



European & Developing Countries Clinical Trials Partnership

DEVELOPING THE DIALOGUE

REPORT OF THE EDCTP
PHARMACEUTICAL INDUSTRY
WORKSHOP

26 JUNE 2012



Towards the second EDCTP programme

The EDCTP Pharmaceutical Industry Workshop is part of a broader effort to foster cooperation of public and private partners for clinical research on poverty-related and neglected infectious diseases in preparation for the second phase of the EDCTP programme (2014-2024).

EDCTP was created in 2003 as a European response to the global health crisis caused by the three main poverty-related diseases (PRDs) of HIV/AIDS, tuberculosis and malaria. Currently EDCTP is a partnership between 14 European Union Member States plus Norway and Switzerland with 47 sub-Saharan African countries. The aim of the programme is to accelerate the development of new and improved drugs, vaccines and microbicides against HIV/AIDS, tuberculosis and malaria through a balanced partnership of European

national research programmes on PRDs with their African counterparts in collaboration with the pharmaceutical industry and like-minded organisations.

The second EDCTP programme is expected to start in January 2014 as part of the European research framework programme Horizon 2020. Its scope is based on the current objectives and achievements and will be expanded to include: all clinical trial phases I-IV including health services optimisation research; other neglected infectious diseases; closer collaboration with industry, like-minded product development partners and development agencies; and collaborative research with other developing countries outside sub-Saharan Africa when possible and desirable.

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Acronyms and abbreviations

BMGF	Bill & Melinda Gates Foundation
CTD	clinical trial dossier
DNDi	Drugs for Neglected Diseases initiative
EC	European Commission
EDCTP	European & Developing Countries Clinical Trials Partnership
EDCTP-II	second phase of EDCTP's programme, which will begin in 2014
EEIG	European Economic Interest Grouping
EFPIA	European Federation of Pharmaceutical Industries and Associations
GCP	good clinical practice
Horizon 2020	financial instrument implementing the Innovation Union, a Europe 2020 flagship initiative aimed at securing Europe's global competitiveness
HAT	human African trypanosomiasis (‘sleeping sickness’)
IPR	intellectual property rights
NCDs	non-communicable diseases
NIDs	neglected infectious diseases
PanACEA	Pan-African Consortium for the Evaluation of Anti-tuberculosis Antibiotics
PACTR	Pan African Clinical Trials Registry
PDPs	product development partnerships
PRDs	poverty-related diseases
R&D	research and development
REMox	Rapid Evaluation of Moxifloxacin in tuberculosis (trial)
SMEs	small and medium-sized enterprises
TB	tuberculosis

1. Executive summary

The European Federation of Pharmaceutical Industries and Associations (EFPIA) and senior representatives of some of the world's major pharmaceutical companies have applauded the work of the European & Developing Countries Clinical Trials Partnership (EDCTP) and declared their willingness to step up the level of their engagement in EDCTP's work against infectious diseases in Africa.

EDCTP was launched in 2003, following a European Parliament and European Council decision to pool resources, funding and activities to achieve a greater impact against the three main poverty-related diseases (PRDs) HIV/AIDs, tuberculosis (TB) and malaria. Partnership is the basis of EDCTP, which currently unites 14 participating EU Member States and two Associated Countries with sub-Saharan African countries and like-minded partners. So far it has supported 57 clinical trials in sub-Saharan Africa, mainly phase II and phase III, against the three main PRDs.

The organisation is now moving towards its second phase (EDCTP-II), which will see an expansion of its remit and activities to include neglected infectious diseases (NIDs) – such as schistosomiasis, human African trypanosomiasis (HAT) and leishmaniasis – and the addition of phase I and IV clinical trials, though the main focus will still remain on phase II and III clinical trials for HIV/AIDS, TB and malaria. Another goal is to strengthen engagement with the private sector through collaborative projects, and to obtain additional support from the pharmaceutical industry. With this in mind, a dialogue between EDCTP and several major pharmaceutical companies has been taking place over the last 12 months. As part of this process a one-day workshop was held at the EDCTP Secretariat in The Hague on 26 June 2012, which was attended by the EFPIA, several major pharmaceutical companies, one global contract research organisation, the European Commission and EDCTP Secretariat. The aim

was to move towards defining a framework for extended collaboration with industry.

Workshop participants heard a review of EDCTP's achievements to date and what it could offer in a partnership with industry: African co-ownership of projects; clinical trials networks that are compliant with good clinical practice (GCP); continuing capacity building in personnel, infrastructure, ethics review and regulatory affairs; and leverage of resources with other partners.

This was followed by an address by the Chairperson of EFPIA's Global Health Initiative Working Group, François Bompert. He spoke of the industry's long-term commitment to working against PRDs in general, which has been stepped up in recent years. EFPIA's view is that the primary focus of EDCTP should remain phase II and phase III trials, conducted in sub-Saharan Africa. However, the proposed expansion into NIDs, phase I and IV trials, and into diagnostics and pertinent elements of health services optimisation research was to be welcomed; and likewise the possibility of activities in other geographical areas. Industry participants also proposed that trials of new products for non-communicable diseases should be given consideration to optimally use capacity built in EDCTP funded clinical trials.

He identified three areas in which the industry could collaborate in EDCTP-II: disease epidemiology, clinical trials and capacity building. Nevertheless, pharmaceutical companies have to optimise the return on their investment and to think in terms of their medium and long-term business objectives in developing countries. Working in this area does pose a number of challenges. Since time is precious, means must be found to minimise delays resulting from ethical and regulatory procedures, and over-complex partnership arrangements should be avoided. Research capacity building – which

can take many forms – was important to the industry, but was not its primary objective. Dr Bompat hoped EDCTP and industry could coordinate their agendas and consider operational alignment. EDCTP could also play an important advocacy role in promoting R&D.

Following the introductory presentations, a far-ranging and frank discussion took place; much of it centring on participants' unanimously held view that expanded EDCTP-industry collaboration could have mutual benefits. For example, pharmaceutical companies could conduct trials in sites already prepared by EDCTP from previous studies; in particular the companies would welcome updated disease epidemiological data from those locations and benefit from shared experience of working there. Acting as a neutral broker for capacity development, EDCTP could help reduce ethical and regulatory delays to a minimum. Another aspect of the brokering role would be bringing together all stakeholders, so that the pharmaceutical industry could have partners 'for the whole journey' of product development.

EDCTP would be aided towards achieving its goals by greater industry support. R&D activities focused on PRDs would be much expanded, and Africa's own research capacity would be increased through the sharing of expertise. The common message from industry was that they will not contribute with cash to EDCTP, but are ready to contribute with their expertise and capacities. It was agreed to explore the establishment of an EDCTP-Industry Fellowship, joint training and mentorship programmes.

EDCTP has noted that phase IV trials investigating specific issues in Africa are 'not happening on their own'. Through a dialogue with industry and researchers in the field, the questions that need to be addressed through such trials can first be identified and then the appropriate research implemented. It was

also observed that much can be achieved if companies normally regarded as rivals work together on global health issues; for example in head-to-head comparisons of products and in developing combination therapies. Industry participants said they recognised this and saw a brokering role for EDCTP in 'pharmato-pharma' collaboration. Improved pharmacovigilance would be among the other benefits of such partnership.

Regarding financial contribution, most industry participants took the view that, while limited support could be provided through social responsibility budgets, pharmaceutical companies did not see themselves as 'funding agencies'. From the EDCTP side, it was made clear that the purpose of the continuing dialogue with industry was not simply to ask for money, but to build partnerships and leverage synergy.

Valuable discussions also took place at the workshop on how to address some of the challenges that increased collaboration would generate – in particular, issues around intellectual property, data sharing and the difficulties in bringing effective drugs to market. Also noted was the need to establish the key issues for new calls for proposals; calls must allow for capacity building and training needs.

Summing up, workshop co-chairs Dr Line Matthiessen (European Commission) and Professor Simon Croft (London School of Hygiene & Tropical Medicine) noted that the following areas had emerged as being of key importance.

- EDCTP is well positioned to work with pharmaceutical companies in developing combination therapies and in conducting head-to-head product comparisons
- Experience has shown that EDCTP is an important broker in product development partnerships and in leveraging of resources with other partners
- EDCTP presents added benefit of African co-ownership of projects; clinical trials networks that are compliant with GCP; and continuing capacity building in personnel, infrastructure, ethics review, and regulatory affairs
- Industry can assist in capacity building, especially in research and financial management, data management and statistics, clinical trial monitoring, joint clinical trial designs, and in the engagement of young scientists. Industry support could be in-kind such as in internships and work placements
- Time constraints, resulting from ethical and regulatory issues, are a major problem for industry, which would value EDCTP assistance as a neutral partner for capacity development in ameliorating the situation
- EDCTP could facilitate the availability of knowledge and quality information on disease epidemiology; trial site capacity including availability of human and infrastructural resources for conducting clinical trials; and country specific factors that affect conducting research
- More phase IV trials are needed: industry and EDCTP should discuss potential for such clinical trials well in advance
- Industry expressed readiness to move into global 'portfolio management' particularly

for NIDs and views EDCTP as a neutral body to mediate this role

- Industry is willing to assist in capacity building through provision of technical expertise, internships, work placements and establishment of EDCTP-Industry Fellowships.

In his concluding remarks, the EDCTP Executive Director, Professor Charles Mgone thanked all participants noting that although the workshop was a momentous event in the partnership between EDCTP and pharmaceutical industry, it should be taken as part of a process and channels of communication should remain open all the time. In the coming months, EDCTP, individual companies and EFPIA will, as a next step, explore on putting some of these recommendation into action including the establishment of EDCTP-industry fellowships.

2. Introduction and presentations

Background

The European & Developing Countries Clinical Trials Partnership (EDCTP) has made major contributions towards a significant increase seen in research intended to reduce the burden of poverty-related diseases (PRDs), until now focusing on HIV/AIDS, malaria and TB. EDCTP has also demonstrated what can be done in this area through use of the partnership approach. There are encouraging signs that what has been achieved can be sustained and indeed expanded.

EDCTP is now seeking to build on its investments and achievements as it moves towards its next phase – [EDCTP-II](#). One key objective is to strengthen the collaboration and involvement of the pharmaceutical sector in the programme. Towards this end the EDCTP General Assembly agreed on the formation of a private sector relations working group, which started work in 2011. The working group is chaired by EDCTP's Executive Director and includes representatives of the EDCTP governing and advisory bodies, plus a coordinator who is part of the EDCTP Secretariat. The required funding has been provided by some of the European partner states. In the context of this initiative, EDCTP has performed a number of company visits and conducted a series of semi-structured interviews with senior personnel in the industry, with a view to eliciting information on their companies' views on a range of key issues – see Box 1. The results of this survey will be available shortly.

A further important step in the process of expanding collaboration with industry was a one-day workshop – held at the EDCTP Secretariat in The Hague on 26 June 2012 – which was attended by the European Federation of Pharmaceutical Industries and Associations (EFPIA), several major pharmaceutical companies, one global contract

research organisation (CRO), the European Commission and EDCTP Secretariat. The aim of the workshop was to attempt to answer the questions that have emerged from the dialogue with industry so far, and to define a framework for extended collaboration between the industry and EDCTP.

Box 1. Key issues addressed in industry survey

1. Identification of potential candidates for clinical trials that fit within the scope and strategy of the EDCTP-II programme
2. Initiation, funding and implementation of the required studies
3. Brokering of suitable partnerships and leveraging of funding, especially for the costly phase III clinical trials
4. Intellectual property rights (IPR), market authorisation and affordability and accessibility of products in poorly-resourced countries
5. Data ownership, including: access to data, publication rights, authorship and information dissemination
6. Design of EDCTP calls for proposals to facilitate closer collaboration with the pharmaceutical industry
7. Joint capacity building including training, internships and EDCTP-industry fellowships.

The workshop was structured according to three main themes, namely priorities, product development and capacity strengthening. This report of the workshop has been prepared according to Chatham House rules; i.e. the names of the main presenters are given but all comments made during the discussions are unattributed.

Participation

The workshop was well attended with representation from most major pharmaceutical companies working on poverty-related diseases, in addition to the EFPIA. Representation was through one to three senior members per company, mostly coming from the operations, external scientific relations, access, PRD, Africa/developing countries and corporate responsibility departments of these companies.

The workshop was co-chaired by Professor Simon Croft (London School of Hygiene & Tropical Medicine) and Dr Line Matthiessen (Directorate-General for Research and Innovation, European Commission).

Presentations

Hannah Akuffo, Chair of the EDCTP-EEIG General Assembly, introduced the workshop. She reminded the meeting of the scale of the burden exacted by PRDs in developing countries and the need to accelerate the research and development of new or improved interventions against these diseases, through the coordination of European member state national programmes working in partnership with sub-Saharan countries. Professor Akuffo went on to describe EDCTP's partnership approach, which involves the European Commission, participating European partner countries, sub-Saharan African countries, and like-minded organisations, e.g. international development agencies and product development partnerships (PDPs). In addition to developing new tools to fight PRDs, support for capacity development and networking is key to the activities of EDCTP. Fifty-seven clinical trials have been funded by the programme so far, with the focus on phase II and phase III trials.

Other accomplishments include: facilitating significant public investment to support PRD research; ensuring joint African-European co-ownership, leadership and stewardship of EDCTP-supported programmes; and research capacity building activities that foster good governance and leadership, the strengthening of regulatory and ethics bodies, and the development and retention of trained personnel within sub-Saharan Africa.

It is proposed that under EDCTP-II all clinical trial phases I-IV, including health services optimisation research, will be supported by the programme, and that neglected infectious diseases (NIDs) will also be included within its remit. Collaborative research involving developing countries outside Africa will be considered. Closer collaboration with private sector organisations will also be sought. The [strategic business plan](#) for EDCTP-II has been developed and current European partner countries have already indicated the volume and form of the support they are likely to provide. These commitments will feed into and support a future legislative process for a decision of EDCTP-II in parallel with the preparations for [Horizon 2020](#). A dialogue has also been established with European countries that are not yet involved with EDCTP, and efforts are being made to enhance the engagement of African

Table 1. Funded clinical trials by area, 2003-2011

HIV/AIDS	27 clinical trials 118M Euro	Drugs	14
		Vaccines	9
		Microbicides	4
Tuberculosis	18 clinical trials 110M Euro	Drugs	7
		Vaccines	7
		Microbicides	4
Malaria	12 clinical trials 76M Euro	Drugs	10
		Vaccines	2

governments. Professor Akuffo encouraged workshop participants to explore what could be achieved through collaboration between industry and EDCTP, and to consider also the barriers that would have to be overcome. She hoped that the discussions would result in an outline strategy defining possible approaches to future calls for proposals and collaborations.

Charles Mgone, EDCTP's Executive Director, presented a comprehensive summary of EDCTP's achievements so far. He emphasised throughout the importance of the partnership approach and the need for good governance. EDCTP's activities go beyond simply the funding of clinical trials to include also capacity development, networking, and strengthening of the R&D enabling environment. The main EDCTP grants scheme is for integrated projects; these include clinical trials, project management, capacity building and networking. Other grant programmes include senior fellowships and grants for health research ethical review capacity development. EDCTP is already playing a role in bringing all the players together for joint calls for proposals by member states, but there is still a need to continue the strengthening of partnerships. Other grant schemes include strategic primer grants and member-state initiated projects.

Professor Mgone set out the sources of the funding of EDCTP administered projects for HIV/AIDS, TB and malaria. Public funding accounts for much the greatest proportion; industry funding has so far played a much smaller role and is confined to TB and HIV/AIDS.

He went on to describe in more detail the process of strengthening trials capacity and the enabling environment, highlighting the role played by EDCTP's [Networks of Excellence](#). He also gave details of EDCTP's involvement in ethics review capacity building, which has included a mapping of ethics review and

regulatory capacities in Africa. The mapping exercise has created a valuable resource for EDCTP, which could also be of use to industry. Professor Mgone discussed EDCTP's activities in supporting the stepwise development of clinical laboratories towards accreditation and infrastructure development, before going on to highlight some EDCTP-funded programmes that illustrated partnerships and global approach: the PanACEA network (shortening and simplifying TB treatment), the REMox study, the Malaria in Pregnancy Consortium, and the joint EDCTP-BMGF call intended to strengthen capacity in HIV vaccine trial sites. He concluded by summarising what EDCTP can offer to industry.

- African co-ownership of projects
- Clinical trials networks that are compliant with good clinical practice (GCP)
- Continuing capacity building in personnel, infrastructure, ethics review, and regulatory affairs
- Leverage of resources with other partners.

François Bompert, who is Vice President and Medical Director, Access to Medicines Department at Sanofi Aventis, spoke to the meeting in his role as Chairperson of EFPIA's Global Health Initiative Working Group. He described *'The role of the pharmaceutical industry in the fight against poverty-related and neglected infectious diseases'*, beginning by stating that the industry had a long-term commitment to working against these diseases. Its R&D budget had been increased in recent years (see IFPMA Status Report 'Pharmaceutical Industry R&D for Diseases of the Developing World, November 2011, www.ifpma.org) and there had already been decades of investment in HIV/AIDS and malaria. Many drug donations had been made and in January 2012 the industry had pledged to provide 1.4 billion treatments for NIDs over the next 10 years. Individually, companies are now working on a total of 82 NID R&D projects, either alone or through

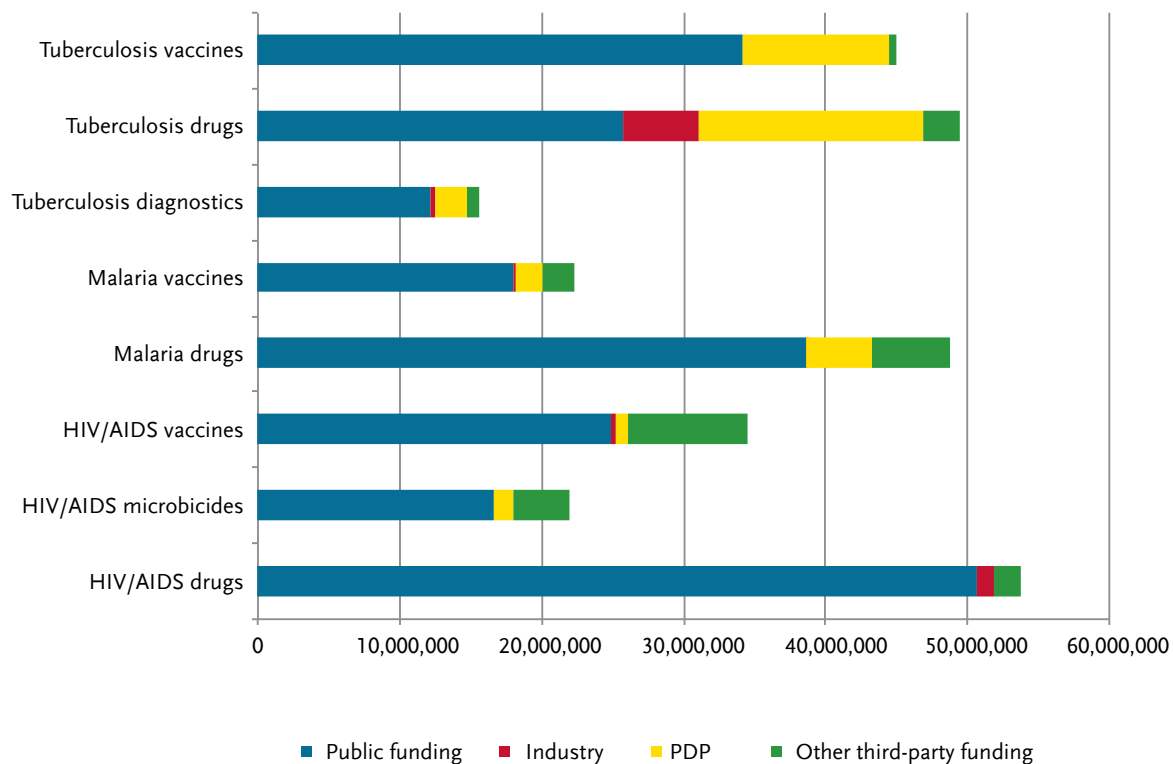


Figure 1. Funding for HIV/AIDS, tuberculosis and malaria (in Euros)

PDPs. This is an industry of ‘decent people’, said Dr Bompert, with a strong sense of corporate responsibility.

EFPIA welcomes the forthcoming launch of EDCTP-II. The Federation’s view is that the primary focus should remain on phase II and phase III trials, conducted in sub-Saharan Africa. However, the proposed expansion into NIDs, phase IV and (under some circumstances) phase I trials, and into diagnostics and health services optimisation research is also to be welcomed; and likewise the possibility of activities in other geographical areas. There are three areas in which the industry can collaborate in EDCTP-II: epidemiology and feasibility studies, clinical trials, and capacity building (including training fellowships, internships and work placement).

Nevertheless, companies have to optimise the return on their investment and to think in terms of medium and long-term business objectives in developing countries. While there is always an element of risk-taking in research, industry must take as few chances as possible; it is necessary to remember that most scientific leads go nowhere. ‘Time is money’ and should not be wasted; adherence to timelines and timely decision making are critical, especially for registration trials. There is also a danger that time can be lost through over-complex partnership arrangements. Industry’s investment in R&D is determined by availability of a lead to follow and a market – sometimes there is one but not the other; sometimes there is no lead and no market! Dr Bompert discussed this issue – and the different strategies required – with regard to HIV/AIDS, TB, malaria and NIDs.

He cautioned that, for industry, capacity building is not the primary objective in clinical trials and that it is hard to implement co-funding when no return on investment can be anticipated. Nevertheless, capacity building – which can take many forms – is important to the industry. He also reminded the meeting of the increasing prevalence of non-communicable diseases in developing countries. EDCTP could consider helping clinical sites expand their capacity beyond infectious diseases – for example, by gathering epidemiological data on non-communicable diseases (NCDs). He applauded the work EDCTP had done so far. He hoped that EDCTP and industry could coordinate their agendas and consider operational alignment. EDCTP could also play an important political role.

Response

François Bompard's presentation prompted a number of comments from other participants in the workshop. Company representatives agreed that industry could provide only limited support for capacity building. Some commented that the remit of EDCTP could indeed be expanded (NCDs and hepatitis B and C, diarrhoeal disease and respiratory infections were all mentioned), but Professor Mgone responded that the range of activities could not be spread too wide; it was necessary to maintain a focus, given the limitations EDCTP-II will face in terms of budget and time constraints. Some participants felt that it was premature to speak of any role for EDCTP as a spokesperson for industry. When asked if he thought industry could play a role in improving pharmacovigilance in Africa, which is still very limited at present, Dr Bompard replied that this was possible, but the primary responsibility for pharmacovigilance lay with countries themselves. Companies should of course be aware whether there are any major safety or other issues with their products, but it is up to the country to investigate issues arising specifically in their region. EFPIA could help in setting up

risk management plans, which would include determining the need for phase IV clinical trials. Regulatory bodies also consider post-registration clinical trials to be a responsibility of pharmaceutical companies.

Christa Janko, EDCTP's Private Sector Relations Coordinator, set out the primary issues requiring the meeting's attention. Firstly, it was necessary to identify priorities, in terms of new products needed and candidate compounds requiring investigation. What kind of trials and which study designs should be chosen? Improved diagnostic tests and combination treatment regimens should be included on the research agenda. It was necessary to establish funding mechanisms, identify suitable trial sites, and determine how the required partnerships could be brokered. Potential barriers to progress also needed to be identified. These include: intellectual property rights (IPR), market authorisation, data ownership and access, and publication rights. She concluded by stressing that Africa did have research capacity and that EDCTP could help the pharmaceutical industry find the capacity it requires. There are many areas of mutual interest between the pharmaceutical industry and EDCTP, as will become clear when the results of the semi-structured interviews are made available; shared problems and possible solutions have already been identified and this meeting will further advance the process.

3. Discussion

Participants agreed that EDCTP's progress so far has demonstrated that there is huge potential to run trials in Africa and produce quality data, providing efficient procedures are followed and all the stakeholders are brought together. Information sharing is an important factor in achieving such collaboration.

The discussion went on to cover a wide range of issues. Frequent mention was made throughout of the fact that increased EDCTP-industry collaboration will be "win-win", with benefits both for the industry and towards achieving the goals of EDCTP. As an example of such mutual benefits, EDCTP can help industry identify appropriate sites for clinical trials and industry can contribute towards building the capacity of those sites. This summary of the discussion focuses first on the benefits of collaboration to the industry and then deals with the benefits towards achieving the goals of EDCTP. The challenges that both sides need to address are then briefly described.

Benefits of collaboration for the pharmaceutical industry

Site preparation

EDCTP's existing programme has ensured that clinical trial sites have been prepared. Many of these have been tried and tested and are able to undertake further trials. Workshop participants from the pharmaceutical industry recognised that access to EDCTP-developed sites would carry several advantages. Nevertheless, some speakers cautioned that Africa must not be seen as a place where patients are 'easy to get'; trials must be relevant to local needs. (Sometimes however, as for example with pneumococcal vaccines, there is a local need for a product that is also required internationally.)

Epidemiology: A lack of epidemiological data from disease foci, endemic regions and communities where trials might be conducted has sometimes held back industry from carrying out research. In particular, data on prevalence, incidence and transmission rates is often unavailable. Several industry participants gave examples of how this obstacle has prevented their companies from conducting trials.

EDCTP's integrated projects and regional Networks of Excellence collect epidemiological data as part of their capacity building activities and this data could be of assistance to industry. It was, however, pointed out that (for example, with regard to the prevalence of drug resistance) the epidemiological situation can change quite rapidly; epidemiological monitoring at trial sites must, therefore, be carried out regularly, which requires well-trained staff and adequate diagnostic capability. The latter is often a key link between epidemiology and trials. It is often harder to train staff in epidemiology than in other research disciplines; one proposal was that EDCTP could establish a fellowship training programme, which industry would support. Another point made was that, when a trial is considered anywhere in the world, the claim is always made that there is 'not enough epidemiological data'! Different companies and organisations have separate objectives and sometimes have data on different aspects of epidemiology. This makes it hard to see the bigger picture. There was a role here for EDCTP to act as a go-between.

But how can additional epidemiological research and monitoring be funded? Several pharmaceutical company representatives indicated that it was not in the immediate interest of the pharmaceutical industry to fund epidemiological research, and that the industry is better able to make its contributions in other areas. But, it was then asked, if EDCTP is going to do more epidemiological work, in order to assist the industry, how will it be rewarded for this? Some funders (including pharmaceutical

companies) are now funding epidemiological mapping projects – is this one way that industry could help? Industry participants did not attempt to answer these questions.

Capacity issues (including human resources): While industry participants recognised that the capacity of an existing EDCTP site could be used for future industry-run trials, companies need to be able to elicit details of the capacity available, including the skills of the staff at the sites. EDCTP can provide this information. Capacity building programmes must be sustainable. Once a trial is completed, new trials are needed to maintain the capacity of the site. However, additional training is often necessary – for example if drug trials are to be followed by a vaccine trial.

Saving time

Delays in obtaining ethical and regulatory approvals can be a serious deterrent to companies that are considering trials. Ethics committees and regulatory authorities can cause difficulties that sometimes seem impossible to overcome. EDCTP is addressing some of these challenges by strengthening the capacity of these bodies.

Knowledge

Pharmaceutical companies often lack knowledge about the situation in specific countries, and how to go about working there. Without information from a range of sources, it is often impossible to see the bigger picture or achieve a holistic view. EDCTP can help in the process of sharing knowledge and experience gained in previous trials, so that it is available for all to use. Knowledge sharing would also make it unnecessary for different companies to approach the same institutions and individuals over and over again to gather the same information.

EDCTP's work in Africa has generated valuable research networks and data related to many

areas relevant to industry: trial registration at the Pan African Clinical Trials Registry (PACTR), epidemiological data, site capacity, ethical review capacity, country-specific regulatory frameworks, etc. So far this knowledge sharing has mainly been on an ad hoc basis (except for PACTR) but a more structured approach could in future be adopted.

Bringing people together

Stakeholders will always have different priorities, but there was a good level of agreement that EDCTP could help close this gap and play a central role in building connections, relationships, synergies and partnerships. An industry participant won strong support when he said that a pharmaceutical company needed partners 'for the whole journey' – from the trial stage on to the final goal – producing an effective product at an affordable price. What is required to make this possible was variously described as a 'counselling agency', a 'forum' and 'an honest broker'. Once again there is a key role for EDCTP to play here. Working with PDPs is now seen as crucial by many companies and again EDCTP can also help broker such relationships.

Sometimes it would be advantageous for companies to work together (for example to undertake head-to-head comparisons of drugs or to investigate new combination therapies). EDCTP could be a neutral broker here.

An important aim in relationship building would be achieving agreement on shared goals (e.g. for TB trials). The concept of 'global portfolio management' then received attention but several industry participants cautioned that there was no single way in which this could be achieved; it would vary depending on the disease, the needs, the market and the scientific leads available.

Participants agreed that facilitation of face-to-face meetings by EDCTP should be seen as a key part of the relationship building role.

Also mentioned in the discussion on relationship building were the industry's concerns regarding the use of low-quality drugs that have not come from the parent company.

Meeting social responsibility goals

Industry speakers repeated that their companies were conscious of their responsibilities toward society; conducting trials offers one way in which such commitments can be met. It was generally agreed by the industry participants that social responsibility budgets were insufficient to fund the development of new products at an affordable price. The best incentive is an adequate financial return on investment. Co-funding would in many cases be the only way forward.

How collaboration could help EDCTP to achieve its goals

Funding

The majority of the funds distributed by EDCTP come from member states, and securing additional support from industry would clearly be desirable. However, company representatives noted there is always 'uneasiness' when expanded financial contributions from industry are mentioned. Pharmaceutical companies are not funding agencies, but may have other resources that they can offer, such as expertise in various fields. It is, in any case not up to industry to decide what good work they want to do – African nations must say what needs there are to be addressed.

However, for the EDCTP side, it was made clear that the purpose of the continuing dialogue with industry is not simply to ask for money; the aim is to build partnerships and

determine what industry's role in these partnerships will be. How can such partnerships be built and how can contributions be secured, in cash or in kind? Industry participants said that EDCTP should be encouraged to approach individual companies directly with specific proposals as opportunities arose, but drawing up a rigid framework to cover all possibilities would not be appropriate. Epidemiology was mentioned as one area where companies would probably *not* wish to assist, as the industry's expertise lies primarily elsewhere.

Improving Africa's research capacity

While EDCTP has already made major steps forward in enhancing Africa's research capacity, it is hoped that further progress can be achieved with industry support. Developing the level of expertise available is one priority. Some companies have already contributed in this area (for example, scientists from the Drugs for Neglected Diseases initiative (DNDi) have been given specialist training). The suggestion that an industry-cofunded fellowship programme, administered by EDCTP, could be established seemed to meet with approval, although no concrete commitments were made. Epidemiological training could perhaps be included in such a programme, although it was noted that this would be harder for industry to provide. Epidemiological expertise is in particularly short supply, notably amongst policy makers – very few people understand the issues. Industry could also contribute in other ways, including sharing the expertise/skills of their staff in those areas where industry has an advantage.

Industry participants responded positively, but said more clarity was needed on precise training needs. Some specific areas were then mentioned: statistics and data management, clinical trial monitoring, and clinical trial and financial management. The latter was seen as particularly important. It was also noted that there have been some recent significant advances

in diagnostics (e.g. in TB) and knowledge and expertise in these new techniques needs to be passed on to those involved in trials. EDCTP and industry could work together with other partners to identify and address training needs.

Expanding trial types

EDCTP wishes to see more phase I and phase IV trials conducted in Africa. Workshop participants focused on the need for phase IV trials. Even in the case of HIV/AIDS research, in which industry continues to invest heavily, phase IV trials investigating specific issues in Africa are ‘not happening on their own’. (For example, the need for paediatric formulations is very much greater in Africa than in the more industrialised countries.) Industry participants were in agreement and said they would welcome collaboration with EDCTP, starting with identification of the questions that needed to be addressed through phase IV trials. However, as was also agreed, this trial phase poses many new challenges – not least because the term ‘phase IV’ often means different things to different people.

Benefits that can be achieved through pharma-to-pharma collaboration

The advantage of combination therapies (primarily to reduce the rate at which drug resistance develops) is now widely recognised. Often drugs that could potentially be combined come from different manufacturers. EDCTP would like to see companies work together in trials of such combinations. Head-to-head comparison of the effectiveness of different drugs is also another area in which companies could collaborate with each other. There was a strong level of agreement with this from industry participants, several of whom went further to say that, in matters of global health, there was a sound case for the industry to work in alliance and not in competition. It was felt that there have already been improvements in industry attitudes in this regard but further changes in the mindset are still needed. If companies could

share expertise it could lead to the development of new drugs that would not result from their individual efforts alone. This was referred to as the ‘pre-competitive’ or ‘non-competitive’ approach. It would be particularly appropriate for diseases where the market was perceived as being poor, for example kinetoplastid infections (human African trypanosomiasis [HAT] and leishmaniasis). A number of industry participants commented that they would like to see their companies working in this way, and that EDCTP could act as a neutral broker (and potential cofunder) in such partnerships. It has already been active in facilitating trials of combination therapies and is willing to do more in this area. One suggestion was that EDCTP could set up a centralised mechanism – such as a portal or a forum – where companies could share experiences on clinical trials and drug development and potential partners could find each other.

However, within quite a lengthy discussion on the issue of pharma-to-pharma collaboration, other speakers from the industry said that competition remained important and its role as the main driving factor should not be forgotten. Without it there was no incentive for companies to ‘jump into the game’.

Other potential benefits

Other potential benefits of collaboration towards EDCTP’s goals were also noted. These included improved pharmacovigilance, improvements to trial sites, and development of the skills of people who work there. There was agreement that people trained in trial skills are also good providers of care, so there is a direct benefit to the communities they serve.

Other issues raised/Challenges and concerns

Intellectual property rights

When partnership programmes are created, the ownership of the intellectual property rights (IPR) must be clearly set out upfront. Difficulties in this area have been cited as a barrier to progress. Workshop participants agreed, however, that the issues are not as complicated as sometimes claimed: 'It is something that we can sort out'. All that matters in the end is whether the products are available and affordable. Partners should share information freely with each other but honour the requirement not to make it available to others. Points made included the following.

- This may require to be done on a case-by-case basis – e.g. medicines that are almost out of patent would be considered differently from newer ones. (There was strong agreement amongst industry participants on this point.)
- Agreement is needed between funders on what will be delivered to the developing world. The conditions on which support will be provided should thus be clearly specified.
- Companies generally do not want to commit themselves to surrendering IPR but might choose not to enforce it. The *management* of IP is the key issue.
- The majority of the investigational products that come to EDCTP from industry will already have been patented, with the exception of situations relating to product label extensions or changes in the indication/clinical use of product.
- If the plan is to sell a drug at a low price in the South and at a premium in the North, (two-tier pricing) then industry needs guarantees that the differential will be respected.

Data sharing

The pharmaceutical industry is now committed to publishing its clinical trial findings in peer-reviewed journals, but journal articles only summarise the research. What is at issue is whether companies will agree to patient-level data being made available to others, who could analyse it. Sometimes this might be done allowing access for a short period only. Databases are now in development that would make such sharing possible for NIDs. Opinions varied as to whether there is a role for EDCTP here.

It is important for regulatory authorities to make clear what they wish to be made available. Often they do not and this is one of the 'regulatory hurdles' that can deter industry from investing. This is something that EDCTP could discuss with regulatory bodies. EDCTP supports different categories of projects and requirements will vary. Note that pressure means that progressively more openness is demanded where projects are funded with public money. Some industry speakers said that research would sometimes produce information that companies did not wish to share.

It should be kept in mind that EDCTP is a funding organisation and not a sponsor of clinical trials. The sponsors, not EDCTP, are therefore responsible for the integrity of the data collected and for the submission of the clinical trial dossiers to the appropriate regulatory agencies.

Different parties might want or need to have access to different data. There is also increasing pressure to make publications available to the scientific community through open access. Further discussion, involving leading international health bodies, is needed on the issue of data sharing. Companies should indicate how they wish to participate and engage.

Conducting phase IV trials

Industry is mainly concerned with phase I, II and III trials but recognises that phase IV trials are necessary to answer ‘bigger picture’ and ‘real life’ questions following product registration. The first issue is identifying which questions have arisen that need to be addressed. Industry recognises that risk management is essential for all products and risk management plans should be in place. However, responsibility for identifying other concerns was felt to lie elsewhere. In the opinion of industry participants, the ‘information gap’ should be defined by those in the field. Others argued that when phase IV work is needed in resource-poor settings, then industry must surely have a role to play. It was also noted that there are different views on what exactly constitutes a phase IV trial.

It was agreed that phase IV trials have different requirements from earlier phase trials. They are conducted in a ‘real world’ setting and issues arise that are not seen in the more strictly controlled settings of earlier trials. EDCTP can help set the agenda for research in a real world setting. Phase IV trials are usually not as costly as phase III, and timing is less crucial, but evaluating impact in real world settings is complex; these can be very difficult trials to implement and interpret. Safety issues do not belong only in the hands of industry; this is a responsibility which must be shared.

In response to the question of what EDCTP should be doing so that more Phase IV trials can be conducted, industry participants suggested that pharmaceutical companies should be approached for discussions once phase II stage has been reached. When multiple funders are involved EDCTP can play a particularly valuable role.

Several industry speakers stressed, however, that each case would have to be treated on an individual basis. In general, collaboration with

EDCTP would be welcomed but what form it would take would vary. It was agreed that EDCTP should set up a small group to discuss the issue further.

Calls for proposals

It is important to establish what the highest priority issues for new calls for proposals are, especially relating to closer involvement of industry. With regard to phase II and III trials, it was noted that funding agency and industry timetables do not necessarily run in parallel; companies are generally more anxious to move forward quickly. Ways must be found to align timetables.

The move to include phase I and IV trials will pose new questions. Calls for proposals for phase IV trials must be done on the basis that such trials will focus on benefits in real life and will be related to the place in which the disease in question occurs. The addition of trials on NIDs will also raise new issues. Industry and EDCTP should hold discussions, as has already been done with phase III trials. The workshop did not establish a standard framework for such discussions and again industry participants noted that cases would vary.

Calls for proposals should also allow for capacity building and training needs. Again research management/budget management, epidemiology and medical statistics were mentioned as key areas. Fellowship training programmes engaging younger clinical scientists were seen as being particularly desirable.

Other areas

Successful completion of phase III trials, with positive results for the product under evaluation, is of course desirable. However, it does create problems in that funding must then be found to bring the product to market. The regulatory aspects of this process will include the need for further trials. It was asked whether companies would be prepared to meet the

costs involved. Industry participants responded that there were limits to what companies could do, and that it would depend on the disease and the market in individual cases. A business plan for product development must always make sense, from the beginning all the way through to market, even in a not-for-profit setting. There are various push-pull mechanisms available. An example given was of a non-profit model where Novartis had an agreement with WHO to enable low-income countries to purchase Coartem either with their own funds or with financing provided by one of the many aid organisations supporting the fight against malaria. When asked whether they thought there was a need for guidelines on product development, industry participants said the issue must be considered on a case-by-case basis; their companies would be willing to discuss each situation with the relevant stakeholders.

It was agreed that too often all the data on treatment of a particular disease in Africa come from just a few countries. It is important to choose a range of trial sites in contrasting locations. Traditionally, trials are usually conducted in countries where it is convenient and pleasant to work. Sometimes, however, it is necessary to conduct research in fragile states, for example to address the burden of leishmaniasis in South Sudan or HAT in the Democratic Republic of Congo (DRC). Industry participants were asked whether their companies would be interested in supporting such research. The issue was recognised as important, but no solutions were proposed.

A recurring issue in the discussions was EDCTP's wish to agree with the industry a standard framework for collaboration. In contrast industry representatives emphasised their companies' openness to proposals but maintained that each case would be treated on its own merits.

4. Conclusions and next steps

Summing up the proceedings as Co-Chair, Simon Croft said that the whole picture of research on PRDs has changed greatly in the last five years, and if the momentum could be maintained there would be 'golden opportunities' to reduce the burden from these diseases. He identified several issues arising in the meeting that required EDCTP's particular attention.

- Combination therapies: industry is well aware of the need for companies to work together in this area, and there is a clear role for EDCTP to play providing both ground for negotiation and a structure for coordination
- Product development partnerships: the industry recognises the importance of working with PDPs and there is a brokering role for EDCTP here also
- Head-to-head drug comparisons: there is a limited availability of sites where such trials can be conducted; EDCTP could assist to ensure that trials are conducted properly, according to good clinical and scientific practices and required quality standards
- Capacity building: there was strong agreement on the need for this; particular areas where industry could assist included research management, epidemiology and statistics, and the engagement of young scientists; industry support could be in-kind (internships and work placements). It was agreed to explore the establishment of an EDCTP-Industry Fellowship and joint training/mentorship programmes
- Regulatory issues: industry faces many problems in this area and would value EDCTP's assistance as a neutral partner
- Knowledge: companies often lack quality information on epidemiology, trial site capacity and availability of resources, and on issues that affect conducting research in specific countries; EDCTP could help supply such information, all of which needs to be continuously updated

- Time constraints: companies want to move forward quickly; they want timelines to be tightened, but with a measure of flexibility; ethical review and regulatory oversight
- Phase IV trials: the need for trials had been agreed; the meeting had not been able to identify the priority questions to be addressed or a standard framework for EDCTP-industry cooperation, but it was clear that the two sides should discuss potential phase IV trials well in advance, with EDCTP taking the initiative to spearhead the collecting of data on safety and effectiveness of products in real-life situations; industry is willing to design and share risk management plans to facilitate this.

The meeting accepted these as being matters requiring attention, but some of the points were not discussed exhaustively. It was agreed that identifying priorities – in terms of products, candidates and combinations – was the most important goal at this stage. Trial design was also seen as a crucial concern; while this will vary between individual diseases, all products must be tested in phase I to IV trials.

An overarching recommendation was that EDCTP should be a major broker to: spearhead knowledge collection and sharing; bring together the various partners (funders, industry, PDPs, and academia both in the South and in the North); stimulate cross-company drug regimen combination clinical trials, and head-to-head cross-company product comparison trials. The latter may be necessary to save time and cost, especially in NIDs, where there is resource limitation in terms of products and clinical trial sites.

Companies were encouraged to attend EDCTP stakeholders meetings, to which they will be invited depending on thematic areas under consideration, when these resume under the current EDCTP Plus programme of preparations for EDCTP-II.

Final remarks

In his closing comments, Charles Mgone said it had been a very useful day in the history of EDCTP. He thanked all of the participants for their contributions. He was also grateful to other companies that had not been able to send representatives for one reason or the other, but had been participating in the dialogue between EDCTP and the pharmaceutical industry.

Many things were happening. The organisation is currently passing through a transition phase (between EDCTP-I and EDCTP-II), while waiting for Horizon 2020. Now that NIDs are to be added to EDCTP's remit, an internal

evaluation of the landscape (for which external help will be added) is taking place. A small committee would be established to focus on industry involvement as EDCTP wants to hear the industry voice and to establish continuous channels of communication. Participants were assured of EDCTP's efficiency in processing calls and the administration of grants. Professor Mgone stressed again that improving EDCTP-industry collaboration is an ongoing process, a work-in-progress. Today's workshop was not a one-off event. One intended output of the workshop is a position paper that can be widely circulated.

Annex 1. List of participants

Name	Organisation
Akuffo, Hannah	EDCTP, Chair General Assembly (Sweden)
Appelmans, An	Institute of Tropical Medicine (Belgium)
Barry, Abdoulie	EDCTP, Director of Finance and Administration (The Netherlands)
Bompart, François	EFPIA / Sanofi (France)
Beattie, Pauline	EDCTP, Operations Manager (The Netherlands)
Brackel, Esther van	GlaxoSmithKlein (Belgium)
Burrone, Esteban	Medicines Patent Pool (Switzerland)
Cardoso, Ana Lúcia	EDCTP, North-North Networking Officer (The Netherlands)
Chinnock, Paul	Rapporteur (United Kingdom)
Croft, Simon	Co-Chair, London School of Hygiene and Tropical Medicine (United Kingdom)
Delft, van Yvonne	Johnson & Johnson/Janssen (The Netherlands)
Dieye, Alioune	EDCTP, Chair Developing Countries Coordinating Committee – DCCC (Senegal)
Goor, Gianpietro van de	European Commission (Belgium)
Hall, Veronica	Emergent BioSolutions Inc. (United Kingdom)
Hayward, Tara	SABIN (USA)
Jaffar, Shabbar	EDCTP, Chair Partnership Board (United Kingdom)
Janko, Christa	EDCTP, Private Sector Relations Coordinator (Austria)
Makanga, Michael	EDCTP, Director South-South Collaboration and Head of the Africa Office (South Africa)
Mathewson, Sophie	EDCTP, Networking Officer (The Netherlands)
Matthiessen, Line	Co-Chair, European Commission (Belgium)
Mgone, Charles	EDCTP, Executive Director (The Netherlands)
Niekerk, Sorika van	Quintiles Africa (South Africa)
Ogwal-Okeng, Jasper	EDCTP, Developing Countries Coordinating Committee – DCCC (Uganda)
Osseni, Raouf	Quintiles West Africa (Benin)
Perry, Mohammed	Johnson & Johnson/Janssen (United Kingdom)
Reinhard-Rupp, Jutta	Merck (Switzerland)
Saville, Melanie	Sanofi Pasteur (France)
Springsklee, Martin	Bayer (Germany)
Stoten, Adam	Oxford Emergent Tuberculosis Consortium Ltd (United Kingdom)
Ter-Minassian, Daniel	Sanofi (France)
Van de Klashorst, Gert Onne	EDCTP, Communications Officer (The Netherlands)
Venter, Johan	Quintiles Africa (South Africa)
Wang, Elaine	Boehringer-Ingelheim (USA)
Webster, Alison	GlaxoSmithKlein (United Kingdom)
Yammine, Mélanie	EFPIA (Belgium)

Colophon

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European & Developing Countries
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Author: Paul Chinnock
Editors: EDCTP Secretariat
Design: Sam Gobin, www.samgobin.nl

Correction note: the graph Figure 1 on page 9
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Europe Office

Postal address
P.O. Box 93015
2509 AA The Hague
The Netherlands

Visiting address
Laan van Nieuw Oost Indië 334
The Hague, The Netherlands

Phone +31 70 344 0880/0897
Fax +31 70 344 0899
E-mail info@edctp.org
Internet www.edctp.org

Africa Office

Postal address
P.O. Box 19070
Tygerberg 7505, Cape Town
South Africa

Visiting address
Francie van Zijl Drive, Parowvallei
Cape Town, South Africa
Phone +27 21 938 0819
Fax +27 21 938 0569

the 1990s, the number of people with a mental health problem has increased in the UK (Mental Health Act 1983, 1990).

There is a growing awareness of the need to improve the lives of people with mental health problems. The Department of Health (1999) has set out a vision of a new mental health system, which will be based on the following principles:

- (i) people with mental health problems should be treated as individuals, with their own needs and wishes;
- (ii) people with mental health problems should be given the opportunity to participate in decisions about their care and treatment;
- (iii) people with mental health problems should be given the opportunity to live in their own homes and communities.

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