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IMPACT ASSESSMENT

Accompanying the document

Proposal for a
DECISION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

on the participation of the Union in a second European and Developing Countries Clinical Trials Partnership Programme jointly undertaken by several Member States

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INTRODUCTION

This Impact Assessment (IA) report accompanies the Commission's proposal for a Decision on the continued participation of the European Union (EU) in a second European and Developing Countries Clinical Trials Partnership programme (EDCTP2). It falls under Article 185 of the *Treaty on the Functioning of the EU*, which foresees the participation of the EU in the joint implementation of national programmes for research and development. It details the findings of the IA required for legislative proposals and represents the ex-ante evaluation required for proposals occasioning budgetary expenditure [1].[1] More specifically, this report addresses the renewal of the EU's mandate and co-funding, as requested by the participating European states [2, 3] and recommended by the independent interim evaluation of the first EDCTP programme (EDCTP1) [4]. The proposal is put forward in the context of the Union's Multiannual Financial Framework (2014-2020) as part of the implementation of the next EU Framework Programme for Research and Innovation, *Horizon 2020* [5].

What is EDCTP?

EDCTP was established in 2003 on the basis of Article 169 of the *Treaty Establishing the European Community* (now Article 185 of the *Treaty on the Functioning of the EU*) [6]. The EDCTP pioneered European countries' endeavour in coordinating national research programmes and the EU in applying - for the first time ever - Article 169 [7, 8]. EDCTP is established as an independent legal entity, a European Economic Interest Group (EEIG), in the Netherlands. Currently, 16 European countries - 14 EU Member States (MS)[2] and 2 Associated Countries (AC)[3] - take part in EDCTP as Participating States (PS). The decision in 2003 allowed the Union to contribute €200 million of co-funding to EDCTP, conditional to national contributions from PS of at least €200 million, while an additional contribution of €200 million was expected from third parties in the private and public sector, including charitable organisations and pharmaceutical companies [6]. With the release of a Strategic Business Plan in 2012 [9], the PS substantiated their plans to continue the EDCTP into a second programme (EDCTP2) and provided a concrete up-front commitment of €552 million.

Why EDCTP?

EDCTP has been conceived to complement the actions implemented under the European Development Fund (EDF) and the Development Co-operation Instrument (DCI) in order to ensure the development and delivery of medical interventions to those in needs. EDCTP is thus part of a coordinated EU response to the global health crisis caused by the three main

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1 Specific background information that may be useful for the reader is provided in footnotes, whereas citations and reference publications are indicated by [*Number*] and refer to the reference list in Annex 8.

2 Member States (MS) participating in EDCTP are: Austria, Belgium, Denmark, France, Germany, Greece, Ireland, Italy, Luxembourg, the Netherlands, Portugal, Spain, Sweden, and the United Kingdom. The following MS are currently not participating in EDCTP: Finland as well as the EU-12 countries that joined the EU in 2004 and 2007, resp.

3 In this document the term "Associated Countries" (AC) refers to currently 12 non-EU countries associated to the Sixth and Seventh EU Research & Innovation Programme (FP6 and FP7, respectively). Associated Countries participating in EDCTP are: Switzerland and Norway.

poverty-related diseases (PRD) - HIV/AIDS, malaria and tuberculosis (TB) - and to the EU's commitment to achieving the Millennium Development Goals (MDG) by 2015[4].

The availability of safe, affordable and effective medical interventions against PRD is a key component in controlling these diseases and reduces their social and economic burden in low income countries. This is particularly needed in sub-Saharan African countries which account for over two thirds of the world's population living with HIV and for nearly three quarters (72%) of AIDS-related deaths and 89% of all malaria deaths. Despite the massive socio-economic burden of PRD, there is a general lack of interest for developing effective medical interventions for PRD due to the limited financial incentives for the private sector, as well as the inadequate capacity to undertake clinical research in disease-endemic areas of sub-Saharan Africa. Without significant and coordinated support from the public sector in close cooperation with the private sector, it is unlikely that new or improved medical solutions for PRD will ever reach those in need.

The most difficult and expensive part of pharmaceutical development is the clinical testing in humans. The main objective of the current EDCTP programme is therefore to support the clinical testing of new or improved medical interventions (drugs, vaccines, and microbicides) against HIV/AIDS, malaria and TB. Secondly, EDCTP aims to build a long-term research partnership between Europe and sub-Saharan Africa through support to local capacity building for clinical research. Thirdly, EDCTP supports cooperation of relevant European national programmes under a single coherent European strategy.

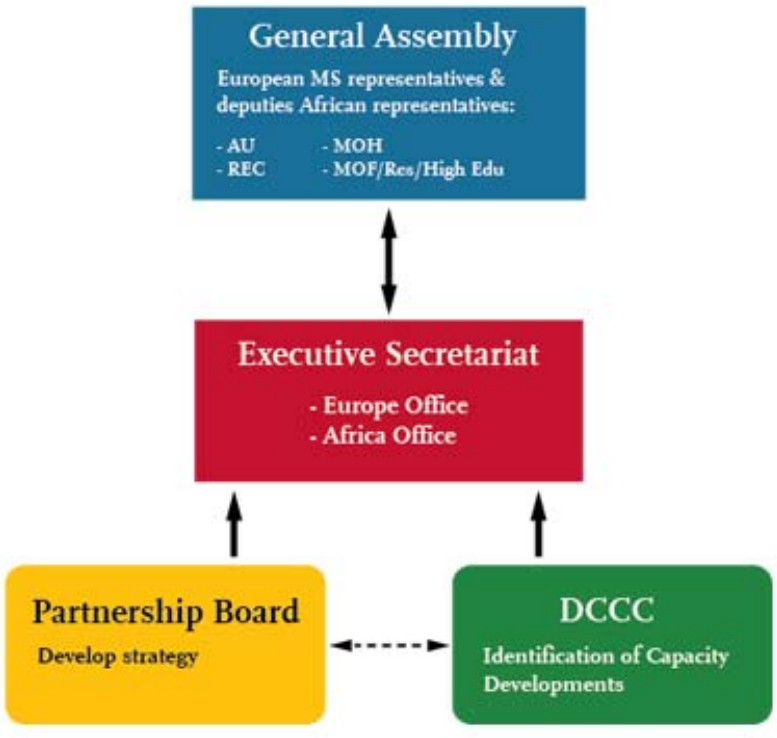

Figure 1: Organisation structure of EDCTP

[4] The health-related MDG are: MDG 4 "Reduce Child Mortality", MDG 5 "Improve Maternal Health", and MDG 6 "Combat HIV/AIDS, Malaria and other diseases": http://www.un.org/millenniumgoals/index.shtml.

How is EDCTP organised?

The EDCTP is established by the participating European states as a European Economic Interest Group (EEIG) in the Netherlands. It consists of the General Assembly (GA) as the governing body and the Executive Secretariat (ExS) as the executive body and dedicated implementation structure (DIS) which is responsible for the administrative, financial and contractual management of the joint research programme (head office in The Hague, and liaison office in Cape Town). The GA is the decision making body of EDCTP composed of delegates of the Participating States, while African representatives are participating as observers. The GA is supported in its decision-making by the Executive Secretariat and two advisory structures (Figure 1): the Partnership Board (PB) composed of independent scientific experts providing scientific and strategic advice, and the Developing Countries Coordinating Committee (DCCC) composed of African senior researchers and policy-makers providing input and advice on African needs and commitments.[5] Regarding the main achievements of EDCTP see section 2.2. The role of the Commission in EDCTP is limited to monitoring the EU co-funding, organising evaluation of EDCTP and participating in the GA as an observer.

How does EDCTP work?

Through the voluntary coordination and pooling of resources from the Participating States (PS), the EU as well as third parties, EDCTP creates a critical mass of resources for specifically supporting late stage clinical trials. EDCTP is therefore complementary to research on PRD funded under the annual work programmes of the EU Seventh Framework Programme for Research and Technological Development (FP7), which funds the preclinical and early clinical phase of pharmaceutical development.

For the current EDCTP, the resources are allocated to research institutions and individual researchers in sub-Saharan Africa and Europe on the basis of competitive calls for proposals and following an independent peer review evaluation and selection process. The research priorities of calls for proposals are developed by the Executive Secretariat in cooperation with the EDCTP advisory bodies (PB, DCCC) and upon consultation of relevant stakeholders[6], and are ultimately agreed by the General Assembly.

Towards the next phase of EDCTP

The current EDCTP is now beyond its active funding period with the last grants involving EU budget awarded in 2012, and the EU co-funding of EDCTP1 fully used.[7] By May 2015, all remaining EDCTP projects will be concluded. The Participating States (PS) aim to continue EDCTP and requested the EU to renew its mandate and participate in the launch of an EDCTP2 programme [3]. To that end, a Strategic Business Plan was released in 2012 [9], in which the current PS describe their plans for an EDCTP2 programme and provide an initial concrete up-front commitment of €500 million. The PS envisage raising their commitment, including with additional funds, to at least €1 billion. They propose to maintain the current geographical focus on sub-Saharan Africa, but plan to extend the scale and scope consisting of (i) doubling the life time of the programme from 5 to 10 years, (ii) including other PRD (in

5 For more information on EDCTP governance: http://www.edctp.org/The_Organisation.724.0.html.

6 For more information EDCTP implementation: http://www.edctp.org/Calls_and_Grants.501.0.html.

7 By 31.12.2012, the EU co-funding of €200 million earmarked for EDCTP1 has been committed fully, more specifically €155.52 million for grants and €44.48 million for non-grants expenditures.

addition to HIV/AIDS, malaria and TB) and addressing all stages of clinical trials (phases I to IV). PS considers that a total budget of at least €2 billion would be required, which means that additional co-funding of at least €1 billion is sought from the EU. Finland, Poland and Hungary have so far indicated their interest to join the initiative [10, 11]. Such an EDCTP2 programme would not only allow for continued clinical exploration of candidate interventions and use of capacities developed under EDCTP1, but would also contribute to the Union's commitment towards the 2012 Rio+20 conference conclusions [12] on the development and achievement of internationally agreed Sustainable Development Goals (SDG), including the Millennium Development Goals (MDG), the EU-Africa strategic partnership [13], and ultimately to the Union's vision of a competitive "Global Europe" [14].

The renewal of the EU's mandate and funding of an EDCTP2 programme is envisaged under the auspices of the next EU Framework Programme for Research and Innovation, *Horizon 2020* (2014-2020). The Commission's proposal for *Horizon 2020* [5] has a specific section on societal challenges, with Health, Demographic Change and Wellbeing as one of the priorities with a proposed earmarked budget of €8.6 billion[8]. EDCTP2 is mentioned as one of the article 185 initiatives eligible for continued support [15]. Apart from supporting clinical trials for PRD through the EDCTP2, the Commission's proposal for *Horizon 2020* contains plans to support other aspects of research on PRD: i) the European Research Council (ERC) will provide opportunities for basic and translational research on PRD;[9] and ii) focused research on PRD could be partially addressed under the next phase of the Innovative Medicines Initiative (IMI), a public-private partnership between the European Commission and the European Federation of Pharmaceutical Industries and Associations (EFPIA) funding all stages of biomedical research in response to public health needs, including tools and technologies addressing bottlenecks in drug development. The actual budget allocation to EDCTP2 is subject to the outcome of the Union's decision on the Multiannual Financial Framework (2014-2020) and *Horizon 2020*.

1. PROCEDURAL ISSUES AND CONSULTATION OF INTERESTED PARTIES

The Commission's Directorate-General for Research and Innovation (DG-RTD) is the lead DG for this initiative [16].

1.1. Organisation and timing

The present IA has been conducted including the following steps:

- Setting up an inter-service Impact Assessment Steering Group (IASG) in September 2009, to oversee the process (section 1.3).
- Preparing a detailed roadmap and consultation plan [16].
- Carrying out an analysis of existing reviews and evaluations of EDCTP (section 1.4).
- Consulting interested parties through an open public consultation which ran from 8 April to 22 June 2010 (section 1.4.1) [17, 18].

8 The total budget proposed by the Commission for *Horizon 2020* is €86.2 billion [5].

9 The Commission proposed for the ERC a major budget of about €13 billion to support excellent science, under the Excellent Science pillar of *Horizon 2020* [5].

- Setting up an independent expert panel in June 2010 to analyse EDCTP with regard to achievements and lessons learnt, current needs and prospects, and provide advice and recommendations for policy options (section 1.4.2) [[19]].
- Gathering the EU Member States in a 'consensus meeting' convened by the Belgium Presidency of the Council of the EU on 27-28 September 2010 followed by consultation (2010-2012) (section 1.4.3) [2].
- Note from the Belgian EU Presidency to the EU Member State's delegations on 18 November 2010 requesting support to the next phase of the EDCTP (section 1.4.3) [3];
- Presenting the preliminary findings to the IASG as well as external experts (2010-2012).
- Consulting the private sector (2011-2012) with regard to potential partnering and financial engagement in EDCTP2 through dedicated meetings (section 1.4.4) [[20]].

1.2. Consultation of the Impact Assessment Board (IAB)

Following the opinion of the Impact Assessment Board, the present IA report was revised as follows: I) The Introduction has been improved with the description of the policy context for this initiative (Article 185), the current programme (EDCTP1) and the Member States' proposal (Strategic Business Plan) for a future programme (EDCTP2). A brief explanation has been provided of how the current programme works in practice, the roles of key actors and the relationship with EU external aid policies and with the Multi-annual Financial Framework (MFF) process. II) The Problem Definition (chapter 2) has been strengthened substantially to improve the intervention logic as regards the continuation and change in scope of the EDCTP programme highlighting the deficiencies of the current programme (EDCTP1) and the drivers of the persisting problems to be considered for the design of the next programme (EDCTP2). III) The Objectives (chapter 3) have been revised to align with the revised intervention logic and focus on the specific problems and drivers described in the Problem Definition (chapter 2). In particular, targets have been set for the increased number of medical interventions against poverty-related diseases that EDCTP aims for. IV) The Options (chapter 4) have been linked to the specific problems and objectives, as well as to the pending decision on the Multi-Annual Financial Framework 2014-2020 (Table 4). V) The assessment of options in the Impact Analysis (chapter 5) has been restructured and the socio-economic impact of the options has been described in more detail. VI) The Comparison of Options (chapter 6) has been revised and further extended with an explicit comparison of options in terms of effectiveness, efficiency and coherence (tables 5 and 6). The expected impact of an increased budget has been highlighted, and the underlying assumptions for the level of matching funding have been further clarified. VII) The Risk Mitigating Strategy (chapter 6) has been reinforced to consider the risks and the consequences if the additional commitment from Member States do not materialise.

Following further comments from the IAB on the low level of third party funding under EDCTP1, the expected level of additional funding for EDCTP2 from public and privat parties, including African countries, has been explained as well as why an extention of the scope beyond sub-Saharan Africa is not considered.

1.3. Inter-service Impact Assessment Steering Group (IASG)

Eight meetings of the IASG were convened between December 2009 and October 2010.[10] The IASG contributed to the IA planning and roadmap, the preparation of the public consultation (section 1.4.1), the terms of reference for the independent expert panel (section 1.4.2), and to the preliminary draft IA report in October 2010. Following the Commission's decision to postpone the renewal of EDCTP and propose EDCTP2 under *Horizon 2020*, the IASG was re-established and met twice between July and October 2012 in order to review the updated IA report, provide advice for improvement, and endorse the final report.[11]

1.4. Consultation and expertise

To gather information, expertise and opinions for the IA exercise, four main groups of stakeholders were consulted from April 2010 to September 2012:[12]

- Interested individuals and organisations at large through an open web-based public consultation (section 1.4.1).
- Experts in the field of international cooperation on PRD through an independent expert panel (section 1.4.2).
- EU Member States through a dedicated "consensus meeting" and European EDCTP participating states through contributions endorsed by the EDCTP General Assembly, (section 1.4.3).
- Third parties supporting clinical development of medical interventions against PRD through bilateral discussions and meetings (section 1.4.4).

In addition, the 2007 and 2009 EDCTP external interim evaluation reports [21, 22], the 2009 internal assessment report [23] and the EDCTP annual reports [24] have been considered for the preparation of this IA report. Annexes 6a and 6b list the recommendations put forward by the 2007 and 2009 external interim evaluations of EDCTP [21, 22].

1.4.1. Public consultation

On 8 April 2010 the European Commission launched a two months public consultation on the future proposal for a second EDCTP programme [17]. The executive summary of the results is provided in annex 4 [18].

The Commission received a total of 235 contributions (137 from Europe, 64 from Africa, 34 from other regions) from the following categories:

- 175 replies from individuals contributing in personal capacity. This included 55% researchers, 11% interested citizens, 15% employees of public organisations and authorities, 7% employees of private non-profit organisations, 2% employees of private for-profit organisations, and 10% others;

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10 The following Commission DGs had been invited to join the IASG: SG, SJ, BEPA, ECFIN, ENTR, ENV, SANCO, JRC, INFSO, REGIO, EAC, JLS, RELEX, TRADE, DEVCO (previously DEV and AIDCO), ELARG, ECHO, and ESTAT. Meetings were held on: 16 December 2009, 3 February 2010, 16 March 2010, 27 April 2010, 23 June 2010, 6 September 2010 and 14 and 28 October 2010.

11 The following Commission DGs (and the EEAS) had been invited to join the re-established IASG: SG, SJ, BEPA, BUDG, HR, AGRI, CLIM, COMP, DEVCO, EAC, ECFIN, ECHO, ELARG, ENTR, ENV, ESTAT, HOME, INFSO, JRC, MARKT, REGIO, JUST, SANCO, TRADE, EEAS. Meetings were held on: 11 July 2012 and 1 October 2012.

12 The consultations conducted comply with the general principles and minimum standards for consultation of interested parties described in the Commission's Impact Assessment Guidelines, SEC (2009) 92.

- 48 replies from organisations/companies, including 31% from private non-profit organisations, 25% from public organisations, 19% from private for-profit organisations, and 25% from other type of organisations;
- 12 replies from public authorities, including 92% replies from centralised authorities (8% others).

The continuation of EDCTP was supported by a majority of respondents (83%). This support was consistent among respondents from Europe (80%) and Africa (92%) as well as across all categories of respondents (87% of individuals contributing in a personal capacity, 75% of organisations, and 67% of public authorities). There was wide support (71%) for the extension of the scope for a new EDCTP programme (65% respondents from Europe, 87% from Africa). However, only 50% of the respondents from public authorities supported an extended scope. Calling for a well-adapted structure, public authorities not supporting an extended scope were in particular in favour of a narrow geographical focus (thus maintaining the focus on sub-Saharan Africa), extension to other diseases only when expected impact on poverty reduction is significant, and of supporting expensive clinical trials in partnership with other funders.

The following types of expansion were supported:

- Extension to phases I and IV clinical trials: widely supported by respondents from Europe (79%) and sub-Saharan Africa (85%), as well as among public authorities (75%), organisations/companies (73%) and individuals (81%).
- Extension to other PRD, such as neglected infectious diseases: the majority of respondents from Europe (60%) and sub-Saharan Africa (70%) were in favour, as well as among public authorities (67%), organisations/companies (58%) and individuals (67%).
- Extension to other geographical areas: a geographical extension was supported by a small majority of organisations/companies (63%) and individuals (56%), whereas only a minority of public authorities (42%) supported the idea.

The outcome of the public consultation was presented and discussed during various meetings and events with stakeholders held between June 2010 and September 2012 where their support was repeatedly confirmed [20, [25], [26], [27]]. In addition, the Commission received joint position papers supported by more than 30 European and international stakeholder organisations in the field of global health [[28], [29]].

1.4.2. Independent expert panel

The panel expressed its support to EDCTP2 with an extended scope that would build on the achievements of EDCTP1 and increase collaborative opportunities in areas with high expected impact and favourable cost-effectiveness (see [19] and annex 5). In particular, the extension of the mandate to all stages of clinical trials (phases I to IV) and to other PRD was considered as most relevant. Geographical extension, however, was considered to be less cost-effective given the particularly high needs in sub-Saharan Africa, although alliances with similar initiatives in other regions of the world were encouraged. Other recommendations included: i) a 10-year lifetime for the new initiative (considering the time needed for clinical trials), ii) a reform of the programme's legal entity (currently a European Economic Interest Group) to allow notably that African countries can formally become members and contribute to EDCTP, and iii) the need to set clear objectives from the beginning with measurable outcomes for the new initiative.

1.4.3. European countries participating in EDCTP

Under the Belgian Presidency of the Council of the EU, a "consensus meeting" among EU Member States (MS) was held on 27-28 September 2010 to discuss EDCTP2 and agree on the way forward [2]. Building upon the progress made under the first initiative, MS expressed strong support for the new initiative. The meeting conclusions were communicated at the Competitiveness Council meeting on 26 November 2010 [3].

The position of MS and other Participating States (PS) of EDCTP was further formalised in a Strategic Business Plan (SBIP) for EDCTP2 published on 30 May 2012 [9, 10]. In this SBIP, PS express their political will and financial commitment for an EDCTP2 programme with advanced integration of their national programmes at scientific, management and financial levels in line with Article 20 of the proposed EU Regulation on *Horizon 2020* [5].

1.4.4. Third parties supporting clinical trials in developing countries

Third parties from the public or private sector, including major funders of global health research, such as the Bill and Melinda Gates Foundation (BMGF) (the 2nd largest global funder of PRD research, providing $448 million in 2011) and the Wellcome Trust (the 4th largest funder of PRD research providing $94 million in 2011), have repeatedly praised the achievements of EDCTP and called for a renewed programme with an extended scope, including neglected infectious diseases and all phases of clinical trials [28, 29, [30], [31], [32]]. Pharmaceutical companies (a sector providing $525 million to PRD research in 2011) including GlaxoSmithKline, Johnson & Johnson, Merck Serono, Novartis and Sanofi and the European Federation of Pharmaceutical Industries and Associations (EFPIA) have also indicated their support to EDCTP2 [20, 32, [33]].

1.4.5. Summary and conclusions

In the consultation process an extension of the scope of the EDCTP2 programme compared to EDCTP1[13] was addressed, where the following was proposed and supported:

- To include other PRDs, such as neglected infectious diseases;[14]
- To support all phases of clinical trials (phase I to IV);
- To NOT expand the geographical scope;
- To increase the duration of the programme.

According to the consultations, there was no convincing support for an extended geographical scope, and the focus should remain in sub-Saharan Africa. Extension of the scope to other PRD, such as neglected infectious diseases, as well as to all phases of clinical development was retained for further considerations. Moreover, the extension of the duration of the EDCTP2 programme to 10 years (instead of the initial 5 years for EDCTP1) was retained for

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[13] The scope of the EDCTP1 programme is "to accelerate the development of new clinical interventions to fight HIV/AIDS, malaria and tuberculosis in the developing countries, particularly in sub-Saharan Africa, and to improve generally the quality of research in relation to these diseases. The EDCTP Programme has been drawn up with a view to stepping up cooperation and the networking of European national programmes, accelerating clinical trials of new products, in particular drugs and vaccines, in the developing countries, helping to develop and strengthen capacities in the developing countries, including the promotion of technology transfer where appropriate and encouraging the participation of the private sector and mobilising additional funds to fight these diseases, including funds from the private sector. Because of the nature of the Programme, a significant part of the funding would be spent in the developing countries." [6]

[14] This extension was already considered in the 2003 EDCTP decision ([6], §12 of the preamble).

further considerations in view of the considerable time needed for preparing and conducting a clinical trials programme (around 8-15 years, see chapter 2). Table 1 summarizes the results of the consultations and the preferences expressed by the different stakeholder groups.

Table 1: Results of consultations with regard to a potential second EDCTP programme.

	Continue EDCTP	Include other poverty-related diseases (PRD)	Support all stages of clinical trials (phase I to IV)	Expand geographical scope	Increase duration to 10 years
Public Consultation [18]	++	++	++	+/-	Not addressed
Independent Expert Panel [19]	++	++	++	-	++
European EDCTP participating states [3, 9]	++	++	++	-	++
Pharmaceutical industry [20]	++	++	++	Not addressed	Not addressed
Foundations and PDPs [28, 29, 30]	++	++	++	++	Not addressed

++/strongly supported, +/supported, -/not supported

2. PROBLEM DEFINITION

Despite the results of the current EDCTP programme and complementary national, EU and international initiatives the **lack of effective and safe medical interventions against poverty-related diseases (PRD) persists** and the socio-economic burden of these diseases remains a limiting factor for a sustainable development of developing countries and in particular in sub-Saharan Africa [12]. Long-term control of PRD will require a combination of both medical innovation and development cooperation [34, 35].

While general improvement of factors such as nutrition, sanitation and infrastructures will surely be important, an effective long-term control will also require the development of new or improved medical products. Previous examples have shown that the development and introduction of new medical products can have dramatic effects. In early 2011, the new meningitis A vaccine (MenAfriVac), which was developed specifically for sub-Saharan Africa, was introduced in a number of African countries in the Sahel area. Since then there have been no cases of meningitis A among people who were vaccinated [36]. An even more dramatic effect has been seen from the introduction of modern antiretroviral treatment (ART) against HIV/AIDS [37]. This has generated significant results, and the number of newly infected people fell from 2.2 million in 2001 to 1.8 million in 2009, while the number of AIDS-related deaths has also been declining significantly in the same period [38]. The development and delivery of effective and affordable ART has been a key component in reaching these impressive goals.

2.1. Problems requiring actions

2.1.1. The persistant high socio-economic burden of PRD

PRD are a heterogeneous group of infectious diseases that disproportionately affect the world's poorest and most marginalised populations.[15] More than one billion people, including 400 million children, suffer from one or more of these diseases and each year PRD cause 13.7 million deaths. HIV/AIDS alone kills an estimated 2 million people every year, while malaria and tuberculosis together kill an estimated 2.2 million people [39, 40, 41, 42]. Other PRD are less deadly but disable, deform and increase the patients' vulnerability to other diseases [43, 44].

Sub-Saharan Africa is disproportionally affected by infectious diseases (Figure 2) with approximately 90% of all malaria-related deaths occurring in Africa in 2010 [42, 45]. This region also accounts for over two thirds (68%) of all people living with HIV and for nearly three quarters (72%) of AIDS-related deaths in 2008 [41, 42]. Africa accounts for 45% of global DALY[16] due to infectious diseases, followed by South-East Asia (30%) and the Eastern Mediterranean region (11%). In relation to the population size, Africa suffers by far from the highest burden with 740 DALY (per 1000 population) compared to 220 for South-East Asia and 250 for the Eastern Mediterranean region [42]. Sub-Saharan Africa is now the only region of the world, where infectious diseases are killing more people than non-communicable diseases [46].

The mortality and morbidity have major economic consequences through their impact on productivity - of individuals, households, communities and nations – and on the costs for healthcare. As example, malaria is estimated to cost Africa over $12 billion per year in direct economic loss, while TB is expected to cost the world's poorest countries $ 3 trillion over the next 30 years [47, 48, 49, 50].

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15 Poverty-related diseases include the three major ones HIV/AIDS, malaria and tuberculosis as well as neglected infectious diseases, which are caused by protozoal, bacterial, viral and helminth infections. The neglected infectious diseases may include, but will not be limited to, the 17 neglected tropical diseases (NTD) that are addressed by the WHO's department for NTD control [51].

16 The number of disability-adjusted life years (DALY) is an indicator of the health burden of a specific disease or group of diseases, such as poverty-related infectious diseases. It provides an estimate of the sum of years of potential life lost due to premature mortality and the years of productive life lost.

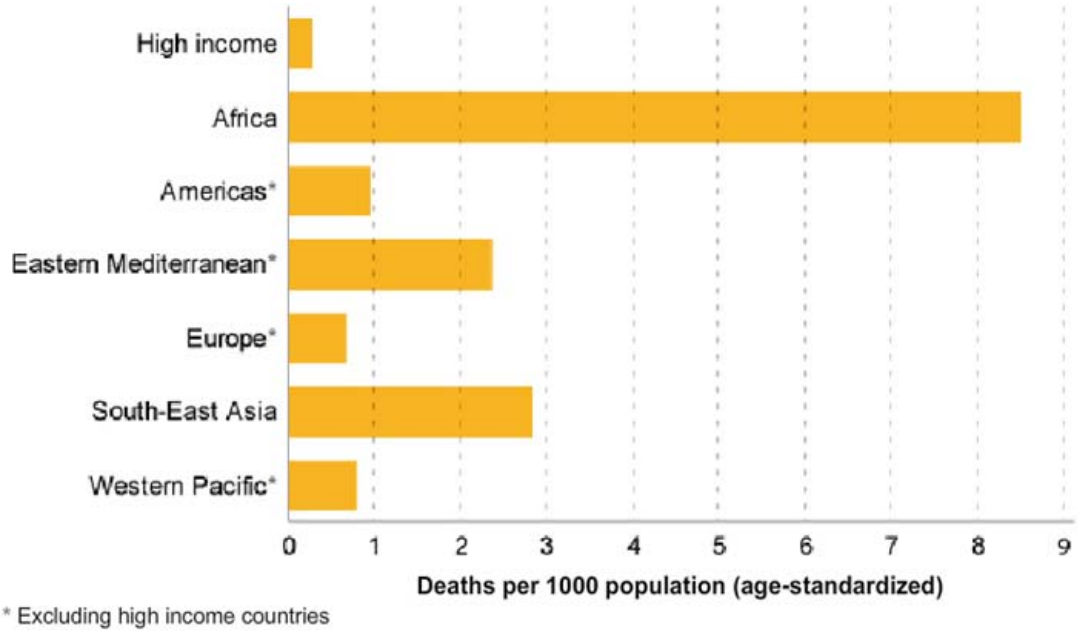

Figure 2: Age-standardized death rates due to infectious diseases, WHO 2004 [42, [51]].

2.1.2. The persistant lack of medical interventions against PRD

Pharmaceutical research and clinical development of new effective medical interventions for PRD is still very limited [47, [52], [53], [54]]. Many drugs and vaccines currently available date back to the early 20th century. For instance, the BCG vaccine against TB was introduced in 1921 and remains the sole vaccine available, and is generally considered highly inadequate [47].

In the period 2000-2009 only 26 new products were developed for PRD, and they were very unevenly distributed with 10 products for HIV/AIDS, 11 for malaria but none for diseases such as tuberculosis, Buruli ulcer, or trachoma [[55]]. There are no effective drugs available for a disease like lymphatic filariasis that results in substantial morbidity and productivity losses in rural areas of Africa, with an estimated $1.3 billion in lost productivity per year [48]. For other diseases, such as sleeping sickness, the only available treatments for severe cases involve highly toxic compounds and complicated dosing regimens that require hospitalization. The few drugs available are in many cases becoming inefficient due to the rise in drug resistance. One of the key strategies against drug resistance of poverty-related diseases is simply to develop new drugs, and thereby get an alternative to apply if/when drug resistance appears.

As of March 2012, there were 374 candidate drugs and vaccines in development against 23 different PRDs (Table 2). This includes candidate drugs and vaccines in all stages of the development pipeline, ranging from discovery phases to late stage clinical trials, but the vast majority of the candidate drugs and vaccines are in discovery and pre-clinical stages (Figure 3). Most of the candidate drugs and vaccines, namely 218 out of the 374 (58%) are for the "big three" diseases: HIV/AIDS, malaria and tuberculosis. The other candidate products in the pipeline could be, for some diseases, the first new therapeutic or preventive interventions in decades.

Table 2: Drug and vaccine candidates for poverty-related infectious diseases (in preclinical and clinical development), status: March 2012 [53].

DISEASE	DRUGS	VACCINES
BIG THREE		
HIV	9 (Microbicides)	48
Tuberculosis	49	45
Malaria	44	23
OTHER NEGLECTED TROPICAL DISEASES		
Buruli ulcer	2	2
Chagas disease	9	0
Dengue	11	13
Fascioliasis	4	1
HAT	10	1
Leprosy	N/A	1
Leishmaniasis	20	7
Lymphatic filariasis	2	2
Onchocerciasis	3	2
Schistosomiasis	4	5
STH: Hookworm	0	2
STH: Ascariasis & Trichuriasis	1	0
Trachoma	N/A	4
OTHER IMPORTANT DISEASES OF POVERTY		
Diarrheal disease	4	N/A
Cholera	N/A	5
ETEC	N/A	11
Rotavirus	N/A	4
Shigellosis	N/A	7
Typhoid fever	N/A	6
Pneumococcal disease	N/A	13

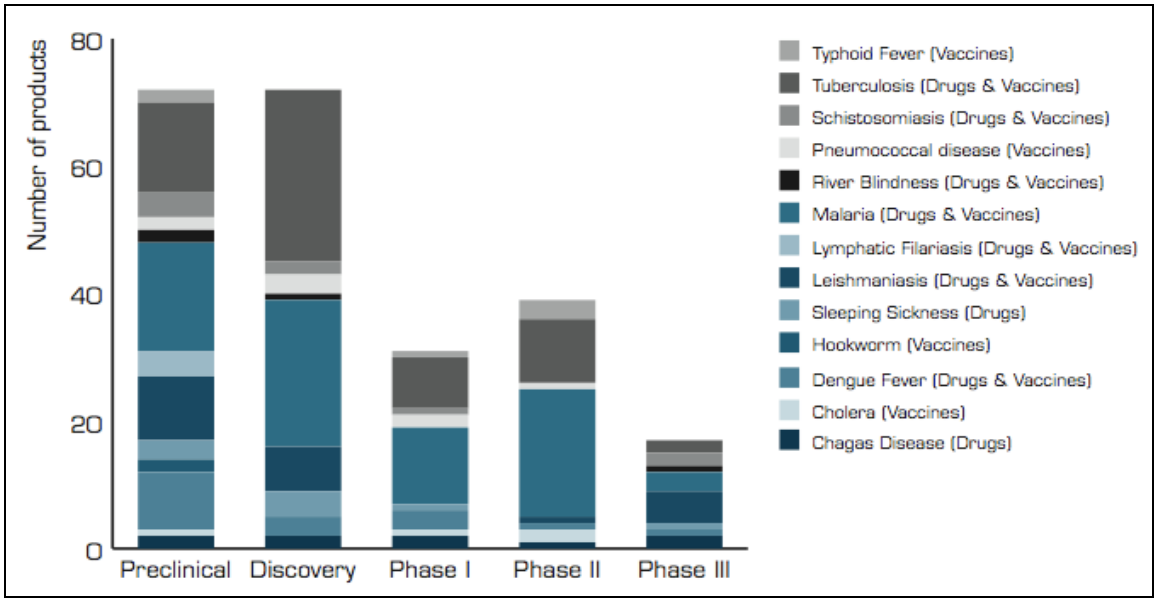

Figure 3: Product pipeline for some poverty-related diseases [47].

Several of the drug and vaccine candidates have been developed with financial support from FP6 and FP7. At least 3 of the vaccine candidates for malaria and two vaccine candidates for leishmaniasis have for instance been financially supported through FP7.[17] The most comprehensive outcome of financial support from FP6 and FP7 is within the area of TB vaccines. Presently, there are 15 TB vaccine candidates in clinical development globally, and

[17] For more information: http://ec.europa.eu/research/health/infectious-diseases/index_en.html.

funding from FP6 and FP7 has been instrumental in supporting 9 of these candidates. Due to previous funding from FP6 and FP7, Europe is therefore in a unique position to develop a new efficacious TB vaccine that would have a major impact on global health. This will require however, that sufficient funding is provided and sufficient critical mass assembled.

2.1.3. The necessity and high costs for clinical trials

Box 1: The role of clinical trials in medical product development.

Before a new medical product can be put on the market, it needs to undergo extensive testing to evaluate the product's safety and efficacy. The testing is done in stages, where the last and most important stages are the clinical trials in human subjects. Clinical trials are conducted in phases. Each phase has a different purpose and answers different questions:

- **Phase 1 trials**: An experimental drug, treatment or vaccine is applied to a small group of people (typically 20-80 individuals) for the first time in order to evaluate the safety, determine a safe dosage range and observe any side effects.
- **Phase 2 trials**: The experimental product is given to a larger group of people (typically 100-300) to test whether it is effective, and to further evaluate the product's safety
- **Phase 3 trials**: The product is given to an even larger group of people (typically 100-3000) to confirm its effectiveness, monitor adverse effects, and compare it to commonly used treatments.
- **Phase 4 trials**: These trials are conducted when the medical product has already been submitted for regulatory approval. In phase 4 trials, the medical product can be tested for additional properties, in additional patient populations and in combination with other treatments.

The most difficult and expensive part of pharmaceutical development is the clinical testing in humans (Box 1). Clinical testing is essential for receiving marketing authorisation by national regulators. A clinical trials programme (Figure 4) typically lasts from 8 to 15 years with an average cost of €500 million per new chemical entity depending on the diseases and product type [47, [56], [57]]. This is broken down into a few million Euros for early stage trials (phase I and IIa) whereas late stage clinical trials (phase IIb, III and IV) can cost hundreds of millions [[58], [59], [60], [61]]. For instance, the clinical development costs for GlaxoSmithKline's RTS,S vaccine against malaria is around €550 million [[62], [63]]. Similarly, it has been estimated that the total cost of developing 2 vaccines against different types of TB would range from $500-850 million on the basis of the current portfolio of vaccine candidates [[64]].

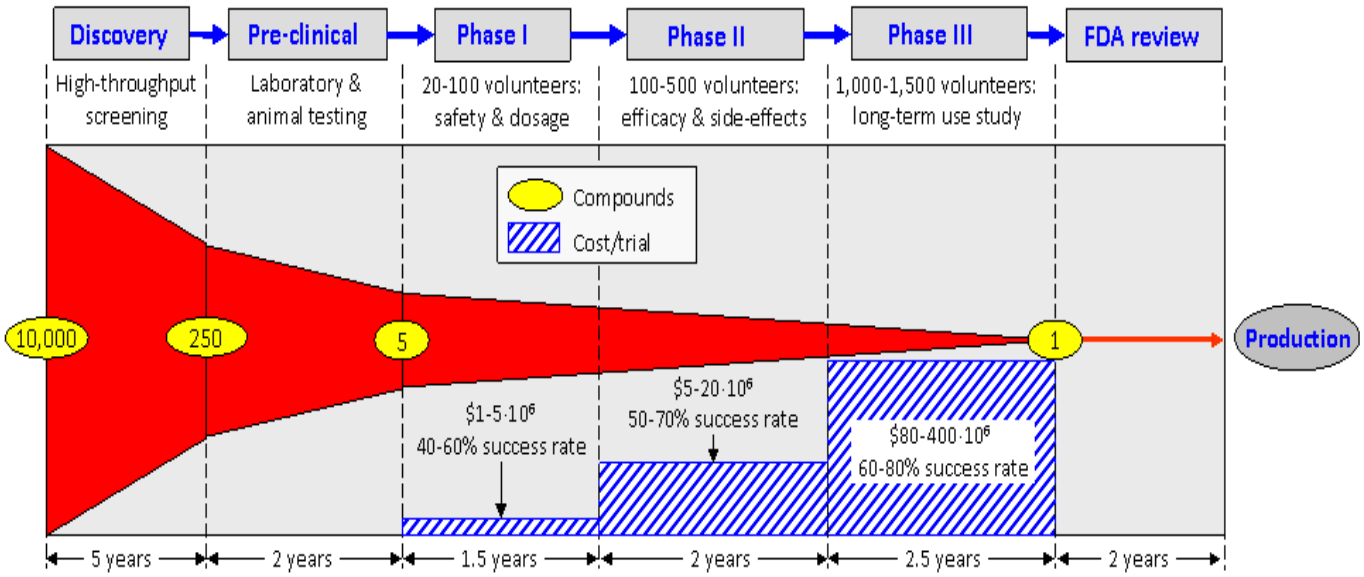

Figure 4: Simplified overview on the clinical development process for a pharmaceutical product [[65]].

2.1.4. The need to focus on sub-Saharan Africa

Africa accounts for 45% of the global disease burden (as measured by DALY, see section 2.1.1) due to infectious diseases, and sub-Saharan Africa is the only region of the world, where infectious diseases are killing more people than non-communicable diseases [42]. Sub-Saharan Africa is also more affected by PRDs than any other region of the world. Approximately 90% of all malaria-related deaths occur in Africa [41, 45], and more than two thirds of all HIV-infected people are living in sub-Saharan Africa. In terms of global public health, there is therefore compelling reasons to focus on combatting PRDs in sub-Saharan Africa, where the potential impact can be greatest.

The mortality and morbidity of PRDs have major economic consequences for sub-Saharan Africa. Malaria is for example estimated to reduce the gross domestic product (GDP) growth by 1.3% per year [66]. The HIV/AIDS epidemic also dramatically impacts the social and economic situation on the continent. Due to the high rates of HIV infection in southern Africa, the life expectancy of the population decreased from 62 years in 1990–1995 to 48 years in 2000–2005 [67]. This is not only a human tragedy; it also results in a massive loss of the most economically productive individuals, affecting the countries' growth rates, health care, education and political stability. Combatting PRDs will therefore have a higher impact on economic development in sub-Saharan Africa than any other region.

With the Lisbon Treaty entering into force, relations with Africa have become an integral part of the EU's overall political, economic, social and humanitarian agenda. This is outlined in the EU-Africa strategic partnership (2007 Joint Africa-EU Strategy (JAES), and the associated Action Plan 2011-2013 outlines a range of important issues, where the African Union and the European Union should work in partnership [13]. One of these issues is an Africa-EU Partnership on Science, Information Society and Space. Africa has the widest scientific divide and therefore less opportunity to use science and technology for socio-economic transformation than any other region of the world. Investments in African scientific capacities have not been prioritized and the continent is also loosing some of its best scientific and technical expertise to other regions through brain-drain. Bridging the scientific divide within African countries and between Africa and other regions, as well as fostering cooperation are therefore important priorities for the Africa-EU partnership. The EDCTP2 addresses all of these aspects and is therefore well in line with the overall objectives of the EU-Africa strategic partnership.

Taken together, there are therefore compelling arguments for focussing EDCTP2 on sub-Saharan Africa, as this will provide the highest political, economical and public health impact.

2.2. Key achievements of EDCTP

As with many pioneering initiatives, EDCTP had a slow start (2003 to 2006) with many initial problems [21], but the 2009 evaluation report recognised that many of these had been successfully addressed: "*its outputs have dramatically increased since 2007, in terms of product orientated clinical trials, networking (nodes of excellence, fellowships) and capacity development embedded within clinical trials (ethical review, regulations)*" [4].

Up to now, EDCTP has funded 241 projects involving 185 African and 70 European research institutions.[18] Among these projects are 55 clinical trials projects involving 88 individual clinical trials which all were subject to ethical clearance from the competent national ethics board(s) in the country or countries in which the trial(s) take place before any EDCTP-funding was granted. The capacities to carry out clinical trials in accordance with European legislation (section 2.8) and international rules and standards of *Good Clinical Practice* [90, 91] needed first to be developed and strengthened in many sub-Saharan African countries, including ethics review capacities and regulatory governance. Therefore, most of the EDCTP-supported clinical trials projects were launched only after 2007/2008 (Figure 5) and are therefore still on-going. Nevertheless, they have already generated more than 350 scientific publications in peer reviewed journals, while the results from 8 clinical trials have so far been integrated in guidelines or recommendations for improved clinical practice (Box 2). It is estimated that around 7 of the clinical trials launched with the financial support of EDCTP will progress to the next phase of clinical testing, and thus require additional funding of around €250-330 million.

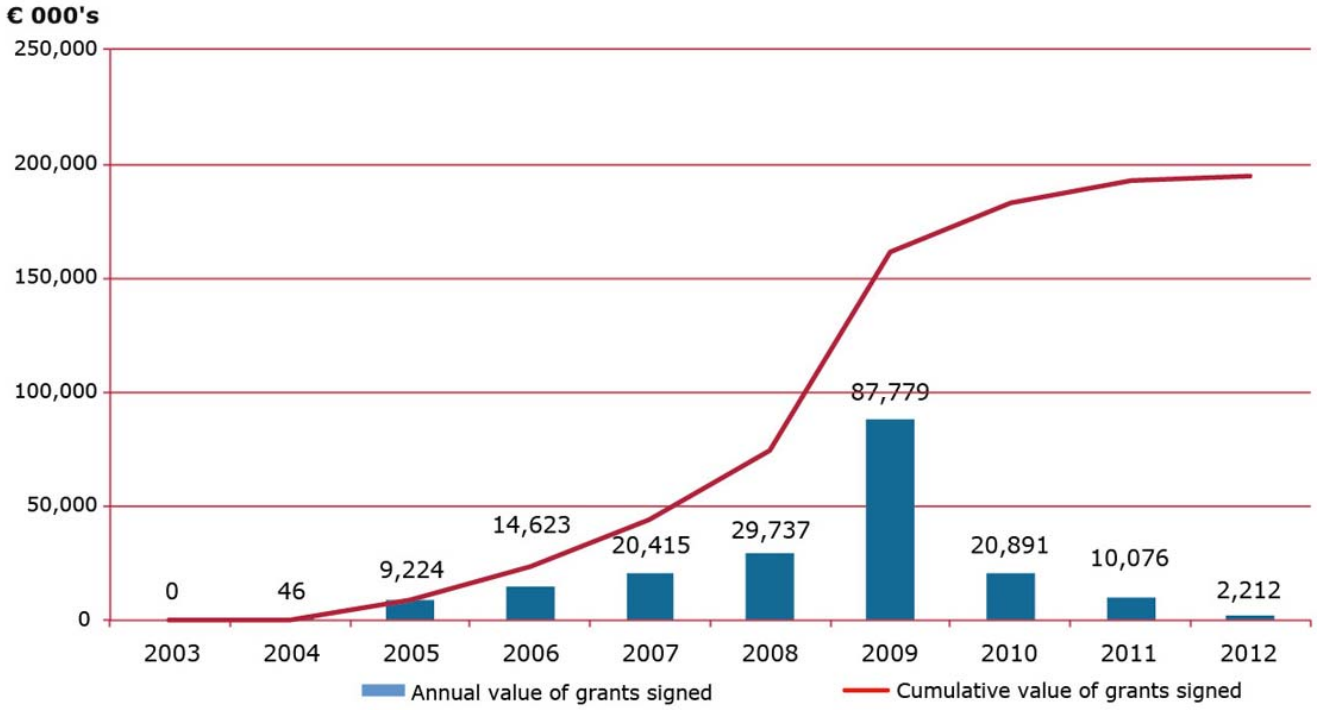

Figure 5: Value of grants signed by EDCTP (2003-2012).

A main achievement of the EDCTP has been to establish a functional organisation that operates according to agreed standards of transparency, accountability and governance in the public sector. EDCTP was the first ever application of Article 169 (now Article 185 TFEU), and therefore a pioneering instrument to develop a new type of long-term, sustainable research partnership among European countries and between European and African countries.

[18] 55 clinical trials projects, 69 fellowships and training grants, 77 projects on strengthening ethical and regulatory capacities, 14 North-North coordination projects, 15 South-South networking projects, 11 strategic primer grants.

This is reflected in EDCTP's governance structure, which involves African policy-makers and researchers in decision-making and priority-setting. This ensures a partnership between African and European countries, built on trust, mutual benefit, and common ownership and leadership. Europe's strong commitment to partnership is reflected in the 75% of EDCTP-funding allocated to African research institutions, and the 49% of clinical trials led by African researchers. The EDCTP has thereby become a good example of a modern North-South collaboration on the basis of equal partnership. This has been recognised at high political level on several occasions, e.g. in the joint statement of the recent EU/South Africa summit [68], in the G8 Declaration on the fight against infectious diseases (G8 Summit, St Petersburg, 2006) [69], and others [30, 31, 55].

While establishing itself as a robust and functioning organisation, the EDCTP has also made important contributions to overcome the key problems drivers for PRD product development during its first decade of operation.

Box 2: EDCTP1 achievements in medical interventions against HIV/AIDS, malaria and TB.

Under EDCTP1, **55 research projects** involving **88 clinical trials** have been funded, promoting African-European and notably trans-African partnerships in clinical trials with more than 100,000 African patients (for therapeutic trials) and healthy volunteers (for vaccine trials): **31 trials on HIV/AIDS, 25 trials on TB, 32 trials on malaria.**

Many of the clinical trials supported by EDCTP1 address the improvement and adaptation of existing medical interventions and drug treatments to specific, vulnerable target groups such as malnourished children or pregnant women. These trials were launched in accordance with ICH standards on good clinical practice [91].

Most clinical trials are still on-going (64 out of the 88). However, some first positive results have been achieved:

- **Kesho Bora study** of highly active anti-retroviral therapy during pregnancy and breastfeeding demonstrated a 43% reduction in HIV infections in infants and more than 50% reduction of mother-to-child transmission during breastfeeding. The findings were presented at the 5th International Aids Society Conference in 2009 and informed the new 2010 WHO guidelines on prevention of mother-to-child transmission of HIV.
- **4ABC study** conducted at twelve trial centres in seven sub-Saharan African countries (Burkina Faso, Gabon, Mozambique, Nigeria, Rwanda, Uganda, and Zambia). More than 10,000 children between 6 and 59 months old were screened and a total of 4,116 children were included in the study and treated. Three novel artemisinin-based combination drugs were found to be safe and efficacious in treating children with uncomplicated malaria. The study informed African Ministries of Health on relative safety and efficacy of available artemisinin-based combination therapies, and its results supported the WHO recommendation of dihydroartemisinin-piperaquine (DHAPQ) as a treatment option for uncomplicated malaria**.**
- **REMoXTB** addresses the rapid evaluation of moxifloxacin in the treatment of sputum smear positive tuberculosis. This study is part of the **PanACEA** Consortium and is evaluating moxifloxacin as a treatment shortening regimen for treatment of tuberculosis. Enrolment was completed in January 2012 and patients are being followed up for 18 months. If the results are positive, the product developers, TB Alliance and the pharmaceutical company Bayer, will seek registration of moxifloxacin as part of a multi-drug regimen for drug-sensitive tuberculosis. This project has made a major contribution to building capacity for regulatory standard clinical trial sites in Africa. If found non-inferior, this regimen will significantly shorten the treatment period of drug-sensitive tuberculosis.
- **Severe Malaria in Children (SMAC) network** demonstrated that 3 doses of iv artesunate over 2 days is as effective as the 5 doses over 3 days regimen) thereby contributing to the development of a lower cost regimen with the potential to reduce the risk of complications and incomplete treatment. A phase III follow-up clinical study completed enrolment of a total of 1046 children with severe malaria, and aims to further optimise the drug administration in the treatment of patients.
- **CHAPAS trial** contributed to the FDA approval in February 2009 and WHO prequalification of Triomune Baby/Junior, a fixed-drug combination formulation for the treatment of HIV in children. This allowed programmes such as the President's Emergeny Plan for AIDS Relief (PEPFAR) and the Clinton Health Access Initiative (CHAI) of the Clinton Foundation to purchase the drug for widespread use in HIV-infected children.
- **HIV-TB Pharmagene** evaluated drug regimens for optimisation of tuberculosis and HIV co-treatment in Africa. The pharmacokinetic and pharmacogenetic data collected on drug-drug interactions will guide treatment policy on optimum dosage.

2.2.1. Budget implementation and leverage effect of EDCTP

Under the EDCTP1 programme, a total of €1'094'411 million was disbursed with €894'411 million contributed by the participating European states and €200 million by the European Union. This includes 241 jointly-funded EDCTP projects with a total budget of €370 million. In terms of commitments, the maximum EU contribution of €200 million to the EDCTP1 programme has been committed fully on these 241 jointly-funded EDCTP project grants and on supporting activities. By 2015, all on-going EDCTP1-funded projects will have finished and the corresponding commitments disbursed. The EDCTP funding activities leveraged additional commitments of €85 million for many of the EDCTP-funded projects, with €14 million from participating sub-Saharan African countries and €71 million from third parties, such as charitable organisations and pharmaceutical companies. This investment has made an important contribution to covering the global investment gap for PRD product development.

2.2.2. Building of clinical research capacity in sub-Saharan Africa

More than 75% of all projects funded by EDCTP (161 projects out of 241) have focused on building human capacity, strengthening research networking and establishing a conducive environment for conducting clinical trials in sub-Saharan Africa in line with European standards (Box 3).

2.2.3. Aligning and integrating the European research landscape for PRD

Besides boosting investments in clinical development and capacities in sub-Saharan Africa, EDCTP has succeeded in triggering structural changes in the traditionally highly fragmented European research landscape (Box 4).

Box 3: EDCTP1 achievements in fostering capacities on clinical trials in sub-Saharan Africa.

- EDCTP1 has provided **420 career and training grants** to African scientists, including 327 postgraduate trainess (183 MSc, 144 MD/PhD), 37 postdoctoral researchers and 50 senior fellows**.** Almost all senior fellows (but one) have remained in their own countries after the training.
- More than **1300 research collaborators in Africa** and more than **750 in Europe** were cooperating in EDCTP-funded activities and benefitting directly or indirectly from EDCTP support.
- Establishment of **four regional networks of excellence**, one in each sub-Saharan African region, i.e. in Western, Eastern, Southern and Central Africa. These networks facilitate the interaction between individual African research teams, help exchange knowledge and pool resources for the conduct and management of clinical trials, including mentoring of less experienced research institutions with experienced ones.
- EDCTP has also funded **74 projects for strengthening ethics and regulatory capacities** in many African countries. This includes support to the establishment of **National Ethics Committees (NECs)** in Benin, Gabon, Mozambique and Rwanda, and the **MARC (Mapping African Research Ethics and Drug Regulatory Capacity)** project, which created an interactive, online map of African countries' capacity to conduct ethics review of health research (www.researchethicsweb.org).
- In collaboration with WHO, EDCTP supported the establishment of **the African Vaccine Regulators Forum** (AVAREF).
- A milestone has been the support to the establishment of the **Pan-African Clinical Trials Registry** (PACTR), which since 2010 has been officially recognised as WHO Primary Registry.

Box 4: The EU-added value and benefits of integrating national programmes.

Clinical trials are of such scale and complexity that **no single country alone can provide the necessary financial/personnel resources or number of patients**, as regards multicentre and/or late stage clinical trials. The EU-level approach on which EDCTP is built allows achieving the required **critical mass of resources**, with EU-funding complementing MS investments.

EDCTP provides a single **common European platform for research cooperation** with sub-Saharan Africa in the fight against PRD. It is instrumental in:

- bringing together and **aligning European public funders** and authorities towards common objectives;
- **brokering new partnerships** between European and African researchers, research institutes and clinical centres;
- **designing common funding strategies**;
- **responding to African needs** and cooperating with national authorities in Africa;
- **attracting and leveraging additional investments** from other public and private funders.

Competitive funding provided by EDCTP through open calls for proposals raises the level of competition from national levels to European level, which in turn results in **spill-over effects** on the quality of research partnerships and projects funded (from bilateral to multi-lateral teams and projects), on the **development of European capacities** and competences, and on the **outcome and impact of public investments**.

EDCTP is **instrumental** in raising **EU's visibility** on the international agenda for global health. It has been mentioned in high-level international meetings, i.e. G8 Declaration on the Fight against Infectious Diseases (2006) at the G8 Summit in St Petersburg (2006) and referred to as **success story** and **role model** for international partnerships between developed and developing countries [74].

This reputation reflects the growing attractiveness of EDCTP to private funders, such as the **Bill and Melinda Gates Foundation**. Such developments could lead other major private funders in the field to join, thus leveraging on private investments.

A wide range of different European public funders in the field now meet on a regular basis to discuss needs and opportunities, and agree on common funding priorities, strategies and procedures. The EDCTP has slowly emerged as the key focal point for pooling European public resources for clinical research in PRD. This is allowing EDCTP to cover research gaps, which previously have been neglected. The EDCTP is thus covering an important gap between promising early discoveries and products ready for final development and delivery to those in need, as recognised in the 2009 interim evaluation report [4]. Such programme coverage is rare, as European research organizations usually focus on the research part, while overseas development agencies typically focus on implementation. Along the lines of covering structural gaps, the EDCTP has also succeeded in changing traditional research collaboration patterns between European and African countries. A typical EDCTP-funded clinical trial project encompasses 9 institutions from 6 different countries, with 5 institutions from 3 African countries and 4 institutions from 3 European countries. According to the 2009 interim evaluation [4], "*this is considered a unique achievement (…) that no other project or funding agency was able to accomplish, and gather all those countries in collaborative networking activities*".

2.3. Lessons learnt from EDCTP

Despite the achievements of the EDCTP so far, a number of shortcomings were pointed out in the 2009 interim evaluation report [4] and the public consultation [18]. Attempts have since been made to fully or partly ameliorate them. Listed below are the key shortcomings and possible solutions to improvements in the next phase of EDCTP.

2.3.1. Need for changing the current scope of EDCTP

As highlighted in the public consultation there is a need to provide continued support for clinical trials of drugs, vaccines and microbicides against HIV/AIDS, malaria and TB. The EDCTP interim evaluation [4] and stakeholder consultation (section 1.4) have also revealed that other PRD such as Buruli ulcer, trachoma, lymphatic filariasis and sleeping sickness may have an even greater need for support. For these diseases there are very few product candidates in late stage clinical trials due to the same underlying obstacles as for HIV/AIDS, malaria and TB. Moreover, many of the other PRD are often found in the same populations and geographical areas as the three major PRD, and even in the same individuals as co-infections. It is therefore justified, scientifically as well as structurally, to extend the scope of EDCTP2 to address all PRD.

The remit of EDCTP1 was focused on phase II and III clinical trials, but there are no compelling scientific reasons for this limitation. A clinical development programme starts with phase I and passes through phases II and III before reaching the market, and ideally the development should be undertaken as a continued process without unnecessary delay between phases. Moreover, the results of the first phase II trial of a new candidate drug or vaccine may sometimes lead to the product developer returning to phase I to undertake adjustments of the product, before proceeding to additional phase II trials. It would therefore be a clear advantage if the EDCTP2 could include phase I trials. Experience from EDCTP1 has also revealed a need for clinical trials that explore improvements of current products for specific groups of people such as pregnant women or people suffering from co-infections or co-morbidities. Similarly, experts and stakeholders have also highlighted the need to stimulate up-take of new medical products by substantiating safety data and pharmacovigilance through post-marketing (phase IV) clinical trials.

As an entire clinical trials programme can typically last 8-15 years it has been recommended by stakeholders, experts and agreed by the Participating States (PS), to increase the duration of EDCTP2 to 10 years to allow the full range of clinical development to be supported.

The current geographic focus of EDCTP still reflects the greatest urgency as sub-Saharan Africa carries by far the highest disease burden in the world as highlighted by the different stakeholders in the public consultation. Any extension of the geographical scope was neither supported by the experts consulted nor by the PS as an enlarged scope would dilute and reduce the impact. Therefore, any change in the geographical scope was ruled out from further considerations in this IA.

2.3.2. Integration of European national programmes should be improved

As pointed out in the previous section, EDCTP1 succeeded to generate significant outcome by integrating a critical mass of resources from national programmes and aligning them to a commonly agreed funding strategy and joint activities. Such a joint programming approach does not only allow to create a critical mass of investments to support complex and costly research projects, which a single country could not support alone, but also to increase the quality and collaboration patterns of research. However, the 2009 interim evaluation pointed out that "*the potential of coordination and integration of European national programmes in the scope of EDCTP has not yet been fully exploited"* [4]. In the period from 2003 to 2011 about 20% of funds spent by PS on clinical research activities against HIV/AIDS, malaria and

tuberculosis were channelled to EDCTP-funded joint activities [70].[19] However, this is an average figure for the entire period, and closer analysis reveals that the level of integration has drastically increased after the initial period, and in the last 5 years it has reached more than 30% (Figure 6). This trend indicates that EDCTP has become established and increasingly used by PS as an efficient structure for European coordination and integration of PRD research activities. In a next phase of EDCTP, further incentives could be developed and implemented to maintain the trend towards greater integration. One example of this continued trend is the establishment PS-lead initiatives.

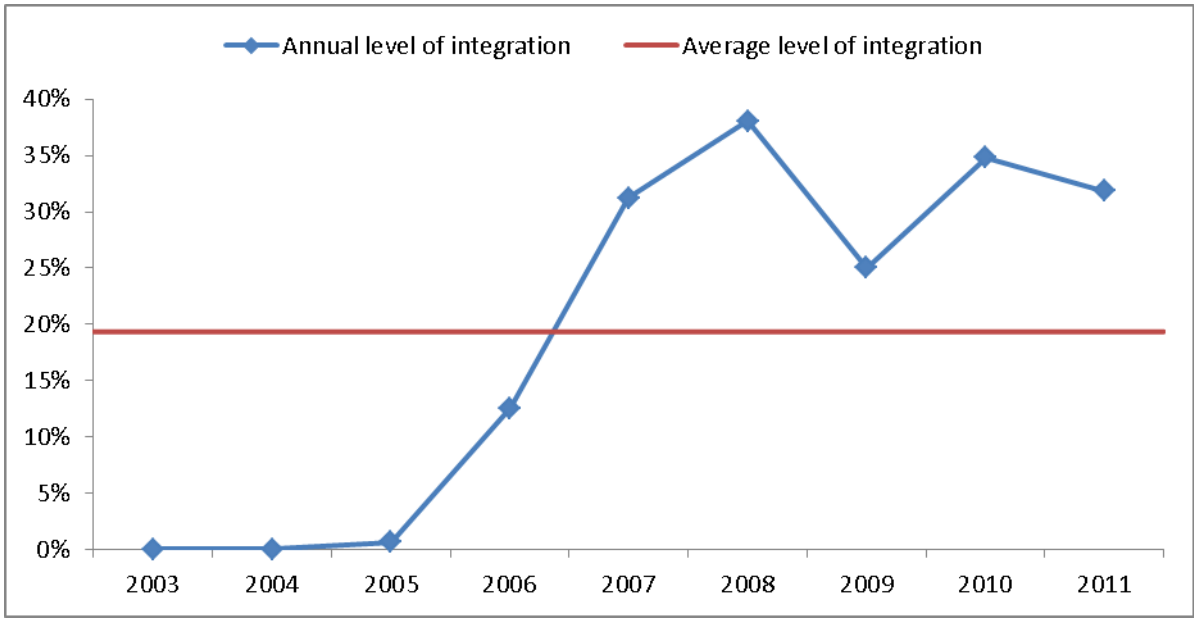

Figure 6: Level of integration of European national programmes through co-investment in EDCTP-funded activities compared to overall investment in the scope of the EDCTP1 programme [70].

2.3.3. Insufficient collaboration with other major funders and pharmaceutical industry

Contrary to initial expectations, raising additional €200 million co-funding from public and private third parties has been highly challenging under EDCTP1. By June 2012, EDCTP had only raised about €70 million from charitable foundations (e.g. BMGF and Wellcome Trust) and pharmaceutical companies. In addition, the pharmaceutical companies have so far mainly contributed to EDCTP-funded trials by supplying and donating medical products that are already authorized for the markets, and where additional post-marketing clinical trials aim to test improved medical intervention regimens.

The lack of clinical research capacities in sub-Saharan African countries has been one of the major obstacles for the private sector to engage in EDCTP1 and to contribute to EDCTP1 activities. In the consultation process for EDCTP2 the pharmaceutical industry recognised, however, that the EDCTP1 programme changed the clinical research landscape in Africa enabling the conduct of clinical trials that meet international standards for scientific, clinical and ethical conduct. Thus, pharmaceutical industry expressed its interest and readiness to join

[19] Over the periode of 2003-2012, 127 million Euros from PS were disbursed to projects which were peer reviewed and selected for funding by EDCTP. Additionally, PS disbursed around €663 million on projects in the scope of the EDCTP1 programme directly through their national programmes [70]. In total, around 790 million were spent by PS through the EDCTP joint programme (20%) and their national programmes (80%).

forces with EDCTP and contribute to the clinical development and testing of medical interventions for poverty-related diseases, as component of their corporate social responsibility policy [20, 33].

The 2009 evaluation report raised the issue of disappointing involvement of third parties and criticized the lack of *"stable working relations with major research funders in the area, or with the pharmaceutical industry"* [4]. Furthermore, public authorities responding to the public consultation emphasized that EDCTP should seek to develop strategic relationships to coordinate and cooperate with similar international funding bodies and initiatives. Some respondents also recommended closer links with relevant African initiatives.

Concrete actions have already been taken to engage in collaboration with major players and harness the impact of EDCTP and Europe as a global player. A Memorandum-of-Understanding (MoU) between the Commission and the BMGF was signed in June 2013 [[71]]. This MoU mentions specifically the EDCTP as a potential area of closer collaboration, and will facilitate future coordination of activities between EDCTP and BMGF, the world's largest private charity funder of global health. A MoU has also been signed by EDCTP and EFPIA in January 2013, and aims to foster cooperation with a focus on joint activities on capacity-building in sub-Saharan Africa [33]. This includes the establishment of an EDCTP-EFPIA industry fellowship programme for training African researchers in clinical trials management at European industry facilities. The programme will also open up the possibility for staff from industry to be trained in running clinical trials in Africa.

In the second phase of EDCTP, more areas of potential common interest must be identified and used as a basis for closer collaboration. The joint selection of product candidates for clinical testing (global portfolio management), the development of combination therapies or head-to-head product comparisons could be areas for EDCTP-industry cooperation. Promising product candidates and improved treatment regimens about to move to the next phase of clinical trials, including expensive marketing authorisation trials (phase III) and post-marketing trials (phase IV), are of particular interest to the pharmaceutical industry. EDCTP provides the opportunity to develop a new business model based on a win-win approach. These potential mutual benefits have been recognised in dedicated meetings with industry and will be further developed under EDCTP2 [20].

2.3.4. Stronger links with EU external policy and development assistance

EDCTP has been conceived to complement the actions implemented under the European Development Fund (EDF) and the Development Cooperation Instrument (DCI) in order to ensure the development and delivery of medical interventions to those in needs (*from bench to bed*). However, this has not been fully achieved as highlighted in the 2009 interim evaluation report's recommendation that the *"General Assembly's members and the Commission should actively seek to expand the financial commitment through the use of additional financial resources such as national development funds and EU funds for Africa"* [4].

Once a medical product has been developed, the remit of EDCTP comes to an end. Yet, the product will still need to reach the patients, which is far from simple in many developing countries. European development assistance provides significant contributions to increase the access to medicines for impoverished communities in developing countries. The impact of both EDCTP and European development assistance could benefit significantly from closer

coordination of actions. This would allow the EU to support a continuum of activities on providing access to medicines starting in the laboratory (supported by the European Research Council, ERC, and the Innovative Medicines Initiative, IMI, the Union's public-private partnership with EFPIA), passing through clinical trials in disease-endemic countries (supported by EDCTP2), until regulatory approval, production and delivery to impoverished populations at affordable prices (supported by European development assistance).

In the second phase of EDCTP, collaboration in the following areas is in preparation:

- The EU contributes to multilateral organisations such as the **Global Fund for AIDS, Tuberculosis, and Malaria (GFATM)** and the **Global Alliance for Vaccines and Immunisation (GAVI)** to provide affordable medicines to poor people in developing countries. The complementarities between EDCTP and these initiatives will be further explored, with the aim of securing a swift introduction and delivery to patients of newly developed pharmaceutical products from the EDCTP.
- Newly developed medical products must be approved by the regulatory authorities before entering the market. However, national and regional capacities to evaluate and monitor new medicinal products are severely limited in most African countries. Strengthening of the **regulatory capacity in sub-Saharan Africa** has been supported by both EDCTP and EDF, the later via a grant to WHO. A future, joint approach should be developed to maximise the impact of EU actions in this area. This should be further strengthened through dialogue and possible involvement of the European Medicines Agency, which has a strategic objective of providing technical assistance in this area.
- Once a new medical product has been developed and enters the market, it must still be followed to monitor any unexpected adverse effects or other safety concerns. However, very few African countries have such a **pharmacovigilance system** in place. EDCTP and EU development assistance could jointly promote the establishment or support the strengthening of regional pharmacovigilance systems in sub-Saharan Africa.
- **Human capacity building** is a prominent component of EDCTPand aims to train medical personnel in clinical research methodology and management, which is pursued by providing grants for short-term trainings, MSc and PhD education programmes, and fellowships for career development. The health systems in Africa are, however, much less specialised than in Europe. In many cases, the same individuals are performing different tasks, some of which could be research, others hospital duties, yet others could be administrative or related to public health aspects. While capacity building is a prominent part of EDCTP, it is formally restricted to clinical research training. However, the complementarities between EDCTP and EU's development assistance in sub-Saharan Africa provides the elements for building a comprehensive EU training programme for medical personnel allowing integration in research, health care and administration. This opportunity should be used as a key component for the EU's sub-Saharan health assistance.

2.3.5. Co-funding rules should be clarified and simplified

The 2009 evaluation report concluded that EDCTP's *"current [national] co-funding arrangements constitute a major source of difficulties and confusion"* [4]. Researchers and organisations responding to the public consultation also called for clearer rules and simplified procedures for co-funding. The Participating States have agreed that for EDCTP2 there will be a common review mechanism and all cofunding will be upfront and detailed in the annual work plan.

2.3.6. Monitoring tools need to be strengthened.

The 2009 evaluation report noted that "*EDCTP should develop a comprehensive framework for process monitoring and evaluation that uses appropriate standard methods and tools and is flexible enough to allow for revisions as needed, based on results of monitoring and evaluation activities*" [4]. Systematic performance, outcome and impact indicators have therefore been developed upfront for EDCTP2 (section 7.2).

2.4. The problem drivers

The persistent lack of effective medical interventions for PRD is affected by five key problem drivers linked to both the nature of the problem and the lessons learnt from the first EDCTP programme:

- Insufficient investment;
- Lack of clinical research capacity in sub-Saharan African countries;
- Fragmented public support;
- Limited scope of the first EDCTP programme;
- Insufficient links to other EU initiatives.

2.4.1. Insufficient investment

The first major hurdle relates to inadequate funding for development of new medical solutions for PRD due to the **market failure**. In 2011, the total global investments in this area has been estimated to approximately $3.2 billion, but a recent WHO report [72] has determined that investments would need to be doubled to $6 billion annually to support the clinical development of promising product candidates, which are currently blocked or severely hampered due to lack of financing. There is thus an annual global investment gap of $2.8 billion for product development for PRD.

Private industry invested a total of $504 million in research and clinical development for PRD products in 2011, representing only 16% of the overall global funding of $3.2 billion. In comparison, 63% came from public authorities and 19% from philanthropic private organisations [73]. Despite a huge unmet medical need, private investments in development of new pharmaceutical products for PRD are thus modest. **Reaching into the markets in low-income countries is not business as usual.** Health systems are typically not functional. Key structures and actors these companies usually rely on are missing. Qualified doctors, proper regulation, efficient logistics systems and health insurance – all these market enablers are frequently lacking or of poor quality. As a result, traditional business models just do not work and public support is essential to bring new medical interventions to the market.

While the first phase of EDCTP has contributed to fill the global investment gap, it is also clear that the magnitude of the gap - $2.8 billion per year - requires a significant increase to make a real impact and to position EDCTP as world leader.

2.4.2. Lack of clinical research capacity in sub-Saharan African countries

Clinical studies on the safety and efficacy of drugs and vaccines need to be conducted in population groups in which these products will actually be used. There are compelling scientific reasons for this, but an additional advantage is that it will facilitate and accelerate uptake into the local healthcare systems.

However, the lack of adequate capacities for clinical trials is a major obstacle for testing PRD products in sub-Saharan Africa. Many countries in sub-Saharan Africa are still lacking the

basic infrastructure and know-how to conduct clinical trials that meet international standards of scientific and ethical conduct [74]. In many countries, the legal framework for conducting clinical trials is insufficient, uncertain or completely lacking with regard to ethical approval, handling of biological material, and governance of intellectual property rights [75]. Another impediment is a shortage of qualified human resources in clinical research and practice. Despite the extensive investments and successes of EDCTP in human capacity building activities, many African countries lack the necessary technical expertise in crucial fields such as data management, project management and leadership of clinical research [3, 19, 20, 23]. The lack of promising career paths to attract and retain excellent researchers and the insufficient number of top research centres, where capacity development could be focused are additional limitations and a major obstacle for the development of medical interventions [75].

74% of respondents to the public consultation stressed the success of EDCTP's capacity building measures in Africa and praised their integration in the clinical trials supported by EDCTP. Many respondents suggested extending these measures.

2.4.3. Fragmented public support

The EU is one of the largest supporters of international health research for tackling PRD [3, 76]. In 2011, six EU Member States (MS) and the EU were among the top 12 public funders of research and clinical development against these diseases. However, European public funding policies and activities in global health research remain highly fragmented into individual national programmes and activities [77, 78]. This fragmentation is characterised by structural, procedural and regulatory diversity, where policies, programmes and activities are organised and supported at national level. This was highlighted in the 2007 and 2009 evaluation reports on EDCTP as being the major barrier to the integration of national programmes and investments [21, 22]. Furthermore, even at national level there is often a significant fragmentation. Funding from national development agencies accounts thus for about 60% of European research funding to PRDs. Research, product development and capacity building for clinical research in developing countries is thus often funded by both research agencies and development assistance agencies, and often with minimal coordination between them.

These factors can result in an overlap or even duplication of efforts and put significant strain on critical bottlenecks (expertise, facilities, funding). A clear example of duplication of efforts exists in the geographical coverage of projects supported by individual MS. Over 50% of clinical trials, capacity building and networking projects (364) are thus concentrated in just three sub-Saharan African countries - South Africa (64), Uganda (49) and Tanzania (79) [77]. In comparison, only one project was carried out in Central Africa. This considerably limits the impact on clinical capacity building across the whole sub-Saharan Africa, which further limits the capacity to undertake multi-site clinical trials across Africa.

Fragmented public programmes with incompatible national funding rules and procedures result in limited diversity and quality of cooperation partnerships as well. In 2010, out of the 210 clinical trials projects on HIV/AIDS, malaria and TB supported by individual MS in sub-Saharan Africa (excluding 40 EDCTP projects), only 29 (14%) involved two or more MS. Similar trends are reported for projects related to capacity building and networking [77]. This reveals a trend where most of MS-led projects are still conducted bilaterally in a direct north-south partnership with limited coordination among European research teams. However, EDCTP funding is contributing significantly to change this pattern by promoting

collaboration among European research teams as it represented the major, if not the sole source of funding for clinical trials projects involving 3 or more MS [77].

The full potential of coordination and integration of European national programmes in the scope of EDCTP has not yet been exploited under the first EDCTP programme.

2.4.4. Limited scope of the first EDCTP programme

As described in previous sections, there is a need to provide continued support for clinical trials of drugs, vaccines and microbicides against HIV/AIDS, malaria and TB, but – as claimed by a majority of stakeholders during consultations and acknowledged by the Participating States in their Strategic Business Plan for EDCTP2 – other PRD such as Buruli ulcer, trachoma, lymphatic filariasis and sleeping sickness may have an even greater need for support. The current scope of EDCTP constrains the exploitation and use of clinical trials capacities built in sub-Saharan Africa under EDCTP1 for clinical trials related to other diseases and medical interventions even though direct benefits to the capacity to deliver healthcare services could be seen. Moreover, as the number of medical products in the development pipeline is limited, such an extended scope would not only mean more opportunities for EDCTP to supporting clinical trials and allow moving candidate products in clinical development from phase I to phase IV, i.e. from the lab to the patients (*from bench to bed*), but also imply less strategic risks for EDCTP since there will be more choices for selecting the most promising product candidates, which in turn would allow for higher impact of EDCTP.

An extension of EDCTP's scope to support all phases of clinical testing and a wider range of PRD with high prevalence in sub-Saharan Africa would thus allow to address the real needs and increase the impact of EDCTP.

2.4.5. Insufficient links to other EU initiatives

EDCTP was initially conceived to interact closely with other relevant EU initiatives, foremost the European programmes for development assistance. So far, this has only happened to a limited extent, but it remains an opportunity to better exploit synergies and achieve greater impact of EU actions in research and development assistance. The remit of EDCTP is restricted to support clinical trials and capacity building for clinical trials. However, in resource poor settings like sub-Saharan Africa, such activities do not exist in isolation, and would achieve a far greater impact if they are integrated and coordinated with the national healthcare systems and programmes.

The EU development assistance supports improvement of health in sub-Saharan Africa through contributions to multilateral organisations and through support to specific projects at national level. Much of this support is allocated to improved access to medicines and capacity strengthening of the weak healthcare systems in the poorest African countries. Coordination between EDCTP activities and EU development assistance on improved access to medicines could therefore ideally create a unbroken innovation chain for access to medicines in Africa, starting with the clinical testing and approval of new medicines to the delivery to the people in need. Similarly, coordination between EDCTP and EU development assistance could establish an integrated plan for capacity strengthening for the healthcare systems in African countries; thereby avoid duplication and competition for the same scarce human resources.

Increased coordination between EDCTP and the EU's development assistance in sub-Saharan Africa constitutes a significant untapped potential that should be better exploited in the future in order to securing a swift introduction and delivery to patients of newly developed medical interventions resulting from EDCTP-funded projects.

2.5. Baseline scenario

In a baseline scenario, the programme would be continued in its present form, mandate, scope and duration. This will require adoption of a new decision continuing the EU participation and funding of an EDCTP2 joint programme with Article 185 TFEU providing the legal basis. The EDCTP activities would remain limited to HIV/AIDS, malaria and tuberculosis, and stay focused on phase II/III clinical trials. Current EDCTP objectives on clinical trials and the integration of the MS' national research programmes would be maintained. Accordingly, the duration and financial commitment from the Participating States would remain stable with at least €200 million for 5 years, matched by the EU with up to €200 million. The combined EU and MS funding would amount to around €400 million *over 5 years*. A contribution of €200 million from other public and private funders would be expected. Such a scenario would not be in line with the Strategic Business Plan of the Participating States [9] which propose to extend the scope and duration of the programme as well as to increase their contribution to at least €552 million for the period 2014-2024.

Under the baseline scenario, a large part of the budget would be needed to financially support the next stage development and testing of the around 7 medical interventions that successfully passed an early stage clinical trial launched with EDCTP1 funding, which requires around €250-330 million. Assets such as infrastructure, equipment and capacities to conduct clinical trials that have been created with the financial support of around €40 million from EDCTP1 would be used in the new programme for new activities, including the integration of these facilities in EDCTP2-funded clinical trials, their adaptation and further development to new specific needs as well as to create complementary facilities and capacities for clinical trials in sub-Saharan Africa.

2.6. Who is affected and how?

Addressing the problem and its drivers would have a high positive impact on health, well-being and economic development of millions of people living in sub-Saharan Africa, and in particular on the children and women of the region who are disproportionately affected by these diseases. Supporting the fight against major poverty-related diseases would also help to safeguard Europe's citizens from these diseases as increasing global mobility (including tourism) and migratory movements mean that Europe may be facing new or returning challenges from infectious diseases. Global warming may further amplify these risks in Europe through the higher prevalence and shift in geographic distribution of these diseases.

Benefits to European and African researchers would also flow from a simple and innovative funding mechanism and from efforts to better coordinate and structure research programmes and activities on poverty-related diseases at European and international level.

Finally, the pharmaceutical industry would be able to contribute to surpass the challenge of these diseases, while sharing the long term benefits of a coordinated set of efforts for capacity building in sub-Saharan Africa, enhancing the industry's ability to provide new medical interventions to patients and markets.

2.7. Need for public intervention at EU level

As outlined above the necessary medical interventions for PRD will not be developed by the private sector alone due to the limited financial incentives. Public intervention at EU level is necessary to bring together compartmentalised national research programmes, help design common research and funding strategies across national borders, and achieve a critical mass of actors and investments required for undertaking resource-intensive clinical trials of new products against poverty-related disease in developing countries, and thereby increase the impact of European activities and investments in this field. Considering budgetary restriction it makes more sense than ever from a purely economic perspective to invest together and make a real difference. Such intervention is in line with the overall provisions of the Treaty on the Functioning of the EU (TFEU), related EU policies and in particular contributes to delivering on the EU's commitments to promote aid effectiveness, inclusive growth and progress towards the achievement of the Millennium Development Goals.

Aiming at strengthening the coherence between EU and national research and innovation programmes, this initiative is embedded into the Treaty's objectives to strengthen the EU's scientific and technology bases (Art. 179.1 TFEU), and to develop a European research area based on cooperation among researchers across borders (Art. 179.2 TFEU), such as through the EU participation in research and development programmes undertaken by several Member States (Art. 185 TFEU). It more particularly contributes to the implementation of the *Europe 2020* strategy [[79]], the *Innovation Union* [[80]] and *Horizon 2020* [5], which call for addressing societal challenges and strengthening international cooperation in research and innovation as a key aspect of the Union's partnership with developing countries. The Commission proposal for *Horizon 2020* makes specific provision for the continuation of the EU's participation and co-funding of an EDCTP2 programme on the basis of article 185 of TFEU [5].

A second EDCTP programme also contributes to the EU's new and extended competences introduced in the Lisbon Treaty on the EU (TEU) with regard to the EU and its Member States pursuing common actions in the field of international relations and cooperation (Art. 21 TEU) and thus to a "Global Europe" [14]. It supports the *EU-Africa partnerships* [13], in particular the *EU-Africa Millennium Development Goals partnership* and the *EU-Africa partnership on Science, Information Society and Space*, and on the implementation of the Commission Communications on *Increasing the impact of Development Policy: an agenda for Change* [[81]] and the *EU Role in Global Health* [[82], [83]]. EDCTP2 is fully in line with the goals of the *European Consensus on Development* [[84], [85]].

2.8. Related EU legislation and initiatives

EDCTP2 will contribute to the Union's commitment towards the 2012 Rio+20 conference conclusions [12] on the development and achievement of internationally agreed Sustainable Development Goals (SDG), including the Millennium Development Goals (MDG), the EU-Africa strategic partnership [13], and ultimately to the Union's vision of a competitive "Global Europe" [14].

It will also contribute to other goals[20] agreed at EU level in the framework of the international sustainability agenda and in line with the Commission Communications on a *Reinforced European Research Area Partnership for Excellence and Growth* [86], on *Partnering in Research and Innovation* [87], on the *EU Role in Global Health* [82, 83], and on *Increasing the Impact of Development Policy: an Agenda for Change* [81]. EDCTP2 is also in line with the goals of the *European Consensus on Development* and the corresponding Code of Conduct [84, 85], the *Charter of Fundamental Rights of the EU* [88], and the *Universal Declaration of Human Rights* [89], and comply with ethical principles included in the revised *Declaration of Helsinki* [90] as well as the *ICH standards on good clinical practice* [91].

Finally, this initiative aligns with the proposed EU Regulation on Clinical Trials [92], which addresses current shortcomings in Europe resulting from too different national legislations hampering product development[21], and is consistent with other EU initiatives aiming at strengthening prevention and control of poverty-related diseases through research, partnerships and international cooperation [93].

3. OBJECTIVES

The objectives have been identified and set on the basis of i) the Union's political goals, ii) the problems and drivers, iii) the achievements and lessons learnt from EDCTP1, and iv) the outcome of the consultations. Figure 6 presents the intervention logic from the problem to the objectives of EDCTP2.

3.1. General objective

In line with the *Union Treaty* (Art 179, 185, 208 TFEU, and Art. 21 TEU), the *Europe 2020* strategy [79], the *Innovation Union* flagship initiative [80] and *Horizon 2020* [5] as well as the Union's commitment towards the 2012 Rio+20 conference conclusions [12] on the development and achievement of internationally agreed Sustainable Development Goals (SDG), including the Millennium Development Goals (MDG), and the EU-Africa strategic partnership [13], the overarching objective of this initiative will be to:

Contribute to the reduction of the social and economic burden of poverty-related diseases in developing countries, in particular in sub-Saharan Africa, by accelerating the clinical development of effective, safe and affordable medical interventions against poverty-related diseases, in partnership with sub-Saharan Africa**.**

3.2. Specific objectives

In order to meet the general objectives supporting the corresponding EU goals and policies, the specific objectives of this initiative are:

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[20] For instance, Declaration of Paris on Aid Effectiveness (2005); the Accra Agenda for Action (2008), the Lisbon Declaration (2007); the Africa-EU Strategic Partnership (2007); the European Programme for Action to Confront HIV/AIDS, Malaria and Tuberculosis through External Action COM(2005)179 final; the EU-US Declaration on HIV/AIDS, malaria and TB, June 2004; EP Report on Major and Neglected Diseases, P6_A(2005)0215; EP Study - Extending the Pipeline - Toward a Comprehensive and Coordinated EU Approach to Poverty Related Diseases, (2008)393786; etc.

[21] The proposed EU Regulation on Clinical Trials could become relevant to EDCTP-funded clinical trials as soon as product registration in the EU is foreseen, in that EU authorities may perform on-site inspections of clinical trials sites, including sites in non-EU countries.

1) **Increased number of new or improved medical interventions against HIV/AIDS, tuberculosis, malaria as well as other poverty-related diseases to the benefit of developing countries**. By the end of the programme at least one new medical product, such as a new drug or a vaccine against TB or any other poverty-related disease, and at least 30 guidelines for improved or extended use of existing drugs will be developed. Moreover, at least 20 candidate products will have progressed in clinical development.
2) **Strengthened cooperation with sub-Saharan African countries in particular on capacity building for conducting clinical trials** in full compliance with the Charter of Fundamental Rights of the EU [88], the Universal Declaration of Human Rights [89], ethical principles included in the revised Declaration of Helsinki [90], and ICH standards on good clinical practice [91], relevant EU legislations, and local ethics requirements of the countries where the clinical activities are to be conducted.
3) **Enhanced coordination, alignment and integration of relevant national programmes** resulting in increased cost-effectiveness of European public investments.
4) **Extended international cooperation** with other public and private funders.
5) **Increased impact due to effective cooperation with relevant EU initiatives**, including the EU development assistance.

3.3. Operational objectives

In order to reach the above-mentioned specific objectives, the following operational objectives have been set, including indicative targets to be met by the end of the EDCTP2 programme in 2024:

- **Support clinical trials (Phase I-IV)** on new or improved medical interventions against poverty-related diseases through partnerships between European and developing countries, in particular sub-Saharan Africa:
  - Target: At least 150 clinical trials supported.
  - Target: Sustain or increase the share in EDCTP-funded clinical trials with African leadership, i.e. at least 50%.
  - Target: At least 1000 peer reviewed scientific articles published.
- **Support research capacity building activities in sub-Saharan Africa** enabling the conduct of clinical trials and contribute to reduce the brain drain:
  - Target: sustain or increase the number of sub-Saharan African countries supported by EDCTP, i.e. at least 30.
  - Target: Double the number of fellowships to African researchers and Ms/PhD to at least 600 compared to EDCTP1 and at least 90% will stay 1 year after the training in Africa.
  - Target: Double the number of capacity building activities supported for conducting clinical trials in sub-Saharan Africa compared to EDCTP1 to at least 150.

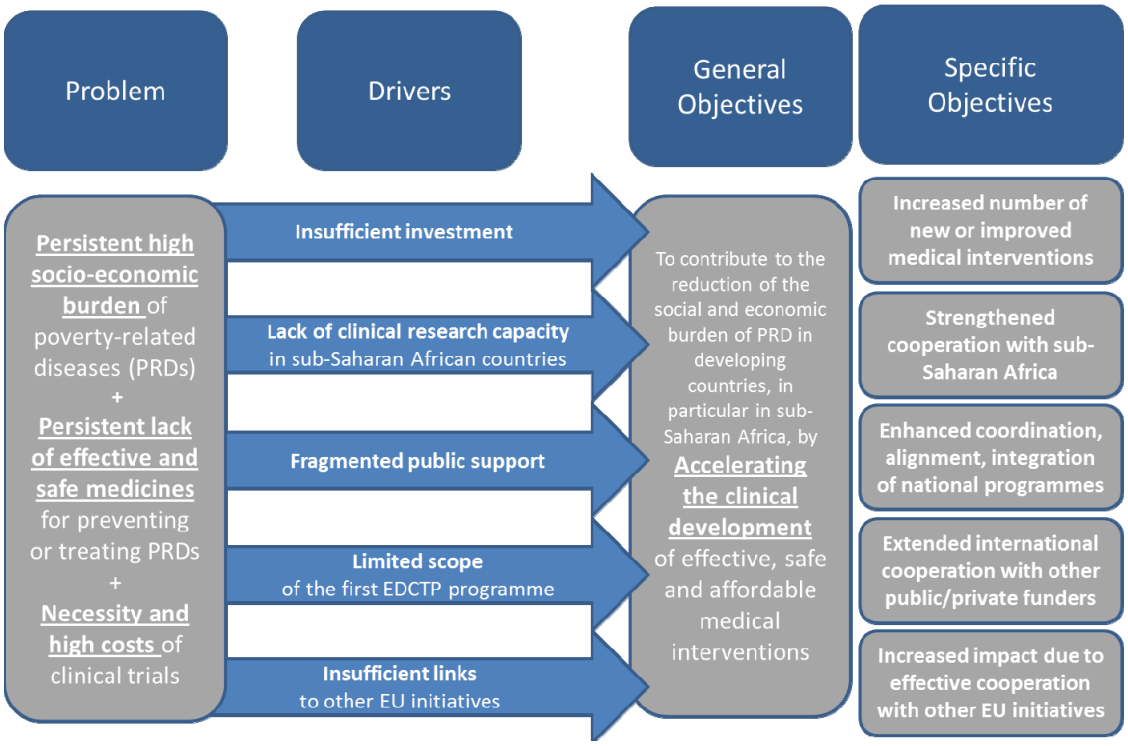


Figure 6: Intervention logic linking the problems requiring action and underlying drivers with the objectives set for EDCTP2.

- **Develop common research agenda, criteria for priority setting and common evaluation:**
  - Target: At least 50% of public investments of participating European states are integrated, aligned or coordinated through the EDCTP joint programme.
- **Increase efficiency of EDCTP programme implementation:**
  - Target: Operating costs below 5% of administered budget.
  - Target: Time-to-Grant[22] below 9 months, and Time-to-Pay[23] below 3 months.
- **Establish cooperation and launch joint actions with other public and private funders**.
  - Target: Increase the contributions received from developing countries to at least € 30 million.
  - Target: Obtain additional contribution, whether public or private, of at least € 500 million.
- **Establish cooperation and launch joint actions with EU, national and international development assistance initiatives** in order to ensure complementarity and enhance impact of the results of EDCTP-funded activities.

4. POLICY OPTIONS

To meet the objectives set out in the previous chapter, the impact assessment considers different policy options and sub-options differing from each other with respect to legal basis, scope, duration, MS and EU contribution to the total budget. Table 3 provides an overview of the six retained policy options and their link to the five building blocks.

22 Time-to-Grant: Time between closure of a call for proposals and signature of the grant agreement.

23 Time-to-Pay: Time between reception of complete financial and technical report until payment of the EU financial contribution.

Table 3: Six policy options composed of five building blocks.

Building Blocks	Policy Option 1	Policy Option 2	Policy Option 3 (baseline)	Policy Option 4a	Policy Option 4c	Policy Option 4c
Legal basis	No EU action	Based on EU programmes (e.g. *Horizon 2020*)	Based on Art. 185	Based on Art. 185	Based on Art. 185	Based on Art. 185
Scope	-	Set by *Horizon 2020*	As EDCTP1*	Extended**	Extended**	Extended**
Duration	-	As *Horizon 2020*: **7 years**	Like EDCTP1: **5 years**	Extended **10 years**[24]	Extended **10 years**[24]	Extended **10 years**[24]
PS funding	-	-	At least **€0.2 bn**	At least **€0.5 bn**	At least **€0.5 bn**	At least **€1 bn**
EU cofunding	-	Set in *Horizon 2020* Annual Work Programme **up to €0.2-1 bn**	up to **€0.2 bn**, matching PS funding	up to **€0.35 bn**, matching PS funding	up to **€0.5 bn**, matching the up-front PS funding	up to **€1 bn (€0.5+0.5 bn)**, matching first an initial €0.5 bn PS funding, and then an additional €0.5 bn PS funding
Overall budget	-	**-**	Like EDCTP1: **€0.4 bn**	Extended scale: **€0.85 bn**	Extended scale: **€1 bn**	Extended scale: **€2 bn**
Share of EU co-funding	0%	100%	up to 50%	up to 40%	up to 50%	up to 50%

* Scope of EDCTP1: a) Developing countries (in particular sub-Saharan Africa); b) Clinical interventions and related capacity-building; c) HIV/AIDS, malaria, tuberculosis.

**Extended scope of EDCTP2: Developing countries (in particular sub-Saharan Africa); Clinical interventions including all phases of clinical trials (phase I-IV) and related capacity-building; HIV/AIDS, malaria, tuberculosis and other poverty-related diseases.

4.1. Option 1: "No EU action"

Under this option, there would be no EU decision to continue participation and financial contribution of the EU and no provisions in EU policies, programmes or funded actions to support EDCTP objectives. European support to clinical trials and related capacity-building would be based only on MS' national programmes. MS could decide to set-up an inter-governmental scheme as an alternative solution. However, the administrative and legal processes to be followed under such inter-governmental schemes are lengthy, difficult and cumbersome. It would require additional costs to set it up and implement, with no guarantee of achieving a high degree of coordination.

4.2. Option 2: "Programme-based"

Under option 2, there would be no EU decision to continue the participation and financial contribution of the EU to support EDCTP objectives. Specific provisions in EU research and development policies and programmes (such as *Horizon 2020*) would allow EU funding to support EDCTP objectives, either in terms of clinical trials or integration of MS' national

[24] EU participation in EDCTP2 has to comply with the provisions of *Horizon 2020*, which provides the EU co-funding to EDCTP2. In particular, EU co-funding to EDCTP2 has to be committed until the end of *Horizon 2020* (i.e. 31.12.2020), while the use of EU funds by EDCTP could last longer.

programmes against PRD. The support to clinical trials and related capacity-building would thus rely on MS' national programmes and EU programmes in the field of PRD.

4.3. Option 3: "Business-as-usual"(baseline scenario)

A new EU decision continuing the participation and financial contribution of the EU to EDCTP2 would be adopted based on the same terms as for EDCTP1 with article 185 of the Treaty on the Functioning of the EU (TFEU) providing the legal basis [6]. EDCTP would remain focused on HIV/AIDS, malaria, and TB, phase II and III of clinical trials, and sub-Saharan Africa. EDCTP1's funding strategy and activities for the coordination and joint implementation of Participating States' (PS) national programmes with the financial participation of the EU would be maintained. The duration and financial commitment from the PS would remain stable with at least €200 million for 5 years, matched by the EU with up to €200 million, respectively. Thus, the total EDCTP2 budget would amount at around **€400 million over 5 years**. Continued support to the existing EDCTP1 portfolio of product candidates would alone consume an estimated €250-330 million, thereby leaving little operational freedom of EDCTP to take in new activities. However, this would not be in line with the Strategic Business Plan from the PS proposing to extend the scope and duration of the programme as well as to increase the total budget for EDCTP2.

4.4. Option 4: "Extended scope"

Under option 4, a new EU decision would be adopted to continue the participation and financial contribution of the EU to the EDCTP2 successor programme on the same legal basis, i.e. article 185 of the TFEU. It will make a significant contribution to bridge the identified global funding gap of $2.8 billion for product development for PRD. It will allow addressing the socio-economic burden of other PRDs (in addition to HIV/AIDS, malaria and TB). It will allow maximising the use of the clinical trial capacities that were developed under EDCTP, and allow supporting the continued clinical development of the most promising product candidates. The increased duration and the provision to fund all stages of clinical trials will make it possible to implement a comprehensive programme that can address a broad range of the obstacles for developing new products for PRD. The extended scope is fully in line with the requests from the PS [2, 3, 9], and in line with the outcome of consultations of the wider public, independent experts, pharmaceutical companies and other stakeholders (section 1.4). The geographical scope would remain focused on sub-Saharan Africa as the world region most affected by poverty-related diseases.

Regarding the overall budget and EU contribution to the EDCTP2 with extended scope, three sub-scenarios are considered in the context of this impact assessment:

4.4.1. Sub-Option 4A: "EU co-funding up to €350 million"

In line with the increased duration and scope, the total budget of EDCTP2 would be **€0.85 billion over 10 years** with an EU contribution up to **€350 million** matching the PS' contribution of at least €500 million as indicated in the SBIP. This means that up to 40% of the combined EU/PS budget for EDCTP2 would be co-funded by the EU.

4.4.2. Sub-Option 4B: "EU co-funding up to €500 million"

The total budget of EDCTP2 would be **€1 billion over 10 years.** The EU would contribute - throughout the duration of *Horizon 2020* [5] - up to **€500 million** to match the PS' firm up-front commitment of **€500 million**. This means that the EU co-funding

would be increased but limited to 50% of combined EU/PS funding. This means that up to 50% of the combined EU/PS budget for EDCTP2 would be co-funded by the EU.

4.4.3. Sub-Option 4C: "EU co-funding up to €1 billion"

As in option 4B, the EU would in a first step contribute up to €500 million to match the PS' firm initial commitment of at least €500 million. In order to provide additional leverage, the EU would contribute up to an additional €500 million to match additional contributions from PS or other entities. The Commission may reduce or cancel this additional contribution, whichever appropriate, based on a negative independent interim evaluation in 2017, and account being taken of the effective capacity of EDCTP2 to plan and manage corresponding additional operations within the duration of the programme and based on an actual spending to the time of the interim evaluation.

Thus, the EU contribution – throughout the duration of *Horizon 2020* [5] – could be up to €1 billion to match at least €1 billion contributions from PS, such that the total EDCTP2 budget would amount at around €2 billion over 10 years. This means that up to 50% of the total EDCTP2 budget would be co-funded by the EU.

The level of partnership and objectives that can be addressed by EDCTP2 for the different financial scenarios, depending on the budget available under the next EU Financial programming period 2014-2020, is summarised in Table 4.

Table 4: Potential of option 3 (baseline) and the sub-scenarios of option 4 to address the specific objectives, due to the budget available.

EU contribution (€ million)	**Level of partnership**	**Specific objectives**
200 (baseline scenario)	PS have committed to contribute €500 million to EDCTP2. A budget at the level of EDCTP1 will not meet the plans of PS, and the proposed expansion of scope for EDCTP2 cannot be met.	Clinical trials will be restricted to HIV/AIDS, malaria and TB. Very limited resources will be available to test new products as €250-330 million will be needed to bring forward the current EDCTP1 portfolio of candidate products. Only 300 African scientists will receive training fellowships. The 4 existing African clinical trials networks will not be expanded. No new products can be expected. The specific objectives of EDCTP2 cannot be met.
Additional 140 (total 340)	The EU contribution will not match the initial commitment from PS. The plans of PS will therefore not be met, and the attractiveness and leveraging effect of EDCTP2 will be limited. EDCTP will remain a niche player, albeit an important one. EDCTP will depend on global partners for setting priorities and supporting costly phase III clinical trials.	Slightly more clinical trials and slightly more African fellowships can be supported, while the scope will expand to all PRDs. The 4 existing African clinical trials networks will be sustained, and expanded to address other PRDs and co-infections. No new products can be expected. The specific objectives can only be partially met.
Additional 160 (total 500)	A total EU contribution of €500 million will match the initial commitment from PS. EDCTP will be able to play an important global role, and will act as an equal partner among other major funders.	About twice as many clinical trials and African fellowships can be supported. The 4 existing African clinical trials networks can be significantly strengthened. Evidence for use of 8-10 existing products for new clinical indications will be provided, but no new products for PRD will be developed. Objectives 2-5 can be achieved and partly objective 1.
Additional 500 (total 1000)	An EU contribution of €1 billion will match the initial €500 million commitments and subsequent €500 million contributions from PS, conditioned by a positive interim	EDCTP will have a magnitude and position that will allow it to support and lead large, ambitious clinical trials. At least 150 clinical trials and 600 African fellowships will be supported. Evidence for

	evaluation of EDCTP. EDCTP can therefore have a major leveraging effect that will attract multiple partners, and precipitate EDCTP as a catalyst for global coordination and cooperation. EDCTP is therefore likely to take a natural leadership role in the global health landscape.	improved or expanded use of more than 30 existing products will be provided. A new, effective drug or vaccine can be achieved. All objectives will be met.

4.5. Other scenarios

Other scenarios include variations of option 3 and 4 considering different legal basis such as articles 184, 186[25] and 187 of the Treaty on the Functioning of the European Union which are neither suitable to address the fragmentation of MS' national programmes nor to ensure continuation of the EDCTP initiative on the short- to medium-term (see Annexe 7 for a detailed analysis of the legal options). Increase of EU development aid would not address the need for development of new or improved medical interventions, which require research and innovation actions.

5. ANALYSING IMPACTS

The section analysis the various impacts of the six policy options (see table 5). Moreover, the economic, social, and environmental impacts as well as the budgetary consequences, including the administrative burden of the six policy options are further discussed in a comparative manner.

5.1. Social and economic impacts

It is difficult to provide exact figures regarding the socio-economic impact of EDCTP as 1) few data are available regarding the socie-economic burden of PRD, and 2) we do not know upfront exactly which drugs or vaccines will be tested. The following section is therefore limited to provide examples of the possible impact.

Option 3 (baseline scenario)

Mortality and morbidity: The disproportionate burden of HIV/AIDS, TB and malaria in sub-Saharan African women and children would be addressed. However, option 3 would not be able to accommodate expensive late stage clinical trials without the participation, co-funding and leadership of other funders. This could limit the potential societal impact significantly. At the same time, option 3 would not address PRDs other than the big 3, which would further limit the social and economic impact. Those PRDs would continue to cause morbidity and mortality and negative downstream social and economic effects. Worldwide productivity losses due to trachoma, for instance, amount to an estimated $2.9 billion [94]. Access to effective treatments and healthcare systems would be improved under this option however, the expected impact would remain limited, as not all PRD would be addressed and the challenges of co-infections/co-morbidities would not be tackled.

Employment: Option 3 would develop local capabilities and create European as well as African highly-skilled jobs, and contribute to reducing Africa's brain drain in these fields. According to a recently published study, European research funding on PRDs in the period 2002-2012 created 13000 new jobs in Europe (many of them highly skilled) while also

[25] The conclusion of an international agreement might, however, be considered on the medium- to long-term as a mean to better associate African countries. This could be a possible outcome of EDCTP2.

creating jobs in Africa [95]. EDCTP1 funding in the period 2003-2012 created 3000 jobs in Africa and 300 in Europe.

Bio-ethics: Compliance of clinical trials projects with international ethical and scientific standards would be maintained under this option and coordinated through EDCTP as a common EU/Africa platform. This would result in improving the impact of these standards, guidelines and indicators.

Ownership and engagement of Sub-Saharan countries: Option 3 would ensure the continuation of EDCTP as a platform for genuine dialogue with African scientists leading to a strengthened promotion of African ownership.

Option 1

Social burden: Compared to option 3, **option 1** would generate much smaller positive impacts on morbidity and mortality of patients in sub-Saharan Africa. Many of the medical products tested in EDCTP1-funded projects are entering into the last phases of clinical development and the discontinuation of the initiative would affect negatively the sustainability of such projects and thus the ability to bring candidate products from clinical development to patients. Efforts to ensure equitable access to treatments and good healthcare settings in sub-Saharan Africa would be maintained under the MS' national programmes. However because of the fragmented national programmes, improvements of the institutional development of health services and of the level of education and training of health professionals would be sub-optimum.

Employment: As underlined by the Independent Expert Panel [19], the discontinuation of EDCTP would thus result in migration and brain drain from sub-Saharan Africa of highly qualified health professionals, who would be faced with fewer career and funding opportunities.

Bio-ethics: Compliance of clinical trials projects with international ethical and scientific standards would be maintained under the MS' national programmes. However, lack of coherent EU/Africa coordination framework to set up standards, guidelines and indicators would limit the impact and follow-up of implementation

Ownership and engagement of Sub-Saharan countries: The political ownership and engagement of sub-Saharan African countries with respect to PRDs would be jeopardised as EDCTP - a success story of EU-Africa partnership - would be discontinued and disappear. A discontinuation would imply the withdrawal of a unique mechanism to engage African partners in a dialogue on clinical research matters with respect to PRDs. This could also impact negatively on the political engagement of sub-Saharan African countries when it comes to cooperation with the EU and its Member States.

Option 2

Morbidity and mortality: Option 2 would be situated between those of options 1 and 3 in terms of, morbidity and mortality, and downstream social and economic impacts.

Employment: Combined volume of EU and MS investments would be more important than for option 1. However, due to persistent fragmentation of the EU and MS national programmes, the impact would be sub-optimum and not sufficient to secure the job opportunities created by EDCTP in sub-Saharan Africa and Europe. In sub-Saharan Africa,

this could lead to health professional migration and brain drain of highly qualified healthcare workers.

Bio-ethics: Similar to option 1.

Ownership and engagement of Sub-Saharan countries: Like option 1, option 2 would jeopardize the political engagement of sub-Saharan African countries with respect to research on PRD and weaken their broader cooperation with the EU and its Member States, since EDCTP provided a unique cooperation platform for brokering and funding EU-Africa research partnerships and cooperation.

Option 4A

Morbidity and mortality: As for option 3, the main achievements of option 4A would be limited to line extension of existing medical products to specific patient groups. As option 4A would have a broader scope than option 3, including all PRDs and all clinical phases, it would nevertheless have a higher social and economic impact as more diseases and disease combinations can be addressed. Like option 3, however, option 4A would not be able to accommodate expensive late stage clinical trials, compromising its ultimate societal impact. Tentative forays would be made into more expensive later stage clinical trials but support would still be focused mainly on less expensive early stage and treatment optimisation clinical trials and on strengthening African clinical research capacities.

Employment: The capacity building actions, including institutional ones and those focused on the training of researchers help to generate long-term economic value by creating highly skilled jobs and sustaining high-quality infrastructures. Jobs will also be created in Europe. An equal number of jobs created under EDCTP1 in Africa and Europe could be expected.

Bio-ethics: Ethical review and regulatory capacities in sub-Saharan Africa would be strengthened.

Ownership and engagement of Sub-Saharan countries: EU's decision to expand the scope of the initiative to all PRD and increase it financial commitment would illustrate the EU and MS's trust toward its African partners and could contribute in strengthened political engagement from sub-Saharan African countries. However, the relative decrease in investments could be perceived by African states and policy-makers as a real disengagement of the EU in the EU-Africa partnership process.

Option 4B

Morbidity and mortality: The main achievements of option 4B would be limited to line extension of existing medical products to specific patient groups. As option 4B would have a bigger budget it would nevertheless have a higher social and economic impact as more diseases and disease combinations can be addressed.

Employment: The positive impact on job creation in both Europe and sub-Saharan Africa and social inclusion and gender equality would be maximised, as all PRD would be addressed. The number of jobs created under EDCTP1 in Africa and Europe would at least be doubled.

Bio-ethics: Similar to option 4A.

Ownership and engagement of Sub-Saharan countries: EU's decision to expand the scope of the initiative to all PRD and increase it financial commitment would illustrate the EU and PS's trust toward its African partners and could contribute in strengthened political engagement from sub-Saharan African countries.

Option 4C

The main importent difference will be that EDCTP under Option 4C would have a magnitude and position that would allow it to support and attract additional funders to support large, ambitious clinical trials. **This makes it realistic that EDCTP would succeed for instance to provide support to the promising global portfolio of TB vaccine candidates, many of which have already been matured for clinical development through funding from FP6 and FP7.** A new TB vaccine would be a huge achievement, as an effective new TB vaccine could prevent more than 105 million cases of TB over a 30 year period. Another example relates to the potential impact of a HIV vaccine. Data from modelling has suggested that an HIV vaccine would reduce the number of new HIV infections in the developing world by a quater over 15 years and preventing 5.6 million new infections. According to a recent report [95] each Euro invested by the EU and its Member States into research on PRDs leverages an equal or greater investment by other donors and generates net benefits to Europe's economy. This option would provide European industry a concrete financial incentive to get closer involved in, engaged with, and connected to global health needs. Such closer industry involvement will also foster the rapid advancement of clinical development from early to later stage trials so that more effective and safe medical interventions reach the patients in need more rapidly.

5.2. Environmental impact

Clinical trials involve the use of equipment and reagents which subsequently need to be disposed of. Under **option 3** (baseline scenario), EDCTP's efforts with respect to the development of environmental risk management standards, guidelines and indicators would be sustained thereby improving the compliance of future EDCTP supported clinical trials projects with good environmental practices. Under **options 1 and 2**, EDCTP’s efforts to strengthen good environmental practice and sustainability, and environmental risk management would be discontinued producing negative environmental impacts. Under **options 4A, 4B and 4C**, EDCTP's efforts with respect to the development of environmental risk management standards, guidelines and indicators would be further strengthened thereby further improving the compliance of future EDCTP supported clinical trials projects with good environmental practices.

5.3. Impacts on Participating States' and EU budgets

Under **option 3** (baseline scenario), the PS on the one hand and the EU on the other hand would each maintain their current (EDCTP1) €200 million financial contribution over a period of 5 years.[26] **Option 1** would produce no additional impact over and above option 3 on PS budgets (their contributions would simply be re-invested into existing national programmes) and a positive impact on the EU budget (no co-funding to EDCTP would be provided). **Option 2** would produce no additional impact on either PS budgets or the EU budget (all PS and EU contributions would simply be re-invested in existing national respectively EU programmes). Controlling for an extended duration, **options 4A and 4B** would increase the PS financial contribution by 25% (from €200 million over 5 years to €500 million over 10 years). As stressed by the PS during their consensus meeting, "*a majority of these funds would not require new budgetary efforts, as many PS contributions would consist of channelling existing resources of the national research programmes through the EDCTP2*", i.e. by increasing alignment and integration of PS' national programmes. **Option 4C** would increase the PS contribution by 150% (from €200 million over 5 years to €1 billion over 10 years). At the same time, and once more controlling for an extended duration, **option 4A** would lower the EU financial contribution by 15% (from €200 million over 5 years to €350 million over 10 years), while **option 4B** would increase the EU contribution by 25% (from €200 million over 5 years to €500 million over 10 years), and **option 4C** would increase it by 150% (from €200 million over 5 years to €1 billion over 10 years).

5.4. Administrative burden impact

EDCTP aims primarily at improving the coordination of PS' national programmes through a common implementation structure. Enforcement costs for both the PS and EU are, therefore, essentially composed of: (1) the "operating costs" incurred by the EDCTP common implementation structure (such as running costs of the EDCTP Secretariat); (2) the "coordination costs" incurred by the participating PS and EU (such as for participating in coordination meetings, for preparing and exchanging information).

Based on the current EDCTP operational management costs (€2.4 million in 2011) and the EU administrative burden calculator, the extrapolated enforcement costs for **option 3** over a 5+3-year[27] period are €20 million (€19.2 million for operating costs, €0.72 million coordination costs assuming participation of 27 MS and the EU). Relative enforcement costs (operating and coordination costs) for option 3 thus amount to 5% of the overall investment made by the EU and the MS (€20 million for a €400 million budget). However, the expected administrative burden for sub-Saharan African countries would be considerably lowered, as through the coordination and integration of EU and national research programmes, EDCTP would facilitate considerably access to funding for African researchers.

Under **options 1 and 2**, the impact on administrative burden and enforcement costs would be positive for the EU, but negative for its MS. The cost involved with the management of

[26] Option 3 provides for the continuation of EU particiaption with the same EU contribution of €200 million as for EDCTP1. Considering inflation and increase in consumer prizes in Europe (OECD Europe: CPI=100 for 2005, CPI=117 for 2012) the nominal value €200 million represent today a real value of around €170 million, i.e. option 3 represents a decrease in EU support of around 15% in real terms.

[27] 5 years of programme duration + 3 years for closing grant execution.

EDCTP would be discontinued, resulting in a saving to the EU. However, option 1 would imply more administrative cost for the PS as activities, which had previously been administered and integrated by the EDCTP secretariat, would have to be handled by individual PS. Option 1 would also imply more administrative burden and costs for researchers, in particular African researchers, since EDCTP as a single gateway to collaborative research funding would be discontinued.

Under **option 4A**, the doubling of both the duration and budget would not have a significant impact on the annual costs and cost-effectiveness of operations such that the estimated operating costs would remain at around 5%, i.e. €43 million. The administrative burden for the sub-Saharan African countries identified in option 3 would be lower under this option due to the extended scope and increased level of coordination and harmonisation among European research funding programmes for sub-Saharan Africa on PRD.

Under **option 4B**, the increased total budget for EDCTP2 would allow making efficiency gains due to economies of scale compared to option 4A. The relative enforcement costs (operating and coordination costs) for the EU and the PS would be reduced to an estimated 4.5%, i.e. €45 million over a 10-year period (calculated on the basis of the combined EU/PS contribution: €1.0 billion). The administrative burden for the sub-Saharan African countries identified in option 4A would be lower under this option due to the extended scale, which facilitates the access to new funding.

Under **option 4C**, the increased total budget for EDCTP2 would allow making additional efficiency gains due to economies of scale compared to option 4B. The relative enforcement costs (operating and coordination costs) for the EU and the PS would be further reduced to an estimated 3.5%, i.e. €53 million over a 10-year period (calculated on the basis of the combined EU/PS contribution: €1.5 billion). The administrative burden for the sub-Saharan African countries identified in option 4B would be lower under this option due to the extended scale, which facilitates the access to new funding.

6. COMPARING OPTIONS

6.1. Overview

As discussed above, and summarised in table 5 and 6, the discontinuation of EDCTP under **options 1 and 2** would produce no or negative impact on PS budgets and a positive or no impact on the EU budget compared to the business-as-usual scenario. The medium- and long-term health and socio-economic costs of these options for sub-Saharan Africa, but also for Europe, however, would be significant and negative. The history of joint programming shows that the discontinuation of the initiative would not be compensated by bilateral or multilateral intergovernmental MS initiatives. Fragmentation would reign. Critical mass of funding, expertise and resources would not be achieved. The effectiveness and efficiency of clinical trials would be affected negatively. The development of effective and safe medical interventions would be compromised. Many of the achievements of EDCTP1 would be at risk. This applies in particular to the durable assets and capacities for the conduct of clinical trials created with the support of EDCTP1 (see section 2.4). None of the 5 objectives for a follow-up to EDCTP1 would therefore be achieved with options 1 or 2. Discontinuing the EU's participation would also undermine Africa's commitment to and confidence in the EU-Africa partnership process as pointed out by the Independent Expert Panel [19]: "*Options 1*

and 2 effectively mean that EDCTP is closed down and many of the gains achieved on the programme in Africa will be damaged or lost. […] These options would be viewed by Africans as a European vote of no confidence in the organisations' largely African management and its current approach to mutual partnership and vision for achieving true partnership in the future. In the short to medium term, this would adversely influence future European-African research and development collaboration in the field of PRD". Last, but not least, discontinuation of EDCTP would also send a serious negative signal, indicating that Europe does not seriously fulfill its political and moral obligation for global health. Given these large-scale negative impacts of options 1 and 2, nearly all stakeholders and respondents to the public consultation rejected the "no EU action" option, while only 9% of respondents supported the "programme-based" option.

The continuation of EDCTP as proposed under **options 3** would make it possible to sustain and continue the activities of EDCTP1. Continued support to existing activities would consume most of the budget, and EDCTP2 would have little freedom to initiate new initiatives. The scope would also remain limited to the present scope, making it impossible for EDCTP to support clinical trials in phase I and IV, and preventing EDCTP in supporting activities related to other PRDs. EDCTP would therefore remain an important European symbol in the global health landscape, but EDCTP would also remain a niche player that mainly supports line extension of existing drugs and targeted capacity building activities.

The continuation of EDCTP with an extended scope as proposed **under options 4** has been requested by the PS and was also supported by 83% of the respondents to the public consultation. Support was high among all categories of respondents, regardless of geographical origin. **Option 4B and C** would allow moving clinical achievements to clinical practice more effectively, reduce the health burden caused by PRDs and in turn relieve the pressure on health budgets and systems in African countries and help to promote economic development. **Option 4C** would even **allow EDCTP to take a global leadership role and prominent position that could attract attention and co-financing from third parties outside of the EU.** While the majority of such funding would eventually flow to sub-Saharan Africa, some of the funding may also benefit the European research community. **Option 4C** would thus **give EDCTP a magnitude and position that would allow it to support large, ambitious programmes throughout the clinical development pipeline.** This makes it realistic that EDCTP under **option 4C** would be able to deliver a new, safe and efficacious product for one of the major PRDs. **Option 4C** would thus allow EDCTP to support the promising portfolio of TB vaccine candidates that has been matured for clinical development through funding from FP6 and FP7. This would be a huge achievement, as an effective new TB vaccine could prevent more than 105 million cases of TB over a 30 year period.

Option 4C would also allow the EDCTP to collaborate with the EU's development assistance programmes to support a comprehensive capacity building for the healthcare sector in the poorest countries in sub-Saharan Africa. Such a programme would have a major positive effect for the functioning of the healthcare systems and the possibilities to retain qualified medical staff in key positions in the healthcare systems in poor countries.

Table 5: Comparative table rating the effectiveness, efficiency and coherency of the policy options.

	Policy Option 1	Policy Option 2	Policy Option 3 (baseline)	Policy Option 4a	Policy Option 4b	Policy Option 4c
EFFECTIVENESS IN ACHIEVING THE SPECIFIC OBJECTIVES	**- √√**	**0**	**0**	**0**	**+ √**	**+ √√**
Clinical Trials: Increased number of new or improved medical interventions against HIV/AIDS, tuberculosis, malaria as well as other poverty-related diseases	- √√	+ √	0	+ √	+ √√	+ √√√
Capacity: Strengthened cooperation with sub-Saharan African countries in particular on capacity building for conducting clinical trials	- √√	- √√	0	0	+ √√	+ √√√
Fragmentation & Cost-effectiveness: Enhanced coordination, alignment and integration of relevant national programmes resulting in increased cost-effectiveness of European public investments	- √√√	- √√	0	+ √	+ √	+ √√
Leverage & Critical Mass: Extended international cooperation	- √√	0	0	0	+ √	+ √√
Coherency: Increased impact due to effective cooperation with relevant EU initiatives, including the EU development assistance	- √√	+ √√	0	0	+ √	+ √√
EFFICIENCY OF IMPLEMENTING THE OPTIONS	**- √√**	**0**	**0**	**+ √**	**+ √**	**+ √√**
Administrative burden	- √	0	0	+ √	+ √	+ √√
Cost-effectiveness	- √√	0	0	+ √	+ √	+ √√
Simplification for researchers	- √√√	+ √	0	+ √	+ √	+ √√
COHERENCY WITH OTHER POLICIES AND PROGRAMMES	**- √√√**	**0**	**0**	**0**	**+ √**	**+ √√√**
Coherency with MS and EU policies and programmes	- √√√	- √	0	+ √√	+ √√	+ √√
Coherency with other EU policies and programmes	- √√	+ √√	0	0	+ √	+ √√
Wider coordination at international level	- √√√	- √	0	0	+ √	+ √√√

- √ = Small negative impact or small costs; - √√ = Medium negative impact/costs; - √√√ = Negative impact/costs; 0 = Neutral (baseline); + √ = Small positive impact/minor savings; + √√ = Medium positive impact/savings; + √√√ = Significant impact/savings.

Table 6: Comparative table summarizing the effectiveness, efficiency and coherency of the policy options.

	Policy Option 1	Policy Option 2	Policy Option 3 (baseline)	Policy Option 4a	Policy Option 4b	Policy Option 4c
EFFECTIVENESS IN ACHIEVING THE SPECIFIC OBJECTIVES						
Increased number of new or improved **medical interventions against HIV/AIDS, tuberculosis, malaria as well as other poverty-related diseases**	The objective will not be met. Only few and smaller scale trials can be expected which may provide some input for improved treatment. No new products can be expected.	The objective will not be met. Some trials can be expected which may provide some input for improved treatment. No new products can be expected.	The objective will not be met. Clinical trials will be restricted to HIV/AIDS, malaria and TB. Very limited resources will be available to test new products as €250-330 million will be needed to bring forward the current EDCTP1 portfolio of candidate products. No new products can be expected.	The objective will partially be met. Will address all PRDs. Some new trials can be expected although the funding will mainly go to follow up from EDCTP1 trials which need to move to next phase. The trials could lead to improved treatment of some specific patient groups. No new products can be expected.	The objective will partially be met. Will address all PRDs. Compared to option 4a, about twice as many clinical trials can be supported. New trials can be expected including funding of follow-up from EDCTP1 trials which needs to move to next phase. The trials should lead to improved treatment of several population groups Evidence for use of 8-10 existing products for new clinical indications will be provided, but no new products for PRD will be developed.	The objective will be met. Will address all PRDs. EDCTP will have a magnitude and position that will allow it to support and lead large, ambitious clinical trials. At least 150 clinical trials can be supported, addressing all PRDs and including large and costly phase III trials. Evidence for improved or expanded use of more than 30 existing products will be provided**. A new, effective and safe drug or vaccine can be achieved, but only under this option.**
Strengthened cooperation with sub-Saharan African countries in particular on **capacity building for conducting clinical trials**	Low, fragmented and based on priorities of European national programmes.	Low; capacity building in developing countries is not a core priority of EU research programmes such as *Horizon 2020*.	Moderate, comparable to EDCTP1. Fellowships for about 300 African scientists, continued support to 4 regional networks and modest support to local ethics and regulatory capacity building. Only 300 African scientists will receive training fellowships. The 4 existing African clinical trials networks will not be expanded.	Moderate, comparable to EDCTP1. Compared to option 3, slightly more African scientists can receive fellowships. The 4 existing African clinical trials network will be sustained, and expanded to address other PRDs and co-infections. Modest support to local ethics and regulatory capacity building.	High. About twice as many African scientists, i.e. 600, can be supported with fellowships. The 4 existing African clinical trials networks can be significantly strengthened. Thorough support to local ethics and regulatory capacity building can be provided.	Very high. Fellowships for at least 600 African scientists can be supported. Contribution to a major EU initiative for capacity building in healthcare in Africa. Comprehensive supporte to the 4 existing African clinical trials networks and thorough support to local ethics and regulatory capacity building can be provided.
Enhanced coordination,	No alignment or integration	Modest coordination on an ad-	Same as EDCTP1.	Higher than EDCTP1. About	Higher than EDCTP1. About	Higher than EDCTP1.

alignment and **integration of relevant national programmes** resulting in increased cost-effectiveness of European public investments		hoc basis. No alignment and integration between European national programmes	About 20-30% of European public funding aligned through EDCTP.	30-50% of European public funding aligned through EDCTP.	30-50% of European public funding aligned through EDCTP.	About 50-70% of European public funding aligned through EDCTP. The levering effect of the higher budget will encourage higher contributions from PS.
Extended international cooperation and increased **leverage of investments from other public and private funders**	Low and based on ad-hoc coordination between individual EU Member States and international initiatives	Moderate, comparable to EDCTP1. Long-term predictability of funding will be difficult and make it difficult to enter into close operational collaboration with international partners.	Moderate, comparable to EDCTP1. The financial volume and flexibility will be insufficient to place EDCTP2 as a world leader, but EDCTP2 could fill key gaps and complement other global initiatives.	Moderate, comparable to EDCTP1. The financial volume and flexibility will be insufficient to place EDCTP2 as a world leader, but EDCTP2 could fill key gaps and complement other global initiatives.	Medium. The financial volume will place EDCTP2 as a flagship initiative, but with limited leveraging effect. In some areas, particularly neglected infectious diseases, EDCTP could play a leadership role.	High. The financial volume will place EDCTP2 as a world leader for clinical trials, and attract direct and indirect contributions from other public and private funders.
Coherency: Increased impact due to effective cooperation with relevant EU initiatives, including the EU development assistance	Low	Medium. Better than EDCTP1 as coordination, contacts and communication can take place through established channels.	Modest, and comparable to EDCTP1. Most resources will be consumed by the core business of EDCTP, making it difficult to establish new actions with complimentary EU initiatives.	Modest, and comparable to EDCTP1. Most resources will be consumed by the core business of EDCTP, making it difficult to establish new actions with complimentary EU initiatives, although the longer duration will make it more attractive.	Higher than EDCTP1. Most resources will be consumed by the core business of EDCTP, but the longer duration and higher total financial volume will make it possible to engage in joint actions with complimentary EU initiatives.	The longer during and higher total financial volume will make it possible to engage in large and long-term programmes in collaboration with complimentary EU initiatives.
EFFICIENCY OF IMPLEMENTING THE OPTIONS						
Cost-effectiveness	National programmes are not coordinated; Lack of critical mass and central implementation structure does not allow to fund costly, multilateral projects and does not allow for economies of scale.	National programmes are not coordinated; EU-funded projects allow for some coordination of nationally-funded actors and activities; Lack of critical mass and central implementation structure does not allow making economies of scale.	Up to 30% of national programmes will be implemented under EDCTP2 with the support of a dedicated implementation structure, operating with harmonised rules and centralised processes which allows for overall cost savings.	Up to 50% of national programmes will be implemented under EDCTP2 with the support of a dedicated implementation structure, operating with harmonised rules and centralised processes which allows for overall cost savings, Further cost savings due to economies of scale and scope.	Up to 50% of national programmes will be implemented under EDCTP2 with the support of a dedicated implementation structure, operating with harmonised rules and centralised processes which allows for overall cost savings. Further cost savings due to economies of scale and scope.	Up to 70% of national programmes will be implemented under EDCTP2, supported by an implementing structure that operates with harmonised rules and centralised processes, which allows for overall cost savings. Further cost savings due to economies of scale and scope.
Administrative burden for MS and EU	Administrative burden for implementing national programmes lies solely with MS. Coordination efforts and related costs would be discontinued resulting in	Even though EU and national programme investments would not be integrated, some coordination activities at EU level funded by EU programmes would imply some	Similar with a dedicated implementation structure managing a small budget. These will remain the same as for EDCTP1, i.e. around 5% of the administered budget.	Similar to option 3 but for a longer duration.	Smaller for a dedicated implementation structure managing a high budget. A higher combined EU+MS budget will create economies of scale and	Smaller for a dedicated implementation structure managing a high budget. A higher combined EU+MS budget will create economies of scale and

	limited cost savings, which do not compensate for the loss of cost-effectiveness.	administrative costs for EU and MS.			reduce operating costs to an estimated 4.5%.	reduce operating costs to an estimated 3.5%.
Estimated average operating costs[28,29,30]	5-10%	5%	5%	5%	4.5%	3.5%
Administrative burden for researchers	Increased administrative burden for the researchers as EDCTP as a gateway to European and national funding would disappear. Researchers would need to apply and comply with rules and procedures of different national programmes.	European efforts against PRD would rely on both EU and MS national programmes with limited coordination. The burden for researchers would increase due to different rules and procedures of EU and different national programmes.	EDCTP as a platform for coordination and integration of EU and MS national programmes would facilitate funding of researchers, and thus reduce enforcement costs for researchers.	Similar to option 3.	Similar to option 3.	Similar to option 3.
COHERENCY WITH OTHER POLICIES, PROGRAMMES						
Coherency with MS policies and programmes	Very limited coherency	National programmes act independently and are only coordinated joint participation in individual EU funded actions.	Up to 30 of national programmes aligned or integrated towards common objectives.	Up to 50% of national programmes aligned or integrated towards common objectives.	Up to 50% of national programmes aligned or integrated towards common objectives.	Up to 70% of national programmes aligned or integrated towards common objectives
Wider coordination at international level	Limited coherency. Based on national activities and initiatives.	Limited coherency. Mainly based on national activities and initiatives, and some EU supported activities.	Some coordination	EDCTP would be an important European contribution to global coordination, yet mainly be a follower of other, larger initiatives.	EDCTP would act as an equal partner to other major initiatives.	EDCTP would have a leadership role in global coordination and priority setting.

[28] Operating costs and annual budget of European research funding agencies in 2011: 11.8% - €746 million (Swiss National Science Foundation); 7% - €561 million (Swedish Research Council); 5%, €54 million (Agence National de la Recherche du SIDA); 4.6% - €3088 million (European Commission, DG-RTD); 3.8% - €195 million (Austrian Science Fund); 2.25% - €2449 million (German Research Foundation); 2.2% - €1300 million (European Research Council).

[29] Operating costs (excluding expenditures for "advocacy and fundraising") and annual budget of Product Development Partnerships (PDPs) in 2011: 12.5% - $284 million (PATH – A Catalyst for Global Health); 8.2% - €26 million (DNDi - Drugs for Neglected Diseases initiative); 14.1% - €48 million (Aeras – Developing New Tuberculosis Vaccines for the World); 13.7% - $83 million (IAVI - International AIDS Vaccine Initiative); 9.6% - $55 million (MMV – Medicines for Malaria Venture).

[30] Operating costs of development assistance agencies are estimated at 7-9% of official development assistance ODA (Florian Kitt: "EU Aid Architecture: Recent Trends and Policy Directions", World Bank Group, January 2010; William Easterly and Tobias Pfutze: "Where Does the Money Go? Best and Worst Practices in Foreign Aid", Journal of Economic Perspectives, Vol 22 (2), 2008, p 29–52).

6.2. Preferred option

From Tables 5 and 6, it is clear that **option 4C** constitutes **the preferred option** as it is the most effective, efficient as well as coherent option. It requires the largest EU budget this approach will transform EDCTP, Europe included, into a major global player taking into account that the annual global investment gap is estimated to be of $2.8 billion in product development for PRDs. It will have sufficient financial volume to provide leadership in developing new safe and efficacious products for one of the three major PRDs or the neglected diseases, for instance in developing a TB vaccine for the world (estimated to cost a further $500-850 million). The impact of a new TB vaccine on the global epidemic is expected to avert 105 million new cases of TB over the next 30 years and reduce the world health costs due to TB by $3 trillion over the next decade. All the current TB vaccine candidates to be tested under EDCTP are in the hands of European private or public organisations. The cooperation with EU and international development assistance programmes will ensure the uptake and distribution of new medical interventions at low costs in sub-Saharan Africa.

This option will also create new investments, jobs and growth both in Europe and in Africa. According to a recent study, 66 cents of every Euro invested by EU governments is reinvested back into European laboratories, universities and companies. Between 2002 and 2010, EU investments on PRD research created over 13,000 jobs in Europe, including many smart, high-value jobs.

It will move EDCTP from a pure collaborative research programme between Europe and sub-Saharan Africa to a programme, which will contribute to the long-term sustainable development of sub-Saharan Africa.

6.3 Risk mitigating strategy

With the prefered option various risks are associated. The different economic, social and environmental impacts discussed above are the impacts that can be achieved if the proposed EDCTP2 programme is implemented successfully. Yet, its full success is not guaranteed a priori. In order for the EDCTP2 programme to tap its full potential, a number of conditions have to be met convincingly. In the current absence of an agreement on the Multiannual Financial Framework for the next programming period 2014-2020 it is not yet known what amount can be made available from the EU budget for EDCTP2.

The serious commitment from all stakeholders involved is needed. The EU contribution is subject to formal commitments from the competent national authorities of the PS and the effective payment of their contributions. The SBIP on EDCTP2 specifies upfront commitments of the PS of at least €500 million [9]. This commitment shall be confirmed by letters from PS.

There is a risk, however, that the additional PS commitment of €500 million will not materialise. The current global economic downturn and related austerity measures may affect the support for clinical development of medical interventions against PRDs. The proposed programme is being designed specifically to mitigate this risk. The release of up to an additional €500 million of EU co-funding to match additional PS co-funding of at least €500 million shall provide an incentive for raising additional funds. However, since this additional EU co-funding is covered by the budget of *Horizon 2020* (2014-2020), an independent

interim evaluation (not later than 2017) will be conducted on the EDCTP2 implementation, including a review of the political support and financial commitments received up to then. The Commission may reduce or cancel this additional contribution, whichever appropriate, based on a negative independent interim evaluation, and account being taken of the effective capacity of EDCTP2 to plan and manage corresponding additional operations within the duration of the programme and based on an actual spending to the time of the interim evaluation.

Second, newly developed effective and safe medical interventions may not generate maximum impact due to the lack of political support from individual African governments. African governments need to engage fully with the outcome of clinical trials, adapt their national health policies, invest in new interventions and make them available through their own public health systems. This requires also their involvement and commitment in the strategic planning of EDCTP2 funding activities, such as in the identification of opportunities and setting of priorities (Box 5) [96]. A stronger link with European development assistance to promote an unbroken innovation chain from "bench-to-bed" will be needed as well in order to maximise the final impact resulting from EDCTP funded projects. EDCTP will therefore be implemented in close collaboration with the Directorate-General for Development Cooperation and the European External Action Service (EEAS).

Third, clinical trials in humans always bear residual health risks. Clinical trials under EDCTP2 must therefore be cleared by the competent national ethics board(s) in the country or countries, where the trial takes place, and copies of the relevant approvals must be presented to the EDCTP secretariat before initiating any clinical trials activities. Clinical trials supported under the EDCTP2 programme must comply with the Charter of Fundamental Rights of the EU, the Universal Declaration of Human Rights, ethical principles included in the revised Declaration of Helsinki, and ICH standards on good clinical practice, and relevant EU legislations, including the relevant rules and guidelines applying to *Horizon 2020* which require that grant proposals are subject to an ethical screening and ethical review [97]. Apart from EDCTP-funded projects being subject to regulatory control by the competent authorities in the country or countries in which the trial(s) take place, EDCTP and the Commission may also conduct ethical reviews and ethical audits during the execution of clinical trials. This will allow verification whether EDCTP-funded clinical trials are effectively conducted according to the ethical provisions imposed by EDCTP.

Box 5: General criteria for priority-setting.

General criteria for setting of priorities as regards the diseases and candidate products that shall be supported for clinical testing could include issues such as:

- **Disproportionately high burden of disease in sub-Saharan African countries:** taking into consideration available data including DALYS, morbidity and mortality, disease foci, and national health priorities.
- **Demonstrated need for new products:** either there is no existing product or there is a need for i) additional products, such as for specific patient groups like children, pregnant women, or HIV-infected individuals, or for ii) suitable formulations for improved compliance in targeted populations, such as single dose and/or fixed combination therapies, and paediatric formulations as appropriate.
- **Availability of products in the pipeline for clinical testing**: as judged by global portfolio analysis but giving priority to products which have been developed in the context of products funded by:

  a) EDCTP,

  b) EU Framework programmes for Research and Innovation,

  c) European national programmes or private sector initiatives.

7. MONITORING AND EVALUATION

The creation of an appropriate monitoring and evaluation system at programme and project level will allow sound assessment whether the EDCTP2 programme is on track and successfully contributing in meeting the identified objectives. It will also play an important role in the mitigation of risks identified in section 6.3. Taking into account the recommendations from the 2009 interim evaluation of EDCTP1 [4] and consultations on EDCTP2 [9, 18, 19], this system will be based on indicators developed in the context of *Horizon 2020* and tailored to the specificities and objectives of EDCTP2. The implementation of this framework and the collection of the related data should be done by the EDCTP Secretariat under the supervision of the European Commission and in coordination with the Participating States and third parties.

7.1. Outline of key principles

Key principles of the monitoring and evaluation system:

- Evidence- and quality-based: section 7.2 suggests quantifiable indicators to be used to measure and assess progress towards the identified objectives and targets set.
- Comprehensive: given the scope of the identified objectives an evaluation framework assessing both the short term and long term achievements of EDCTP2 is necessary and could be composed of the following:
  - Updates on indicators of EDCTP2 published annually.
  - Annual reports on the implementation of EDCTP2 programme giving detailed information on its performance and progress towards meeting its objectives and targets.
  - An independent interim evaluation of EDCTP2, carried out by an expert panel convened by the European Commission, will be conducted not later than 2017, with a specific focus on the implementation so far, the quality of the research and innovation against PRD under way, progress towards the objectives and targets set, and recommendations for possible improvements.

  - At the end of the EDCTP2 programme, and not later than 2023, an independent evaluation of EDCTP2 reviewing the performance and quality of the EDCTP2 implementation and funded activities will be conducted.
  - A final independent evaluation carried out by an expert panel convened by the European Commission will be conducted not later than 2026.
- Supported by Participating States: due to the significant level of integration of national programmes required for EDCTP2, Participating States have to provide detailed evidences on the nature and volume of direct and indirect national contributions to the EDCTP2 joint programme.

The Commission will also ensure that all actions taken and supported in the context of the EDCTP2 programme respect the Charter of Fundamental Rights of the European Union [98] and are in line with the ICH standards on good clinical practice [91].

7.2. Proposed indicators

Operational Objectives	Indicators / Targets by 2024
Support clinical trials (Phase I-IV) on new or improved medical interventions against poverty-related diseases through partnerships between European and developing countries, in particular sub-Saharan Africa	**Number of clinical trials supported** Target: at least 150
	Number of new medical products delivered Target: at least 1
	Number of medical interventions proceeding to further development (through additional trials or next phase) Target: 20
	Number of clinical trial results integrated in guidelines or recommendations for improved clinical practice or submitted to regulators. Target: 30
	Share of EDCTP-funded clinical trials with African leadership Target: at least 50%
	Number of peer reviewed scientific articles published Target: at least 1000
Support research capacity building activities in sub-Saharan Africa enabling the conduct of clinical trials and contribute to reduce the brain drain	**Number of African countries** involved in EDCTP-funded projects Target: at least 30
	Number of capacity building activities supported for conducting clinical trials in sub-Saharan Africa Target: at least 150
	Number of fellowships to African researchers and Ms/PhD Target: at least 600
	Number of African researchers supported by EDCTP fellowships **staying in Africa at least 1 year after the end of the training.** Target: at least 90%

Develop common research agenda, criteria for priority setting and common evaluation	**Share of public investments of participating European states** integrated, aligned or coordinated through the EDCTP joint programme Target: at least 50%
Raise additional co-funding for EDCTP2 activities from Participating States (PS), including funds raised by PS and EDCTP from other public and private third parties.	**Volume and share of co-funding from EU and PS**, including funds raised by PS and EDCTP from other public and private third parties Target: Achieve a leverage effect of EU co-funding of at least 1, i.e. €1 EU co-funding generating at least €1 co-funding from PS, including funds raised by PS and EDCTP from other public and private third parties. Target: PS contribute at least additional €500 million to EDCTP2, including co-funding from new PS, and other parties, whether public or private, to EDCTP2 activities. Target: Increase the contributions to EDCTP2 from developing countries to at least €30 million
Increase efficiency of EDCTP programme implementation	**Operating costs** Target: below 5% of administered budget.
	Time-to-Grant Target: below 9 months
	Time-to-Pay Target: below 3 months

CONCLUSION

EDCTP1 has been an innovative measure both from a policy, legal and administrative standpoint. In operation for almost a decade, it is now on track in delivering significant results, ranging from the impact of its support to clinical trials in sub-Saharan African countries to engaging those countries in a true partnership with the EU and the European states participating in EDCTP.

Building on the achievements and lessons learnt from EDCTP1, the conclusion of this impact assessment is that, the option consisting in the EU to

i) respond to the PS request and continue its participation in EDCTP,
ii) extend the scope and duration of the EDCTP2 programme,and
iii) increase the financial contribution to the EDCTP2 programme (under *Horizon 2020*), including additional financial provisions

is the most cost-effective in terms of effectively addressing the problems and underlying drivers linked to the social and economic burden of poverty-related diseases in sub-Saharan Africa, and in meeting the identified objectives.

Such an expansion of the scope and scale of the EDCTP2 programme should be built on the extended pooling of resources from PS by aligning more of their direct activities under the umbrella of a Joint Programme with common objectives and goals to reach a total of at least €500 million which the EU would match with €500 million co-funding. In addition, EDCTP would be assigned the objective to raise at least another €500 million co-funding from its PS with the EU providing up to an additional €500 million to match this additional PS co-funding.

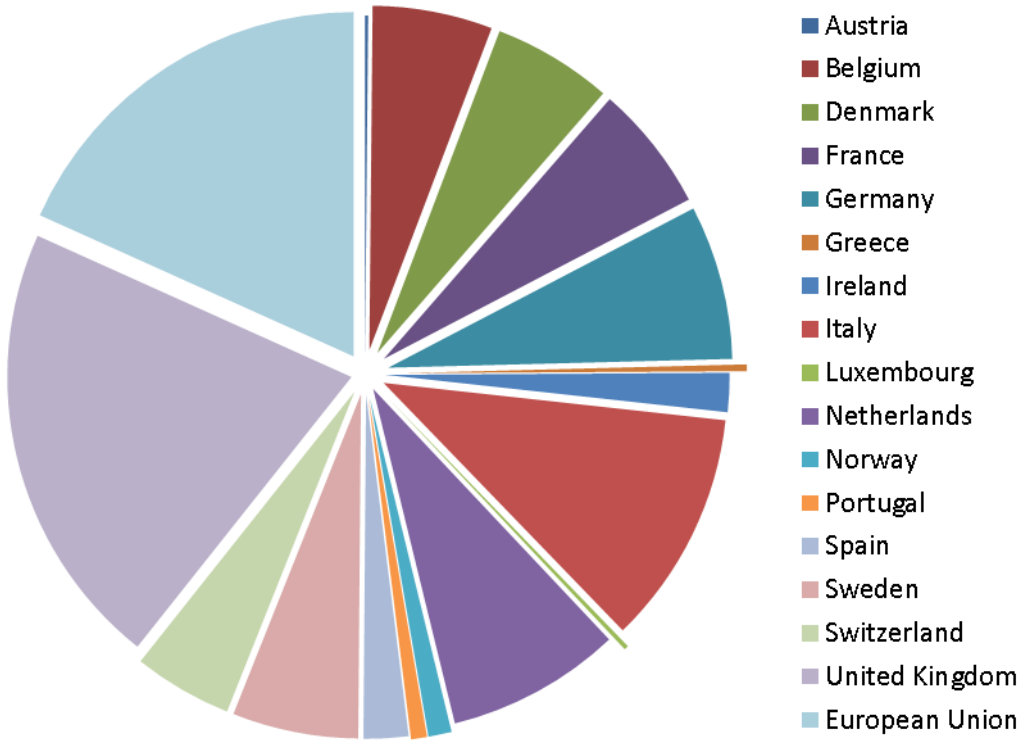
ANNEXES

ANNEX 1: LIST OF ACRONYMS AND ABBREVIATIONS

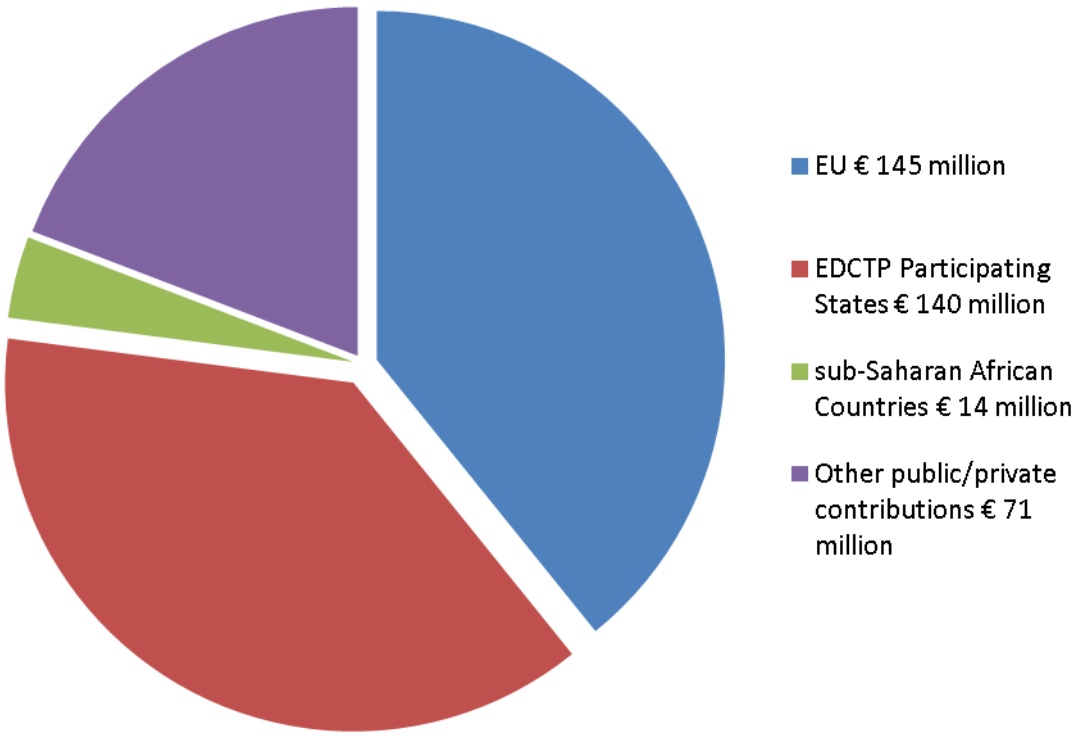
AC	FP6/FP7 Associated Country
ACT	Artemisinin-based Combination Therapies
AIDS	Acquired Immuno-Deficiency Syndrome
BMGF	Bill and Melinda Gates Foundation
DALY	Disability-Adjusted Life Year
DCCC	EDCTP Developing Countries Coordination Committee
DCI	Development Cooperation Instrument
EDF	European Development Fund
ERA	European Research Area
EDCTP	European and Developing Countries Clinical Trials Partnership
EDCTP1	First EDCTP joint programme
EDCTP2	Second EDCTP joint programme
EEIG	European Economic Interest Group
EFPIA	European Federation of Pharmaceutical Industry Associations
ExS	EDCTP Executive Secretariat
FP6	Sixth Framework Programme of the European Community for research, technological development and demonstration activities (2003-2006)
FP7	Seventh Framework Programme of the European Community for research, technological development and demonstration activities (2007-2013)
GA	EDCTP General Assembly
HIV	Human Immunodeficiency Virus
Horizon 2020	EU Framework Programme for Research and Innovation (2014-2020)
IA	Impact Assessment
IAB	Impact Assessment Board
IASG	Impact Assessment Steering Group
IEE	Independent Expert Evaluation
IER	Independent Expert Review
MS	EU Member State
MDG	Millennium Development Goal
NID	Neglected Infectious Diseases
NTD	Neglected Tropical Diseases
PB	EDCTP Partnership Board
PDP	Product Development Partnership
PRD	Poverty-Related Diseases
PPP	Public Private Partnership
PS	European EDCTP Participating State
SBIP	EDCTP2 Strategic Business Plan

TEU	Treaty on the European Union
TFEU	Treaty on the Functioning of the European Union
TB	Tuberculosis
WHO	World Health Organization

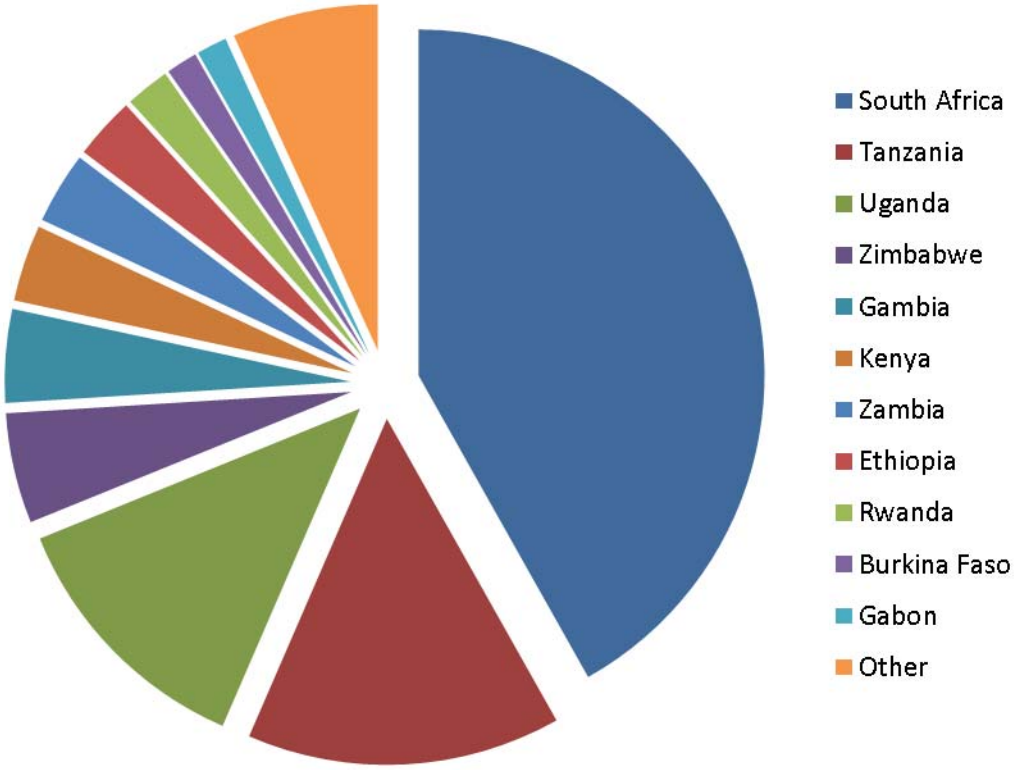
ANNEX 2A: DISBURSEMENT OF FUNDING BY EDCTP AND THE PARTICIPATING STATES UNDER THE EDCTP1 PROGRAMME - TOTAL: €1'094 MILLION (TOTAL PAYMENT APPROPRIATIONS, EXCLUDING DISBURSEMENTS FROM THIRD PARTIES).



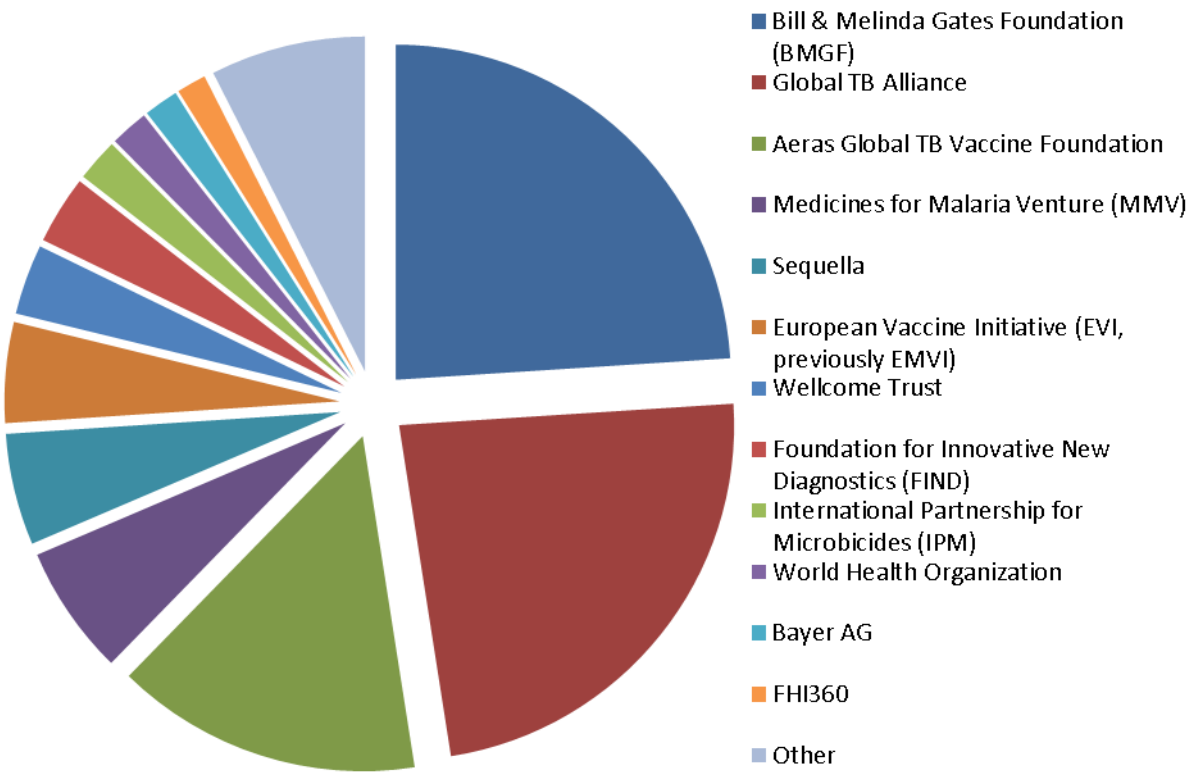
ANNEX 2B: TOTAL VOLUME OF EDCTP1 GRANTS, AND SHARE OF COFUNDING - TOTAL: €370 MILLION IN TOTAL (TOTAL COMMITMENT APPROPRIATIONS, INCLUDING COMMITMENTS FROM THIRD PARTIES).



ANNEX 2C: FINANCIAL COMMITMENTS FROM SUB-SAHARAN AFRICAN COUNTRIES TO EDCTP1-FUNDED ACTIVITIES: €14 MILLION IN TOTAL.



ANNEX 2D: FINANCIAL COMMITMENTS FROM THIRD PARTIES, INCLUDING THE PRIVATE SECTOR TO EDCTP1-FUNDED ACTIVITIES: €71 MILLION IN TOTAL.



ANNEX 3: NUMBER OF PARTICIPATIONS IN EDCTP1-FUNDED ACTIVITIES BY COUNTRY.

Sub-Saharan Africa	Number of projects in which the country participates	Europe	Number of projects in which the country participates
South Africa	65	UK	83
Tanzania	52	The Netherlands	50
Uganda	47	Germany	40
Kenya	32	Belgium	38
Burkina Faso	25	France	32
Zambia	24	Switzerland	31
Gabon	22	Spain	21
The Gambia	21	Sweden	20
Mozambique	21	Italy	18
Ghana	20	Austria	16
Malawi	17	Denmark	14
Senegal	17	Ireland	7
Zimbabwe	17	Norway	7
Cameroon	16	Luxembourg	2
Ethiopia	15	Slovakia	1
Nigeria	13	Finland	1
Mali	12		
Rwanda	8		
Botswana	6		
Benin	6		
Guinea Bissau	4		
Democratic Republic of Congo	4		
Ivory Coast	4		
Republic of Congo	4		
Guinea	4		
Liberia	2		
Madagascar	2		
Namibia	1		
Togo	1		
Sudan	1		

ANNEX 4: MAIN CONCLUSIONS FROM THE PUBLIC CONSULTATION. (REFERENCE [18] FOR THE FULL REPORT)

A public consultation was held from 8 April to 22 June 2010, inviting the EDCTP stakeholders (i.e. researchers, research institutions, regulatory authorities, funding agencies, pharmaceutical companies, etc.) and the public at large to express their views on the need for and nature of a renewed EDCTP initiative. This consultation took place through an online questionnaire to inquire support for different policy options identified and to canvass stakeholders' opinions in targeted areas of particular interest. The questionnaire was accompanied by a public consultation document, a specific privacy statement and links to other supporting material.

In response to the public consultation launched in 2010 the Commission received a total of 235 contributions broken down as follows:

- *175 replies from individuals contributing in a personal capacity. This included 55% researchers, 11% interested citizens, 15% employees of public organisations and authorities, 7% employees of private non-profit organisations and 2% employees of private-for-profit organisations;*
- *48 replies from organisations/companies, including 31% from private non-profit organisations, 25% from public organisations, 19% from private for-profit organisations and 13% from other type of organisations;*
- *12 replies from public authorities, including 92% replies from centralised authorities (8% others).*

The separation into these categories was taking into account when interpreting results to ensure balanced conclusion. Geographically, respondents were distributed as follows: 137 from Europe, 64 from Africa and 34 from other regions.

As part of this consultation, a set of different policy options for a second EDCTP programme were presented and stakeholders invited to indicate their preference. These options included:

- *Option 1 - No EU action: there would be no EU decision to continue participation and financial contribution of the EU to the EDCTP initiative after the expiration of the current funding phase.*
- *Option 2 - Programme based: no EU decision to continue participation and financial contribution of the EU to the EDCTP initiative after the expiration of the current funding phase. Provision is however made in EU research policies and programmes to support EDCTP objectives.*
- *Option 3 - Business as usual: a new EU decision continuing the participation and financial contribution of the EU to a second EDCTP programme under the same terms.*
- *Option 4 - Extended scope: as in option 3, a new EU decision continuing the participation and financial contribution of the EU to a successor EDCTP programme would be adopted. However, the scope of the second EDCTP programme would be expanded, by including other poverty-related diseases (such as neglected infectious diseases), other forms of medical products and interventions (such as diagnostics), all phases (I-IV) of clinical trials, and/or developing countries in other geographical areas.*
- *Another option*

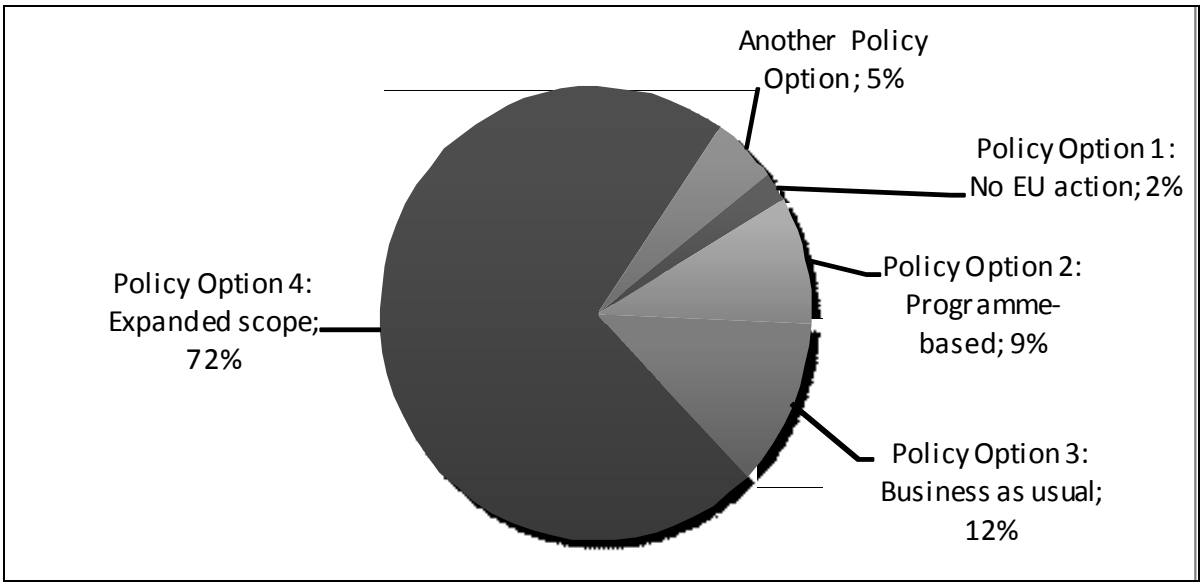
The continuation of EDCTP was supported by a majority of respondents (83% of respondents). This support was consistent for respondents from Europe (80%) and Africa

(92%) as well as across all categories of respondents (87% of individuals contributing in a personal capacity, 75% of organisations, and 67% of public authorities).

Most respondents (71%) were in favour of an expansion of the scope of a new EDCTP programme, with clearer majority (86%) among those who were in favour of a continuation of EDCTP. This support for an extended scope was consistent for respondents from Europe (65%) and Africa (87%) but not for all categories of respondents where only half of the respondents from public authorities supported an expanded scope (76% of individuals contributing in a personal capacity, 63% of organisations, 50% of public authorities). Public authorities not supporting an extended scope were in favour of keeping a narrow geographical focus (sub-Saharan Africa), of addressing other diseases only when expected impact on poverty reduction is significant, and of supporting expensive clinical trials in partnership with other funders, while also calling for an EDCTP structure that is well-adapted to an extended scope [12].

Looking at the support specific types of expansion received by the respondents of the public consultation, a more coherent picture results across all social and geographical categories for expanding the scope:

- *to phases I and IV clinical trials: majority of respondents in favour in EU (79%) and Sub-Saharan Africa (85%), as well as among public authorities (75%), organisations/companies (73%) and individuals (81%); and*
- *to other infections: majority of respondents in favour in EU (60%) and Sub-Saharan Africa (70%), as well as among public authorities (67%), organisations/companies (58%) and individuals (67%).*



However, a geographical extension was less supported (see figure below), in particular by the public authorities (42%).

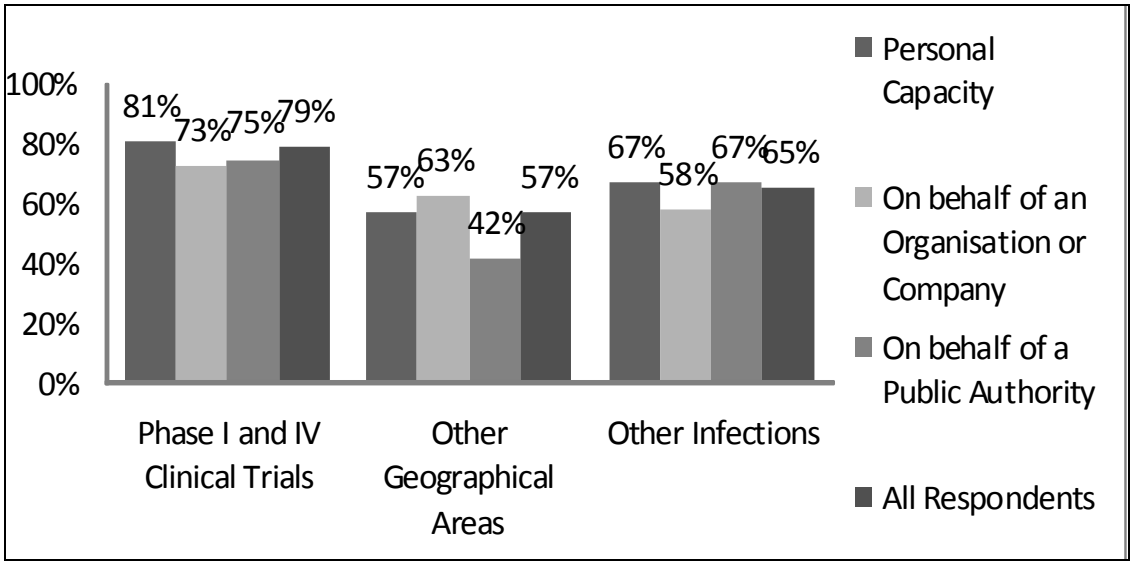
As part of the consultation, stakeholders also identified possible objectives to be pursued in the context of a renewed, second EDCTP programme. This notably includes:

- *objectives with social impact: help ensure access to the products of research findings (87%), improve health care benefits and equal treatments (87%), improve public*

understanding of clinical trials (74%), promote cultural exchange through research (72%) and improve public awareness of ethics (72%); and

- *objectives with economic impact: promote collaboration between research and development funding institutions (86%), promote academic research (81%), facilitate the introduction and dissemination of new products, technologies and production methods (80%), reducing the cost of clinical trials (68%) and promoting industrial research and facilitating job creation (48%).*

Finally, respondents expressed broad support for the creation of a "common pot"[31] *to reduce operational complexity and simplify and streamline co-funding (81% in favour) and a better involvement and cooperation with third parties, such as international funding bodies (83%), large pharmaceutical and biotechnology industries (57%), and SMEs (55%).*



[31] Under a real common funding pot ("common pot") , national contributions are pooled together and managed by a common implementation structure (such as the EDCTP Secretariat) according to agreed common procedures to select and support the best research proposals identified by peer review and independently of national rules.

ANNEX 5: EXECUTIVE SUMMARY OF THE 2010 REPORT RELEASED BY THE INDEPENDENT EXPERT PANEL CONTRIBUTING TO THIS IMPACT ASSESSMENT. (REFERENCE [19] FOR THE FULL REPORT)

An expert panel[32] was convened in July-August 2010 to contribute to the ex-ante impact assessment of a renewal of the EDCTP grant (EDCTP2), commenting on the 4 options for the future identified by the EC: 1) No EU action, 2) Programme –based option, 3) the 'Business as usual' option , i.e. a continuation of the EDCTP with identical scope, and 4) the 'Expanded Scope Option' giving EDCTP 2 an extended mandate to i) other geographical regions than Africa, to ii) other diseases (NIDs) and/or iii) to Phase-1 and Phase-4 clinical trials.

The panel reviewed the problem definition as formulated by the European Commission (EC) and examined the political, financial, economic and social impacts of the four proposed paths forward. Sources used were: EDCTP-related documents, a literature review and interviews with key-informants (EC staff, High Representative of the EDCTP, Executive Director of the EDCTP and staff of the EDCTP African Office in Cape Town).

*Since inception in 2003 [*until the release of this expert report in August 2010*], there have been numerous accomplishments. The 142 projects funded (~€ 269 million from the EC and EU MS) by EDCTP involve 136 institutions from 29 sub-Saharan countries, 42 institutions from 16 European countries and 51 other partners from non-profit organizations and private sector groups. These (almost all still on-going) projects include 44 clinical trials: 20 on HIV/AIDS, 14 on tuberculosis and 10 on malaria. The infrastructure and training of individuals to conduct these trials is a substantial accomplishment. There were over 100 peer-reviewed publications related to EDCTP-funded research.*

The panel endorses the problem definition as formulated by EC in terms of i) burden of disease, ii) lack of capacity for clinical research and development in Africa and EU iii) fragmented R&D landscape. Given the accomplishments so far, the panel is of the view that to maximize the political and socio-economic impact of EDCTP2, it should get an expanded mandate (as foreseen under Option 4, Expanded Scope). Expansion to phase 1 and 4 trials is justified. Geographical expansion seems not relevant at this stage. The countries involved should primarily be the sub-Saharan countries but EDCTP2 should be encouraged to engage in alliances with other regions. EDCTP2 should be allowed to work on other NIDs as needed by the participating African countries.

In addition, the expert panel recommends that any EDCTP2 program should, from the start, outline clear objectives with measurable outcomes both in clinical research as well as in capacity strengthening. It also recommends that the governance structures of EDCTP be modified to include the EC as voting members and eventually to grant full voting rights to the African partners. Monetary funding from the collaborating sub-Saharan African nations would enhance sustainability and lead to true partnership.

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[32] The members of the panel were:
- Arnold L. Christianson MD, PhD, Professor and Head of the Division of Human Genetics, National Health Laboratory Service and University of the Witwatersand, Johannesburg, South Africa.
- C. Jo White MD, independent consultant, Blue Bell, PA, USA.
- Marleen Boelaert MD, PhD, Professor of Epidemiology, Department of Public Health, Institute of Tropical Medicine, Antwerp, Belgium.

ANNEX 6: RECOMMENDATIONS FROM THE 2009 EDCTP1 INTERIM EVALUATION. (REFERENCE [22] FOR THE FULL REPORT)

Part 3 of the Independent Expert Evaluation report focuses on conditions for a possible grant agreement under FP 7 for a second EDCTP Programme under article 169 of the Treaty (EDCTP 2). In preparation for a possible Second Programme, the Panel formulates the following recommendations to the EDCTP:

7.1. The General Assembly should finalize proposals on how each country intends to fund EDCTP2 and each member should consult accordingly with their Minister(s) in charge.

7.2. The EDCTP should engage in a profound outreach activity towards MS who are not substantially contributing to the Programme and towards EU countries not yet members of the EDCTP.

7.3. For the purposes of EDCTP2, the General Assembly composition and voting rights should be restricted to representatives from countries who have made the necessary financial commitments in cash or in kind, as it is the case in several EU research projects based on Article 169 of the Treaty.

7.4. General Assembly members must be able to operate with a political and financial mandate from their government and be in a position to effectively coordinate EDCTP with relevant national activities.

7.5. General Assembly members and the Commission should actively seek to expand the financial commitments through the use of additional financial resources such as national development funds and EU funds for Africa.

7.6. The General Assembly should continue to review the number of EDCTP Bodies, clarify their respective roles and review the number of meetings in order to reduce costs and improve the efficiency of its communication, especially on the Website, where all corporate minutes should be made public.

7.7. The Chair person of EDCTP General Assembly must have the authority to discuss financial and policy matters with the Commissioner and relevant Ministers.

7.8. The EDCTP General Assembly should adopt, as soon as possible, a coherent Second Programme (EDCTP2) with a clear strategy linked to the EU Health Research and existing national policies on poverty diseases. The EDCTP should continue to focus on clinical trials and operational research for the introduction of new technologies for HIV/AIDS, TB, and Malaria.

7.9. The Panel supports the current efforts and encourages EDCTP to develop more comprehensive indicators for assessing EDCTP's activities. According to the panel, this assessment should include two complementary components:

- *Monitoring the performance of the Programme,*
- *Evaluating the impacts on research capacity, with a view to reduce the disease burden of HIV/AIDS, Malaria and Tuberculosis in sub-Saharan Africa.*

7.10. In particular, the EDCTP General Assembly should develop more specific key performance indicators and monitor, on an annual basis, the EDCTP Key performances, including:

- *Number, quality of implementation and output of clinical trials,*
- *Number, quality of implementation and output of capacity building projects,*
- *Number, quality of implementation and output of networking activities,*
- *Performances of EDCTP Secretariat in The Hague and Cape Town,*
- *Measuring cost efficiency and effectiveness,*

- *Number and quality of EDCTP links with other global health initiatives in the field,*
- *Number and quality of EDCTP links with industry in the field.*

7.11. The EDCTP General Assembly should adopt a transparent information and communication.

Annex 7: Potential legal basis for EDCTP2.

To address the objectives specified in chapter 3 (subsequently referred to as "EDCTP2 objectives"), EU intervention and funding could be based on the following articles of the Treaty on the Functioning of the EU, addressing the European research area and making provisions for its achievements:

- **Article 182** provides the legal basis for establishing the multi-annual Framework Programme, including budgetary provisions. The next Framework Programme for Research and Innovation, *Horizon 2020*, foresees funding of individual researchers, research teams and consortia, as well as co-funding programmes implemented by other European funding agencies [5]. EU intervention based only on Article 182, and on *Horizon 2020* more specifically, would imply direct budget implementation by the Commission by calls for proposals to allocate grants for the value of the Union contribution to EDCTP. This would hamper common funding of costly clinical trials by multiple funders. A possible *Horizon 2020* €200 million grant to EDCTP (programme co-fund) cannot be envisaged. In addition to its significant amount and the lack of a sound legal basis for multiannual commitments, it would not allow the Union to play any proactive role and to participate in the national research programmes of MS. Thus, basing EU intervention on this article would imply a discontinuation of the EDCTP joint programme, and of the corresponding process of integration of national programmes.
- **Article 184** provides the basis for implementing the multi-annual Framework Programme, to establish supplementary programmes involving the participation of certain MS only, which shall finance them subject to possible Union participation. Such supplementary programmes established under this article are components of the EU Framework Programme and therefore *de facto* EU programmes. Thus, integrating national programmes under this article would mean dissolving or reducing national programmes and re-directing corresponding funding to a single EU programme with rules decided by the Union. Such an approach would fail to effectively address the fragmentation of national policies, programmes and activities, and would certainly fail to find sufficient support from MS. Thus, this legal basis has been ruled out.
- **Article 185** is the legal basis of the current EDCTP1 programme. It allows the Union, in implementing the multiannual Framework Programme, to make provision, in agreement with the MS concerned, for participation in research and development programmes undertaken by several MS, including participation in the structures created for the execution of those programmes. Thus, it specifically foresees the establishment of dedicated implementation structures for the execution of the joint programme(s) and the Union's participation in such dedicated implementation structure. The existence of a dedicated implementation structure (the European Economic Interest Group which manages the programme through the EDCTP Secretariat) provides for economies of scale to the profit of the Union and EDCTP member states.
- **Article 186**, while making provision for cooperation with third countries and international organisations, does not specifically address joint implementation and integration of national programmes. International agreements, by nature, may derogate from the Treaty if so accepted by ratifying bodies. It would allow establishing a dedicated implementation structure as international organisation and thus granting membership to non-EU countries. This article would provide the basis for the transformation of EDCTP from a European to an international initiative. However, the establishment of an international agreement that would also bind MS - with their

activities. This would lead to a much more complex and lengthy adoption process, involving national ratifications, and consequently to a significant funding gap between EDCTP1 and EDCTP2. The establishment of an international agreement on the basis of Article 186 could, however, be a long-term future prospect for EDCTP provided that it succeeds in increasing the level of integration of national programmes and achieving a critical level of at least 50% integration. Hence, this legal basis has been ruled out from further considerations in this IA.

– **Article 187** on the other hand relates to the establishment of joint undertakings or any other structure for the efficient execution of Union research, technological development and demonstration programmes. An Article 187 decision is for the Council alone, and one cannot envisage that powers vested to the Parliament with regard to Article 185 could be so bypassed. Article 187 is strictly a mean of implementation of a Framework Programme activity, notwithstanding its use for the establishment of public-private partnerships through Joint Technology Initiatives in accordance with other Framework Programmes decisions or regulations. In addition, and referring strictly to the establishment of a Joint Undertaking, i.e. a Union legal body, the 2009 EDCTP interim evaluation report [4] underlined the long period necessary for the creation of such Joint Undertaking. This legal basis was therefore ruled out from further considerations.

Alternative solutions exist through the setting up of inter-governmental agreements. However, the administrative and legal processes which typically have to be followed under such inter-governmental schemes are lengthy, difficult and cumbersome.

In conclusion, Article 185 is the best legal basis for continuing EU participation and support to EDCTP, while Article 182 (*Horizon 2020*) provides the legal basis for EU financial support to EDCTP (established under Article 185) but also for direct EU funding of individual activities in the scope of EDCTP2 objectives, if EU participation and support to EDCTP is discontinued.

ANNEX 8: REFERENCES

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