Independent External Review Report

European and Developing Countries

Clinical Trials Partnership

(EDCTP Programme)

Review conducted by the IER / EDCTP Panel:

Wim Van Velzen (Chair),
Adetokunbo O. Lucas, Allyson Pollock, Jean Stéphenne
and Fernand Sauer (Rapporteur).

Executive Summary

The European and Developing Countries Clinical Partnership (EDCTP) was established in 2003 by 15 European countries to develop new clinical interventions and adapt existing treatments to address the needs of sub-Saharan Africa in the field of poverty related diseases. It is meant to create a sustainable and genuine research partnership between European and African countries.

The EDCTP is mainly funded through a grant of € 200 million under the 6th Framework Programme for European Research. The duration of the grant agreement was extended to 2010, at no extra costs and with a number of conditions attached.

At the request of Commissioner Janez Potočnik, an independent external review (IER) was conducted between January and July 2007 to provide recommendations on how the EDCTP could better integrate Member States' national programmes and increase clinical trial and capacity building activities through a stronger partnership with Africa.

The IER panel analysed all the documentation available, held six meetings and conducted several interviews with representatives from the Commission services, Permanent Representations, European Parliament. In depth discussions took place with the new Executive Director, and representatives from the various EDCTP bodies and institutes or organisations working with EDCTP.

The report describes the objectives, structures and the present situation of the EDCTP Programme. It analyses the difficulties facing this first research initiative based on Article 169 of the Treaty.

A **majority of IER panel members** ask the EDCTP to focus on the areas of:

- product clinical investigations,
- general conditions for conducting clinical trials,
- and optimal conditions for drug use.

They request the EDCTP to improve significantly its results over the next 18 months if new funding under FP 7 was to be provided.

The report contains their key recommendations relating to the following aspects:

- improvements of the current EDCTP Programme,
- conditions for a new EDCTP financing decision under the 7th Framework Programme,
- prerequisites for new research programmes based on Article 169.

Professor A. Pollock expressed **a dissenting opinion**, recorded in Part 4 of the report.

The annexes to the report provide background information on the impact of the three major poverty related diseases (HIV/AIDS, tuberculosis and malaria), the potential for product development and other health interventions, ethical issues and intellectual property rights, the current EDCTP projects, lists of African partners and major donors, as well as public documents used by the panel.

Independent External Review Report

on the European and Developing Countries Clinical Trials Partnership (EDCTP Programme)

Poverty related diseases, especially HIV/AIDS, tuberculosis and malaria, constitute a major public health emergency, as well as a formidable obstacle to economic development in sub-Saharan Africa. A summary description of the impact of the 3 diseases is given in annex 1.

The need to confront these diseases, as expressed in the UN Millennium Development Goals and in successive G8 declarations, led the Commission to initiate specific action programmes in 2001 and 2005 and to issue various communications to the Council and the European Parliament.

Applied research into new, more effective and affordable drugs and vaccines is part of this global approach by the European Union to improve prevention and treatment of the three diseases. Product development and strengthening of health systems should go hand in hand. Ideal drugs for mass treatment in developing countries may be different from those that can only be used in a strictly monitored hospital environment (see annex 2).

The Brussels European Council meeting of 8 and 9 March, 2007 endorsed a Council Report[1], which mentioned the EU support to the development of new preventive technologies such as vaccines and microbicides. The ongoing dialogue between the EU and African partners to identify mutual benefits and needs for cooperation in the area of research was illustrated by the EDCTP Programme. The European Council reiterated the importance of the Lisbon objective of spending 3% of GDP on research and development by 2010. It stressed the need for synergy between Community programmes and to improve the transformation of research findings into innovative products, with knowledge sharing between all partners.

The international community has promised to work towards the goal of universal access to HIV/AIDS prevention, treatment, care and support by 2010. At its meeting in Heiligendamm, on 8 June 2007, the G8 has renewed its pledge to support African efforts to strengthen health systems more broadly, including support for long-term plans and better institutional coordination and to address the feminisation of the pandemic, including mother to child transmission.

The G8 reaffirmed their commitment to scale up their efforts towards the goal of universal access, the Millennium Development Goals for fighting HIV/AIDS, malaria and tuberculosis as well as strengthening of health systems by providing at least a projected US$ 60 billion over the coming years. They noted the increasing demand by the board of the Global Fund to Fight AIDS, TB and Malaria and stated that the Global Fund continues to enjoy their full support.

[1] "The EU and Africa: Towards a Strategic Partnership", approved by Council on 11.12.2006.

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PART 1:

IER / EDCTP TASKS AND KEY RECOMMENDATIONS

1.1. Key recommendations from the I E R Panel

1.2. Terms of reference and membership of the IER Panel

1.3. IER methodology, activities and meetings

PART 1: IER TASKS AND KEY RECOMMENDATIONS

The European and Developing Countries Clinical Partnership was established by 15 European countries to develop new clinical interventions and adapt existing treatments to address the needs of sub-Saharan Africa in the field of poverty related diseases. It is meant to create a sustainable and genuine research partnership between European and African countries.

Research and Development of adapted medicines should target effective, safe, affordable, easy to apply and culturally acceptable products. There is also an urgent need for new drugs, vaccines and diagnostic tools, in particular because of drug resistance. The involvement of competent African scientists at all stages of R&D will help optimise the formulation, effectiveness and utility any new product. Appropriate clinical and epidemiological studies carried out in sub-Saharan Africa will help to ensure that any resulting products are more readily accepted and compatible with health systems in these countries.

The EDCTP was launched in 2003. It has, until now, been mainly funded through a grant agreement under the 6th Framework Programme for Research and Technological Development of the European Union, for a duration of 5 years[2]. In June 2007, the duration of the grant agreement was extended to 2010, at no extra costs and with a number of conditions attached. International health research will be addressed again under FP7 (2007-2013), with the possibility a new grant for EDCTP, depending on achievements and needs.

The difficulty for the EDCTP Programme in combining two major tasks should not be underestimated: integrating national clinical trials programmes and working with scientists and clinicians in Africa. This is a very long-term ambition, which can only produce progressive results if all interested partners understand their responsibilities and respect their commitments, which must be renewed from time to time. The EDCTP is unique in providing a strong influence to African scientists and this should be reinforced and institutionalised in future.

The European Commission has asked for an independent external review (IER) of the EDCTP Programme. The IER should provide recommendations, on how the EDCTP should integrate Member States' national programmes and support clinical trial and capacity building activities through a stronger partnership with Africa.

The Independent External review Panel analysed all the documentation made available by the Commission, EDCTP and IER Panel members since January 2007 and held six meetings between January and July 2007. Several interviews were held with representatives from DG Research, DG Development, Permanent Representations, and European Parliament. In depth discussions took place with the new Executive Director, representatives from the EDCTP General Assembly, Partnership Board, DCCC, ENNP and EDCTP Secretariat. Interviews took place with representatives of national institutes and other organisations in contact with EDCTP.

This report contains some key recommendations, a description of the present situation of the EDCTP Programme and an analysis of the difficulties facing this first research initiative based on Article 169 of the Treaty, accompanied by more detailed suggestions.

[2] Decision N° 1209/2003/EC of 16.6.2003, OJCE N° L 169/1 of 8.7.2003

1.1 Key recommendations from the Independent External Review of EDCTP

The **opinion of a majority of members** of the Independent External Review Panel is that:

1. The EDCTP must strictly comply with its mandate under Annex 1 of Parliament and Council Decision N°1209/2003/EC and focus on the following activities:

a) Effective coordination of product clinical investigations within a clearly defined public health strategy and involving strong partners in Europe (including industry) and in Africa to avoid fragmentation.

b) Improving the general conditions for conducting clinical trials in Africa, taking into account the existing regulatory and ethical constraints.

c) Studying the optimal conditions of use of drugs and vaccines against the three diseases in an African context (access, affordability and distribution), in comparison with other public health interventions.

2. For the EDCTP Programme to continue, the Member States who created and own the EDCTP should endeavour to take all necessary measures to provide the promised levels of financial support and to drastically improve the EDCTP governance and performance.

3. If by end of 2008, the EDCTP did not improve significantly in terms of visible and tangible outputs and results, in line with key recommendations 1.1 to 1.5 (see table), the panel does not recommend the renewal of the financing decision under FP7, based on Article 169 of the Treaty."

4. One member of the IER panel, Pr. A. Pollock, decided to abstain. Her reasons for a **dissenting opinion** are given in Part 4 of the report.

IER / EDCTP KEY RECOMMENDATIONS
1. To the EDCTP:
1.1. Define a clear, convincing and realistic EDCTP strategy with a common shared vision, clearly defined contributions from each partner and equitable sharing of results.
1.2. Make the General Assembly more political and create an Executive Steering Committee.
1.3. Expand association with major Product Development Public/ Private Partnerships for access to know-how and to provide visibility. Keep an inventory of and contacts with other similar programmes, to avoid unnecessary duplication.
1.4. Renew calls for appropriate projects to be submitted rapidly to attract the best public/private partnerships and to participate in major R&D initiatives such as MVI, IAVI and on TB.
1.5. Simplify and streamline co-funding, from a virtual to an actual common pot (by 2009), in order to reduce operational complexity and allow African initiation of EDCTP projects.

2. To the EDCTP Member States:

2.1. Interested Member States should renew their "EDCTP vows" in Council; accept reforms to EEIG structures, and directly finance an EDCTP " common funding pot".

2.2. In the General Assembly, the decision making should be restricted to Member States who provide financial contributions with representation at the highest appropriate national level and to African representation; other member would become observers, starting in 2008.

2.3. The African presence in the General Assembly should be reinforced, with decision-making status for representatives from African countries or regional organisations.

2.4. Member States should refrain from imposing national criteria, and accept one integrated scientific and ethical evaluation conducted by EDCTP, utilising a pool of the best national experts.

2.5. Member States should enforce the Article 169 concepts in their own countries on a sustainable basis, involving national parliaments when required, and report back annually to the EDCTP and the Commission on progress in implementation.

3. To the European Commission, in relation to future EDCTP activities:

3.1. Report to the Council and Parliament about the current status, in anticipation of the 2008 review.

3.2. Create a joint DG Research / DG Development platform to engage in a dialogue with the EDCTP.

3.3. Reformulate health research strategy before any new decision to finance EDCTP from FP7, in particular on the three diseases.

3.4. Consult African Governments on EDCTP future and international health research under FP7.

3.5. Involve African Governments at an early stage to link capacity strengthening to national strategies, in order to ensure sustainability.

3.5. Submit a new funding proposal to the Council and Parliament, before FP 7 mid-term review, provided that:

- Interested Members States political/budgetary/administrative commitments are clear.
- The EDCTP programme integrates the relevant national ones, with a common funding pot.
- The EDCTP governance is properly adjusted and more open to African partners.
- The EDCTP performance complies with targets from the EDCTP Roadmap.

4. To the European Commission, in relation to new Article 169 initiatives:

4.1. Set out future Article 169 pre-conditions, preferably in a guidance communication.

4.2. For an Article 169 Programme to become and remain successful, there must be pre-existing national programmes, strong commitment by Member States to provide funding and irreversible national support.

4.3. Before EU money becomes available, there must be: common work-plan; sound governance structure; fixed national financial contributions; clear evaluation criteria and procedures; clear deliverables; solutions for the liability issue.

1.2. Terms of Reference and membership of the IER Panel

In December 2006, Commissioner Janez Potočnik asked the IER Panel members:

- To assess, with a focus on improving future operations and results, the EDCTP Programme performance:
  - in integrating with National Programmes in the spirit of art.169 of the EU Treaty
  - as an operational structure (carrying out Clinical trials, Capacity building and Networking activities)
  - in forming a partnership with African Countries.

- To recommend actions for improving the performance of the EDCTP programme and its outputs; in this context, the role of the European Commission should also be addressed.

- To address the role of EDCTP in the broader international research and development agenda, taking into account the nature and values of the Programme and its comparative advantages.

- To suggest alternative or complementary approaches for the EU to finance research on infectious diseases in Africa.

- On the basis of this assessment, to draw possible lessons to be learnt and recommendations for future initiatives on the basis of art.169.

Details on the mandate are given in annex 7 to this report.

The European Commission appointed a multidisciplinary team of five individuals to conduct the Independent External Review:

- **Adetokunbo O. Lucas**, MD studied medicine at Durham University, graduating with honours in 1956, followed by postgraduate training in internal medicine and public health. From 1960 to 1976, he taught internal medicine and public health in Ibadan, Nigeria. He directed the WHO Tropical Diseases Research Programme, 1976-86. Later, he was appointed Professor of International Health at Harvard University, He serves on expert and advisory committees of various organisations both national and international.

- **Allyson Pollock** is professor and director of the Centre for International Public Health Policy at the University of Edinburgh. Her background and training is in public health medicine. She has an extensive research and teaching experience in the areas of epidemiology, research methods, and international health policy. She was previously professor of Health Policy at the School of Public Policy, University College, London and director of Research & Development at University College London Hospitals' NHS Foundation Trust.

- **Fernand Sauer (Rapporteur)** studied Pharmacy at Strasbourg and Law at Paris University. After a few years in France as hospital pharmacist and health inspector, he became the Head of Pharmaceuticals at the European Commission and the first Executive Director of the European Medicines Agency in London (1994-2000). Director for Public Health from 2001 to 2005, he is now an Honorary Director General of the European Commission, member of the French High Council for Public Health and of the Academy of Pharmacy.

- **Jean Stéphenne** has overseen Glaxo-SmithKline Biologicals since 1991, as President and General Manager since 1998. He joined the company in 1974 and served as Vaccine Plant Director and R&D Director from 1981 to 1991. Mr Stéphenne is an engineer in Chemistry and Bio-industries (University of Gembloux) and has a degree in Management (Louvain). He is a member of the European Association of Vaccines Producers, of the Management Committee of the Belgian Companies Federation and member of the Board of several Belgian companies.

- **Wim Van Velzen (Chair)** advises Covington & Burling LLP clients on European institutional affairs, legislation and accession issues. He is particularly involved in energy, ICT and R&D policies. Since 1989, he has worked extensively in Central and Eastern Europe, and more recently, in the Balkans and Turkey. He was a Member of the European Parliament from 1994 to 2004, where he became Vice-President of the EPP-ED group. He is currently Chairman of the Rathenau Institute; member of the Committee of Wise Men advising the Dutch government on research; Chairman of the Dutch Roadmap Committee for Research infrastructure; member of the Supervisory Board of the Technical University of Twente.

1.3. IER methodology, activities and meetings

The IER Panel reviewed a mass of documentation from the European Commission services, the EDCTP public and internal documents, the World Health Organization and other international organisations, and documents produced or communicated by members of the Panel. All official documents, minutes, notes from interviews, mission reports and personal contributions were classified and archived on a private Web site (CIRCA/EDCTP Independent External Review). The list of published source material used by the IER panel is given in Annex 8.

The Panel greatly appreciated the organisational support provided by Dario Zanon and Ana-Rita Figueira, from DG Research. Ana-Rita Figueira ensured co-ordination and full secretariat support (minutes, dissemination and archiving of documentation, Circa site) to the Panel and, in particular, to the rapporteur.

Several exchanges with Commission officials took place during the IER meetings, in particular, for DG Research: Octavi Quintana Trias, Bernard Mulligan, Manuel Romaris, Arnd Hoeveler, Andreas Holtel and, for DG Development: Juan Garay Amores and André Vanhaeberbeke (expert).

The IER Panel met the main representatives from the EDCTP: the Chair and vice-Chairs of the General Assembly: Diana Dunstan (MRC-UK) Bruno Gryseels (Tropical Medicine, BE) Stefano Vella (Istituto Sanita, IT); the Executive Director Charles Mgone; the Haut Représentant Pascoal Mocumbi; Laura Brum, ENNP Chair; EDCTP staff members: S. Belcher, C. Naus, D. Cole and F. Ntoumi. Written responses from EDCTP to IER questions were received on 27 March, 4 May and 4 July.

Separate interviews were conducted by IER members as follows, with feed back provided to the other Panel members:

- **W. Van Velzen**: Permanent Representations from Germany, Denmark, France, Netherlands, Portugal, Slovenia, Spain, UK; members of the European Parliament; Chair of NWO (hosting EDCTP), ex-Commissioner Busquin, MEP.

- **W. Van Velzen, together with F. Sauer**: Charles Mgone (EDCTP Director); Kurt Vandenberghe (Cabinet Potočnik); Lluis Riera (Director, DG Development).

- **A. Lucas**: Simon Agwale, Chair of DCCC; participation in EDCTP meetings in Douala, 8 to 11 May 2007: Nodes of excellence, DCCC, and ENNP/DCCC.

- **A. Pollock**: Diana Dunstan, Mark Palmer and Sheena McCormack (Medical Research Council-UK); Andrew Hall, Richard Hayes, Peter Smith and Lucy Bradshaw (London School of Hygiene and Tropical Medicine); Chris Hentschel (MMV), Prof. Awa Marie Coll-Seck (RBM), Dr Bernard Pécoul (DNDI), Dr Odile Leroy (European Vaccine Intitiative), Robert Ridley (Special Programme for Research & training in Tropical Diseases), Simon Agwale (Innovative Biotech Ltd).

- **J. Stéphenne**: Seth Berkley (IAVI), Chris Elias and C. Loucq (MVI/PATH); Magdalena de Azero (European Vaccine Manufacturers) and various industry sources.

- **F Sauer**: Patrice Debré chair of Partnership Board and Jean-Pierre Girard, GA vice-Chair; participation in EDCTP Stakeholders' meeting on HIV treatment, Madrid, 24 May 2007.

The Independent External Review Panel held six IER meetings, from January to July 2007:

- **Initial IER meeting**: Brussels, 8 January 2007. Briefing from relevant Commission services (RTD & DEV). First discussion of mandate, working methods, relevant documentation. First encounter with EDCTP General Assembly Chair and two Vice-Chairs.

- **Second IER meeting**: The Hague, 1 and 2 March 2007. Designation of W. Van Velzen Chair, F. Sauer rapporteur. Full discussion with DG DEV expert, EDCTP Secretariat, Chair of GA and vice-Chairs, Haut Représentant, ENNP. Request for written contributions from EDCTP.

- **Third IER meeting**: Brussels, 29 March 2007. Input from IER members on: EDCTP strategy and relations with national centres, DCCC and African involvement, ethical and IP issues, attractiveness and incentives for industry, donors and national research agencies.

- **Fourth IER meeting**: Brussels, 24 April 2007. Discussion of written responses from EDCTP and contributions from panel members on Article 169, EDCTP governance, African partnership, attractiveness, IPR issues, views from Members States and European Parliament.

- **Fifth IER meeting**: Brussels, 31 May 2007. Discussion of preliminary draft report circulated by rapporteur and of contributions from other panel members. Outcome of exchanges with EDCTP director and DG DEV. Orientations on IER report.

- **Final IER meeting**: The Hague, 6 July 2007. Following a teleconference on 28 June, and a drafting group meeting on 5 July, presentation to and discussion with EDCTP and Commission services of pre-final draft circulated by rapporteur on 29 June.

- **Transmission of final IER Report to Commissioner on 12 July 2007**.

PART 2:

EDCTP OBJECTIVES, STRUCTURES AND ACTIVITIES

1.1. Setting up the EDCTP Programme

1.2. EDCTP in the context of EU activities related to poverty diseases:

a) EU development aid

b) EU research on poverty diseases

1.3. EDCTP objectives

1.4. EDCTP structures

1.5. EDCTP finances and main activities

1.6. EDCTP evaluation processes

1.7. Implementing the EDCTP ”Roadmap 2010”

PART 2 EDCTP OBJECTIVES, STRUCTURES AND ACTIVITIES

At a political level, the EDCTP was hailed as a flagship for North-South cooperation and as the first and most powerful example of scientific cooperation based on Article 169 of the Treaty. The Brussels European Council of 8 and 9 March 2007 invited the Commission to present new proposals for initiatives based on Article 169, to follow on this first example of a research programme conducted by several Member States, with budgetary support from the European Union.

Article 169 of the Treaty of Nice
"In implementing the multiannual framework programme, the Community may make provisions, in agreement with the Member States concerned, for participation in research and development programmes undertaken by several Member States, including participation in the structures created for the execution of those programmes."

2.1. Setting up the EDCTP Programme

The principles and design of the EDCTP programme were discussed in 2001 between representatives of the interested Member States and the Commission and set out in a concept document finalised in Vienna, in June 2002. The EDCTP was formally set up in The Hague as a European Economic Interest Group (EDCTP-EEIG) on 26 June 2003[3]. The EDCTP-EEIG statutes, the act of incorporation adopted under Dutch law and the EDCTP internal regulations[4] do not contain any formal obligation for the participating countries in terms of support, funding, or programme integration.

In anticipation of the creation of the EDCTP structure, the Commission had proposed[5] to support this initiative with a significant contribution from the 6th research framework programme. The short explanatory memorandum and financial statement that accompany the proposal do not contain an impact assessment or a description of the national programmes to be coordinated. These documents or the above mentioned concept document do not state to what extent Developing Countries, international organisations, representatives from health industry or relevant non-governmental organisations had been involved or consulted during or after the preparatory phase.

The EDCTP secretariat is hosted by the Dutch Organisation for Scientific Research (NWO), which provides facilities and services. A second office was established in Cape Town, hosted by the South African Medical Research Council. The suitability of both sites have been subject to review and recommended for lease extensions until 2010. African partners tend to criticise Cape Town for not being close enough, geographically and culturally. They also suffer from visa requirements in Africa and Europe, especially when travelling to EDCTP meetings. It has been suggested that another African office could be opened at a more appropriate site where the first office might migrate to by 2010.

[3] EDCTP current membership: AU, BE, DK, DE, GR, SP, FR, IR, IT, LU, NL, PT, SW, UK as well as Norway and Switzerland.
[4] The EDCTP internal regulations were adopted in July 2004 and modified in August 2006.
[5] COM (2002) 474 of 28/08/2002

The European Council and Parliament decided[6] to contribute € 200 million from the European Research Area appropriation and specified several formal conditions concerning: governance, involvement of African countries, scientific excellence, ethics, intellectual property and financial rules. This decision does not impose any collective or individual obligation on the participating Member States. It merely expresses expectations but does not make the EU contribution conditional upon other sources of funding. Whereas condition N° 13 states that the participating countries "have agreed to coordinate and implement jointly activities aimed at contributing to the EDCTP programme", it simply notes that "the overall value of their national participation is estimated at EUR 200 million". Whereas condition N° 14 expresses the hope that "activities linked to obtaining additional funds, whether public or private, estimated at EUR 200 million, are provided for in the implementation of the EDCTP Programme".

Given the general nature of the financing decision, the Commission laid down more precise contractual conditions when signing the grant agreement for the EU subsidy to the EDCTP on 15 December 2003. This grant agreement describes in detail the "Joint Programme of the Action" (JPA), at a total cost of € 400 million. The EU contribution is limited to the same amount as that provided by the participating countries, up to € 200 million.

In response to an EDCTP request[7] for a cost neutral extension of the Programme, Commissioner Janez Potočnik accepted to extend the duration of the initial grant agreement until September 2010, at no extra-costs and with 4 conditions attached:

- The EU contribution to EDCTP management costs should not exceed € 15 million.
- The EDCTP should provide a detailed roadmap and indicators of national programme integration.
- The Member States must match the EC contribution by co-funding or direct contributions.
- The EDCTP plan and timetable must show an increase in number of clinical trials and capacity building in Africa.

In theory, the Member States who own the EDCTP could engage in other regions of the world and in supplementary activities outside the EU financing instruments, if they are ready to provide the appropriate extra funding.

2.2. EDCTP in the context of EU activities related to poverty diseases

Africans face considerable health problems in general: limited access to prevention and health care information, insufficient capacities of their health care systems, shortage of health professionals. Confronting the HIV/AIDS epidemic, tuberculosis and malaria has become the top priority at world level for the World Health Organization ("Roll-back Malaria" and "Stop TB"), the World Bank and specialised UN bodies such as UNAIDS. The "Global Fund to fight AIDS, tuberculosis and malaria" was set up in 2001 as a financial instrument, based on a partnership between governments, civil society, the private sector and affected communities to direct resources to areas of greatest needs. With a secretariat of 240 people in Geneva, the Global Fund has so far attracted € 7 billion and committed € 1.2 billion to support 154 programmes in 93 countries.

The international community has promised to work towards the goal of universal access to HIV/AIDS prevention, treatment, care and support by 2010, including addressing mother to child transmission. The G8 supports African efforts to strengthen health care systems more

[6] Council and Parliament Decision N° 1209/2003/EC of 16.6.2003
[7] Letter of 24.02.2006 from the Chair of the EDCTP General Assembly.

broadly, including through support for long-term plans and better institutional coordination. This is mainly done through development aid funding.

a) EU development aid

The European Union together with its Member States represent 57% of public development aid worldwide (€ 48 billion in 2006). The global EU support to health in over 100 developing countries is estimated at € 625 million per year. The EU Member States and Commission are together the leading donor for the "Global Fund". Over the last 5 years, the Commission contribution was about € 50 million per year. On 31 May, the President of the Commission pledged € 100 million for 2007 and proposed a further € 300 million over the following three years.

The European programme for action[8] to confront HIV/AIDS, malaria and tuberculosis through external action (2007-2011), endorsed by Council in May 2005, targets four areas for Commission activities, in partnership with the Member States and other key players:

- affordable pharmaceutical products,
- strengthening regulatory capacities,
- developing new tools and interventions such as vaccines and microbicides,
- strengthening partnerships with multilateral agencies.

This programme for action makes several references to EDCTP and public-private-partnerships, capacity building for health research and training, medical care coverage for the population concerned by clinical trials. Three new projects of potential interest to the EDCTP were identified, requiring a total amount of € 14.4 million in funding. An older project, covering some of the EDCTP scope for malaria, is still subsidised by DG Development (AMANET). The Commission also supports partnerships with key organisations such as the International AIDS Vaccine Initiative (IAVI) and the International Partnership for Microbicides.

b) EU Research in the field of poverty diseases

When it comes to health research, international efforts are limited. At a ministerial summit held in Mexico in November 2004, 24 health ministers issued a statement on health research asking "the international health research community to accelerate the development of essential drugs vaccines and diagnostics and to ensure the equitable delivery of those interventions". The WHO Initiative for Vaccine Research (IVR) provides an inventory of public health vaccines at the R&D stage. The WHO special programme for research & training (TDR) produced a "Ten-year vision and strategy" paper in December 2006.

Under the 6th research framework programme, besides the EDCTP subsidy, another € 258 million were earmarked for collaborative research[9] on HIV/AIDS, Malaria and Tuberculosis. From 2002 to 2006, the responsible Unit in the Commission's Research DG was able to commit, with a team of 12 people, all the corresponding funds: 43% for vaccine development, 48% for drugs and other treatments, 6% for microbicides and 3% for new diagnostics. In terms of diseases, HIV/AIDS represents half of the amount, malaria 26% and TB 24%.

In addition, DG Research funded, under the 6th framework programme, 27 projects on neglected infectious diseases (€ 44 million), 12 projects on health systems (€ 20 million) and 8 projects on reproductive health (€ 14 million). DG Research projects are exclusively conducted through calls for proposals, whereas EDCTP can also pursue a brokering approach where players and products can be identified and brought together.

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[8] COM (2005) 179 of 27/04/2005.

[9] See DG RTD publication "Combating deadly diseases", Project synopses 2007.

Additional advantages for the EDCTP are the possibility to fund clinical trials beyond phase I and to focus on science in Africa. DG Research has also developed numerous guidelines on evaluation procedures, project integration, ethics and intellectual property, which could also be used by EDCTP.

It appears that the EDCTP initiative was initially triggered by a desire for greater efficiency and better coordination, expressed by national agencies already involved in clinical trials in Africa. There is no suggestion that product development is the only or the most important input to the global effort to improve health in Africa. Capacity strengthening programmes will fail if not closely linked to the national objectives, priorities and strategies of African governments. Without early and clear involvement of African governments it would be difficult to assure sustainability of the strengthened institutions, as recommended in the strategy paper on capacity that DCCC submitted in 2006.

It should be noted that most clinical trials on HIV/AIDS, malaria and tuberculosis are conducted by the pharmaceutical industry worldwide, and only a few by public research institutes. They generally include multiple clinical centres around the world and rarely concentrate on African countries only.

2.3. EDCTP objectives

The statutes of the EDCTP-EEIG contain 2 general objectives:

- The cooperation of the members to promote new clinical interventions to fight the 3 diseases in developing countries.
- To serve as a common execution structure for the EDCTP Programme in the sense of Article 169.

EDCTP activities to be subsidised under the EU framework programme are defined in annex 1 of Decision N° 1209/2003/EC of Parliament and Council. The activities to be funded could be redefined or expanded in a future FP7 financing decision.

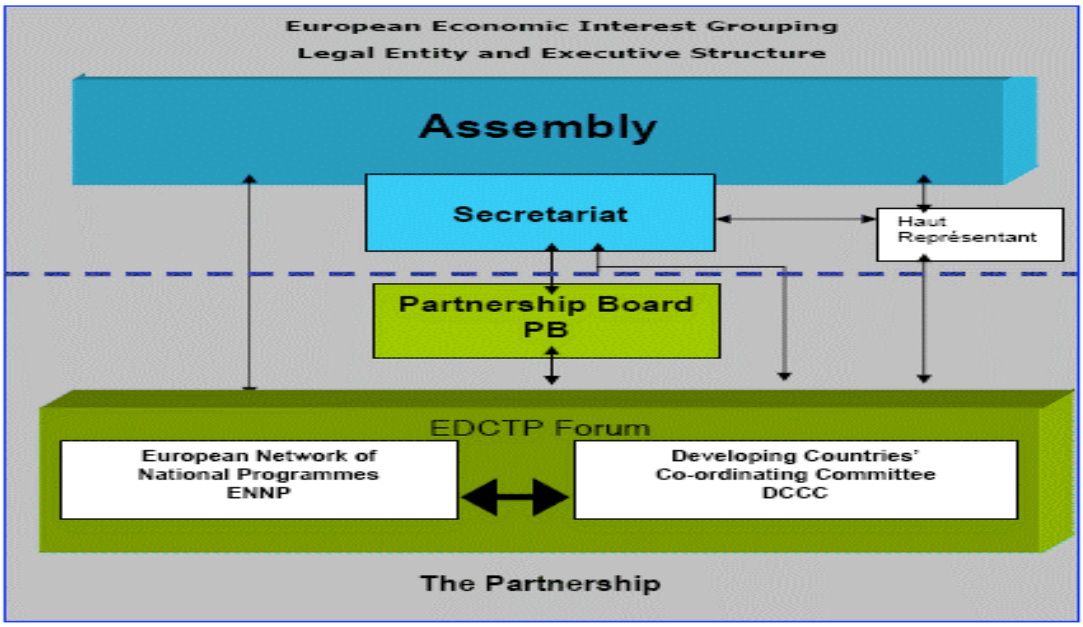
Description of EDCTP Programme activities financially supported by the EU budget
1. Activities linked to networking and coordination of: *(a) European national programmes;* *(b) the activities carried out in developing countries.*
2. RTD activities linked directly to the development of new products and the improvement of existing products against the three diseases (HIV/AIDS, malaria and tuberculosis), suited to the specific requirements of the developing countries, i.e. that they are effective, easy to use, new and as affordable as possible: *(a) support for clinical trials in the developing countries, taking into account, in the design of the trials, coexisting infections and giving due consideration to sexual and reproductive health;* *(b) strengthening of capacities in the developing countries.*
3. Activities planned to ensure the development, visibility and sustainability of the EDCTP Programme:

(a) activities to promote the EDCTP Programme to ensure a high profile at European or international level; *(b) activities linked to obtaining the necessary funds, including those from the private sector, to enable the EDCTP Programme to develop as planned, including beyond the period covered by this decision;* *(c) regular reporting on the implementation of the EDCTP Programme with special emphasis on its public-interest value.*
4. Basic activities for the EDCTP Programme such as secretariat services and the management of information concerning clinical interventions against the three diseases (HIV/AIDS, malaria and tuberculosis).”

2.4. EDCTP structures

The formal governance structure of the EDCTP comprises:

- a **General Assembly** – the decision making body made up of 16 representatives of the Member States and observers (Chairs of the PB, DCCC and ENNP; EU Commission and Switzerland), The GA has delegated North/North and North/South networking tasks to the European Network of National Programmes **(ENNP**), an informal working party of contact persons,
- an advisory **Partnership Board (PB)** (12 independent experts from Europe & Africa),
- **the Developing Countries Coordinating Committee (DCCC)** giving the views of 14 scientists from developing countries on institutional and human capacity development,
- a **Secretariat** led by the **Executive Director** facilitates the work and implements the EDCTP plans, in compliance with the legal and financial obligations of the EU and other sponsors,
- a **Haut Représentant** acting as an EDCTP advocate for political support and funding.



2.5. EDCTP finances and main activities

The EDCTP has three sources of funding: from the EU budget, from concerned Member States and from Third Parties. The EU grant agreement requires that EU funding must be matched by an equal amount of funds from the Member States and limited to € 15 million for administrative costs.

Year	Contribution: (€ million)	Spent: (€ million)	Overall spending, since 2003:
2003	EC: 19.79	0.21	• 30.9 % spent on management costs • 44.5 % on clinical trials + capacity building • Total committed to end 2007: € 60 mio In 2006, 49.2% spent in Africa in the form of: Grants 3.38, Cape Town 0.73, DCCC+PB 0.31
2004	EC: 4.61	3.15	
2005	EC: 3.95	4.30	
2006	MS: 1.01 *	8.40	
Total	29.36	16.06	

** Member States direct contributions (cash + kind) have recently increased to € 37 million including 7.5 million from UK, 2 million from Spain and Sweden, 1.25 million from Ireland*.

The output of EDCTP so far has been limited. Nevertheless, 69 grants have been approved, or are under contract negotiations (€ 40 million in total). These include 24 training awards, 19 for clinical trials, 14 for ethics support, 11 for networking and 1 for clinical trials registry support, involving 75 different institutions in sub-Saharan Africa (see Annex 3: EDCTP projects).

This table on EDCTP expenditure in the main areas of activity shows a relative decrease in management costs and an important effort on information. The amounts spent in Africa have now reached half of the total expenditure. The low spending and the limited number of projects do not warrant a separate analysis of the EDCTP performance in each area of activity.

Area	Spent in 2005 (€1000)	Spent in 2006 (€1000)	% In 2006
North-North networking	189	787	9,3
South-South networking	284	631	7,5
Clinical trials	1 017	2 246	26,7
Capacity building	778	1 839	21,9
Advocacy/fundraising	242	400	4,7
Management	1 796	2 202	26,2
Information	1	297	3,5
Total	4 305	8 402	100,0

2.6. EDCTP evaluation processes

Review procedures were prepared in collaboration with the Norwegian and UK Medical Research Councils and described in some 30 Standard Operation Procedures adopted in consultation with the Dutch funding agency ZonMW and published on the EDCTP site[10]. Eligibility and selection criteria for applications are stated in the call publication. When there is limited national expertise, very few products and sites, the EDCTP may choose to develop a brokering action plan to select an eligible application.

[10] See in particular the EDCTP guideline for reviewers, 28 November 2006.

EDCTP has assembled a pool of reviewers through the various constituencies who are checked for conflicts of interest. All proposals are reviewed by two independent external experts as well as two members of the Scientific Review Committee (SRC). The SRC meeting produces a ranking of proposals, submitted to the Partnership Board with a full SRC report. The General Assembly makes the final decision on the basis of PB recommendations. It takes 6 to 9 months, overall, between receiving the proposal and the final decision. The results and reports are accessible to national agencies but not to the general public.

All clinical trials require previous ethics clearance through a national ethical board and projects that do not meet ethical criteria are rejected. All clinical trial projects are registered with the South African Cochrane Centre (ATM Clinical Trials Registry). EDCTP also supports the work of various ethical committees in Africa.

Decision N° 1209/2003/EC makes EDCTP funding conditional on the formulation of the provisions relating to intellectual property rights in such a way that they also aim at ensuring that the people of developing countries have easy and affordable access to the research results produced by activities under the EDCTP Programme and to the products directly deriving from its results. The basic principle is that the EDCTP will favour the transfer of IP-rights to ensure production and availability of affordable medicines to the people in need in developing countries.

2.7. Implementing the EDCTP "Roadmap 2010"

In response to a request from the Commission, linked to the grant extension, the EDCTP produced a detailed roadmap at the end of 2006. In June 2007, the General Assembly adopted a new strategy, on proposal from Dr Mgone, and agreed as proposed that it should be developed to include key performance indicators, both for internal and external purposes. It was also agreed that a time work plan should be drawn up over the summer. Good relationships have been established with the Bill and Melinda Gates Foundation (BMGF), with a € 20 million joint call, announced on "World Aids Day", 1 December 2006 (BMGF: € 7 million, Member States: € 6.7 million and the EC: € 6.7 million).

The EDCTP has opted to change its approach and offers larger awards that focus on product orientated clinical trials and built into the calls the networking (nodes of excellence, fellowships) and capacity development elements (ethical review, regulations). New efforts have been made to solicit third-party involvement and funding. A new database and tracking system that includes automatic alerts, countdowns and target milestones for contract negotiation has been developed and will be implemented.

The EDCTP has initiated a series of stakeholders meetings and has announced new calls:

- Malaria vaccines (Copenhagen, January), call in July 2007 (14.4 mio €)
- Tuberculosis vaccines (The Hague, April), call in July 2007 & May 2008 (11.2 mio €)
- Nodes of excellence (Douala, May), call in July 2007
- HIV/AIDS treatment (Madrid, May), call in January 2008 (6.6 mio €)
- Tuberculosis treatment (Dublin, May), call in August 2007 (14.3 mio €)
- HIV Microbicides (Oslo, June), call in February 2008 (8.1 mio €)
- Ethics and regulatory affairs (Geneva, June), and follow-up in liaison with WHO
- Malaria in pregnancy (Vienna, June), call in August 2007 (9.1 mio €)
- Malaria treatment (Vienna, June), call in August 2007 (9.1 mio €)
- HIV vaccines (Antwerp, September), call in February 2008 (7.2 mio €)
- Three rounds of calls for senior fellowships, in August 2007/2008/2009

PART 3:

MAIN ISSUES AND SUGGESTIONS

FROM EXTERNAL REVIEW

3.1 Need for EDCTP improvements during the extension period: *(2007/2010)*

a) Improving EDCTP policies

b) Improving EDCTP governance

b) Insufficient results, so far

c) Improving EDCTP operations

3.2 Need for interested Member States to reinforce their commitments

3.3 Conditions for funding future EDCTP activities under FP 7: *(2010/2013)*

3.4 Prerequisites for new Article 169 research programme initiatives

PART 3 MAIN ISSUES AND SUGGESTIONS FROM EXTERNAL REVIEW

The design and goals of EDCTP are ambitious, perhaps over ambitious. The terminal goal of relieving poverty in Africa by improving the control of three major diseases is challenging. EDCTP is further complicated by including additional goals within the process of operating the programme, these are:

- Involvement of national research programmes of the European countries.
- Capacity strengthening in Africa within a network of collaborating centres.

Two important prerequisites for Article 169 were missing when the EDCTP was created: the real status of national programmes jointly undertaken by certain Member States, the pre-existence of structures created for the execution of such programmes. In addition, there was no previous tradition of cooperation between the Member States; the common EDCTP-EEIG structure only came into existence after adoption of the EU financing decision.

The EDCTP had a very difficult start from mid 2003 to 2006. National agencies did not fully understand the implications of Article 169 in terms of fresh funding, joint ownership and sharing of expertise. Even now, most national agencies are not yet prepared or enabled to finance EDCTP activities directly. When offering so-called “joint activities”, they often require separate calls and evaluations and insist on a systematic “juste retour” for their own researchers. Such legal and administrative limitations are an obstacle to programme integration and make the EDCTP coordination complex, bureaucratic and unattractive for industry as well as for African researchers.

It should have been anticipated that the organisation of this complex programme would require careful and detailed planning and negotiations to establish its main components. For example, the fact that some of the European countries have not established national research programmes has been a constraint. Some of the European countries need to review their national research policy and make revisions that would facilitate their collaborating with other European countries, African institutions and with WHO and other international organisations.

Similarly, the EDCTP programme tacitly assumes that investments into selected African institutions would lead to sustainable capacity strengthening. Experience has shown that such projects tend to fail unless there is a clear involvement of the host government, which provides assurance of continuing support when external aid ceases.

Initial projections of a quick start-off were unrealistic and it has taken this long period to mobilise the essential components of the programme. The first three years have not been entirely lost but have been used in working out in more detail the nuts and bolts of a complex programme. With hindsight, EDCTP could have been launched into scientific work more quickly using a simpler European Research Area design. A second more ambitious phase could have been launched later to achieve integrated collaboration of European national research programmes and long-term enhancement of research capacity in African countries.

In response to criticism by the Commission, the EDCTP made a significant effort in 2006 to remobilise its constituencies and overcome some of the difficulties. The new Chair and some General Assembly members undertook to consolidate the working practices (EDCTP Guidelines and SOP’s), to improve the Website and to address the governance issues, giving more attention to ideas from the Developing Countries Coordinating Committee (DCCC). The Haut-Représentant, Pascoal Mocumbi deployed considerable efforts to raise the visibility of EDCTP in Europe and Africa. The newly appointed Executive Director, Charles Mgone has accelerated the pace of improvements and reacted positively to comments and suggestions from the IER Panel.

3.1 Need for EDCTP improvements during the extension period (2007/2010)

a) Improving EDCTP policies

To reduce poverty in Africa, the EDCTP has to address three major diseases for taking products from pre-clinical to clinical phases II, III and beyond. The € 200 million EU subsidy risks being spread too thinly across the field to meet the high expectations placed on EDCTP. The identification and processing of the most suitable candidate for the development of public goods, as soon as possible, for countries in need, should take precedence.

The specific contribution from EDCTP should be to promote clinical trials, to intensify the development of new and improved drugs and vaccines for the control of HIV/AIDS, malaria and tuberculosis. A narrow interpretation of this goal would imply that northern partners would provide candidate drugs and vaccines that African scientists would test in well designed clinical trials. A broader interpretation of the goal is a true partnership in which both the northern and southern partners are involved in all aspects of product development including:

- Specification of the characteristics of the desired products;
- Relevant clinical pharmacology/immunology and epidemiological studies;
- Design of Phase I and Phase II trials even if these are to be carried out in the North;
- Sustainable improvement in the capacity of African institutions to conduct relevant research.

EDCTP was meant to coordinate national programmes of research of Member States. It is now clear that some of the EU countries have not developed comparable national programmes. The EDCTP programme could stimulate some Member States to review the organisation of health research and develop credible national programmes. The persistence of complex overlapping national mechanisms and commitments are a sign of scepticism towards the EDCTP.

The EDCTP does not yet have a clear and coherent research strategy*)*. It should improve the legibility and clarity of its planning documents. It should define a precisely timed action plan, with financial targets and deliverables (precise in 2007/ 2008, tentative for 2009 and 2010), performance indicators and external benchmarks.

Strict compliance with ethics is clearly very important for the protection of patients and healthy volunteers and for the reputation of EDCTP and the EU as a whole. All clinical trials require previous ethics clearance through a national ethical board and projects that do not meet ethical criteria should be rejected. All clinical trial projects are registered with the South African Cochrane Centre (ATM Clinical Trials Registry). EDCTP also supports various ethical committees in Africa. However, EDCTP's guideline on ethics is a list of reference documents and the policy should be spelled out in more detail. A summary of how ethical judgements were carried out on specific EDCTP projects should be prepared by sponsors and made available on the Website, for scrutiny.

On Intellectual Property Rights (IPR), the EDCTP states that a general policy is difficult to define given the various combinations of potential partners and that specific Intellectual Property Rights issues should be addressed on a project–by–project basis. Nevertheless, as announced on the EDCTP Website, a policy paper should be adopted as soon as possible to address tiered pricing agreements, availability and easy access to affordable new medicines. More details on ethics and IPR issues are given in Annex 4.

Participating Members States should show their commitment to engage in a joint programme. Offering budgetary support or other resources in kind should not be left to their discretion. National funding could also help increase the headroom for EDCTP administrative expenditure, by analogy with WHO administrative practices for specially funded programmes.

The lack of direct funding from most Member States is the main explanation for the very slow start and major under spending by EDCTP. Because of the lack of flexibility of most national programmes, which prevent direct funding or financing teams from other Member States, the current co-funding mechanisms appear cumbersome and discouraging for any applicant, especially researchers from African countries. This, combined with the stringent EU financial regulations, led to bureaucratic compromises, overcautious approaches, no industry participation and a lack of dynamism of the EDCT Programme so far. The EDCTP calls should be better structured, taking for example, FP7 calls as a model, but avoiding overlap with calls from DG Research.

The so-called “integrated activities” refer in fact to normally run national activities. The concerned Member State only has to label them unilaterally as of potential interest for EDCTP and to certify the activity as a budget contribution to the Joint Programme. Whereas such practices might have been acceptable in the start-up period, they should be progressively abandoned and replaced by truly integrated programmes, entirely run and financed by the EDCTP budget, secured on a foreseeable mid-term basis.

b) Improving EDCTP governance

The EDCTP governance structure is complex and has given rise to multiple conflicts between individuals and between the various bodies. There now seems to be a better understanding and dialogue. Some of the difficulties have been due to the instability and weakness of the Secretariat (4 executive directors in 4 years, including one interim director), the lack of understanding by Member State agencies of the challenges and consequences of an article 169 programme. The governance is now beginning to work better.

All EDCTP bodies should quickly redefine and agree on mandates for all EDCTP components, and their respective obligations, in order to avoid late inputs of scientific strategy, action plans and parts of the annual reports. The General Assembly should formalise and implement as soon as possible the main recommendations stemming from the self-assessment exercise conducted in 2005 and all improvements announced in the 2006-2010 EDCTP Roadmap. The EDCTP should also have a clear mandate to enter into partnerships with industry and other third parties, provided public interests are well protected.

General Assembly members should have a high position at home to be able to supervise all relevant national activities and to mobilise national funds directly. One or two meetings a year should be sufficient to decide on strategy, policy, funding and appointments, avoiding micro-management as was the case previously. There is a need to further strengthen African representation in the General Assembly (African countries or regional organisations). The GA should also create a small Steering Committee to provide more regular support to the Executive Director, with GA chair, Vice-Chairs and donor countries only, PB and DCCC chair, possibly by videoconferences.

The **Partnership Board** should develop its independent and high level expert role in defining the scientific content of the EDCTP strategy and work programmes, calls for proposals, stakeholders meetings and recommending joint activities between Member States and African institutions or scientists. It should in future better document its scientific strategy and its capacity to supervise peer review and scientific excellence.

The **DCCC's** contribution has greatly improved over the last 18 months, focusing on centres of excellence and capacity development. It has started to liaise more effectively with African governments with the help of the Haut Représentant and the members of the Secretariat from Cape Town. DCCC membership may have to be broadened to increase the engagement of African governments. Regional health bodies are now well represented[11].

The Haut Représentant will from now on be based at the African Office in Cape Town to allow more time to meet with African leaders and secure their involvement.

The Secretariat is small and has to outsource work, in particular to NWO. It should acquire more expertise by rotation of National or Commission scientific officers and administrators on secondment. The leadership of the Executive Director is crucial in managing the EDCTP as a small enterprise with several stakeholders and clients. This requires excellent negotiation and management skills, besides knowledge of the scientific and multi-cultural environment. Lessons should be drawn from past executive directors' instability, and management weaknesses at secretariat level.

c) Insufficient results, so far

The output of EDCTP so far has been very limited. The succession of directors caused major disruption and an excessive number of meetings with little in the way of results. The first call (February 2004) had to be cancelled because of serious problems with the review procedure. The slow EDCTP start was the subject of sharp criticism in "The Lancet" and in "Nature Medicine" in July and August 2005. The second call (June 2005) gave rise to excessive delays in securing trial sponsorship, finalising co-funding, changes in protocols and lack of preparedness of the investigators. For the third call: only € 4.76 million from a budget of € 6.1 was committed, due to the poor quality of the rejected proposals.

Past performance cannot be considered satisfactory in terms of volume of activities and results, in view of the available financial resources. During the first 3 years, the EDCTP has not been able to fulfil its promises and has not shown sufficient operational capacity to properly allocate EU research funds. The initial awards of various separate small grants on capacity development (PhD's, fellowships, ethics, regulatory support), networking and conduct of clinical trials, have created some awareness, but were time consuming and not always cost-effective. In future, the EDCTP programme should no longer be regarded as bureaucratic and complicated, rather as helpful.

Whilst the European Commission's own € 258 million budget for research on the three diseases was spent normally, the EDCTP budget shows a massive under-spending (but no apparent irregularities):

- From FP6 € 200 million, less than € 40 million will be committed by the end of 2007,
- From € 200 million expected from Member States, only € 37 million will have been received directly by the end of 2007,
- From € 200 million expected from Third Parties, only € 7 million has been received so far (from the Bill and Melinda Gates Foundation).

Nevertheless, the EU financial interests appear to have been well protected by the strict clauses of the initial grant agreement and by the additional contractual requirement imposed with the extension, especially on co-funding.

[11] WHO-AFRO, West African Health Organisation (WAHO), Organisation de Coordination pour la Lutte contre les Endémies en Afrique Centrale (OCEAC), East, Central and Southern African Health Community (ECSA).

d) Improving EDCTP operations

In 2007, the EDCTP initiated a cycle of stakeholders meetings. These stakeholder meetings seem a very laudable initiative. It is not evident that the stakeholder meetings are having the expected results. Furthermore, they have attracted limited attention from the concerned national agencies, or from the pharmaceutical industry, in terms of presence and seniority. Also, it may have been preferable to present the partners upfront with a clear strategy and a tentative action plan on all these subjects, rather than hope that participants would be able to formulate the way forward on each topic in just one session. Instead of fragmented calls, it might be preferable to launch massive and well-structured annual calls, visible to a large number of potential partners, as is the case in DG Research.

The EDCTP should now be in a better position to set realistic priorities and regroup the various activities around clinical trials, taking on board DCCC concepts on capacity building and nodes of excellence. The ENNP has for some time been working to establish what activities are in fact existing joint programmes resulting from cooperation between the members of EDCTP and what activities have the potential to develop from initiatives of a single Member State into joint programme activities, either with or without EDCTP funding. Development of new initiatives between EDCTP and a number of national agencies collaborating together on a relevant research project also falls within this category.

When making an inventory of possible activities, calls and brokering, the EDCTP should look beyond the circle of national institutes. The EDCTP could try to associate with a few worldwide clinical studies for know-how and visibility, as was already done with AMANET or the African AIDS Vaccine Programme. The Secretariat should keep an inventory of and maintain good contact with other similar programmes to avoid duplication. In order to show that improvement is being achieved, the Executive Director should quickly set up and publish on the Web a monthly one-page table with key performances indicators.

Direct funding of EDCTP projects avoids the grantee having to prepare multiple sets of technical and financial reports in differing formats and face multiple evaluations, which can be very time consuming, inefficient and confusing. It is easier to complete the EDCTP reports, including co-funders' contributions. The co-funding institutions receive the EDCTP reports and detailed administrative tasks can be delegated at no cost to the EDCTP Secretariat. These may include budget negotiations, contract drafting, legal matters, reviewing of annual financial and technical reports, project monitoring and appropriate international financial auditing. When a grantee reports to separate bodies the risks of errors occurring and double counting of costs between the financial reports of the funders' increases significantly.

The EDCTP should explore mechanisms for achieving a smoother running of the programme within the present restrictions dictated by Art.169. As an example, an African regional organization, OCEAC has recently earmarked US$ 20 million for health research in Central African countries. Could this be used as a resource to meet the co-funding requirements thereby giving African scientists more flexibility in initiating partnership programmes?

It takes 6 to 9 months, overall, between receiving the proposal and the final decision. The results and reports are accessible to national agencies but not to the general public. Hence, supervision of scientific excellence depends entirely on the Executive Director and the Partnership Board, but cannot be judged by the scientific community at large. The host, NWO, has the impression that EDCTP could have used more intensively the know-how and experience of NWO/Zon-MW in order to gain time and efficiency.

The EDCTP should associate with international Product Development Public-Private Partnerships and build on successful African networks where a significant level of expertise

and capacity is already in place. In order not to leave behind some African countries, the EDCTP must also encourage weaker institutions (in particular in Central Africa) to join in through a south-south mentorship programme. Following the recent stakeholders' meeting in Douala, The EDCTP should build on and collaborate with pre-existing networks in Eastern, Western, Central and Southern Africa, rather than create new ones (see annex 5).

The new EDCTP communication officer position should be used to implement a communication plan to make EDCTP an attractive and visible player to the scientific community worldwide, especially in the EU and Africa, and to African health scientists, health officials, regional organisations and industry. There is also a real need to improve internal written communication: legibility and clarity of minutes, strategy, action plans, annual reports and all key official documents.

IER suggestions on EDCTP policies, governance and operations

EDCTP policies:

1. Revisit scope, set realistic priorities and regroup the various activities around clinical trials, taking on board DCCC concepts on capacity building and nodes of excellence.
2. Define a clear, convincing and realistic EDCTP strategy, with common shared vision, clearly defined contributions expected from each partner, equitable sharing of results.
3. Define a precisely timed draft action plan, with financial targets and deliverables (precise in 2007, 2008, tentative for 2009 and 2010), performance indicators and external benchmarks.
4. Simplify and streamline co-funding, from virtual to actual common pot, in order to reduce operational complexity and allow African initiation of EDCTP projects
5. Publish on the Web a summary of ethical judgements on specific EDCTP projects.
6. Publish an EDCTP Intellectual Property policy to address availability and access to medicines.

EDCTP governance

1. Redefine and agree on mandates of all EDCTP components, and their respective timely inputs.
2. Improve dialogue among all components, especially GA/PB.
3. Make the General Assembly more political.
4. Create Executive Steering Committee: Executive Director, with GA chair, Vice-Chair and donor countries only, DCCC chair & HR.
5. Broaden DCCC membership to increase engagement of African governments and organizations.
6. Reinforce scientific independence and level of Partnership Board with adequate firewall protection from political and other external pressures.
7. Draw lessons from past Executive Director instability and management weaknesses at secretariat level.

EDCTP operations

1. Improve structure and quality of calls. Shorten time to contract to 3 months after evaluation. Borrow more from FP 6 and FP 7 guidelines and NWO knowledge.
2. Fully implement quality assurance to show and guarantee scientific excellence of call designs, evaluation and final acceptance. Publicise summary assessments for the scientific community.
3. Associate with major Product Development Public/Private Partnerships for know-how and visibility. Keep an inventory of and maintain contacts with other similar programmes to avoid duplication.
4. Involve Northern and Southern partners in all aspects of product development: product specifications, design of all clinical phases (pharmacology/immunology/epidemiology), including trials in Europe, and capacity strengthening of African research institutions.
5. Set up and publish on the Web a monthly one-page table with key performance indicators
6. Implement a communication plan to make EDCTP an attractive and visible player:
- to the scientific community worldwide and especially in the EU and Africa
- to African health scientists, health officials and regional organisations
7. 1mprove legibility and publish on the Web: minutes, annual reports and key official documents.

3.2. Need for interested Member States to reinforce their commitments

The discussion of the most appropriate structure for EDCTP seems to have focused on the European Economic Interest Group model, which is mentioned in the Council and Parliament financing decision. Unfortunately, not only is the EEIG model complex, but it also has several shortcomings. It does not allow representatives of Developing Countries to participate as full members in the decision-making General Assembly. Neither can Commission representatives fully participate "in the structures created for the execution of the programme" as required in Article 169.

A useful comparison could have been drawn at the time with the European Organisation for Research and Treatment of Cancer (EORTC), founded in 1962 as an international organisation under Belgian law, to develop, conduct and coordinate clinical trials. In a different area of intervention, EORTC provides a good example of successful research cooperation, clinical trial sponsorship and sound funding mechanisms at European and International level.

A feedback from Permanent Representations and members of the EDCTP General Assembly shows that most Member States are not aware of the complexities and conditions attached to Article 169. Some officials from Permanent Representations declared that the EDCTP was only accepted under pressure from the Commission. Member States with a high political profile in Africa, do not want to lose control or visibility of their own national flagship projects. Several Member States are not yet ready to accept that their money is being spent on foreign research teams. In most countries research activities could not even be integrated into a national programme, let alone into a Community programme. Within countries, national institutions often compete for the same limited funds. Governments did not make fresh funds available for participation in the new EDCTP Programme.

The Commission should report back to Council and Parliament about current difficulties and possible solutions, in anticipation of the formal report due mid 2008. In this report, the Commission should help Member States identify the best ways to reform the current EDCTP structures and requirements for "common funding pot" and true programme integration. The Commission could also help Member States define typical national implementing measures and incentives for national agencies to better co-operate with EDCTP in future. The Commission could also consider whether Article 170 (international agreements) could be used to reinforce African presence in EDCTP if the EEIG instrument in itself presented legal limitations.

It is the responsibility of the Member States who own the EDCTP to re-establish true ownership and reinforce their mutual commitment towards the common structure and programme they accepted to create in 2003. This could be achieved by a strong Council Resolution, renewing the "EDCTP vows" and agreeing to provide fresh money to a common pot according to a pre-determined allocation key. The Member States concerned should agree to fund directly and significantly the EDCTP on a yearly basis. They should also accept that programme integration really takes place in terms of a single EDCTP procedure for planning, launching and evaluating calls, with no national strings attached.

The interested Members States should jointly revise the EEIG statutes to define the mutual commitments in terms of budget and programme integration. EDCTP decision-making (General Assembly) should be restricted to the donor European countries represented at the highest possible level and opened to representative African partners. Other partners could retain an observer status

Where necessary, the Member States should involve their parliaments to adopt the necessary national budgetary and administrative implementation measures. They should also improve internal coordination of related national activities and provide incentives to national institutes who are ready to cooperate. Concerned national institutes should explicitly address EDCTP activities in their official programming and annual reporting.

IER suggestions to EDCTP Member States and to the Commission

1. The Commission to report to Council and Parliament about current difficulties and possible solutions, in anticipation of the formal report due in mid 2008.

2. Interested Member States should renew their “EDCTP vows” in Council and accept reform to the EEIG.

3. The Commission should help Member States define appropriate national implementation measures.

4. Member States should agree to contribute to a “common funding pot” according to a pre-determined allocation key.

5. In the General Assembly, the decision making should be restricted to financial contributors with representation in the GA at the highest national level; other member will become GA observers.

6. African presence in the General Assembly should be reinforced, with decision-making status for African donors (country or regional organization).

7. Member States should refrain from imposing national criteria, and accept one single integrated scientific and ethical evaluation, conducted by the EDCTP, utilising a pool of the best national experts.

8. Member States should enforce the Article 169 concepts at home on a sustainable basis, involving national parliaments, and report back annually to the EDCTP and the Commission on implementation measures.

9. Member States should improve internal coordination of related national activities; provide incentives to national institutes ready to include EDCTP in their programming and annual reporting.

10. The Commission should encourage public/private partnerships in the field.

3.3. Conditions for funding future EDCTP activities under FP 7 (2010/2013)

Before the 7th Framework programme mid-term review in 2009, the Commission may consider favourably a new proposal to Council and Parliament to renew the funding of EDCTP under FP7, provided that:

- The interested Members States political, budgetary and administrative commitments are clear;
- The EDCTP programme integrates with the relevant national ones (common funding pot and evaluation);
- The EDCTP governance structures are properly adjusted and more open to African partners;
- The EDCTP performance complies with targets in the EDCTP Roadmap (November 2006).

The EDCTP roadmap contains a number of indicators that are not yet in place. The Commission should review these indicators with EDCTP and set out the exact targets to be achieved by the end of 2008 as a pre-condition for a new financing proposal under FP 7. The EDCTP must provide the Commission with a clear mapping of national programmes and trends to show the potential added value of future EDCTP activities.

For the Commission, there is a need to reassess the place of the three diseases compared to other neglected diseases and to other health research objectives. In addition, on the basis of FP6 experience, product development must be put in perspective compared to other aspects of health research in the field, which would complement future EDCTP tasks. Questions about evidence based priority setting (clinical trials versus primary health care and sanitation) and the extent of consultations with health researchers in Africa were repeatedly raised during IER panel discussions with representatives from DG Research. It appears that the EDCTP initiative was initially triggered by a desire for greater efficiency and better coordination, expressed by national agencies already involved in clinical trials in Africa.

Product development is not the only research input to the global effort to improve health in Africa. The Report by John Bowis and the European Parliament resolution adopted in June 2005 on major and neglected diseases in Developing Countries outlines future orientations for EU development aid and research policies and calls for the activities of the EDCTP to be broadened to include other neglected diseases and other phases of clinical development[12]. The synergies between FP 7 and development aid activities related to poverty diseases must be considerably reinforced. The Commission must ensure greater coherence between the various activities sponsored by its services, given the growing number and complexity of international partnerships and initiatives in the field (see annex 6).

The European Commission and the EU Member States have played a major role in the revision of the WHO International Health Regulations, which came into force in June 2007. The EU activities to fight HIV and tuberculosis have been strengthened, with the recent creation of the European Centre for disease prevention and control in Stockholm[13]. At a very recent meeting between the new WHO Director General, Margaret Chan, the President of the Commission, and Commissioners Kyprianou and Potočnik, the prospect of meeting African health ministers in Bamako in 2008 was discussed. This would be an excellent opportunity for the European Commission to consult African Governments on the future of EDCTP activities and on priorities for international health research and other health activities

[12] PE 357.813 of 22/06/2005, European Parliament Committee on Development
[13] www.ecdc.europa.eu

of interest to Africa. African governments should also be asked on this occasion to link EU capacity strengthening efforts to their national strategies, in order to ensure sustainability.

Successive Commission communications on poverty related diseases refer to the links to be made with the EDCTP. The Programme for action on poverty diseases makes several references to the EDCTP and public-private-partnerships, capacity building for health research and training, medical care coverage for the population concerned by clinical trials. Nevertheless, the IER panel did not find evidence that these principles had been sufficiently applied by DG Development in synergy with the EDCTP and DG Research. The relevant inter-service meeting, chaired by DG Development, did not meet for more than a year and never involved any representative from the EDCTP. DG Development representatives do not attend EDCTP meetings, where they could have highlighted the new development principles which contain clauses on: ownership, a stronger voice for Developing Countries, priority setting and affordability.

Nevertheless, the Haut Représentant, P. Mocumbi, met recently with the Director-General of DG Development and makes regular contact with local representatives from DG Development in Africa. It was suggested that DCCC members should also be introduced to delegation members. At a meeting with IER panellists, the new director in charge, Luis Riera agreed to have a fresh look at the situation in terms of synergies, overlaps and DG Development presence and support for the EDCTP.

DG Development is willing to include health research in the health sector policy dialogue, especially in countries where the Commission provides significant budgetary support, allowing longer-term national strategies to be pursued. Health programming guidelines could mention specific issues on health research.
Other areas of more specific collaboration could be made through links with activities to confront the crisis on human resources for health, or with the Health and Development Innovative Consortium (a network of ACP universities around AIDS research).

It is imperative to establish internally a joint DG Research / DG Development platform to engage in a real and continuous dialogue with the EDCTP and to support capacity building around EDCTP core tasks. Regular institutionalised meetings at director level between EDCTP, DG Research and DG Development would be most appropriate to establish and formalise an appropriate level of cooperation. It should include, where appropriate, representatives from the Public Health Directorate (DG Sanco) and from the European Medicines Agency (EMEA). Since last year, EMEA has played a special role[14] in advising WHO and international organisations on scientific issues related to Research and Development and to the evaluation of medicines used outside Europe.

It would be useful for the EDCTP to come up with a 'test case' for DG Development, to show real commitment. If clinical trials were successful, DG Development should commit to take care of the costs of treatment of the target population.

[14] www.emea;europa.eu and Article 58 of EMEA Regulation EC N° 726/2004.

Suggestions to the Commission, in relation to future EDCTP financing under FP7

1. Define, in consultation with the EDCTP, parameters for 2008 evaluation and conditions for future FP7 financing before mid-term, taking into account the targets set in the EDCTP Roadmap of 2006.

2. Create a joint DG Research / DG Development platform to engage in a real and continuous dialogue with EDCTP and support capacity building around EDCTP core tasks, including where appropriate, DG Sanco and the EMEA.

3. Revisit the three diseases and the neglected diseases research strategy: product development versus other aspects of health research in the field, to complement future EDCTP tasks.

4. Consult African health ministers on EDCTP future activities and the direction for EU international health research.

5. Submit a new Article 169 funding proposal to Council and Parliament, before FP 7 mid-term, provided that:

- Interested Members States political/budgetary/administrative commitments are clear;
- The EDCTP programme integrates the relevant national ones: common funding pot/evaluation;
- The EDCTP governance is properly adjusted and more open to African partners;
- The EDCTP performance complies with targets in the EDCTP Roadmap.

6. Consider combining Article 170 with the next Article 169 funding proposal to reinforce African presence in the EDCTP.

3.4. Pre-requisites for new Article 169 research programme initiatives

In principle, the EDCTP Programme, as described in the concept document of June 2002, could have received financial support from the EU framework programme in various ways other than Article 169:

- As a supplementary programme under Article 168 of the Treaty, involving certain Member States only, who provide national financing subject to possible Community participation;
- As an international agreement between the EU and Developing Countries (Article 170);
- As a joint undertaking or any other structure necessary for the efficient execution of the Community research programme (Article 171).

The IER panel did not see any documents discussing these various options for the EDCTP. At the time, there was no concrete experience of structures based on any of these articles of the Treaty. The reflections seem to have focused on the Article 169 option, in order to allow the Community to participate in programmes undertaken by several Member States and in their executive structures.

With hindsight, an integrated Community structure, or agency under Article 171 could have given European Institutions greater control and responsibility for the management of the EDCTP Programme, in close cooperation with national agencies and possibly the pharmaceutical industry[15]. Furthermore, an international agreement based on Article 170 could have been considered to reinforce the role of Developing Countries in the EDCTP Programme and structures.

A CREST discussion paper of January 2006 recognised that a combination of scientific, managerial and financial integration is essential to implement an Article 169 programme on a long-term basis. Whilst the legislative system of some Member States does not allow them to give public financial support to foreign institutions, the setting up of a dedicated common budget would require, in most of the other countries, approval by their national parliament, to be renewed every year.

The Brussels European Council of 8 and 9 March 2007 invited the Commission to “present proposals for Joint technology initiatives in selected sectors of strategic importance”. It is also invited the Commission “ to present proposals for initiatives based on Article 169 in order to provide Community participation in RTD Programmes undertaken by several Member States with a view in both cases to launching the most advanced ones in 2007.”

There appears to be a strong demand from Several Member States for new research initiatives based on Article 169. A major condition for success is the existence of a true cross-European ownership, with joint programmes between the interested Member States and autonomous and well functioning pre-existing structures.

The Commission should make new proposals only when the pre-conditions, implied by Article 169, are fully met. In particular, the Commission should:

- Assess the reality and added value of the national programmes to be integrated;
- Assess the performance and suitability of pre-existing common structures;

[15] See Proposal for a Council regulation setting up the Innovative Medicines Initiative Joint Undertaking, based on Article 171 COM (2007) 241 of 15/05/2007.

- Require a clear joint ownership statement, a pact with long-term obligations and sanctions;
- Define general rules for a common funding pot or other possible national contributions.

Therefore, for an Article 169 Programme to become and remain successful the Commission should verify that:

- There are well identified national programmes;
- There are available budgets, or a strong commitment to make such budgets available;
- The participating Member States show a political commitment with irreversible conditions;
- These commitments have sufficient political support in the particular Member State;
- Member States are ready to take the necessary administrative and budgetary steps, and other implementing measures, involving their national Parliament when required.

As a consequence, Member States not fulfilling the above mentioned conditions should not have access to an Article 169 programme. The Council and Commission must agree a mechanism to exclude Member States unable to fulfil these conditions during the implementation, under a clause to be formulated in the Article 169 Decision.

Before an Article 169 project can start:

- There must be a common work-plan for the project including: objectives, strategy and organisation;
- The financial contributions for each participating Member State are fixed;
- The Article 169 Entity has full control on how to spend the money;
- Member States cannot determine unilaterally how and with whom to spend the funds;
- There is a clear governance structure[16], approved by the Member Sates and the Commission;
- There are clear milestones and deliverables;
- There are clear evaluation procedures and criteria; the overall criterion is one of excellence.

The allocation of Community money should be strictly linked to the completion of milestones and deliverables, to be checked through an external evaluation procedure. There should be a clear division of tasks between the Article 169 Entity and the Commission in terms of information exchange and reporting,

Only if these conditions are fulfilled should the Commission report to the Council that Community money can be made available. When these conditions are met, the "common funding pot" requirement is less essential.

In addition, given the misunderstandings in the setting-up of the EDCTP, the Commission would be well advised to adopt a more pedagogical approach with Member States during the preparation of the initiative. The interested Commission departments should be ready to monitor the newly created entities during start-up, and provide continuous support later.

[16] Member States representation at a level to take decisions in the Board, with a clear distinction between contributing and non-contributing Member States; a clear description of competences, role and decision-making of each part of the structure, in particular of the Director.

To ensure coherence between different initiatives, the Commission should set out Article 169 pre-conditions in a guidance communication, giving criteria for choice between Article 169, other Treaty Articles or lighter ERA options and a strong budgetary "common funding pot" requirement.

For external research initiatives, in particular for "European neighbourhood policy", the Commission might consider combining Articles 169 and 170 to cover a foreign presence in decision-making.

Suggestions to the European Commission for new Article 169 initiatives

1. Set out future Article 169 pre-conditions, preferably in a guidance communication:

- Set criteria for choice between Article 169, other Treaty Articles or lighter ERA options;
- Assess the reality and added value of National programmes that are to be integrated;
- Assess the performance and suitability of pre-existing common structures;
- Require a clear joint ownership statement, a pact with long term obligations and sanctions;
- Define general rules for the common funding pot or other possible national contributions.

2. For an Article 169 Programme to become and remain successful:

- There must be pre-existing national programmes;
- There must be available budgets, or a strong commitment to make them available;
- The participating Member States must demonstrate an irreversible commitment;
- The Commission verifies sufficient political support in the particular Member State;

3. Before EU money becomes available:

- There must be a common work-plan, objectives, milestones, sound governance;
- The financial contributions per participating Member State are fixed;
- The Article 169 entity has full control on how to spend the money;
- There is adequate representation at a level where individuals can take decisions;
- There is a clear evaluation procedure; the overall criterion is one of excellence;
- Community money allocation is strictly linked to milestones and deliverables.

PART 4:

DISSENTING OPINION

BY PROFESSOR A. POLLOCK

PART 4 DISSENTING OPINION BY PR. A. POLLOCK

1.0 *The position of the majority report is premised upon the continuation of EDCTP as a global public private partnership for clinical trial research in support of product development. It is my view this recommendation is based on an overly restrictive interpretation of our terms of reference (section1.2, majority report). As well as focusing on EDCTP operations and performance, we were also asked to consider the role of the EC and EDCTP in the broader international research and development agenda, and to suggest alternative or complementary approaches for the EU to finance research on infectious diseases in Africa. This is the basis of my dissenting note.*

2.0 On the basis of the evidence received EDCTP has not met and is unlikely to meet the objectives laid out for it, unless it is substantially reformed with respect to political accountability and its own internal strategy. As documented in section 3.1 of the majority report, the complex governance arrangements and cofunding requirements have resulted in a major underspend.

2.1 The EDCTP programme was actioned under Article 169, title XVIII of the EC Treaty, an article that had never been implemented before. As a result, European research funds were hypothecated for use by 15 of the 27 member states on condition of matched funding from participating states being made available to EDCTP; and a complex and independent structure was established which is administratively and politically removed from the EU's main decision-making bodies . As highlighted by the majority report the absence of political representation from member states and political representation from African countries as full members in the decision-making General Assembly, is problematic. Currently EEIG and PB board members comprise academics each with their own institutional affiliations but no formal political accountability. With the exception of networking activities of DCCC in Africa and member state networking on the partnership board, the EDCTP is replicating many EC roles in commissioning research programmes but with less political accountability and strategic direction.

2.2 It is my view that the majority report recommendations which are intended to strengthen governance will not resolve the continuing ambiguity with respect to political control and accountability.

2.3 The EC has provided no evidence to support the establishment of EDCTP as a global health partnership. Since the inception of EDCTP in 2002 there has been a rapid expansion in the number of global health partnerships. The Commission and member states also support other global health partnerships some of which focus on clinical trials and product development, and drug procurement. Questions have already been raised about the adequacy of the governance arrangements of global PPPs and the deficiencies are not yet sufficiently identified or understood. However the EC has conducted no formal evaluations of these partnerships and there is no systematic account or evaluation of EC and member state funded global health partnerships conducting research on clinical trials in the sphere of the three neglected diseases which are the remit of EDCTP.

2.4 During the course of our enquiry we were told that this review is important for three reasons:

a) The EDCTP has been hailed as a flagship for Article 169 and member state cooperation. It has been proposed that before the 7th Framework programme mid-term review in 2009, the Commission should consider a new Council and Parliament proposal to redirect 10% of FP7 budget (total 6.6 billion over a further five years) to EDCTP.

(dissenting opinion by Pr A. Pollock, continued)

b) The European Parliament adopted in June 2005, a resolution on major and neglected diseases in Developing Countries which outlines future orientations for EU development aid and research policies and "calls for activities of the EDCTP to be broadened to include other neglected diseases and other phases of clinical development"[17].

c) Article 169 is now being used in other areas and lessons learned from EDCTP will be applied more widely.

2.5 In view of the limited evidence and evaluation of the implications of the model for political control and accountability I cannot support a recommendation for conditional acceptance of the EDCTP model, let alone an expansion of its remit - see Recommendation 1.0.

3.0 The first objective of EDCTP is "Networking and co-operation between the participating national programmes to increase their efficiency and impact and overcome the fragmentation of European research in this field. ***The most powerful means of networking research programmes is by the joint implementation of programmes or large parts of programmes.*** *This will contribute to realising the principles of the European Research Area in this field of research." While there is evidence of strong networking between research institutes of member states there is as yet no compelling evidence of joint implementation of programmes or large parts of research programmes.*

3.1 During the course of our enquiry we were unable to locate a comprehensive strategy for public health research on neglected and poverty related diseases in Africa. Neither DG Res nor DG Dev could provide us with a comprehensive strategic overview of EC activities in Africa and there was no evidence that EDCTP had sought to establish an overview of member states research activities and strategies in Africa. Without these it is not possible to see where EDCTP sits in the context of either member states or EU research strategy for neglected diseases and poverty alleviation in Africa - see Recommendations 2, 3, and 4.

4.0 The second objective of the EDCTP is the "Acceleration of the development of new products by supporting clinical trials in the Developing countries, thus promoting transfer of research into clinical practice thereby strengthening Europe's R & D excellence on the global market".

4.1 Effective drug development and transfer of research into clinical practice presupposes fully functioning health systems, drug distribution and delivery systems, and epidemiological surveillance systems which can be adapted, modified or added to in the event of effective and safe products becoming available. Commission officials have stressed that the driver for EDCTP is product development. EC staff and other interviewees including those from global health partnerships working on products suggested that health systems strengthening is not part of the EU programme but are the remit of WHO or are country level responsibilities within Africa. However, the distinction between product development and health systems is not sustainable in practice. Fragmented and weakened health care and drug distribution systems pave the way for counterfeit medication, fraud, loss of bioavailability, lack of access, misuse, poly-pharmacy and iatrogenic disease and make it impossible to distribute products to patients effectively and efficiently - see Recommendation 5.

[17] PE 357.813 of 22/06/2005, European Parliament Committee on Development.

(Dissenting opinion by Pr. A. Pollock, continued)

4.2 Under the 6th research framework programme, besides the EDCTP subsidy, another EUR 258 million had been earmarked for collaborative research[18] on HIV/AIDS, Malaria and Tuberculosis including clinical trials. There is weak evidence that EDCTP has sought to coordinate its activities with EC and member state funded programmes including those global public private partnerships which focus on product development - see Recommendation 6.

4.3 EDCTP remit is to contribute to a comprehensive policy on poverty related diseases in developing countries through product development. The majority report has found that EDCTP strategy with respect to product development is weak. This is a fundamental problem of EDCTP.

5.0 The transfer of research into clinical practice requires a wider public health perspective including the complex environmental, structural, material, cultural, behavioural and regulatory factors which may impede public access to products. We were unable to ascertain EC strategy for working with African partners with respect to:

- *population surveillance and epidemiological monitoring*
- *the capacity of government and non government procurement systems, drug distribution and drug delivery systems to deliver safe accessible affordable and effective products;*
- *public health needs within health systems and capacity of health systems to respond to needs*
- *manufacturing capacity*

5.1 Monitoring and surveillance:

Most countries in Africa have no capacity to monitor mortality and morbidity of the whole population and survey and sample estimates are used in their place. A product development plan should have regard to the capacity (skills and costs) required to evaluate and monitor the impact of products on population health in the short and long term.

We found no evidence of a strategy within EDCTP to address population surveillance in Africa, or of collaboration with In-Depth, a network dedicated to establishing surveillance in 22 countries - see Recommendation 7.

5.2 Accessible and affordable medicines:

Provision 209/2003/EC makes EDCTP funding conditional on the formulation of the provisions relating to intellectual property rights to ensure that the people of developing countries have easy and affordable access to the research results and to the products directly deriving from EDCTP results.

The basic principle is that the EDCTP will favour the transfer of IP-rights to ensure production and availability of affordable medicines to the people in need in developing countries, it is not known whether this is the case in practice. EDCTP has general guidance but states that a formal policy is difficult to define, given the various combinations of potential partners. Specific IP-rights issues are addressed on a project–by–project basis.

[18] See DG RTD publication "Combating deadly diseases", Project synopses 2007.

(Dissenting opinion by Pr. A. Pollock, continued)

IP is inseparable from the role of sponsorship since it is the sponsor who controls publication rights, patient data and IP. We found no evidence that the EDCTP had seriously addressed IP or sponsorship issues - see Recommendation 8.

6.0 The third objective of the EDCTP is "Strengthening clinical research capacities in the Developing countries in the fight against the three poverty-related diseases, in line with European development and co-operation objectives. This aim would also help establish a long term sustainable and genuine partnership between Europe and the Developing countries."

6.1 Capacity building was defined by some interviewees as infrastructure and training of personnel. Shortages of core skills were highlighted in statistics, data management, epidemiology and clinicians. Neither the EC nor the EDCTP has conducted a systematic, country by country, needs assessment of requirements for capacity building within and across Africa.

6.2 The absence of a comprehensive needs assessment of the requirements for capacity building in Africa countries poses threats for health systems. DFID and the World Bank have highlighted the ways in which aid can weaken already fragile public health systems by creating new inequities and redirecting resources away from other public health programmes. We heard evidence that trials for new vaccines had further weakened public health systems in some African countries often by taking key staff and personnel away from healthcare.

6.3 We heard accounts of clinical research/ trial sites in Africa which do not have funding when EDCTP funded trials come to an end. We also heard how the short term focus and short term funding of donor countries undermine the longer term strategic investments required for sustainable research infrastructure. All interviewees were concerned that EDCTP should not become a CRO for industry, and that African scientists and researchers must be enabled to pursue original research which is not limited to clinical trials or to clinical trials which are solely focused on product development. The EC needs to consider how to ensure capacity building is sustainable across all its funded programmes for Africa - see Recommendation 9.

ALTERNATIVE RECOMMENDATIONS TO THE EUROPEAN COMMISSION BY PR. A. POLLOCK

In relation to the future of EDCTP (Governance):

Recommendation 1: *Given the failure of the EDCTP to meet its objectives and the serious concerns about political control and accountability, the EU should work with member states to take urgent steps to remedy the deficit in public governance and accountability within the model. It could, for example, with the agreement of member states, incorporate EDCTP under direct administrative control of the EC.*

In relation to the broader international research agenda:

Recommendation 2: *The EC should work with governments in Africa to provide a coherent and comprehensive account of the public health research strategy for Africa. It should show how member state activities and funding and EC activities and funding for research into product development on the three diseases sits within the broader framework of public health research.*

Recommendation 3: *DG Research / DG Development/ DG Sanco and DG AidCo should conduct joint strategic reviews of all EC funded clinical and public health research in Africa to ensure overall coherence with the public health strategy.*

Recommendation 4: *The EC should give a comprehensive account of all EC funded research activities in Africa including global health partnerships, with respect to product development, health systems, drug delivery, drug procurement and distribution and population surveillance and show how they reflect the priorities of African governments.*

Recommendation 5*:The EU strategy should establish the conditions required for the supply of accessible and affordable essential medicines to African countries by undertaking, with the relevant governments, an audit of and research into manufacturing and production capacity, drug procurement systems, drug delivery and health systems in the target countries. The preparatory work for this should be undertaken by the EC and assist the FP7 midterm review for research priorities.*

Recommendation 6: *The EC, together with governments of African countries, should conduct a systematic review of all clinical trials developments and clinical capacity for all poverty related diseases with specific reference to Africa.*

Recommendation 7: *The EC should work with African countries to develop a strategy and funded implementation programme for country wide population surveillance and monitoring systems to look at the short and long term consequences of drug delivery programmes within a public health framework. This should be done before the FP7 mid- term review.*

Recommendation 8: *The EC should conduct a formal review of technology transfer, IP and drug supply agreements across all EC funded research. IP policy with respect to EC funded research should not be determined on a case by case basis. The EC should establish a formal policy with African countries in respect of IP that is consistent with its goal of providing accessible and affordable pharmaceutical products for Africa. This review should inform the mid term FP7 review of research.*

Recommendation 9*: The EC should work with the governments of all African countries to undertake a comprehensive needs assessment of the requirements for capacity building for clinical research and health systems, and which demonstrates the contribution of each of the EC Service Directorates to it.*

ANNEXES

TO THE IER / EDCTP REPORT

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ANNEX 1

SUMMARIES ON HIV/AIDS, TUBERCULOSIS AND MALARIA

Extracts taken from http://www.edctp.org/Home.162.0.html)

HIV/AIDS

AIDS is caused by the human immunodeficiency virus (HIV) transmitted through sexual intercourse, blood transfusion, and unsafe drug-injecting practice, and from mother to child during pregnancy, delivery or breastfeeding. There is no vaccine or cure yet for AIDS, but combined antiretroviral treatment helps.

The global number of people living with HIV/AIDS is estimated at 40 million, including 2.5 million children under 15 years. People newly infected with HIV in 2003 totalled 5 million, including 700.000 children. AIDS deaths in 2003 totalled 3 million (i.e. 8.200 people per day), including 500.000 children. Regional HIV/AIDS statistics show that sub-Saharan Africa accounts for 27 million adults and children living with HIV/AIDS with 3.2 million new infections in 2003, representing 70% of the global total; The HIV/AIDS epidemic continues to expand rapidly in many parts of the developing world, including in sub-Saharan Africa, with devastating demographic effects. The most urgently needed measures are those that will slow the spread of infection.

Progress with the development of HIV vaccines has been disappointing. While trials of candidate vaccines are of the highest priority, second generation new vaccines may become available for phase I/II testing in the next 5 years. Nonetheless, it will be important to develop capacities to conduct clinical trials, in anticipation of future candidate vaccines. More promising, on a shorter time scale, is the possibility that vaginally applied microbicides may protect women against HIV infection. The expertise necessary for the evaluation of vaccines and microbicides has substantial overlap and there are common capacity development needs.

In recent years, effective anti-retroviral therapies have been developed and applied in Developing Countries (DC's) that, while not curing the infection, have dramatically prolonged survival and lowered morbidity and mortality in those HIV-infected. Few infected individuals in DC's currently have access to these therapies, in large part because of their cost. The development and evaluation of simpler and cheaper regimens would greatly facilitate their deployment in DC's. In parallel with such expanded access, it will be important to monitor the emergence of resistance against these drugs.

At present there is only 1 clinical trial on a potential HIV vaccine funded by a National Programme (NP). However, new vaccine candidates are likely to come out of the pipeline soon. Regarding treatment of HIV, 14 clinical trials are currently taking place or planned. Eight European and 11 African nations are involved these projects (budget about 18,5 million euros). With respect to microbicides, 8 clinical trials are planned within the next 5 years, involving 2 NP's and 5 African nations (budget about 23 million euros).

In addition, 3 NP's and 7 African countries are involved in studies on the intervention against mother to child transmission. Some of the NP activities concerning HIV are joined efforts. Presently, 9 out of the 15 NP's are involved in HIV clinical trial related activities. There is a need for identification of synergies and the coordination of NP in this area.

The resources that are available for clinical trails on HIV in the NP in the coming 5 years may exceed 91 million euros. In the future, more data on the NP will be gathered and NP will be become increasingly aligned with EDCTP principles. Therefore, EDCTP predicts that the total HIV related budget available in the NP would change.

Further information can be found under: http://www.unaids.or
http://www.who.int/topics/hiv_infections/en/ http://www.theglobalfund.org/en/

Tuberculosis

Tuberculosis (TB) is a contagious, airborne infection. Infected people incur a 10% risk of developing active TB. If untreated, 50% of patients with active TB will die in a 5- year period. Weakening of the immune system, e.g. via HIV infection, increases the risk of developing active disease. Early detection and treatment of infectious cases is the primary control measure.

One third of the world's population is currently infected with TB bacilli. If control is not further strengthened it is estimated that, between 2002 and 2020, 1000 million people will be newly infected, over 150 million will get sick and 36 million will die of the disease. The global incidence rate of TB is growing annually at approximately 0.4%, but much faster in sub-Saharan Africa. Globally, 9% of all new TB cases in adults are attributable to HIV- infection, but in Africa the figure reaches 31%.

There are an estimated 8 million new TB cases in the world annually from which 2 million deaths occur every year. The largest burden of disease is in South East Asia and sub-Saharan Africa. In Africa the TB epidemic is fuelled by the HIV epidemic. 70% of the 14 million people co-infected with both pathogens in the world live in Africa.

To successfully control tuberculosis, effective medical and biomedical tools, and trained health staff should be available. Better drugs (shorter, more effective therapeutic regimens), better vaccines, and improved diagnostic tests for tuberculosis are required. There is a clear need for new scientific advances to address gaps in available interventions against tuberculosis.

Drugs that can rapidly kill latent (persistent) organisms, or vaccines that can prevent their activation in the presence of HIV, are greatly needed. Of all potential interventions, such an advance will have the greatest impact on tuberculosis control. Some European national programmes are already involved in funding of clinical trails evaluating vaccine candidates and drugs.

The treatment of tuberculosis is recognised as one of the five most cost-effective health interventions in the world today. But, the treatment period is long (6-8 months), and often results in patients interrupting their therapy schedule. Treatment schedules need to be shorter and simpler, if the problems of non-compliance and of ineffective service provision are to be overcome.

Co-infection with HIV leads to activation of latent infection and to an accompanying rapid escalation in the incidence of tuberculosis. Therefore, it is central to a tuberculosis control strategy to stop rapid progression of TB infection to disease and improve success rates in tuberculosis/HIV co-infected individuals who develop the disease. These patients often relapse after initial bacterial clearance. A new approach is needed to not only improve the initial clearance, but also reduce relapse rate after treatment. New anti-tuberculosis regimens are needed, in association with compatible anti-retroviral treatments. Clinical trials of tuberculosis drugs are time consuming, lasting up to 5 years on average. Therefore, there is a need for surrogate markers of drug efficacy to enable early decisions on the potential of new drug regimens.

The general aim of tuberculosis vaccine trials is to produce affordable and accessible vaccines. Research on the development of novel vaccination strategies has been intensified in many European research institutions in the recent past. These strategies comprise subunit vaccines, DNA vaccines and live attenuated vaccine strains. Several of these new candidates have entered pre-clinical testing and gave promising results in animal tuberculosis models. After further testing, some of these vaccine candidates have either entered or will enter phase I/II trials soon and phase III trials after 2006.

Further information can be found under: http://www.who.int/tdr/diseases/tb/default.htm

Malaria

Malaria is caused by a single-celled protozoan parasite of the genus Plasmodium. It is transmitted to humans via the bite of infected female mosquitoes, which have previously ingested parasites from another infected human individual. The parasite undergoes its reproductive phase inside the mosquito vector before being passed on to the next human victim. Upon infection the parasite multiplies initially in the liver cells; these infected liver cells then rupture to release multiple so-called merozoite cells into the blood stream, where the parasite then enters the red blood cells.

Malaria exists in 100 countries, with the disease being most prevalent in the poorer tropical areas of Africa, Asia and Latin America. Four Plasmodium species infect humans, the most lethal of which, Plasmodium Falciparum is the most prevalent in Africa.

The number of people infected with malaria is estimated to be more than 1 billion worldwide, with around 500 million clinical cases every year and an annual death toll due to malaria exceeding 1 million deaths. Around 90% of all mortalities occur in Africa, mostly affecting young children and pregnant women. Malaria is Africa's leading cause of under-five mortality (20%) and constitutes 10% of the continent's overall disease burden. It accounts for 40% of public health expenditure, 30-50% of inpatient admissions, and up to 50% of outpatient visits in areas with high malaria transmission. Economic losses in Africa due to malaria are estimated to be more than € 10 billion annually.

Treatment and control have become more difficult with the spread of drug-resistant strains of parasites and insecticide-resistant strains of mosquito vectors. Insecticide-impregnated bed nets are very efficient in reducing the exposure to mosquitoes. The choice of drugs depends on the resistance pattern in the area. The parasite becomes more and more resistant to classical drugs like Chloroquine or Sulfadoxin-pyrimethamine. To avoid resistance, use of combination drugs appears to be more efficient and has therefore been recommended by WHO as first-line treatment strategy. Preventive measures would be most efficient and cost-effective, and thus the search for a vaccine continues. Although it is difficult to predict when such a vaccine will become available, considerable progress has been made in research over the past decade and a number of candidate vaccines are currently in clinical trials.

The number of effective and affordable drugs available to treat malaria is still limited. Furthermore, the emergence and spread of drug-resistant parasites and insecticide-resistant mosquitoes have rendered inadequate some of the traditional mainstays of malaria control. Despite these obvious constraints to the development of new interventions against malaria, significant improvement has been achieved with the increasing availability of Chinese products belonging to the artemisinin family. This has led to the identification of new and effective anti malarial combination regimens. However, most of these compounds are not widely available because they do not conform to international standards of production and development. These developments should be completed as a priority.

We are now witnessing a renewed interest in anti malarial drug and vaccine discovery and development. The pipeline of new products that may be undergoing clinical development is richer now than ever before. There are a few MVI phase II trials ongoing for a malaria vaccine. In 2008, the first malaria vaccine will undergo large-scale phase III trials, with a huge potential impact on public health, in particular, pediatric mortality. Increasing attention is being given to the availability of adequate trial sites in Developing Countries and to the training of staff to conduct GCP trials. The levels of malaria control that are needed may not be achieved with the use of single interventions. In this context, evaluation of combined strategies will help inform policy of the most cost effective package of interventions for malaria control in a given epidemiological setting.

Further information can be found under: http://www.mim.su.se/
http://www.who.int/tdr/diseases/malaria/default.htm http://malariavaccine.org

ANNEX 2

PRODUCT DEVELOPMENT AND PUBLIC HEALTH INTERVENTIONS

Source: contribution from Pr. Adetokunbo O. Lucas

The Millennium Development Goals (MDG's) identified specific targets for the control of malaria, tuberculosis and HIV/AIDS. These diseases persist, partly because of the lack of effective technologies for their control and also because of the weakness of the health services and other factors associated with poverty. A combined strategy is required to achieve the MDG's in relation to these three diseases:

- Technological innovations to provide more effective tools for the control of these diseases; and
- Strengthening of the health systems to ensure equitable access to chemotherapy and other interventions.

It would be useful to learn lessons from recent experience in tackling other diseases in poor developing countries. A combined approach including product development as well as strengthening of the health service delivery systems, has proved highly successful in some programmes:

Leprosy

For many decades, the control of leprosy was based on the use of single therapy with dapsone, a drug that was introduced around 1947. A major challenge was the increasing resistance of the leprosy bacillus to dapsone – up to 30% of newly diagnosed cases. In spite of an annual spending of US$30 million by various international charitable organizations dedicated to leprosy control, the prevalence of the disease remained static for several decades through to the mid 1980's. At an estimated cost of US$ 14 million over a nine-year period, the World Health Organization (WHO) through its Tropical Diseases Programme (TDR) sponsored research that led to the development of multiple drug therapy (MDT). A global programme for the elimination of leprosy, based on MDT, aimed to reduce the prevalence of active disease below 1 per 10,000 in every country. By the target date of 2005, most endemic countries, including African countries, had reached this goal and the remaining problem areas are being tackled with a real expectation of eliminating leprosy within the foreseeable future.

Onchocerciasis

Onchocerciasis, the infection that causes river blindness, was highly endemic in parts of West Africa and Latin America. The Onchocerciasis Control Programme in West Africa was initially based on vector control of entire river basins, starting first with the Volta river and later extending to the Sene-Gambia basin. Major transmission areas in Nigeria and elsewhere were not included in this programme. WHO/TDR in collaboration with Merck Inc. developed a new drug, ivermectin for the treatment of onchocerciasis. The African Programme for Onchocerciasis Control (APOC) distributes the drug, given orally once a year, through a newly devised mechanism: *"The Community-Directed Treatment with Ivermectin (CDTI) is the delivery strategy of APOC. It empowers local communities to fight river blindness in their own villages, relieving suffering and slowing transmission. After just 8 years of operations, APOC has established 107 projects, which in 2003 treated 34 million people in 16 countries."*[19] *Merck Inc. donates the drug in a programme that supplied over 60 million doses in 2006.*

[19] http://www.who.int/blindness/partnerships/APOC/en/

Trachoma

The current global strategy for the elimination of trachoma, the commonest cause of preventable blindness, is based on four interventions: Surgery for chronic cases, Antibiotics for current infections, Face washing and Environmental sanitation to reduce fly breeding. This so-called SAFE strategy was developed on the basis of laboratory work, clinical trials and field research that showed the best methods for applying the individual components. Instead of using local application of tetracycline ointment daily for 6 weeks, the programme uses azithromycin, an oral drug in a one-day treatment; the Pfizer drug company donates the drug for use in this programme. Early results from the affected countries is showing encouraging results

These and other cases e.g. the progressive elimination of Chagas' disease from endemic areas in South America, show the value of a combined approach of research involving product development complemented by health services research as well as innovations aimed at ensuring equitable access to the new products and effective delivery of services.

ANNEX 3

INDICATIVE LIST OF EDCTP PROJECTS

Extracts from http://www.edctp.org/Home.162.0.html)

Capacity Building

PABIN: "Establishing an African Coordinating Office for Ethics"
AMANET: “Creating web-based research training courses in biomedical research ethics for Africans”
University of Stellebosh, S. Africa: “Enhancing Research Ethics Capacity and Compliance in Africa”
Medical Research Council, Zimbabwe: “Building National Capacities in Health Research Ethics.”
Cardiff University, UK: “Developing a distance learning research ethics course for East Africa”
University of Neuchâtel, CH: “Training and Resources in Research Ethics Evaluation for Africa”
University of Malawi: “Building Capacities in ethical Review and Clinical Trial Monitoring».
Nigerian Institute of Medical Research: “Capacity Strengthening of Nigerian Researches and Ethics."
Vienna School of Clinical Research: "Training on Ethical Aspects of Clinical Research for members of African National Ethics Committees and for African physicians/investigators"
Paulina Tindana, Navrogo Health Research Centre, Ghana: “A proposal for Strengthening Capacity of Six Research Ethics Committee in Ghana”
Medical Research Council, Zimbabwe: “Strengthening the Medical Research Council in Zimbabwe”
Makarere University, Uganda: “Supporting research through enhancement of the IRB processes.”
University of Malawi: “Proposal to strengthen the College of Medicine Ethics Committee."
University of Ibadan, Nigeria: “Strengthening the Capacity of Researches Ethics Committees.”

Networking Grants

Jenny Hill, Liverpool School of Tropical Medicine: “A North-South working group to support the design integrated research proposals for malaria in pregnancy”
Marleen Temmerman, Ghent University: “Strengthening laboratory capacity and nutrition skills in the context of an ICH GPC clinical trial for the prevention of mother-to-child transmission of HIV”
Margarita Navia from Recerca Biomèdica, Spain: “Ifakara_Lambarene_Manhiça Partnership”
Robert Colebunders, The Institute of Tropical Medicine, Antwerp, Belgium: Workshop on Tuberculosis Immune Reactivation Inflammatory Syndrome (TB IRIS)
Andrew Hall from London School of Hygiene and Tropical Medicine, UK: “Masters courses in clinical trials for sub-Saharan Africa”
Abraham Aseffa from Armauer Hansen Research Institute (AHRI), Ethiopia: “Strengthening the National Tuberculosis Research Network in Ethiopia”
Amina Jindani from International Consortium for trials of chemotherapeutic agents in tuberculosis (INTERTB), UK: “A proposal to establish a network of sites, in sub-Saharan Africa, to conduct clinical trials in tuberculosis and to build their capacity to participate in multi-centre trials”
Sheena McCormack from Medical Research Council, UK: “Identifying the common learning needs of investigators working in poverty-related diseases in African settings.”
Daniel Kyabayinza from Regional Center For Quality of Health Care (RCQHC), Uganda: “KIDS-ART-LINC: network of clinical centers treating HIV-infected children with antiretroviral therapy."

Training Awards

Louis Marie Yindom (Gambia): “The role of human leukocyte antigen (HLA) and killer immunoglobutin – like receptor (KIR) in HIV-2 infection: a key component to HIV vaccine design.”
Getnet Yimer Ali, Ethiopia: “Anti tuberculosis – anti retroviral drugs induced hepatotoxicity and introduction of these drugs at the level of CYP 450 metabolism”
Leah Mwai, Kenya: “Understanding the mechanism of resistance to lumefantrine by Plasmodium falciparum”
Charles Arama, Mali: “Host immunogenetic factors involved in the susceptibility to malaria in sympatric ethnic groups (Dogon and Fulani) in Mali”
Ramatouli Janha, Gambia: “investigating the effects of inactive CYP2C19 alleles on chlorproguanil pharmacokinetics in adults and in children with mild malaria following Lapdap® treatment”

Mthiyane Thuli, South Africa: “Reconstruction of TB antigen specific IFN-y responses in TB-HIV co-infected participants”
Bornwell Sikateyo, Zambia: “An assessment of the understanding of the informed consent process by participants in microbicide intervention trials in Zambia”.
Sunny Oyakhirome, Gabon: “MSc in Public Health”
Alasan Jobe, Gambia: “MSc in reproductive and sexual health research”
Else Carole Eboumbou Moukoko, Camerron: "Identification of Plasmodium falciparum parasite virulence markers for the evaluation of the impact of malaria control intervention."
Dr Antony Kebba, Uganda: “Patterns of HIV-1 specific CD8+ T cell epitope recognition determining plasma viral load trajectory and set point following HIV-1 infection”
Dr Molebogeng Xheedha Rangaka, South Africa: “Immunological investigation of the HIV-tuberculosis associated immune reconstitution inflammatory syndrome”
Issa Nebie, Burkina Faso: "Understanding the mechanisms underlying the difference in susceptibility to malaria in an area of hyperendemic malaria in Burkina Faso."
Didier Koumavi Ekouevi, Cote d'Ivoire: Preventing per-partum transmission of HIV-1 in Africa: tenofovir based alternatives in the light of future treatment options
Abdoulaye Djimde, Mali: "Assessment of the Public Health Benefit of artemisine based combination therapies for uncomplicated malaria treatment in Mali"
Alexis Nzila, Kenya: "Understaning the mechanism of piperaquine resistance"
Abraham Alabi, Gambia: "Development and evaluation of high throughput, cheap and reliable assays for monitoring HIV-1 and HIV-2 viral loads in ARV programmes and clinical trials in DCs"
Maowia Mukhtar, Sudan: "The burden of tuberculosis in eastern Sudan: epidemiology and drug resistance patterns of Mycobacterium tuberculosis isolates"
Willem Hanekom, South Africa: "BCG-induced immune correlates of protection against tuberculosis"
Dr David Nwakanma, The Gambia: “Evaluation and implementation of high throughput PCR-based method for diagnosis and measurement of Plasmodium falciparum parasitaemia in clinical trials”

Clinical Trials

Jimmy Volmink, South African Cochrane Centre: “Proposed HIV/AIDS, Tuberculosis and Malaria Clinical Trials Registry in Sub-Saharan Africa”
Paul van Helden, South Africa: "Surrogate markers to predict the outcome of anti-tuberculosis therapy"
Conceptta Merry, Ireland: “Determining the optimal doses of antiretroviral and antituberculous medications when used in combination for the treatment of HIV/TB in co-infected patients”
Stephen Gillespie, United Kingdom: "Rapid Evaluation of Moxifloxacin in the treatment of sputum smear positive tuberculosis: REMoxTB"
Amina Jindani, United Kingdom: "A controlled clinical trial to evaluate high dose rifapentine and moxifloxacin in the treatment of pulmonary tuberculosis"
Peter G. Kremsner, Germany: “Artesunate for severe malaria in African children”
Umberto d'Alessandro, Belgium: "Evaluation of 4 artemisinin-based combinations for trating uncomplicated malaria in African children"
Chifumbe Chintu, Zambia: CHAPAS Trials: Children with HIV in Africa: Pharmacokinetics and Adherence of Simple Antiretroviral Regiments"

ANNEX 4

ETHICS AND INTELLECTUAL PROPERTY RIGHTS ISSUES

Source: compilation by Fernand Sauer

Ethical aspects in clinical trials conducted in Developing Countries

Clinical trials that breach ethical guidelines in the developed world should not be permitted in developing countries. The EU, US and Japan, in the framework of the International Conference on Pharmaceutical Harmonisation (ICH) and in collaboration with WHO, adopted in 1995 a major guideline on good clinical practices which incorporates the CIOMS Helsinki Declaration on Ethics (informed consent, ethics review committees, etc…). All trials in Europe must conform to these rules. Unethical trials conducted elsewhere are not accepted in a submission for marketing approval of a medicinal product in the EU (Directive2001/20/EC).

The European Group of Ethics (EGE), an independent body which advises the European Commission on ethical aspects of science and technology published on 4th February 2003 an opinion[20] based on the assertion that "the fundamental ethical rules applied to clinical trials in industrialised countries are to be applicable everywhere".

This publication covers cultural relativism, informed consent, the role of ethics review committees, building research capacity, standards of care for patients in trials, placebo control trials, patent issues, and the role of traditional medicine.

Many issues in the developing world arise from problems that rarely occur in the West. How does one obtain informed consent from people who cannot read and write? Who oversees the trials in areas where ethical review committees are unknown?

Africa's own clinical research capacity remains limited. International solidarity must ensure that the developing world shares the benefits of medical research. The European Union should provide leadership to guarantee Africans "the power to enjoy the basic right to health".

Strict compliance with ethics is clearly very important for the protection patients and healthy volunteers and for the reputation of EDCTP and the EU as a whole. All clinical trials require previous ethics clearance through a national ethical board and projects that do not satisfy for ethical reasons are rejected. All clinical trial projects are registered with the South African Cochrane Centre (ATM Clinical Trials Registry). EDCTP also supports various ethical committees in Africa.

However, EDCTP's guideline on ethics is a list of reference documents and the policy should be spelled out in more details, taking into account the results of the international conference on “Ethics, research and Globalisation”, organised by the Commission in Brussels on 14 and 15 may 2007.

Furthermore, a summary of how ethical judgements were carried out on specific EDCTP projects ethical should be prepared by sponsors and made available on the Website, for scrutiny.

[20] *Opinion no. 17, Ethical aspects of clinical research in developing countries (ISBN 92 894 5373 7).*

Intellectual Property Rights at EDCTP

The rules regarding the protection dissemination and use of knowledge were re-defined in 2002 for the 6th Framework Programme. They are summarised below in combination with extracts from a short guideline taken from the EDCTP Website.

Decision 1209/2003/EC of the EDCTP makes funding conditional on the " formulation of provisions relating to intellectual property rights in such a way that they also aim at ensuring that the people of developing countries have easy and affordable access to the research results produced by activities under the EDCTP Programme and to the products directly deriving from its results." Participants own the intellectual property of the knowledge resulting from the project. The EDCTP, while accepting the need for strong IP-rights protection in developed countries, will not seek in general IP-rights protection in developing countries. Each party to an EDCTP project remains the owner of its pre-existing know-how, but shall make it available as needed for carrying out the project.

Where appropriate, the owner of knowledge will provide adequate and effective protection for knowledge capable of industrial or commercial application. Participants may publish information on the knowledge acquired under the project, provided this does not affect the protection of that knowledge.

Knowledge shall be disseminated by the participants within a reasonable period. Every grantee will need to establish a dissemination plan with timelines. The EDCTP will ensure that the results of the research will, wherever possible, be in the medical and scientific literature. The EDCTP will, by contract, always retain the right to publish research results in case a grantee does not publish all the results. The role played by local scientists will be properly and fully acknowledged through authorship of publications.

The provisions relating to access rights are the same for all participants. Access rights to knowledge shall be granted on a royalty-free basis, unless other conditions were agreed upon.

The basic principle is that the EDCTP will favour the transfer of IP-rights to ensure production and availability of affordable medicines to the people in need in developing countries. The EDCTP will agree on these issues with the grantees but in certain circumstances retain the right to handle IP-rights issues. When collaborating with the EDCTP, industry will probably accept preferential pricing but not concede all IP rights.

The EDCTP states that a general policy is difficult to define given the various combinations of potential partners and that specific IP-rights issues should be addressed on a project–by–project basis.

The EDCTP Website announces a future policy to address tiered pricing agreements, including provisions on the time schedule, availability and easy access to affordable new medicines; and the dissemination of knowledge in order to inform policy decisions.

On 2 April 2007, the Health Directorate of DG Sanco organised with WHO Europe an important seminar on Public Health, Innovation and Intellectual Property, with the participation of the EDCTP. The discussions held during this seminar[21] could help the EDCTP to formulate its future policy. Also relevant are the DNDi's (Drugs for Neglected Diseases Initiative) Intellectual Property Policy document published in December 2004 and the report produced on the subject by a special WHO commission in 2006. The best practises as discussed by WHO will serve as examples in making interventions readily available at an affordable price to people in developing countries, in accordance with the policy on tiered product pricing under Regulation EC/ 953/2003.

[21] See presentations under http://ec.europa.eu/health/ph_international/int_organisations/who_en.htm

ANNEX 5

AFRICAN STUDY CENTERS AND KEY PARTNERS

Source: indicative list communicated by Jean Stéphenne

Country	Institution	Disease Interest	Key partners
Angola			
Benin	Regional Center for Entomological Researches of Cotonou	Malaria	AMANET
Botswana	The Botswana-Harvard AIDS institute partnership for HIV research	HIV	Harvard University
Burkina Faso	Centre National de Recherche et de Formation sur le Paludisme (CNRFP)	Malaria	
	Muraz Centre, Bobo-Diouolasso	Malaria	Institut de Médecine Tropicale, Antwerpen
	Muraz Centre, Nanoro	Malaria	Institut de Médecine Tropicale, Antwerpen, Brescia University
	The Nouna Health Research Centre	Malaria	
Burundi			
Cameroun	Organisation de Coordination pour la Lutte contre les Endémies en Afrique Centrale (OCEAC)		
Cape Verde			
Central African Republic			
Chad			
Comoros			
Congo, Republic of			
Congo, Democratic Republic of The	Kalembelembe Pediatric Hospital / BOMOI Health Center, Kinshasa	HIV	University North Carolina
Cote d'Ivoire	Pierre Richet Institute	Malaria	AMANET
Djibouti			
Equatorial Guinea			
Eritrea			
Ethiopia	Jimma Institute of Health Sciences	Malaria	AMANET
Gabon	Albert Schweitzer Hospital (HAS), Lambarene, Gabon	Malaria	University Tubingen, Germany
	Centre International de Recherches Médicales de Franceville	Malaria	AMANET
The Gambia	Medical Research Council Laboratories (MRC),	Malaria, Pneumococcus, Hib, HIV	Medical Research Council (UK), INDEPTH
Ghana	Kumasi Centre for Collaborative Research (KCCR), Agogo, Ghana	Malaria	Bernhard Nocht Institute
	Navrongo Health Research Centre (NHRC)	Malaria	INDEPTH London School of Hygiene and Tropical Medicine
	Kintampo Health Research Centre (NHRC),	Malaria	INDEPTH London School of Hygiene and Tropical Medicine
	Noguchi Memorial Institute for Medical Research	Malaria	
	Northern Region Malaria Project (NORMAP), Bulpeila Tamale, Ghana	Malaria	Institute Tropical Medicine Berlin
Guinea			
Guinea-Bissau	Bandim Health Project		Staten Serum Institute,

			Denmark
Kenya	Kenya Medical Research Institute, Kilifi	Malaria	Wellcome Trust, UK
	Kenya Medical Research Institute, Kisumu	Malaria	Walter Reed USA
	Kenya Medical Research Institute,	HIV	Centers for Disease Control, USA
	Kenya AIDS Vaccine Initiative (KAVI),	HIV	IAVI, Oxford & Nairobi University
Lesotho			
Liberia			
Madagascar			
Malawi	Kamuzu Central Hospital (KCH), Lilongwe,		University of North Carolina
	University of Malawi & Wellcome Trust, Blantyre	Malaria	Wellcome Trust UK Liverpool School of Tropical Medicine
	Centers for Disease Control, Blantyre		Centers for Disease Control, USA
	Blantyre Malaria Project / Ndirande Research Clinic		College of Medicine Center for Vaccine Development, School of Medicine, University of Maryland / Michigan State University College of Osteopathic Medicine
Mali	University of Bamako		AMANET, EMVI, College f Medicine Center for Vaccine Development, School of Medicine, University of Maryland
Mauritania			
Mauritius			
Morocco			
Mozambique	Centro de Investigacao em Saude de Manhica, Mozambique Centre Instituto Nacioanl de Saude	Malaria, Hib, Pneumococcus,	Hospital Clinic of Barcelona
Namibia			
Niger	Research Center for Meningitis and Schistosomiasis (CERMES)		AMANET
Nigeria	Cellular Parasitology Programme, Department of Zoology, University of Ibadan University of Enugu		
	University of Ibadan		
Rwanda			
Sao Tome and Principe			
Senegal	Institut de Recherche pour le Développement (IRD), Niakhar, Senegal		Institut Français de Recherche Scientifique pour le Développement en Coopération – Centre
	Institut Pasteur de Dakar		
Seychelles			
Sierra Leone			
Somalia			
South Africa	National Malaria Research Programme: Medical Research Council (South Africa)		
Sudan	The Blue Nile Research and Training Institute (BNRTI)		AMANET

	Faculty of Medicine, University of Khartoum		AMANET
Swaziland			
Tanzania	Ifakara Health Research Development Centre (IHRDC),		Swiss Tropical Institute
	Joint Malaria Project (JMP),		University Copenhagen, London School of Hygiene and Tropical Medicine
	Amani Medical Research Centre		AMANET
Togo	National Malaria Control Programme (Ministry of Health – Togo)		AMANET
Uganda	Med Biotech Laboratories		Nsambya & Apac hospitals
	UVRI		IAVI/Wellcome Trust/MRC
	Makerere University	Malaria, HIV, Telemedicine	University of California, San Francisco, John Hopkins' University, IDRC
	Infectious Disease Institute	HIV	Academic Alliance, Pfizer
	Mulago hospital	HIV, malaria, TB	Makerere University, Case Western Reserve
	Joint Clinical Research Center	HIV	UVRI, Makerere medical School
	Mbarara University	Malaria, HIV	Lund University in Sweden, University of California, San Francisco,
Zambia	Tropical Diseases Research Centre (TDRC), Mpongwe Ndola, Zambia		AMANET
Zimbabwe	Blair Research Institute (BRI)		AMANET

ANNEX 6

MAJOR DONORS

Source: Indicative list provided by Jean Stéphenne

Major donors to HIV/AIDS PDPs

IAVI:

Government
Basque Autonomous Government, Canada (Canadian International Development Agency)
European Union, Ireland (Irish Aid), Netherlands (Ministry of Foreign Affairs), Norway (Ministry of Foreign Affairs), Denmark (Ministry of Foreign Affairs), Sweden (Swedish International Development Agency *and* Ministry of Foreign Affairs), United Kingdom (Department for International Development), United States (U.S. Agency for International Development)
Corporations
Becton, Dickinson and Company, Continental Airlines, Google Inc.,Henry Schein, Inc.
Merck & Co., Inc. , Pfizer Inc
Foundations
Alfred P. Sloan Foundation, Armin & Esther Hirsch Foundation, Avrum Katz Foundation
Bill & Melinda Gates Foundation, Broadway Cares/Equity Fights AIDS, The Cynthia and George Mitchell Foundation, The Glickenhaus FoundationThe Haas Trusts, The Hale Foundation
The John D. Evans Foundation, Louis and Anne Abrons Foundation, The New York Community Trust, Nora Ephron and Nicholas Pileggi Foundation, James B. Pendleton Charitable Trust, The Rockefeller Foundation, The Starr Foundation, Until There's a Cure Foundation, The William and Flora Hewlett Foundation

International Partnership for Microbicides:

Government
Belgium (Belgian Development Cooperation), Canada (Canadian International Development Agency), Denmark (Ministry of Foreign Affairs), European Commission, France (Ministry of Foreign Affairs), Germany (Federal Ministry for Economic Cooperation and Development)
Ireland (Irish Aid), Netherlands (Ministry of Foreign Affairs), Norway (Royal Ministry of Foreign Affairs), Sweden (Ministry for Foreign Affairs & Department for Research Cooperation)
United Kingdom (Department for International Development), United States (United States Agency for International Development), The World Bank
Foundations
Bill & Melinda Gates Foundation, The Rockefeller Foundation

Major donors to tuberculosis PDPs

TB Alliance:

Government Ireland (Irish Aid), Netherlands (Ministry of Foreign Affairs), United Kingdom (Department for International Development), United States (U.S. Agency for International Development)
Foundations
Bill & Melinda Gates Foundation, The Rockefeller Foundation

Aeras TB vaccine Foundation:

Government
United States (Centers for Disease Control), Netherlands (Ministry of Foreign Affairs)
Denmark (Danish International Development Agency)
Foundations
Bill & Melinda Gates Foundation

Major donors to malaria PDPs

Medicines for Malaria Venture

Government

Ireland (Irish Aid), Netherlands (Minister for Development Cooperation), Switzerland (Swiss Agency for Development and Cooperation), United Kingdom (Department for International Development), United States (U.S. Agency for International Development), World Bank

World Health Organization (Global Malaria Programme & Special Programme for Research and Training in Tropical Diseases)

Corporations

ExxonMobil, International Federation of Pharmaceutical Manufacturers & Associations

Foundations

Bill and Melinda Gates Foundation, Rockefeller Foundation, Wellcome Trust

Malaria Vaccine Initiative

Governments

United States (U.S. Agency for International Development)

Foundations

Bill and Melinda Gates Foundation

ANNEX 7

TERMS OF REFERENCE

Independent External Review of the European and Developing Countries Clinical Trials Partnership (EDCTP Programme)

Purpose and Scope of the independent external review of the EDCTP Programme

The European and Developing Countries Clinical Trials Partnership (EDCTP) has been set up with the purpose to create a **new genuine partnership with Africa, with industry, between Member States and between African countries**.
The EDCTP is a partnership between 14 EU countries, Switzerland and Norway on one hand, and African countries on the other. It aims to join relevant European national research programmes and their African partners to develop new clinical tools against AIDS, malaria and tuberculosis.
EDCTP should concentrate on the real needs of Developing Countries, who are involved in setting the priorities and establishing a strategy of the EDCTP research agenda. At the same time, EDCTP should reduce the compartmentalisation of research in Europe by bringing greater coherence and coordination of national research activities. Its mandate is to promote a long-term structuring effect between European and Developing Countries' research policy and to help to integrate different policies in a coherent context.
The legal, operational and financial structure of the EDCTP is provided by the European Economic Interest Group (EEIG) through its two organs, namely the EEIG Assembly and the Secretariat. The EEIG Assembly is the final decision-making authority in which all participating European states are represented. The Secretariat, headed by the Executive Director, is responsible for the day-to-day running of EDCTP. The EEIG Assembly is assisted by the Partnership structure, which is the strategic planning arm comprising the scientific and regional expertise necessary for steering the EDCTP programme
Constituents of the Partnership include the Partnership Board (PB), the European Network of National Programmes (ENNP) and the Developing Countries Co-ordinating Committee (DCCC). The EDCTP was officially launched on 15 September 2003 for a duration of 5 years with funding provided through a contract under the EU's 6th Framework Programme for Research and Technological Development (FP6).

In July 2006 a **no-cost extension** of 2 years, with a number of conditions in connection, was accorded to accommodate for the long duration of clinical trials projects that otherwise would exceed the duration of the EDCTP programme.
The Health theme under FP7 (2007-2013) will contribute to international efforts addressing global health problems, including possibly EDCTP, depending on EDCTP's achievements and future needs.
In this context and with a view to maximising the chances of maximising results in the future, the European Commission is launching an independent external review (ER) of the EDCTP. The ER's objective is to make recommendations on how to enhance this unique initiative, looking forward to the next 5 to 10 years.
Enhancing the EDCTP involves integrating Member States' national programmes and supporting more and more quickly clinical trial and capacity building activities through a stronger partnership with Africa.

The ER will:

1) Assess, with a focus on improving future operations and results, the EDCTP Programme performance:
    - as integration of National Programmes in the spirit of art.169 of the EU Treaty
    - as operational structure (Clinical Trial, Capacity building and Networking activities)
    - as a partnership with African Countries

2) Recommend actions for improving the performance of the EDCTP programme and its outputs; in this context, the role of the European Commission should also be addressed

3) Address the role of EDCTP in the broader international research and development agenda, taking into account the nature and values of the Programme and its comparative advantages

4) Suggest alternative or complementary approaches for the EU to finance research on infectious diseases in Africa

5) On the basis of this assessment, draw possible lessons to be learnt and recommendations for future initiatives on the basis of art.169.

Some suggestions are given for some key questions relating to each of these main issues (points 1-5 above). Any other question that the External Review Committee feels necessary to address for accomplishing the task can be added.

Committee Membership

The ER will be conducted by a multidisciplinary team of personalities appointed by the European Commission. The External Review Committee (ER Committee) will be composed of a maximum of 5 experts: 1 from Africa, 3 from Europe (from politics, from industry, from science) + 1 Rapporteur.
The ER Committee will have a Chairperson and one Rapporteur (elected by the other members)
The overall committee will have a broad perspective of tropical disease research and capacity building. Collectively, the members will have expertise that focuses on:

- Understanding of the European Research Community
- Knowledge of the financial mechanisms for funding research at EU level
- Technical experience of clinical trials and capacity building in Africa
- Knowledge of conducting research in resource-poor settings

Rapporteur

The duties of the Rapporteur will be the following:

− To organize meetings of the ER Committee
− To follow-up and provide the documentation that the committee requests
− To communicate with committee members
− To carry out selected interviews on behalf of the Committee
− To carry out reviews of documentation and data analysis as requested by the Committee
− To write-up and edit the final report

Obligations of the External Review Committee

The obligations of the ER Committee will be:

− To inform the EC of all relevant information sources utilised for accomplishing the task
− To treat documents in a confidential manner
− Not to publish review results or outputs without permission from the EC
− To return (or destroy as appropriate) all documents used in the ER
− To report in a timely manner any possible conflicts of interest
− To produce reports as outlined below

Methodology

The methodology for the ER could include, but not necessarily be limited to:

1. Desk review of documents, reports of EDCTP
2. Interviews with the staff of the Secretariat
3. Interviews with the EC services
4. Interviews, mostly by telephone, video conference, and questionnaire with, and desk review of feedback from:
   - EEIG General Assembly Members,
   - High Representative,
   - Partnership Board members,
   - DCCC members,
   - ENNP members,
   - Current and potential future contributors, as well as other relevant scientists, actors and stakeholders in the fields of research.
5. Any additional sources of information or procedure to obtain views and feedback on the performance, role, and set-up of EDCTP that the Committee feels to be necessary to accomplish the tasks set forth in these terms of reference.

The ER Committee has the right, if it feels it necessary, to conduct visits in Europe and Africa. The ER Committee could, if it feels it necessary, invite stakeholders to Brussels for interviews. The final report of the findings and recommendations of the ER Committee will be written in English.

Indicative Work plan

Duration

The ER will be carried out between 25 December 2006 and 30 June 2007.
The ER Committee work will be of 22 working days with the following time allocation:

- 1 day briefing in Brussels
- 20 working days (with 5 meetings planned)
- 1 day for a final meeting in Brussels with EC Services & EDCTP

For the Rapporteur 47 days of works are foreseen.

Initial Meeting: Brussels

Scope: Objectives of the External Review
Briefing of the ER Committee with relevant services in EC Headquarters (DG RTD F3)

Final Meeting: Brussels

Scope: Presentation and discussion of the initial findings of the review (the draft to be circulated previously).
ER Committee, EC services (DG-RTD), & EDCTP constituencies (Chair of GA and vice chairs, ED, HR, Chair of PB, Chair of DCCC, Chair of ENNP)
The Final report, submitted to the EC, will take into account the relevant recommendations and as appropriate, issues raised in the final meeting.

Budget

The total Budget foreseen for the ER is **176.669 €**.

Important note:
It should be taken into consideration that one Secretary from DG-RTD services could be detached from normal duties in order to support the Committee for five months on a part time base.

ANNEX 8

LIST OF PUBLIC DOCUMENTS MADE AVAILABLE TO THE IER PANEL

List compiled by Ana-Rita Figueira, DG Research, European Commission

EU Institutions		
Programme for Action: Accelerated action on HIV/AIDS, malaria and TB in the context of poverty reduction – COM(2001) 96	Commission	21 Feb. 2001
Health and Poverty Reduction in Developing Countries – COM(2002) 129	Commission	22 Mar. 2002
EDCTP Concept document – EDCTP Steering committee meeting	EU/EDCTP Steering committee	20 June 2002
Proposal for a decision of the EP and Council – COM(2002) 474	Commission	10 Sept. 2002
Ethics conference 2002: 'The ethical aspects of biomedical research in developing countries'	European Group on Ethics (EC)	1 Oct. 2002
Ethical aspects in Clinical Research in Developing Countries – Opinion n° 17	European Group on Ethics (EC)	4 Feb. 2003
Decision No 1209/2003/EC of the E. Parliament and the Council	OJCE N° L 169/1 of 8.7.2003	16 June 2003
"North-South Partnership for Health Systems Research: 20yrs of experience of EC support" – report to the European Commission	Commission	2004
EC portfolio for Health, AIDS and Population (HAP) in develop. cooperation (Fact Sheet on Human and Social Development)	Commission	May 2004
A Coherent European Policy Framework for External Action to Confront HIV/AIDS, Malaria and Tuberculosis – COM(2004)726	Commission	26 Oct. 2004
European Court of Auditors report PF-1828 (6046)	European Court of Auditors	6 July 2005
A European Programme for Action to Confront HIV/AIDS, Malaria and TB through External Action (2007-2011) – COM(2005)179	Commission	27 Apr. 2005
A European programme for action to confront HIV/AIDS, malaria and tuberculosis through external action (2007-2011) – 9278/05	EU Council	24 May 2005
The EU and Africa: Towards a strategic partnership	EU Council	11 Dec. 2006
Report on major and neglected diseases in developing countries A6-0215/2005	EU Parliament	22 June 2005
The EU programme for action targeting HIV/AIDS, Tuberculosis and Malaria (Fact Sheet 13 on Human and Social Development)	Commission	Dec. 2005
The EU programme for action targeting HIV/AIDS, Tuberculosis and Malaria (Fact Sheet 13 on Human & Social Development)	Commission	Dec. 2005
Budget Line for Poverty-Related Diseases (Fact Sheets on Human and Social Development: No 16)	Commission	Dec. 2005
Programming Guidelines for Country Strategy Papers Health AIDS and Population (HAP)	Commission	
Letter from the Commissioner J. Potočnik on no-cost extension	Commission	2006
EUROPAID Annual Report	Commission	2006
Guidelines on Proposal Evaluation and Selection Procedures	Commission	
Terms of Reference for EDCTP Independent External Review	Commission	9 Nov. 2006
Green Paper: European Research Area new perspectives; COM(2007)161	Commission	4 Apr. 2007

International Organisations		
Sourcebook for Evaluating Global and Regional Partnership Programmes	World Bank	2007
HIV/AIDS Slowing in Africa with Help from NGOs, Drugs, and Condoms	World Bank	June 2007
The Africa multi-country AIDS programme 2000-2006	World Bank	2007
Priority Medicines for Europe and the World	WHO	Nov. 2004
The African Regional Health Report	WHO	2006
Malaria and HIV Interactions: implications for public health	WHO	June 2004
Global Tuberculosis Report	WHO	2007
"Public health innovation and Intellectual Property Rights"	WHO	2006
The Aidspan guide to round 7 applications to the Global Fund	Aidspan	8 Mar. 2007
TDR 10-year Vision and Strategy	WHO-TDR	Dec. 2006
Making a difference: 30 years of Research and Capacity Building in Tropical Diseases	WHO-TDR	June 2007
Global Fund against AIDS/TB/Malaria Annual Report	Global Fund	2005
Report on Global AIDS Epidemic	UNAIDS	May 2007
NEPAD Health Action ; Health Strategy	NEPAD	
DNDi Intellectual Property Policy	DNDi	Dec. 2004
Medicines for Malaria Venture (MMV) Independent Evaluation	MMV	May 2005
MMV and Intellectual Property Rights	MMV	June 2007

Articles in the press		
Mirowski and Van Horn "CRO and the commercialization of scientific research"	Social Studies of Science	Aug. 2005
Petryna "Clinical trials offshored: on private sector science and public health"	Bio Societies	2007
"Africa begins malaria vaccine trial"	BBC News	5 Mar. 2007
" Older TB vaccines 'work better'"	BBC News	18 Mar. 2007
"Arrest call over Uganda AIDS fund"	BBC News	1 May 2007
"Big pharma's shameful secret"	Bloomberg	Dec. 2005
"Take the guessing out of African aid"	Financial Times	2 Mar. 2007
"Two new drugs offer options in HIV fight"	Int. Herald Trib.	28 Feb. 2007
"A cheaper, easier malaria pill"	Int. Herald Trib.	1 Mar. 2007
"Study finds HIV/AIDS treatment goals for developing world unmet"	Int. Herald Trib.	29 Nov. 2007
"Safety concerns halt trials of HIV microbicide"	Int. Herald Trib.	1 Feb. 2007
"Scientists rail against Europe's absence in AIDS research"	Nature medic.	Aug. 2005
Lehner *et al* "EU and EDCTP strategy in the global context: recommendations for preventive HIV/AIDS vaccines research"	Vaccine	July 2005
"Europe's science bureaucrats should learn from Gates' success"	Lancet editorial	2 July 2005
"Fight against infectious diseases" - G8 St. Petersburg	Press article	16 July2006
"Virulent TB in South Africa may imperil millions"	Int. Herald Trib.	27 Jan. 2007
"Malgré des progrès, le bilan de santé de l'Afrique reste "dramatique"	Le Monde	22 Nov. 2006
"Ambitious scheme for developing world trials in 'big trouble"	Nature	
"Changing funding patterns in Tuberculosis"	Nature	Mar. 2007
“WHO’s new Stop TB strategy”	Lancet	18 Mar. 2006

EDCTP	
Incorporation EDCTP-EEIG (legal entity document)	26 June 2003
Internal Regulations for the EDCTP-EEIG	22 July 2004
EDCTP Self-assessment	29 Apr. 2005
Summary recommendations of working group following up on EDCTP self-assessment	2005
NWO - EDCTP agreement on hosting the EDCTP Secretariat	6 Sept. 2005
EDCTP Standard Operative Procedures	1 Oct. 2005
Revised Internal Regulations for the EDCTP-EEIG	09 Aug. 2006
Formal request for extension of term to RTD Commissioner J. Potočnik	21 Feb. 2006
EDCTP Roadmap – approved by the General Assembly	22 Nov. 2006
Joint call for proposal: 'Capacity building in preparation for preventive HIV vaccine trials'	1 Dec. 2006
Guidelines for EDCTP Stakeholder meetings	19 Jan. 2007
EDCTP African Office hosting institution review	12 Feb. 2007
Review of the European hosting institution (NWO) for EDCTP	12 Apr. 2007
EDCTP Annual report 2005	
Joint Programme of the Action 2004	
Joint Programme of the Action 2005	
Joint Programme of the Action 2006	
Interim Technical Report 2003	
Interim Technical Report 2004	
Interim Technical Report 2005	
Interim technical Report 2006	
EDCTP Communication Strategy 2006-08	
EDCTP Strategy for 2007-2010	
Africa office - Annual report 2006	

Report on EDCTP 3rd Annual Forum Stockholm	11 Oct. 2006
Tuberculosis Vaccines – Stakeholders' meeting, The Hague	11 Apr. 07
Report on EDCTP First Investigators' meeting Cape Town	25 July 06
EDCTP Guidelines for stakeholder meetings	
EDCTP Guideline on Intellectual Property Rights	
EDCTP Guidelines on Ethics	