be considered for possible partnership for NTDs projects: researchers, academia, patient representatives, organisations and family, disease networks, stakeholders from affected communities, communities marginalised, civil society, industry (big pharma, biotech, SMEs), regulatory agencies (EMA, AMA), National Ethics Committees, public bodies, public-private partnerships organisations, NGOs and philanthropic foundations, international (e.g., WHO) and national organisations (EDCTP), national health programmes per disease, community health workers and clinicians, pharmacists and associations, military, beneficiaries of former EU-funded projects, insurance companies, African regional centres of excellence (e.g., IEC).

7.6 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. Global Health EDCTP3 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. Global Health EDCTP3 will aim to advance the clinical pipeline of vaccines against these diarrhoeal diseases. As the number of efficacious vaccines increases, research and development work to evaluate innovative vaccine delivery mechanisms, including combination vaccines, will be a priority to reduce the number of vaccination visits and improve vaccine uptake.

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

Adjacent sectors to be encompassed as part of the diarrhoeal disease calls when possible: health education (fellowship programmes, training…), public-private partnerships (product development for diagnostics/drugs/vaccines, policy and advocacy), digital health and AI, regulatory capacity and pharmacovigilance, local manufacturing and sustainability, education and training, migration, community trust, transparency, health financing, agriculture and food programmes, AMR, climate change, disaster response, urbanisation and mobility, veterinary products (potential candidates for medicinal products human use), WASH, nutrition, cancer and mental health.

Stakeholders to be considered for possible partnership for diarrhoeal disease projects: researchers, academia, patient representatives, organisations and family, disease networks, stakeholders from affected communities, communities marginalised, civil society, industry (big pharma, biotech, SMEs), regulatory agencies (EMA, AMA), National Ethics Committees, public bodies, public-private partnerships organisations, NGOs and philanthropic foundations, international (e.g., WHO) and national organisations (EDCTP), national health programmes per disease, community health workers and clinicians, pharmacists and associations, military, beneficiaries of former EU-funded projects, insurance companies, African regional centres of excellence (e.g., IEC).

7.7 Lower respiratory tract infections (LRTI)

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 newborns 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 specific and non-specific impact of 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 Global Health. (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.

Adjacent sectors to be encompassed as part of the LRTI disease calls when possible: health education (fellowship programmes, training…), public-private partnerships (product development for diagnostics/drugs/vaccines, policy and advocacy), digital health and AI, regulatory capacity and pharmacovigilance, local manufacturing and sustainability, education and training, migration, community trust, transparency, health financing, AMR, disaster response, urbanisation and mobility, veterinary products (potential candidates for medicinal products human use) and mental health.

Stakeholders to be considered for possible partnership for LRTI projects: researchers, academia, patient representatives, organisations and family, disease networks, stakeholders from affected communities, communities marginalised, civil society, industry (big pharma, biotech, SMEs), regulatory agencies (EMA, AMA), National Ethics Committees, public bodies, public-private partnerships organisations, NGOs and philanthropic foundations, international (e.g., WHO) and national organisations (EDCTP), national health programmes per disease, community health workers and clinicians, pharmacists and associations, military, beneficiaries of

former EU-funded projects, insurance companies, African regional centres of excellence (e.g., IEC).

7.8 Preparedness and response to emerging/re-emerging infectious diseases

Global Health EDCTP3's key aim is to enable countries in sub-Saharan Africa to prepare for, prevent, and effectively manage infectious disease outbreaks. Global Health EDCTP3 will continue the EDCTP Emergency Funding Mechanism that has allowed rapid mobilisation of research funding without a call for proposals in exceptional and 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 or pandemic potential are a persistent threat to global health security, as well as to public health in many African countries (26) and to socioeconomic development, as the COVID-19 pandemic or the Mpox outbreak has underscored.

It is vital to strengthen capacity for preparedness to address emerging/re-emerging infectious diseases and to undertake rapid evaluation of interventions in clinical trials when outbreaks occur, and treatments are inadequate or lacking entirely.(27) Evaluation in different settings of the safety and efficacy of new health technologies is needed to take into account 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. Longitudinal cohorts, if they already exist in outbreak areas, may be able to play a role in initial pandemic surveillance and assessment of clinical status and immune responses. The establishment of regionally linked strategic cohorts that could be pivoted rapidly to research on emerging infectious diseases will be considered. Supporting the maintenance of existing observational and interventional clinical studies with baseline continuous research activities could allow the recruitment of patients right from the onset of an outbreak.

FAIR and rapid data sharing is essential to accelerate research advances especially during an epidemic or pandemic. The development of data hubs and analytics for the storage, sharing, and analysis of research data, including the linkage of genomics and clinical data to support rapid identification and analysis of infectious threats is essential to inform rapid public health actions. These data sharing efforts could be facilitated through the creation of regional structures to enhance genomic surveillance and rapid-response capabilities, levering experience from the European COVID-19 Data Platform.

Global Health EDCTP3 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, Global Health EDCTP3 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, health research systems preparedness,

technology support for home-based self-care, impact on the health care workforce, and distributed health care delivery for Global Health EDCTP3 priority infectious diseases.

In addition, during the COVID-19 pandemic the research landscape has seen the emergence of large-scale, multi-country platform trials using master protocols and adaptive trial designs. Important results for treatment options for COVID-19 patients were delivered in a timely manner through these trials. Adaptive platform trials study multiple interventions for a single disease, with interventions allowed to enter or leave the platform according to data generated during the trial. Encouraging the implementation of adaptive platform trials in LMICs could improve the quality of clinical research by harmonising research efforts across different LMICs through forming clinical trial networks across multiple institutions in different countries. Hence, the Global Health EDCTP3 will encourage the use of innovative clinical trial designs such as adaptive platform trials and common protocols adapted to the regional context in global health research. It will support capacity building to enhance the understanding of specific trial designs, trial implementation, and data analysis, for research teams as well as for relevant ethical and regulatory committees along with the inclusion of (early stage) vaccine development of new vaccine products to address recent EID outbreaks in Sub-Saharan Africa.

Given Global Health EDCTP3'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 Global Health EDCTP3 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) The COVID-19 pandemic has shown the important role that social science plays in tackling misinformation and in better understanding vaccine hesitance, the stigma of infection, and impacts on individual mental health. Hence, social science needs to be core to broader epidemic pandemic and research response activities.

Adjacent sectors to be encompassed as part of the emerging/re-emerging disease calls when possible: health education (fellowship programmes, training…), public-private partnerships (product development for diagnostics/drugs/vaccines, policy and advocacy), digital health and AI, regulatory capacity and pharmacovigilance, local manufacturing and sustainability, education and training, migration, community trust, transparency, health financing, agriculture and food programmes, AMR, climate change, disaster response, urbanisation and mobility, veterinary products (potential candidates for medicinal products human use), WASH, nutrition, cancer and mental health.

Stakeholders to be considered for possible partnership for emerging/re-emerging projects: researchers, academia, patient representatives, organisations and family, disease networks, stakeholders from affected communities, communities marginalised, civil society, industry (big pharma, biotech, SMEs), regulatory agencies (EMA, AMA), National Ethics Committees, public bodies, public-private partnerships organisations, NGOs and philanthropic foundations, international (e.g., WHO) and national organisations (EDCTP), national health programmes per disease, community health workers and clinicians, pharmacists and associations, military,

beneficiaries of former EU-funded projects, insurance companies, African regional centres of excellence (e.g., IEC).

7.9 Climate crisis-related infectious disease

Global Health EDCTP3 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 diseases, 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. (30)

For higher impact, climate crisis-related infectious diseases research will be addressed through joint calls with other (EU or private) funding instruments.

Adjacent sectors to be encompassed as part of the climate crisis-related projects, when possible: health education (fellowship programmes, training…), public-private partnerships (product development for diagnostics/drugs/vaccines, policy and advocacy), digital health and AI, regulatory capacity and pharmacovigilance, local manufacturing and sustainability, education and training, migration, community trust, transparency, health financing, disaster response, urbanisation and mobility, malaria, NTDs, emerging and re-emerging infectious diseases, non-communicable diseases (NCDs) (e.g., asthma or stroke), diarrhoeal diseases, AMR, WASH, vector control, nutrition, cancer and mental health.

Stakeholders to be considered for possible partnership for climate crisis-related projects: researchers, academia, patient representatives, organisations and family, disease networks, stakeholders from affected communities, communities marginalised, civil society, industry (big pharma, biotech, SMEs), regulatory agencies (EMA, AMA), National Ethics Committees, public bodies, public-private partnerships organisations, NGOs and philanthropic foundations, international (e.g., WHO) and national organisations (EDCTP), national health programmes per disease, community health workers and clinicians, pharmacists and associations, military, beneficiaries of former EU-funded projects, insurance companies, African regional centres of excellence (e.g., IEC).

7.10 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. (31,32)

Global Health EDCTP3 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 Global Health EDCTP3's scope will help 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.

In view of the horizontal nature of AMR, intersecting with almost every other health issue, a stronger focus on the intersectionality of AMR, notably un patients with other major co-morbidities such as HIV/Advanced AIDS or TB, would allow to fully understand the impact and future need of effective antibiotics.

Adjacent sectors to be encompassed as part of the AMR disease calls when possible: health education (fellowship programmes, training…), public-private partnerships (product development for diagnostics/drugs/vaccines, policy & advocacy), digital health and AI, regulatory capacity and pharmacovigilance, local manufacturing and sustainability, education and training, migration, community trust, transparency, health financing, agriculture and food programs, climate change, disaster response, urbanisation and mobility, WASH, nutrition and mental health.

Stakeholders to be considered for possible partnership for AMR projects: researchers, academia, patient representatives, organisations and family, disease networks, stakeholders from affected communities, communities marginalised, civil society, industry (big pharma, biotech, SMEs), regulatory agencies (EMA, AMA), National Ethics Committees, public bodies, public-private partnerships organisations, NGOs and philanthropic foundations, international (e.g., WHO) and national organisations (EDCTP), national health programmes per disease, community health workers and clinicians, pharmacists and associations, military, beneficiaries of former EU-funded projects, insurance companies, African regional centres of excellence (e.g., IEC).

7.11 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. (33)

To ensure it does not spread its resources too thinly to achieve impact, Global Health EDCTP3 will retain a core focus on infectious diseases, 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.

Global Health EDCTP3 will therefore support studies on interventions to prevent or treat non-communicable diseases in patients with infectious diseases (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 Global Health EDCTP3 scope.

Recognising the importance of patient-centred approaches to healthcare, Global Health EDCTP3 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.

Adjacent sectors to be encompassed as part of the NCDs calls when possible: health education (fellowship programmes, training…), public-private partnerships (product development for diagnostics/drugs/vaccines, policy and advocacy), digital health and AI, regulatory capacity and pharmacovigilance, local manufacturing and sustainability, education and training, migration, community trust, transparency, health financing, agriculture and food programmes, AMR, climate change, disaster response, urbanisation and mobility, nutrition, cancer and mental health.

Stakeholders to be considered for possible partnership for NCDs projects: researchers, academia, patient representatives, organisations and family, disease networks, stakeholders from affected communities, communities marginalised, civil society, industry (big pharma, biotech, SMEs), regulatory agencies (EMA, AMA), National Ethics Committees, public bodies, public-private partnerships organisations, NGOs and philanthropic foundations, international (e.g., WHO) and national organisations (EDCTP), national health programmes per disease, community health workers and clinicians, pharmacists and associations, military, beneficiaries of former EU-funded projects, insurance companies, African regional centres of excellence (e.g., IEC).

8. Portfolio of foreseen activities and resources

The Global Health EDCTP3 programme will use a range of funding mechanisms as necessary to achieve its objectives.

Support for clinical trials and related studies: Support will be provided for clinical research activities and clinical trials, as well as other epidemiological or observational studies, including the integration of associated social science research in these 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, community engagement and empowerment, 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, among European researchers, and among African researchers, institutions, and sites (including support for regional Networks of Excellence in sub-Saharan Africa): including, for example, institutional capacity building through teaming of northern and southern institutions to commonly develop business plans for southern institutions aimed at strengthening their long-term research strategy and sustainability; (3) foster collaboration with public and private funders; and (4) promote communication with policy makers and the public to raise awareness about 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.

Global Health EDCTP3'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 2).

Resources: The total resources for calls for proposals to be launched under the Global Health EDCTP3 JU amount to about 740 m Euro. The largest share will be invested in support for clinical trials and related studies, followed by support for capacity building, with the lowest share to be invested in support to career development. The estimated amounts are 600, 100 and 40 million euros, respectively. These resources will be complemented by investments from the members of the JU, to be invested for the largest part in own activities, as well as investments from contributing partners.

9. Monitoring and Evaluation Framework

Global Health EDCTP3's Monitoring & Evaluation (M&E) framework aims to establish a systematic and structured approach to tracking Programme results across all stages of its lifecycle, providing evidence to support timely adjustments in its activity plans and strategic decision-making.

The Framework has been developed through document analysis and targeted consultations with Global Health EDCTP3 staff, EDCTP Association, and with input from the Global Health EDCTP3 Stakeholder Group, Scientific Committee, and Governing Board.

The framework is intended to serve as a living, flexible, and adaptable tool, to be refined over time as the programme implementation advances, global health priorities evolve, and practical insights emerge. Adjustments may be needed based on the actual effort required to measure certain indicators, the resources available, and the data realities in specific contexts - factors that will only become fully clear when measurement of specific indicators is being done.

The framework includes the following **components**:

1. Programme logic

The foundation of the M&E Framework, outlining the specific public health improvements to which the programme seeks to contribute, and the pathway through which it aims to trigger those improvements. The programme logic summarises the expected causal chain of programme results, illustrating how resources and activities are expected to generate specific deliverables - outputs, how these outputs are expected to lead to immediate effects - immediate outcomes, and how these, in turn, are anticipated to contribute to broader, longer-term changes - intermediate, long-term outcomes, and impact.

The programme logic is illustrated in Figure 3, in its version of July 2025.

2. Comprehensive list of indicators

Information that shows the extent to which envisioned activities have been implemented and expected results have been achieved. Indicators align with the Programme logic, covering all levels from activities to outputs, to outcomes, and to the impact.

The list contains donor-mandated indicators and Global Health EDCTP3-specific indicators. The former include:

- Horizon Programme Key Impact Pathways indicators (KIPs) that are measured directly by the Horizon Programme and data provided to the Global Health EDCTP3 team upon request.

- Joint Undertaking (JU) common indicators, shared across all JUs.
- Indicators deriving from EC Reporting requirements for reporting under the Regulation 2021/2085 ('Single Basic Act').

Additionally, Global Health EDCTP3-specific indicators have been included to track results unique to the Programme that are not sufficiently covered by the donor-mandated ones.

The figure below, illustrating the Programme logic, indicates which activities and results are to be measured with donor-mandated indicators, Global Health EDCTP3-specific indicators, and core indicators.

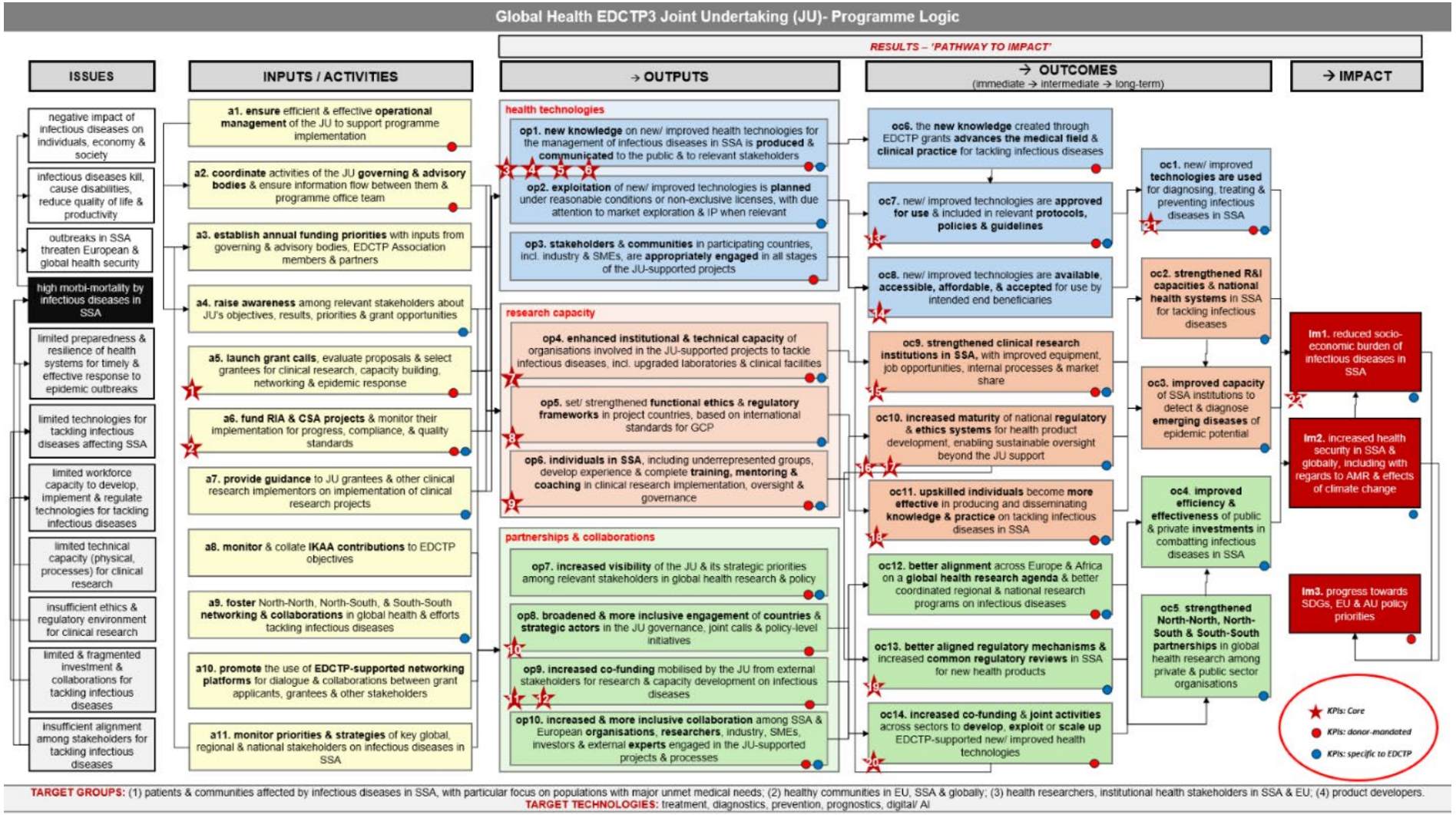


Figure 3 Programme logic.

3. Core indicators

A selection of up to 25 key indicators providing a high-level snapshot of the programme performance. These are drawn from the full list, ensuring alignment with Global Health EDCTP3's objectives.

While the comprehensive list of indicators enables an in-depth analysis of the programme's performance across specific thematic areas, components, or cross-cutting issues, the core indicators provide a concise overview of the Programme's overall performance.

The values of a selected set of indicators, relevant to each stage of the programme lifecycle, will be presented and analysed in each Global Health EDCTP3 Annual Activity Report, and featured in presentations and communication materials throughout the year.

The table below contains the list of core indicators as of July 2025.

#	Core indicators
Level: activities	
1	# projects selected for funding, with signed Grant Agreements
2	grant amounts allocated to projects (EUR), committed and actual
Level: outputs	
3	# new/ improved medical interventions that progressed through clinical development due to the JU support and for which evidence on safety, efficacy, or usability was generated by a JU-funded project, with description
4	# new/ improved medical interventions for which evidence on safety, efficacy, or usability was generated by a JU-funded project, with description
5	# medical interventions for which evidence on effectiveness, feasibility, acceptability, or scalability was generated through JU-funded implementation research, with description
6	# research datasets or databases established, maintained, or made accessible through JU-funded projects, with description

7	# laboratories and clinical facilities upgraded with the direct contribution of a Global Health EDCTP3-funded project
8	# countries with newly established or revised ethics and/or regulatory frameworks with the direct contribution of a Global Health EDCTP3-funded project
9	# researchers who receive(d) Global Health EDCTP3-funded fellowship/ research/ training grants
10	# entities with which Global Health EDCTP3 has formal collaboration agreements
11	financial (€) and in-kind contributions, committed and actual [direct leverage]
12	amount of public and private investment mobilised with the initial investment from the Programme
Level: immediate & intermediate outcomes	
13	# medical products resulting from EDCTP-funded projects pre-qualified by WHO recommendations and/or that received regulatory approval to be marketed, with description
14	# new/improved medical products known to be available for use by end beneficiaries, with description
15	# and % of Global Health EDCTP3-supported laboratories and clinical sites demonstrating improvements in diagnostic capacity by the end of project completion
16	# and % countries that received EDCTP support for strengthening their regulatory frameworks that attained regulatory systems maturity level 3 or higher on the WHO benchmarking scale
17	# and % countries that received EDCTP support for strengthening their ethics systems with national ethics committees having achieved international accreditation
18	# and % researchers involved in EDCTP grants who joined implementation teams in other research initiatives addressing infectious diseases in SSA after receiving EDCTP support

19	# of SSA countries or regulatory authorities participating in shared review processes, harmonized frameworks, or mutual reliance mechanisms for clinical trials or health product approvals
20	additional investments triggered by the EU contribution, notably for exploiting or scaling up results (linked to but outside the partnerships, including qualitative impacts and success stories) [indirect leverage]
Level: long-term outcomes & impact	
21	# of new/ improved technologies that became integrated into healthcare services, national healthcare programmes, or disease-specific initiatives, with description
22	DALY (disability-adjusted life years; total years of healthy life lost due to illness, disability, or premature death) for relevant infectious diseases in relevant populations of SSA

10. Other potential European Partnerships of relevance

Calls for research projects supported through the Horizon Europe partnerships will be launched by the partnership whose scope is most relevant for the specific topic. Only in the case where it can be very well justified (e.g. pandemics) can multiple partnerships launch calls with topics in the same areas of research.

Name	Short description of the aim
Innovative Health Initiative (IHI)	(a) contribute towards the creation of an EU-wide health research and innovation ecosystem that facilitates translation of scientific knowledge into innovations, notably by launching at least 30 large-scale, cross-sectoral projects, focussing on health innovations; (b) foster the development of safe, effective, people-centred and cost-effective innovations that respond to strategic unmet public health needs, by exhibiting, in at least 5 examples, the feasibility of integrated health care products or services, with demonstrated suitability for uptake by health care systems. The related projects should address the prevention and/or management of diseases affecting the EU population, including contribution to Europe's Beating Cancer Plan; (c) drive cross-sectoral health innovation for a globally competitive European health industry, and contribute to reaching the objectives of the new Industrial Strategy for Europe and the Pharmaceutical Strategy for Europe.
One Health AMR	Bring together the many aspects of antimicrobial resistance (AMR) to overcome fragmentation of the AMR research landscape, and integrate the various different research fields (addressing human health, animal health, food safety and environment). Contribute to the EU One health action plan against AMR that provides the framework within which action should be taken.
Animal health: fighting infectious diseases	Bring sustainable and innovative solutions to tackle infectious animal diseases, including those transmitted between animals and humans (zoonoses) and to contribute to the fight against anti-microbial resistance, implementing the One Health concept. Support sustainable animal production, reduce trade barriers, and protect consumers

Large-scale innovation and transformation of health systems in a digital and ageing society	Boost research for uptake, scale-up and transfer across and within EU countries of innovative solutions (incl. technological innovations and organisational innovations) in order to accelerate the transformation of national/regional health care systems. Establish a research and innovation platform that would bring together not only the different actors but also health data across health care systems to enable data-driven policy and exchange.
Fostering an ERA for Health research	Establish a flexible and more effective coordination between programme owners (typically ministries) and programme funders (typically funding agencies) of the numerous networks established in the European Research Area (ERA) for Health and Well-being. It would focus on establishing a strategic research agenda and joint funding strategy between major European funders, public and private, on translational health research and innovation.
Key Digital Technologies	Maintain the European Electronics Components and Systems industry at the technological forefront and contribute to boosting the EU's competitiveness, including that of its industries by providing essential components and software as well as the related manufacturing infrastructure in Europe and national strategies
High Performance Computing	Establish an integrated world-class supercomputing & data infrastructure and support a highly competitive and innovative HPC and Big Data ecosystem.
Smart Networks and Services	Enable the infrastructure basis in terms of key technologies and deployment for Next-Generation Internet services used by citizens and for "smart" services required by vertical sectors such as transport, energy, manufacturing, health and media.

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12. List of abbreviations

Acronym	Full term / definition
AMR	Antimicrobial resistance
CSA	Coordination and support action
EDCTP	European & Developing Countries Clinical Trials Partnership
ERA	European Research Area
EU	European Union
FAIR	Findable, accessible, interoperable, and reusable
GH	Global health
Global Health EDCTP3	Global Health EDCTP3 Joint Undertaking
HIV/AIDS	Human immune deficiency virus / Acquired immunodeficiency syndrome
IHI	Innovative Health Initiative
LMICs	Low- and middle-income countries
MD	Medical doctor
NIDs	Neglected infectious diseases
PhD	Philosophy doctor
R&D	Research & development

Acronym	Full term / definition
R&I	Research & innovation
RIA	Research & innovation action
SDG	Sustainable Development Goal
SWOT	Strengths, weaknesses, opportunities, threats
SRIA	Strategic research and innovation agenda
TB	Tuberculosis
TMA	Training and mobility action