



E D C T P

European & Developing Countries Clinical Trials Partnership

STAKEHOLDER MEETING

HEALTH RESEARCH ETHICS
AND
REGULATORY AFFAIRS

ANTWERP, BELGIUM
28-29 NOVEMBER 2013



Towards the second EDCTP programme

The EDCTP Stakeholder Meetings on Health Research Ethics and Regulatory Affairs are part of a series of thematic stakeholder meetings planned to contribute to the shaping of the strategy and funding approach of the second EDCTP programme. EDCTP has held further stakeholder meetings on HIV/AIDS, tuberculosis and other mycobacterial infections, malaria, and neglected infectious diseases. The Stakeholder Meeting on Capacity Development will take place in Berlin on 3 July 2014.

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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 16 European countries, the European Union and sub-Saharan African countries. The aim of the programme is to accelerate the development of new or improved drugs, vaccines, microbicides and diagnostics for 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 will start in 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.

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Acronyms and abbreviations

AMRH	African Medicines Regulatory Harmonisation initiative
AU	African Union
AVAREF	African Vaccine Regulatory Forum
CC&DW	Creative Consulting and Development Works
CERMES	Centre for Medical and Health Research
COPAB	Pan African Congress for Ethics and Bioethics
EDCTP	European & Developing Countries Clinical Trials Partnership
EDCTP ₂	second EDCTP programme
EMA	European Medicines Agency
GCP	Good Clinical Practice
GMP	Good Manufacturing Practice
H ₃ Africa	Human Heredity and Health in Africa (research programme)
IRB	institutional review board
ITM	Institute of Tropical Medicine, Belgium
KEMRI	Kenya Medical Research Institute
MARC	Mapping African Research Ethics and Drug Regulatory Capacity
NACCAP	Netherlands-Africa Partnership for Capacity Development and Clinical Interventions against Poverty-related Diseases
NEC	National Ethics Committee
NEPAD	New Partnership for Africa's Development
NRA	national regulatory authority
REC	research ethics committee
SAC	EDCTP Strategic Advisory Committee
TRREE	Training and Resources in Research Ethics Evaluation
UNESCO	United Nations Educational, Scientific and Cultural Organization
WHO	World Health Organization
WHO-AFRO	WHO African Regional Office

1. Executive summary

The EDCTP Stakeholder Meetings on Health Research Ethics and Regulatory Affairs were hosted by the Institute of Tropical Medicine (ITM) in Antwerp, Belgium, on 28 and 29 November 2013.

Health research ethics

The following expected outcomes had been set for the first day of the meeting:

- Review of the current status of ethics capacity in sub-Saharan Africa
- Results from an external evaluation of the EDCTP₁ ethics programme
- Identification of key ethics capacity gaps, opportunities and barriers to progress
- Recommendations that will contribute towards the EDCTP strategy for supporting ethics capacity development.

Dr Michael Makanga, EDCTP Director South-South Cooperation and Head of Africa Office, presented a brief overview of the programme's activities and achievements since its launch in 2003, with particular emphasis on ethics, going on to describe the expanded scope of the EDCTP₂ programme, which will begin in 2014. Seventy-five (75) ethics projects were funded, of which 53 are now complete. Activities have included training; establishment and strengthening of ethics capacity at institutional and national levels; and dynamic mapping of ethics capacity in Africa. Developing ethics capacity will remain one of the capacity development priorities in EDCTP₂.

Dr Odile Oukem-Boyer, Director of the Centre for Medical and Health Research (CERMES), Niger, gave the keynote address, in which she discussed the research ethics landscape over the last decade and considered the prospects for sub-Saharan Africa. There has been considerable growth in activity, of which she cited many examples, but it is unclear as to how effective and how

sustainable these various programmes will be. Many sub-Saharan African countries are still lagging behind in relation to research ethics activities. Her recommendations to EDCTP included: support a biennial summit of national bioethics advisory bodies; promote use of the Training and Resources in Research Ethics Evaluation (TRREE) online training tool; translate training materials into French and Portuguese and promote their use; expand the Mapping African Research Ethics Review Capacity (MARC) project and promote its use.

Discussion

Further recommendations were then made from the floor:

- Advocacy is needed to create greater awareness of ethical issues
- Effective quality controlled training with measurable impact is essential
- Ensure compliance with national legislation for institutional and national ethics structures
- Performance enhancement is needed to improve the quality and quantity of the work done by sub-Saharan Africa's research ethics committees (RECs)
- The aim must be universal coverage – all countries must have research ethics capabilities
- Devise ways to counter biopiracy
- Research ethics capability will only be sustained if there are financial contributions from within sub-Saharan Africa itself.

Prof. Anton van Niekerk, Stellenbosch University, presented a summary of the evaluation of EDCTP's ethics grants programme, conducted by Creative Consulting and Development Works (CC&DW), which analysed the achievements of the 75 EDCTP-funded ethics grants projects across sub-Saharan Africa. The findings fell into five areas: Mapping African Research Ethics and Drug Regulatory Capacity (MARC); promoting the establishment and strengthening of national ethics committees (NECs) and institutional review boards (IRBs); supporting ethics training

activities, including development of online training programmes; networking; and grant management. A series of recommendations was made in each area. Overall recommendations to EDCTP included:

- Recognise the uneven research ethics review capacity of African countries; determine where it is best for EDCTP to invest
- Foster existing relationships through continued support
- Determine how future funding arrangements will be made; ensure countries with weaker capacity are provided with support to write funding proposals
- For ethics committees with very limited capacity, it is important to support the grantee throughout the process, and provide them with seed funds rather than awarding large grants, which they may not have the capacity to administer
- Maintain a relationship with other donors and acquire an understanding of their focus and budgets, to help decide where EDCTP can best invest its money and minimise the potential for duplication of funding
- Expand EDCTP's strategic role in research ethics in Africa
- Conduct an evaluation to better understand the needs of researchers with regard to ethics.

Discussion

A far-ranging discussion followed this presentation; topics included:

- Many of the problems identified are not unique to Africa; they also affect RECs in Europe and elsewhere
- Collaboration with relevant organisations is essential for synergy and avoidance of duplication
- More work needs to be done to strengthen ethics capacities at national levels
- North-South 'partnership ethics' also require attention

- Training:
 - should not be too theoretical and should make use of case studies
 - should be assessed for quality
 - should include group training for committees and training of trainers
- The requirement to apply for EDCTP grants in English compromises the success rate of francophone and lusophone researchers
- Funding is usually provided for three years; however, this is too short; quality takes time and it takes a longer time to establish an ethics committee from scratch
- The legal position was not allowed for in the evaluation, but should in future be included
- Informed consent is a key issue. EDCTP should work with the private sector to make consent forms simpler
- Many fundamental aspects of research ethics (e.g. informed consent) need research to determine how people perceive the issues
- More information is needed on ethics procedures in different sub-Saharan African nations
- The issue of 'sovereignty' was raised; countries have a right to adopt different procedures, but a level of standardisation can be achieved without compromising sovereignty
- Genomics is anticipated to bring about a massive increase in complexity in ethical decision making
- A source of income is needed for the sustainability of ethics committees. A transparent mechanism for charging should be considered
- In determining the level of ethics committee performance, the time taken to complete the review of a protocol is an important consideration.

Prof. Dominique Sprumont, University of Neuchâtel, Switzerland, gave a presentation on online ethics training programmes and the standardisation of ethics training.

To maintain public confidence in research, education is needed that emphasises the importance of protecting participants in trials. Research ethics education programmes – to promote awareness and appreciation of human research protection issues – must be provided to members of research ethics committees and to all members of the research team, and must be included at the earliest possible stage of professional training. E-learning is not the only way forward, but offers many advantages; preferably, both online and onsite training should be used.

Prof. Sprumont went on to describe the TRREE training tool.

Dr Christiane Druml, Medical University of Vienna, gave a presentation entitled ‘Global Ethics Perspective’. Her focus was the need for research ethics review in sub-Saharan Africa, common structural errors, and ways to achieve harmonisation.

She outlined the three types of ethics committees: bioethics committees that advise government, research ethics committees that review research protocols, and clinical ethics committees that focus on individual cases. In many countries; however, there remains a lack of clarity as to ‘who does what’. She identified the following challenges: multiple review, maintaining standards of care, capacity building, fostering international cooperation, and avoiding the ‘brain drain’. She highlighted the following needs: improve the African-wide system, initial and continuing training for REC members (in English, French and Portuguese), and quotas for gender representation.

EDCTP should use its strength to maximise harmonisation in sub-Saharan Africa. It should cooperate with other international organisations and respect African cultural differences while maintaining an international focus.

Discussion

The remainder of the stakeholder meeting was devoted to contributions and discussions from the floor. Amongst the wide range of issues raised, the following emerged as being of particular importance:

- Harmonisation is key. It is not enough to establish separate ethics review projects. Harmonisation of ethics review terminology and standard operating procedures and guidelines are of particular importance. A consultative platform would help achieve harmonisation
- All countries must have appropriate legislation on health research ethics. A degree of standardisation should be aimed for, without compromising sovereignty. EDCTP may have a role to play, by working with the African Union (AU), for instance
- EDCTP should refocus its training support on countries with the greatest needs
- Training priorities include: identifying the right software and platforms for e-learning, training ethics committee administrators to help reduce delays, and embedding training within all projects. A balance of e-learning plus face-to-face training is required
- EDCTP should work towards greater flexibility in grants management and communication
- EDCTP should continue to collaborate with other organisations, such as WHO, to achieve synergies. It should support research ethics networks
- Sub-Saharan African countries themselves must take over programmes such as MARC and TRREE and ensure that they are sustained
- EDCTP should continue to evaluate and monitor progress in the ethics projects it supports (including training), and maintain its efforts to ensure the effectiveness of ethics committees.

In closing the ethics meeting, Prof. Mgone noted the enthusiastic level of participant engagement. EDCTP is already active in some of the areas mentioned and the additional suggestions made will be given serious attention.

Regulatory affairs

The following expected outcomes had been set for this meeting:

- Review of the current status of regulatory capacity in sub-Saharan Africa
- Identification of key regulatory capacity gaps, opportunities and barriers to progress
- Recommendations that will contribute towards the EDCTP strategy for supporting regulatory capacity development.

Dr Michael Makanga reminded participants of EDCTP's mission, objectives and scope, its achievements overall, and its activities in the area of regulatory affairs, listing a number of key achievements. He also outlined the recommendations made at the previous regulatory affairs stakeholder meeting (Geneva, 2007), before proceeding to discuss the forthcoming transition to EDCTP2.

Mr Lahouari Belgharbi, WHO, gave the keynote address. WHO activities include the pre-qualification service for vaccines and medicines, strengthening national regulatory authorities, and efforts to develop and sustain production. One concern is that, while vaccine demand continues to increase, the number of vaccine-producing countries is decreasing; Senegal is now the only African vaccine-producing country.

EDCTP and other funding organisations should focus on the following when considering where to make investments:

- Coordinate investment and support at three levels: global, regional and country

- Align strategically with regional and global initiatives
- Avoid duplication of efforts; seek to boost or fill gaps
- Provide support that can be integrated into existing institutional development plans developed by the national regulatory authorities (NRAs) that are monitored and supervised
- Focus investment on human resources, with an emphasis on staff who will remain on the project for at least five years
- Develop a roster of experts as mentors that can be used quickly and regularly to assist other programmes.

Of these, coordination and investment in people (particularly women) were emphasised as the most important.

A presentation on behalf of the New Partnership for Africa's Development (NEPAD) Agency was given by **Mr Gordon Katende Sematiko** of the National Drug Authority of Uganda.

His focus was on the African Medicines Regulatory Harmonisation (AMRH) initiative, established to support sub-Saharan African countries in improving public health by increasing access to good quality, safe and effective medical products and technologies. AMRH's main strategic directions are: regulatory capacity development; knowledge generation and leveraging; and governance, management and partnerships. Mr Sematiko outlined activities in all these areas and the planned move towards a more streamlined structure for the initiative.

Ms Emer Cooke, European Medicines Agency (EMA), gave a European perspective and described a range of activities taking place in Europe that might be relevant to capacity strengthening in sub-Saharan Africa. There are now opportunities to use Europe's best scientific resources to evaluate products that would not be used in Europe. She reviewed the types of training activities at EMA and the tools available; the

preferred EMA approach is to extend existing EU activities to non-EU regulators. She also referred to the EU's Article 58 which allows EMA's Committee for Medicinal Products for Human Use (CHMP) to give opinions on medicinal products for human use that are intended exclusively for markets outside the EU¹.

Discussion

The meeting was then opened to comments from the floor. A discussion took place on the need to be clear on 'what ethics does' and 'what regulatory does', which often varies between different settings. Clear boundaries on roles and responsibilities should always be defined; EDCTP, EMA and NEPAD could each assist in this process.

Improvements in management, coordination and communications were all seen to be needed in the area of regulatory affairs. The following actions by EDCTP were proposed:

- Provide financial support to build regulatory capacity; however, this also needs commitment from African governments
- Promote the agenda of the African Vaccine Regulatory Forum (AVAREF) and ensure that the tools developed for AVAREF are more widely used
- Support the training of administrators of regulatory committees
- Assist in the area of pharmacovigilance
- Find out what works in Africa.

Dr Samba Cor Sarr, Vice-Chair of the African Vaccine Regulatory Forum (AVAREF) described how AVAREF uses a network approach to stimulate progress towards regulatory harmonisation of clinical trials of vaccines and medicines in the WHO-AFRO region.

AVAREF has clearly defined the respective roles and responsibilities of RECs and National Regulatory Authorities (NRAs). Dr Sarr described

AVAREF's clinical trials applications process, and summed up the lessons learned from progress made so far. A high level of expertise and commitment exists in sub-Saharan African countries, and mutual recognition and acceptance of common challenges provide an incentive to create the space to work together. Capacity building activities provide a foundation for a path towards harmonisation and the design of 'authentic learning' opportunities. These activities should feed into institutional development plans.

Ms Christine Mathieu, speaking from her experience as a lawyer who negotiates contracts for the Clinical Trials Centre, University Hospitals Leuven, gave a European perspective on clinical trials sponsorship by academic and research institutions. Amongst the initiatives she described were the International Conference on Harmonization of technical requirements for registration of pharmaceuticals for human use, and European Directive 2001/20 EC(2), which seeks to clarify and harmonise existing legislation. Harmonisation has not been achieved within Europe; a failure to harmonise legislation reduces the number of trials that can take place and leads to many practical problems.

Dr Delva Shamley, University of Cape Town, continued the theme of clinical trials sponsorship by academic and research institutions. The sponsor of a clinical trial holds 'ultimate responsibility' for its initiation, management and financing, and must support the researcher to conduct rigorous research that meets international standards. Non-commercial sponsors face many challenges, including their duty to maintain good clinical practice (GCP), adequate monitoring and insurance cover. Conducting trials in resource-poor settings is becoming more complicated.

Needs identified by Dr Shamley included:

- A database of clinical trial insurance in sub-Saharan Africa (to compensate participants in case of harm)

¹ Article 58 of Regulation (EC) No 726/2004; see also EMA website www.ema.europa.eu (Article 58 Q&A)

- Defined internal and reciprocal monitoring systems
- Sharing of information on data management tools
- Better dialogue on the donor-sponsor relationship.

Discussion

Contributions from the floor responding to the two presentations on trials sponsorship by academic and research institutions included:

- The challenges faced by non-commercial sponsors, mainly due to inadequate funding, are considerable and more severe in Africa
- EDCTP should probably not become a sponsor of trials, but could help find sponsors, develop organisations to become sponsors and help them respond to challenges
- Other suggested ways in which EDCTP can help included:
 - Change legal status to become an association²
 - Ensure RECs check whether trial sponsors really are capable of taking on the role
 - Provide training in sponsorship
 - Act as a clearing house
 - Assist with the adoption of new technologies.

It was also noted that within the last few years there has been a proliferation of new initiatives. It is difficult to remain up to date with all of them and the lack of coordination is of concern.

Final discussion

The regulatory affairs meeting then proceeded to its final discussions. One of the co-Chairs, Dr Ofori-Anyinam, said that the priority areas identified for action, concerned:

- Pharmacovigilance
- Interface between ethics committees and regulatory bodies
- Management training
- Coordination and exchange of information
- Addressing the challenges of trial sponsorship.

Needs in other areas included:

- An insurance database for sub-Saharan Africa
- Better monitoring of capacity building
- Creation of awareness of regulatory needs at AU level.

Further observations were then made from the floor:

- EDCTP could, for example, confine its funding to countries with adequate ethics committees and NRAs
- AVAREF should be supported and its role extended; AVAREF can help find ways to strengthen the capacity of NRAs and ethics committees and to clarify their roles
- EDCTP could support the ethics programme of the AU's consolidated plan of action on science and technology
- EDCTP to create awareness of the importance of pharmacovigilance and the need for phase IV trials.

Participants were reminded that EDCTP works under the Horizon 2020 scientific programme and some of the suggestions fall outside what would be regarded by the EU Parliament as scientific research.

The co-Chairs concluded that important issues were raised, which trialists face every day. Thanking participants, Prof. Mgone said EDCTP's Strategic Advisory Committee would now consider all the recommendations made.

² It has since been decided that the implementation structure for EDCTP₂ will be an association under Dutch law.

2. Health research ethics

The EDCTP Stakeholder Meeting on Health Research Ethics was hosted by the Institute of Tropical Medicine in Antwerp, Belgium, on 28 November 2013 and was attended by 56 participants from research institutions, funders and international organisations.

Opening session

Prof. Bruno Gryseels, Director of the Institute of Tropical Medicine, Belgium, welcomed participants, noting that ethical considerations should be central in the planning of research. Informed consent is one ethical issue, but not the only one. Young researchers need ethical training and it is good that EDCTP is active in this area.

Prof. Charles Mgone, EDCTP Executive Director, thanked everyone for their attendance. The recommendations from the previous stakeholder meeting on research ethics, held in Geneva in 2007, had been followed by EDCTP ‘to the letter’; the contributions made in the current meeting would be taken equally seriously.

Dr Elizabeth Bukusi, of the Kenya Medical Research Institute (KEMRI), and co-Chair urged participants to get to know each other and contribute fully to the meeting, noting its four expected outcomes:

- Review of the current status of ethics capacity in sub-Saharan Africa
- Results from an external evaluation of the EDCTP₁ ethics programme
- Identification of key ethics capacity gaps, opportunities and barriers to progress
- Recommendations that will contribute towards the EDCTP strategy for supporting ethics capacity development with particular reference to:
 - Priority areas to address in ethics calls for proposals

- Areas of potential synergy with other ethics capacity strengthening initiatives.

Dr Michael Makanga, EDCTP Director South-South Cooperation and Head of Africa Office, presented a brief overview of the programme’s activities and achievements since its launch in 2003, with particular emphasis on ethics, going on to describe the expanded scope of the EDCTP₂ programme, which will begin in 2014.

Seventy-five (75) ethics projects were funded, of which 53 are now complete. No new calls for ethics projects were launched in 2012 or 2013, but developing ethics capacity will be a core part of EDCTP₂. EDCTP has supported ethics training³ in sub-Saharan Africa through:

- Development of online training programmes
- Funding courses on ethics through formal training courses, such as diplomas or certificates
- Projects with training components, such as GCP and human subjects protection training
- Establishment and strengthening of ethics capacity at both institutional and national levels with the objective of making these committees functional and independent
- Coordination and mapping of ethics and regulatory activities.

Dr Makanga listed the six recommendations on ethics that were made in Geneva (2007):

- High-quality ethics review of clinical research to be done by ethics committees in host countries
- Ethics review capacity to be strengthened in countries and areas where EDCTP supports clinical trials
- Support training and strengthen NEC/IRB infrastructure

³ See the EDCTP Project portfolio: http://www.edctp.org/fileadmin/documents/our_work/EDCTP_project_portfolio.pdf

- Open calls for proposals
- Collaboration where possible, to avoid duplication and add value
- Encourage applications from countries and geographical areas known to have inadequate ethics review capacity
- Dynamic mapping of existing and new ethics capacity, and of organisations involved in developing this capacity in sub-Saharan Africa.

Dr Odile Ouwe Missi Oukem-Boyer of the Centre for Medical and Health Research (CERMES), Niger, gave the keynote address, in which she discussed the research ethics landscape of the last decade, both globally and in sub-Saharan Africa.

In recent years there has been much activity in the area of research ethics. WHO's ethics and health initiative (2002) led to the establishment of the organisation's [Department of Ethics and Social Determinants](#) and the [UN Inter-Agency Committee on Bioethics](#). There have also been a number of relevant publications, conferences and workshops. Within Africa several continental, regional and local initiatives have been launched, including online courses and workshops. Nevertheless, many countries in Africa are still lagging behind in relation to research ethics activities.

Dr Oukem said it was unclear to what extent all these initiatives have been successful and whether they will be sustainable. Awareness has improved, but many areas still need attention, including legislation, and professionalisation of training for researchers and members of RECs. Without effective RECs, there is a danger that unethical research will take place. She called for 'universal coverage' of RECs and the establishment of an African accreditation body, which could be modelled on [FWA](#)⁴ or other successful collaborations.

Human Heredity and Health in Africa ([H3Africa](#)) is one research programme that poses many ethical challenges related to informed consent, community engagement, creation of cell lines, and the education of RECs on these complex issues. Such research creates issues for policy makers, researchers, RECs, NRAs, communities, and both funding and hosting nations.

Dr Oukem's suggestions to EDCTP included:

- Support a biennial summit of national bioethics advisory bodies
- Promote use of the [TRREE](#) online training tool
- Translate training materials into French and Portuguese and promote their use
- Support regional ethics committees
- Consider establishing an African accreditation body and a centralised registry
- Expand the Mapping African Research Ethics Review Capacity (MARC) project and promote its use⁵.

Discussion

- The quality and quantity of work done by sub-Saharan Africa's RECs must be improved; despite all the training courses, there are still too many delays. 'Performance enhancement' is the goal
- Bridging gaps between stakeholders is key; communities and REC members should be given assistance to understand technical issues
- Research ethics capability will only be sustained if there are financial contributions from within sub-Saharan Africa itself
- EDCTP needs to be aware of the ethical concern of biopiracy. When rich-country researchers take samples of local plants and patent them, poor countries lack the means to defend their rights.

⁴ Federal-wide Assurance for the Protection of Human Subjects

⁵ See www.researchethicsweb.org.

In her role as co-Chair, **Dr Abha Saxena** (WHO), identified the main issues emerging from the opening session as being the need for: advocacy to create greater awareness of ethical issues, legislation, training, an African regulatory body, and the achievement of universal coverage. There should be no ‘blanks’ on the map of Africa. She also noted that researchers should be required to obtain and retain written evidence of ethical approval of their studies, and to provide this when required.

Prof. Anton van Niekerk, Director of the Centre for Applied Ethics, Stellenbosch University, South Africa, presented a summary of the evaluation of EDCTP’s ethics grants programme, which was conducted by Creative Consulting and Development Works (CC&DW). Prof van Niekerk acted as the ethics technical expert during the evaluation.

In order to establish the impact of EDCTP’s support in strengthening ethics activities, CC&DW analysed the achievements of the 75 EDCTP-funded ethics grants projects across sub-Saharan Africa. The findings fell into five areas:

- Mapping African Research Ethics and Drug Regulatory Capacity (MARC)
- Promoting the establishment and strengthening of National Ethics Committees (NECs) and Institutional Review Boards (IRBs)
- Supporting ethics training activities, including development of online training programmes
- Networking
- Grant management.

A comprehensive series of recommendations was made in each area. CC&DW produced a series of overall recommendations to EDCTP:

- Recognise the uneven ethics capacity of African countries and determine where it is best for the programme to have a presence
- Foster existing relationships through continued support for high impact EDCTP₁ investments
- Determine how future funding arrangements will be made, to ensure that countries with weaker capacity are provided with support to write funding proposals that meet a competitive standard
- Should a proposal be accepted, make available continuing capacity and mentoring to ensure that the grantee is supported, to ensure they adhere to the rules, implement the grant according to the work plan, and meet reporting requirements
- Provide grantees from institutions with limited administrative and financial management capacity with seed funds, rather than large grants, which they may not have the capacity to administer
- Maintain a strategic relationship with other funders and acquire a good understanding of their focus and overall budgets, to help decide where EDCTP can best invest money and minimise the potential for duplication of funding
- Expand its strategic role in investment in ethics in Africa
- Support this strategy through increased internal human resource capacity and operational budget, plus regular evaluation
- Conduct an evaluation to better understand the needs of researchers with regard to ethics.

Discussion

- Many of the problems identified are not unique to Africa; they affect ethics committees in Europe and elsewhere
- As several organisations are now active in research ethics, care is needed to avoid duplication of efforts. Collaboration,

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- especially with WHO as an example, is essential and will create synergies
- More work needs to be done to strengthen ethics capacities at national levels in order to facilitate the establishment and monitoring of ethics committees, and the development of the guidelines necessary to achieve national harmonisation and consensus. Ethics review should be embedded within national research systems
 - ‘Partnership ethics’ also requires attention. This will require training on negotiation skills, intellectual property issues, and the principles of fair collaboration. African researchers often need advice on contractual matters. Forums for the discussion of case studies might be useful
 - Training is needed for individuals, but group training for committees is also important, as is the training of trainers. Training of trainers will address the gap between ethics committees and academia
 - Several speakers said the requirement to apply for EDCTP grants in English compromises the success rates of francophone and lusophone researchers. It was suggested that EDCTP should allow applications in French and hire translators. Alternatively, applications could be reviewed by French or Portuguese speakers. The cost of and accuracy of translations were discussed as potential challenges hampering effective review of applications that are not in English
 - It was noted that the National Institutes of Health (NIH) (USA) has so far provided most of the funding for health research ethics in sub-Saharan Africa. Funding for ethics projects is usually provided for 18 months to three years, but this is too short, as has already been found in Europe. Quality takes time and more time is needed to establish a new ethics committee
 - Training should not be too theoretical and should make use of case studies. Ideally, those receiving training should be taken on field trips immediately after their courses and encouraged to apply, in practice, the knowledge and skills acquired
 - The environment in which ethics committees work and the relevant laws that are in place have a big impact on their performance. It was noted that the legal position was not allowed for in the evaluation
 - Informed consent is a key issue. Consent forms are usually written by company lawyers and are not easily understood by participants and communities. It was recommended that EDCTP work with the private sector to make consent forms simpler and more comprehensible
 - Many fundamental aspects of research ethics (including informed consent) need more research to determine how people perceive the issues
 - Countries vary considerably in what they are doing and some have no ethics procedures in place at all. Empirical data is needed to establish what is happening in different sub-Saharan African countries
 - The issue of ‘sovereignty’ was raised; countries have a right to adopt different procedures, even though this can create complications when multi-site trials take place across borders. However, a level of standardisation can be achieved without compromising sovereignty
 - A source of income is needed to ensure the sustainability of ethics committees. A good transparent mechanism for charging could be considered
 - Genomics is anticipated to bring about a massive increase in complexity in ethical decision making. Advice may be available from elsewhere
 - In determining the ethics committee’s performance, the time taken to complete the review of a protocol is an important consideration
 - The need to facilitate joint ethics review of clinical trials proposal applications was emphasised. Several advantages were highlighted: the additional expertise can

improve quality, save time, avoid late occurring reviews and requests for change, and enhance capacity through knowledge sharing.

Commenting on the remarks made from the floor, Prof. van Niekerk said that – while some of the points raised fell outside the remit of the evaluation – he agreed with much that had been said, e.g. on the universality of some of the problems and the language barrier. There are advantages in a degree of standardisation in ethical guidelines; however, one size does not fit all. Researchers often distrust RECs so it is important that the committees themselves should be evaluated.

Summarising the discussions, the co-Chair considered the following to be of particular importance:

- The legislative framework should be included in future evaluations
- Training is often needed on specific issues
- The quality of training can be hard to assess
- A global expert pool for advice could be established, without compromising sovereignty of individual countries in decision making
- Online discussion forums could also provide useful support
- The advantages and disadvantages of joint reviews should be investigated further and experiences with this approach shared
- Decisions are required as to whether EDCTP should fund national ethics committees, and research into ethics itself.

Afternoon session

Prof. Dominique Sprumont, Institut de Droit de la Santé, Université de Neuchâtel, Switzerland, gave a presentation on online ethics training programmes and the standardisation of ethics training. Research ethics is a

complex issue involving many stakeholders. Many e-learning programmes are now available, making it hard to make the appropriate choice. A workshop was held in Hermance, Switzerland, in January 2013 to begin the process of establishing standards for e-learning programmes. This led to publication of a paper on consensus standards.⁶

It was agreed at the workshop that, to maintain public confidence in research, education is needed that emphasises the importance of protecting clinical trial participants. Research ethics education programmes must be provided to promote awareness and appreciation of human research protection to members of research ethics committees and to all members of the research team, and must be included at the earliest possible stage of professional training. Training should deal with all forms of research involving humans. E-learning is not the only way forward, but offers many advantages; preferably, both online and onsite training should be used.

The workshop produced recommendations on: developer/provider qualifications, learning goals, learning objectives, and content for introductory e-learning courses. Methods and training materials should be in line with learning objectives, and take into account technical restraints, such as low bandwidth. Participants should be provided with references and online resources for further study. Courses should include an assessment of the course. Course providers should seek recognition of the course for continuing professional development credit.

The rest of Prof. Sprumont's presentation focussed on the development of the Training and Resources in Research Ethics Evaluation ([TRREE](#)) training tool. TRREE is collaborative, collegial and multi-directional (North–South, South–North, South–South, North–North). It

⁶ Williams JR, Sprumont D, Hirtle M, et al. 2013. J Med Ethics. Epub ahead of print. doi:10.1136/medethics-2013-101572.

reflects African and European perspectives within an international vision, and is based on universal ethical and legal principles. TRREE has been online since 2009. As of November 2013, over 25,000 participants have registered and nearly 9,000 have completed the course. New countries continue to join, and new modules and new languages are being added. Plans for the future include development, with AVAREF, of a new set of e-learning tools relating to regulation in the field of vaccines and other medicinal products. TRREE, in collaboration with AVAREF, is expanding to include training on regulatory affairs. It was noted that the GCP courses are more popular than ethics since GCP is demanded by regulators.

Dr Christiane Druml, Medical University of Vienna, gave a presentation on the global ethics perspective. She said she would focus on the need for ethical review in sub-Saharan Africa, highlight common structural errors, and suggest ways to achieve harmonisation. Principles should always lead the way; we must not delay new research, but we must protect those involved. Coordination and strengthening of the ethics and regulatory environment within sub-Saharan Africa is already a core part of EDCTP's activities, but more needs to be done.

There are three types of ethics committees: bioethics committees that advise government, research ethics committees (including IRBs) that review research protocols, and clinical ethics committees that focus on individual cases, (e.g. end-of-life decisions, organ allocation). In many countries there remains a lack of clarity as to 'who does what'. Dr Druml traced the history of health research ethics, noting such landmarks as the Nuremberg Code (1947) and the 'birth of the ethics committee' with the First Amendment of the Declaration of Helsinki (1975). She also noted the establishment of the European Group on Ethics in Science and New Technologies⁷ which considers ethical

aspects of clinical research in developing countries and aims to provide advice to the European Commission on the ethical aspects of implementing EU-funded research activities in countries which differ culturally or economically from Western Europe.

Challenges that have emerged include: multiple review, maintaining standards of care, capacity building, fostering international cooperation, and avoiding the 'brain drain'. She highlighted the following needs: to improve the African-wide system, initial and continuing training for ethics committee members (in English, French and Portuguese), and establishing quotas for gender representation. Sub-Saharan Africa can learn from what has been done elsewhere, including from the deficiencies in the European system.

She concluded with the following 'take-home messages':

- Use EDCTP's strength to maximise harmonisation in sub-Saharan Africa
- Cooperate with other international organisations (e.g. NIH, UNESCO and WHO *inter alia*) to profit from their systems
- Respect African cultural differences, but maintain an international focus.

Comments and recommendations

The remainder of the ethics stakeholder meeting was devoted to comments and recommendations.

- Ethics committees must consider both the science and the ethics of a research proposal. This is never ideal. Some participants were concerned that ethics review could 'compromise scientific freedom'. Others disagreed with this view

⁷ http://ec.europa.eu/bepa/european-group-ethics/welcome/index_en.htm

- The AU is the right political platform to push legislation on ethical review, so that all countries have the necessary laws in place
- It must be noted that ethics committees have to review all research proposals involving human participants, not just clinical trials
- Avoiding harm is central; social as well as physical risks should be considered. Clinical trials may disrupt existing routine health care systems in some settings; the wider impact of a trial should be allowed for in the review process and reflected in training programmes
- Human and animal researchers should collaborate more. A 'Pan-African Centre for Disease Control' is needed with both human and animal infections within its remit
- Doubts were expressed about the long-term sustainability of MARC, TRREE and other projects. Many initiatives that had been performing well have now been lost. Sub-Saharan African countries themselves must take over these programmes and ensure that they are maintained
- Research is required on research ethics (such as issues around informed consent)
- As a funding strategy, EDCTP could concentrate on national leading institutions rather than distributing its funding over several institutional review boards.
- Monitor ethics committee performance and train committee members
- Support training of ethics committee administrators
- Refocus training on countries with the greatest needs
- Network support
- Support African participation in global efforts
- Support regional ethics governance structures
- Flexibility in grants management and communication
- Reduce language barriers by considering to accept proposal applications in all three EDCTP official languages
- Develop synergy with others in the field
- Ensure sustainability
- Establish legal frameworks through engagement with the AU
- Mapping of ethics review capacity
- Launch a consulting platform with a view to achieving harmonisation.

Discussion then continued, focusing on the following areas.

Training

- Priorities include: identifying the right software and establishing new platforms for e-learning, training ethics committee administrators to help reduce delays, and embedding training within all projects (so that those trained can use their skills in subsequent studies)
- Focus on training a cadre of trainers in each country, to ensure sustainability, and empowering countries to develop their own capacities
- A balance between e-learning and face-to-face training (including case studies) is needed; those who can access face-to-face training should use it

Co-Chair **Dr Elizabeth Bukusi** closed the first part of the afternoon discussions, noting that the need for harmonisation had emerged as a key issue – it was not enough to establish separate ethics review projects. Ethical language harmonisation, including terminology used, standard operating procedures and guidelines, is of particular importance.

Co-Chair **Dr Abha Saxena** introduced the final discussions by highlighting some of the needs identified so far:

- Members of initiatives, such as the UNESCO bioethics committees, might be able to help in some aspects of training
- EDCTP should consider funding students to attend courses already in operation
- US training programmes should be considered, but only adopted if considered relevant for sub-Saharan Africa
- New issues, such as genomics, will create a need for specialist training.

Monitoring and evaluation

- Criteria should be agreed to determine whether training courses are successful, i.e. do trained staff members employ their skills effectively?
- EDCTP should ensure that the ethics training programmes it supports are quality controlled by external bodies
- Overall time to approval was proposed as one measure of ethics committee efficiency. However, it should not be the only indicator. Support the development of indicators to assess functionality of Research Ethics Committees (i.e. assessment of independence, transparency, expertise, efficiency, relevance, etc.).

Network support

- Current useful informal networking between ethics committees should be encouraged
- Some participants feared that networking could cause further delays in ethical approval. Others argued against this view saying it would concern general issues, not individual proposals
- EDCTP could consider supporting national forums where ethics committees and others are brought together and priorities identified.

African participation in global efforts

No strong views were expressed as to whether EDCTP should provide support in this area. There were no objections, but it did not emerge as a priority. It was noted that the costs involved in attending global summits, for example, are significant.

Flexibility on grants management and communications

- The duration of grants for ethics projects should be reviewed, but while the duration of the grant may be increased, the aim must still be cost effective execution and sustainability
- In deciding how much should be given to support an ethics committee, allowance should be made for individual circumstances, avoiding a restrictive approach
- EDCTP could consider supporting training for French and Portuguese speakers in completing application forms, or consider funding the translation of the forms (and of the documents applicants must read in order to complete the forms).

Legal frameworks

- Legal and ethical frameworks should be considered concurrently – one influences the other. In order to establish the guidelines that are needed, EDCTP should collaborate with the AU, regional economic communities and non-governmental organisations. Advocacy is important
- Support establishment of independent ‘governing bodies’ operating within legal frameworks to regulate good practice within research ethics committees, improve minimum standards, and move towards accreditation
- Some participants called for a basic set of laws to be introduced across Africa, but concerns was expressed that the stakeholder

meeting should not make specific legal recommendations, but advise instead whether EDCTP should involve itself in this area. Once a country adopts a convention it should move towards passing a new law. This can be difficult and EDCTP could perhaps offer help.

Consulting platforms and harmonisation of efforts

- Sometimes local ethics committees are ‘pushed around’ by the ethics committee of a big international research institute or funding agency; a platform could help achieve a fairer situation
- Support establishment of closed forums for discussion of complex ethical issues on research projects being evaluated by more than one ethics committee, and for sharing of ethics comments on multi-country projects
- Support joint reviews of complex and high risk trials learning from the DNIDA experience
- When bringing experts together, EDCTP should ensure that it is not just the academic community that is involved.

Other

- Ethics governance structures in H3Africa projects will be important, but other funders are looking into the issue, so EDCTP may not have to include this in the list of priorities
- EDCTP may not need to provide ethics support at an international level, but it should explore ways of working with, for instance, WHO, UNICEF and UNESCO among other players within individual countries
- The declaration of the UN convention on biodiversity clashes with current rules on intellectual property - EDCTP should involve itself here.

Conclusion

Prof. Mgone concluded the ethics stakeholder meeting, noting that some of what had been recommended could be implemented immediately, in collaboration with EDCTP’s partners, as EDCTP was already active in this area. “Some things are in the kitchen, some are already in the pot.” Other activities proposed would take more time to reach fruition.

Networking and synergy was mentioned by many participants, which was very much in line with EDCTP policy and practice. Prof. Mgone thanked all those present for their exceptional level of engagement, and particularly thanked Dr Odile Oukem, the Chairs and EDCTP staff involved in organising the stakeholder meeting.

3. Regulatory affairs

The EDCTP Stakeholder Meeting on Regulatory Affairs was hosted by the Institute of Tropical Medicine in Antwerp, Belgium on 29 November 2014 and was attended by approximately 57 participants from research institutions, the pharmaceutical industry, national and international regulatory bodies and international organisations.

Opening addresses

Prof. Bruno Gryseels, Director of the Institute of Tropical Medicine, welcomed all those present. Clinical trials, he said, are different from other studies in many respects and permission to run a trial brings with it great responsibility for the health of the volunteers. Clinical trials pose many difficult questions, including whether regulations restrict scientific enquiry. A clinical trial involves many stakeholders, who must understand each other and know their respective roles. He anticipated that many of these issues would be discussed during the meeting.

Prof. Charles Mgone, EDCTP Executive Director, thanked participants for coming and for their attendance. The views of regulators, as delivered at the stakeholder meeting in Geneva (2007), had helped shape the first stage of the EDCTP programme and now input for EDCTP2 was being sought.

The co-Chairs of the meeting introduced themselves – **Prof. Christian Burri** is Head of Medicines Research at the Swiss Tropical Institute, and **Dr Opokua Ofori-Anyinam** is a Director of Global Clinical Development at GSK Vaccines (Belgium). They stressed that it is not possible for EDCTP to solve all the problems that surround regulatory affairs; the meeting therefore should seek to be practical. They reminded participants of the expected outcomes of the meeting:

- Review of the current status of regulatory capacity in sub-Saharan Africa
- Identification of key regulatory capacity gaps, opportunities and barriers to progress
- Recommendations that will contribute towards the EDCTP strategy for supporting regulatory capacity development with a particular focus on:
 - Regulatory activities to prioritise for future funding
 - Areas of potential synergy with other regulatory capacity strengthening initiatives.

Dr Michael Makanga, EDCTP Director South-South Cooperation and Head of Africa Office, reminded participants of EDCTP's mission, objectives and scope; its achievements overall (including the grants scheme, the work supported so far, and the establishment of the Networks of Excellence); and its activities in the area of regulatory affairs.

The regulatory affairs stakeholder meeting in Geneva (2007) recommended the following:

- Work with WHO and other partners in the implementation of the priority regulatory activities in sub-Saharan Africa
- Develop a strategic approach to facilitate regulatory capacity alignment, including mapping of regulatory capacity
- Support training and systems development in pharmacovigilance and in drug safety monitoring and evaluation
- Establish joint training and dialogue between stakeholders
- Develop self-assessment tools for national regulatory authorities
- Develop systems for situation analysis and mapping of capacity
- Explore ways of expanding the WHO database to enable ready sharing of information and cross-cutting activities.

EDCTP's activities regarding regulatory affairs have been implemented through collaboration with WHO. Support has been provided for the assessment and capacity strengthening of the national regulatory environment of various sub-Saharan African countries, leading to the following key achievements:

- EDCTP and NACCAP⁸ funding led to the formation of the African Vaccine Regulators Forum (AVAREF)
- Training of regulators and members of ethics committees from eight sub-Saharan African countries on clinical trials authorisation
- Training on vaccine quality, GCP and site inspection for regulators from ten countries.

Dr Makanga went on to discuss the transition to EDCTP2; stakeholder meetings such as this one play an important part in the process, especially in drawing up the strategic and operational business plans and the work programme.

Mr Lahouari Belgharbi, WHO, gave the meeting's keynote address, beginning with the background and history of WHO's work on regulatory matters since 1996. WHO activities include the prequalification service for vaccines and medicines, which (though not very well known) assists over 120 countries. WHO also seeks to strengthen national regulatory authorities (NRAs); activities here began with training, as the human factor is important. Efforts to develop and sustain production also form part of WHO's work in this field. The keynote address focused on three areas, namely, market authorisation, pharmacovigilance and clinical trials.

One concern noted by Mr Belgharbi is that, while vaccine demand continues to increase,

the number of producing countries decreases. Africa needs well regulated production, but Senegal (where there is a prequalified vaccine) is the only African country that is still producing vaccines. There used to be 12 African vaccine-producing countries. Maintaining production in Senegal is therefore very important.

He went on to discuss WHO activities in more detail, listing the various strengths and gaps that have been identified. He highlighted the following challenges:

- Competing agendas for timing and priorities
- Actions are not globally coordinated to ensure coherence and effectiveness of investment
- Critical resources are not strategically aligned
- Not all partners are aware of what is happening
- Fatigue and poor institutional memory: potential for wasted resources and duplicated efforts
- Monitoring by WHO is essential and must continue. However, WHO has no budget for these activities and relies on EDCTP and other funders. For example, EDCTP has funded planning workshops and meetings for African vaccine regulators.

It was recommended that EDCTP and other funding organisations focus on the following items when considering where to make investments:

- Coordinate investment and support at three levels: global, regional and country
- Align strategically with regional and global initiatives
- Avoid duplication of efforts; seek to boost initiatives or fill gaps
- Provide support that can be integrated into existing plans that are monitored and supervised

⁸ Netherlands-Africa Partnership for Capacity Development and Clinical Interventions against Poverty-related Diseases.

- Focus investment on human resources with emphasis on staff who will remain on the project for at least five years
- Develop a roster of experts as mentors who can be used quickly and regularly to assist other programmes.

In summing up, he emphasised the need for coordination and the importance of investment in human resources, particularly women. The high rate of staff attrition is of great concern and requires urgent attention.

A presentation on, ‘The African regulators’ perspective’, was then given on behalf of the NEPAD Agency by **Mr Gordon Katende Sematiko** of the National Drug Authority of Uganda. His focus was on the African Medicines Regulatory Harmonisation (AMRH) initiative, established to support sub-Saharan African countries in improving public health by increasing access to good quality, safe and effective medical products and technologies.

AMRH creates a platform on which to build sub-Saharan Africa’s regulatory capacity; 85% of sub-Saharan Africa (70% by population) is now covered in the process and the regional economic communities are among the major stakeholders. The main strategic directions are:

- Regulatory capacity development
- Knowledge generation and leveraging
- Governance, management and partnerships.

Mr Sematiko outlined activities in all these areas and described the planned move towards a more streamlined structure for AMRH.

Ms Emer Cooke of the European Medicines Agency (EMA) gave a European perspective on strengthening regulatory capacity in sub-Saharan Africa. She outlined the respective roles of the EMA and the European Medicines Regulatory Network. She described a range of

activities taking place in Europe that might be relevant to capacity strengthening in sub-Saharan Africa, saying there were now opportunities to employ Europe’s best scientific resources to evaluate products that would not be used in Europe. She reviewed the types of training activities at EMA and the tools available. Also mentioned were the Paediatric Medicines Regulatory Network, pharmacovigilance inspector training activities, GCP workshops, and support for capacity building organised by third-party organisations.

She referred to the EU’s [Article 58](#) which allows the Committee for Medicinal Products for Human Use (CHMP) to give opinions on medicinal products for human use intended exclusively for markets outside the EU. Article 58 provides, she said, a valuable tool for capacity building⁹.

EMA seeks to extend existing EU activities to non-EU regulators where possible, but it does not provide funding to enable non-EU regulators to travel. There is significant scientific experience within EMA and its networks, which could potentially be used. Resources are limited, however, and EMA needs to improve its understanding of the needs of non-EU regulators.

Discussion

- EDCTP can learn a lot from EMA, particularly with regard to the conduct of clinical trials. It was noted, however, that legal barriers prevent EMA from sharing its inspection reports
- The ethical issues that arise in trial registration, which are dealt with by ethics committees, are different from those arising in regulatory affairs. A discussion took place on the need to be clear and distinguish between ‘what ethics does’

⁹ Article 58 of Regulation (EC) No 726/2004; see also EMA website www.ema.europa.eu (Article 58 Q&A)

and ‘what regulatory does’, as this varies in different settings. There seem to be different approaches in Anglophone and Francophone countries. Clear boundaries on roles and responsibilities should be defined, but in practice there are often grey areas. This is an issue for EDCTP to address in some way; for example it could facilitate training and ethics–regulatory discussions in order to create model guidelines and document best practices. EDCTP could potentially help individuals clarify the roles of their respective bodies. The NEPAD Agency could assist by making recommendations; however, this would not be mandatory

- EDCTP’s role is to provide financial support to build capacity, but this also needs commitment from African governments. EDCTP should obtain clarity from organisations like the AU and NEPAD Agency as to the needs for capacity building, and continue to work closely with WHO, for example
- EDCTP could do more to promote the agenda of AVAREF and ensure that the tools developed for AVAREF are more widely used
- EDCTP should support the training of administrators for regulatory and ethics projects – they cannot do an efficient job if they do not understand the science and the issues. Their training should be practical. An online information system would enable them to obtain advice from experts
- After some discussion, it was agreed that EDCTP should assist in the area of pharmacovigilance, which is very weak in Africa and must be improved.¹⁰ Most health ministries have departments with pharmacovigilance responsibilities, but often nothing is recorded and no action taken when problems arise at local level. EDCTP already intends to support phase IV trials that address the issue of pharma-

covigilance. EDCTP should also engage in advocacy emphasising the importance of pharmacovigilance, determine the relevant parties in individual countries and bring them together. It could support the training needed to enable recognition of adverse reaction signals. Cross-border collaboration is important; perhaps EDCTP could help meet transport costs

- EDCTP could support national regulatory authorities where drug registration is still paper-based and more advanced electronic systems are needed. Pharmacovigilance must also be improved. Most training materials are only in English – new materials and training courses are needed and again EDCTP could help.

Co-Chair **Dr Ofori-Anyinam** noted that the meeting had not discussed whether there was a role for EDCTP in market authorisation, i.e. speeding up access to new drugs. In her view a priority for EDCTP was to find out what works *in Africa*.

Co-Chair **Prof. Christian Burri** said the issues which had stood out most in the morning’s discussions were pharmacovigilance, and the need for better management, coordination and communication.

Afternoon session

Dr Samba Cor Sarr, vice Chair of the African Vaccine Regulatory Forum (AVAREF) and from the Senegal National Health Research Council, opened the afternoon session. Launched in 2006, AVAREF uses a network approach to stimulate progress towards regulatory harmonisation of clinical trials of vaccines and medicines in the WHO-AFRO region. Capacity building is seen as a priority. Twenty (20) African countries are now AVAREF members, with three others under consideration. A range

¹⁰ This issue was the subject of a previous stakeholder meeting: ‘Post-Registration Medicinal Products Safety Monitoring in sub-Saharan Africa’.

of international partners support the initiative. AVAREF's website and all its meetings are trilingual. The respective roles and responsibilities of ethics committees and NRAs have been defined as follows.

- Ethics committees: review and approve human research studies, audit sites to ensure compliance with good clinical practice/good clinical laboratory practice (GCP/GCLP), and review data
- NRAs: review clinical trial applications for products for use in humans, approve importation of medicinal products for use in humans, inspect manufacturing facilities to ensure compliance with good manufacturing practice (GMP), review common technical documents, provide market approval, and ensure post-marketing surveillance.

Dr Sarr went on to describe the review process for clinical trial applications in more detail. Many lessons were learned from the progress made so far including:

- A high level of expertise and commitment exists in sub-Saharan African countries
- Mutual recognition and acceptance of common challenges provides an incentive to work together
- Capacity building activities provide a foundation for a path towards harmonisation and the design of 'authentic learning' opportunities. These activities should feed into institutional development plans
- Increasing ownership by countries has been achieved, as signalled by their confidence to identify and propose future joint initiatives.

Ms Christine Mathieu, speaking from her experience as a lawyer who negotiates contracts for the Clinical Trials Centre, University Hospitals Leuven, gave a European perspective on clinical trials sponsorship by academic and research institutions.

She referred to the European Directive 2001/20.EC(2) which seeks to clarify and harmonise existing legislation. Harmonisation has not; however, been achieved within Europe; national legislations vary in many respects. A failure to harmonise legislation reduces the number of trials that can take place and leads to many problems at the level of daily practice: for example, the costs and administrative burden are high, there are different obligations regarding insurance, and different approaches on the issue of privacy.

Key changes to regulations have recently been proposed that will be GCP-based; the aim is to streamline. Timelines have been set for their introduction. Harmonisation therefore presents both a challenge and an opportunity.

Dr Delva Shamley, University of Cape Town, continued with the theme of clinical trials sponsorship by academic and research institutions. It is widely accepted that the sponsor of a clinical trial holds 'ultimate responsibility' for its initiation, management and financing, and must support the independent researcher to achieve rigorous research of an international standard. There are challenges in the regulatory oversight of North-South collaborative research: multiple (or absent) regulatory/ethics procedures, varying levels of regulatory 'stringency', and varying approval times. A focus on procedural requirements can lead to a neglect of ethical issues. Dr Shamley spoke of the challenges non-commercial sponsors face including their duty to maintain good clinical practice, adequate monitoring and trial insurance cover, plus additional context-related challenges. Limited sponsor infrastructure often means either expensive outsourcing or gaps in the quality system. She called for adapted approaches and tools for ensuring full protection of participants and populations and compliance with research standards. Dr Shamley identified the following needs:

- Turn capacity development programmes into practice
- Establish a database of clinical trial insurance in sub-Saharan Africa, to compensate participants in case of harm
- Define and agree on internal and reciprocal monitoring systems
- Share information on data management tools
- Develop an improved donor-sponsor relationship dialogue.

Running trials in resource poor settings is here to stay, but it is becoming more complicated. Sponsors and funders should work more closely together.

Comments and recommendations

There were contributions from the floor responding to the two presentations on clinical trial sponsorship by academic and research institutions.

- We are seeing a proliferation of initiatives in the area of regulatory affairs. It is difficult to keep up to date with them all – who should coordinate them?
- Finding non-commercial clinical trials sponsors is a bottleneck. Most European centres do not have the capability to be sponsors and the problems faced in Africa are bigger. Inadequate funding is the problem
- Many African countries are moving towards national health insurance. This should be taken into account in setting up trial insurance
- It is probably best that EDCTP does not become a sponsor of trials. However, it could find sponsors, develop organisations to become sponsors, and help them respond to challenges, such as new and existing regulations and directives

- Other suggested ways in which EDCTP can help included:
 - Change its legal status to become an association (Note: already decided). Ensure that ethics committees and NRAs check whether intending trial sponsors really are capable of taking on the role. Alternatively, EDCTP could commission independent auditing of prospective clinical trial sponsors
 - Support training in sponsorship on a continuous and sustainable basis
 - Act as a clearing house, particularly in the areas of training, pharmacovigilance, and the identification and introduction of new technologies.
- AVAREF was praised by several participants, who inquired as to how it developed its procedures. Dr Sarr explained that there were three working groups that examined issues, such as protocol submission and funding. AVAREF is an advisory body that allows sovereignty to be preserved
- The Global Health Network provides free training and resources that could benefit EDCTP partners and help them address some of the issues discussed in this meeting
- The Chairperson of the Pan African Congress for Ethics and Bioethics (COPAB) expressed an interest in working closely with EDCTP, and reported that COPAB is working on a legal framework endorsed by the AU.

Final discussion

Dr Ofori-Anyinam (co-Chair) grouped the needs that had emerged under the following areas:

Pharmacovigilance: improve outcome reporting; strengthen passive reporting; strengthen

targeted approaches; develop electronic systems.

The ethics–regulatory interface: clarify respective roles and responsibilities and eliminate grey zones; map the ethics committee/NRA legal framework.

Management training: basic training for scientists in project management; advanced training for project managers and administrators; basic and advanced training in accounting and finances; training on the legal framework; training for regulators.

Coordination and exchange: funding of regulatory mentorship activities and coordination with EMA or other first-tier NRA capacity building, establish cross-border exchange mechanisms (South-South).

Trial sponsorship: addressing the challenges faced by sponsors; training applicants in sponsorship.

Other: create an insurance database for sub-Saharan Africa; monitor capacity building; ensure sustainable funding for the Pan-African Clinical Trials Registry (PACTR); create awareness of regulatory needs at AU level; EDCTP should discuss the impact of the adapted EU trial directive; how to coordinate and communicate between the many new initiatives.

Additional observations were then made from the floor:

- AVAREF should be supported and its role extended; AVAREF can help find ways to strengthen the capacity of NRAs and ethics committees and to clarify their roles
- EDCTP should create awareness of the importance of pharmacovigilance and the need for phase IV trials. Participants were asked to remember that EDCTP works under the Horizon 2020 scientific

programme; some of the suggestions made in this meeting may fall outside of what would be regarded by the EU Parliament as scientific research. EDCTP, in consultation with the Strategic Advisory Committee (SAC), should decide what should be implemented. Other agencies, such as WHO, may be more appropriate to implement some of the items listed.

Final remarks

Prof. Christian Burri (co-Chair) said that the meeting had discussed issues that frustrate trialists. Many of these frustrations, for example delays attributed to the review of clinical trials protocol applications, are more severe in Africa. Nevertheless, it is encouraging to learn that they are receiving much warranted attention.

Prof. Mgone thanked everyone for their contributions, in particular the co-Chairs. Prof. Gryseels is one of the founders of the EDCTP programme and the meeting benefited greatly from his input. EDCTP's SAC will now consider all of the recommendations made. The SAC will determine what is within the programme's scope and what can be realistically achieved, working with partners, as appropriate.

Prof. Gryseels expressed his pleasure that ITM was able to contribute by hosting a meeting addressing issues that ITM trialists confront every day. His final suggestion was that EDCTP should talk more to Europe's development ministers, who have so far contributed little in this area.

Annex 1. List of participants of the Stakeholder Meeting on Health Research Ethics

Name	Institution	Country
Akkoyun, Akin	Projekträger im Deutschen Zentrum für Luft- und Raumfahrt e.V. (PT_DLR)	Germany
Aseffa, Abraham	Armauer Hansen Research Institute (AHRI)	Ethiopia
Becker, Loren	Global Health Technologies Coalition at PATH	United States
Berkis, Uldis	Study and Research Administration	Latvia
Breugelmans, Gabrielle	EDCTP	Netherlands
Bompart, François	EFPIA/Sanofi	France
Bukusi, Elizabeth	Kenya Medical Research Institute	Kenya
Burri, Christian	Swiss Tropical and Public Health Institute	Switzerland
Buvé, Anne	Prince Leopold Institute of Tropical Medicine (ITM)	Belgium
Chinnock, Paul	EDCTP	United Kingdom
Desclaux, Alice	Institut de Recherche pour le développement (IRD)	France
Dieye, Alioune	Institut Pasteur Dakar	Senegal
Effa, Pierre	Pan African Congress for Ethics and Bioethics (COPAB)	Cameroon
Fakier, Nuraan	EDCTP	South Africa
Gryseels, Bruno	Prince Leopold Institute of Tropical Medicine (ITM)	Belgium
Hirsch, Francois	French National Alliance for Life and Health	France
Hoogervorst, Suzanne	EDCTP	Netherlands
Ijsselmuiden, Carel	COHRED	Switzerland
Kone, Bather	African Union Commission	Nigeria
Kruger, Mariana	Stellenbosch University	South Africa
Liquori O'Neil, Alessandra	United Nations Interregional Crime and Justice Research Institute	Italy
Little, Katherine	Wellcome Trust	United Kingdom
Makanga, Michael	EDCTP	South Africa
Mazarati, Jean-Baptiste	Rwanda Biomedical Center	Rwanda
Mbacham, Wilfred	University of Yaounde	Cameroon
Mgone, Charles	EDCTP	Netherlands
Mokgatla-Moipolai, Boitumelo	COHRED	Botswana
Ndebele, Paul	Medical Research Council of Zimbabwe (MRCZ)	Zimbabwe
Nyika, Aceme	Public Health Projects in Africa (PHPAfrica)	Zimbabwe
Nyirenda, Thomas	EDCTP	South Africa
Ofori-Anyinam, Opokua	GSK	Belgium

Olesen, Ole	EDCTP	Netherlands
Otim Onapa, Maxwell	Uganda National Council for Science and Technology (UNCST)	Uganda
Ouwe Missi Oukem, Odile	CERMES	Niger
Pandya, Lara	EDCTP	Netherlands
Peeters, Koen	Prince Leopold Institute of Tropical Medicine (ITM)	Belgium
Pereira, Daniela	EDCTP	Netherlands
Pinxten, Wim	Prince Leopold Institute of Tropical Medicine (ITM)	Belgium
Ravinetto, Raffaella	Prince Leopold Institute of Tropical Medicine (ITM)	Belgium
Sarr, Samba Cor	Senegal National Health Research Council (Conseil National pour la Recherche en Sante - CNRS)	Senegal
Saxena, Abha	WHO	Switzerland
Shamley, Delva	University of Cape Town	South Africa
Sikwese, Kenly	African Community Advisory Board (AFROCAB)	Zambia
Solbakk, Jan Helge	University of Oslo	Norway
Sprumont, Dominique	Institute of Health Law, TRREE, University of Neuchâtel	Switzerland
Strub Wourgaft, Nathalie	Drugs for Neglected Diseases Initiative (DNDi)	Switzerland
Tangwa, Godfrey	Cameroon Bioethics Initiative (CAMBIN)	Cameroon
Toure, Aissatou	Institut Pasteur de Dakar	Senegal
Van Loggerenberg, Francois	The Global Health Network, The University of Oxford	United Kingdom
Van Niekerk, Anton	Stellenbosch University	South Africa
Verdonck, Tine	Prince Leopold Institute of Tropical Medicine (ITM)	Belgium
Verellen, Jef	Prince Leopold Institute of Tropical Medicine (ITM)	Belgium
Verlinden, Ann	Prince Leopold Institute of Tropical Medicine (ITM)	Belgium
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Wassenaar, Douglas	University of KwaZulu-Natal	South Africa
Yammine, Melanie	EFPIA	Belgium

Annex II. List of participants of the Stakeholder Meeting on Regulatory Affairs

Name	Organisation/Institution	Country
Akkoyun, Akin	Projektträger im Deutschen Zentrum für Luft- und Raumfahrt e.V. (PT_DLR)	Germany
Aseffa, Abraham	Armauer Hansen Research Institute (AHRI)	Ethiopia
Breugelmans, Gabrielle	EDCTP	Netherlands
Burri, Christian	Swiss Tropical and Public Health Institute	Switzerland
Buvé, Anne	Prince Leopold Institute of Tropical Medicine (ITM)	Belgium
Caturla, Mercè	Janssen Infectious Diseases	Belgium
Chinnock, Paul	EDCTP	United Kingdom
Cooke, Emer	European Medicines Agency (EMA)	United Kingdom
Dieye, Alioune	Institut Pasteur Dakar	Senegal
Faillat-Proux, Valérie	Sanofi Access to Medicines	France
Effa, Pierre	Pan African Congress for Ethics and Bioethics (COPAB)	Cameroon
Fakier, Nuraan	EDCTP	South Africa
Gryseels, Bruno	Prince Leopold Institute of Tropical Medicine (ITM)	Belgium
Fournier, Bertrand	Janssen Research & Development	Netherlands
Habarugira, Jean-Marie	EDCTP	Netherlands
Hoogervorst, Suzanne	EDCTP	Netherlands
Jepsen, Søren	Statens Serum Institut	Denmark
Kasule, Mary	Council on Health Research for Development	Botswana
Khoma, NE	Medicines Control Council	South Africa
Kone, Bather	African Union Commission	Nigeria
Kouyate, Bocar Amadou	Ministry of Health	Burkina Faso
Lahouari, Belgharbi	World Health Organisation (WHO)	Switzerland
Liquori O'Neil, Alessandra	UNICRI	Italy
Madicke, Diagne	Direction de la pharmacie et du Medicament, Ministere de la Sante	Senegal
Mbacham, Wilfred	University of Yaounde	Cameroon
Makanga, Michael	EDCTP	South Africa
Mathieu, Christine	Clinical Trial Center	Belgium
Mgone, Charles	EDCTP	Netherlands
Ndebele, Paul	Medical Research Council of Zimbabwe (MRCZ)	Zimbabwe
Nyirenda, Thomas	EDCTP	South Africa
Ofori-Anyinam, Opokua	GSK	Belgium
Olesen, Ole	EDCTP	Netherlands
Pandya, Lara	EDCTP	Netherlands

Pereira, Daniela	EDCTP	Netherlands
Ravinetto, Raffaella	Prince Leopold Institute of Tropical Medicine (ITM)	Belgium
Sarr, Samba Cor	Senegal National Health Research Council (Conseil National pour la Recherche en Sante - CNRS)	Senegal
Saxena, Abha	WHO	Switzerland
Sematiko, Gordon Katende	National Drug Authority	Uganda
Shamley, Delva	University of Cape Town	South Africa
Spathopoulou, Thania	European Medicines Agency	United Kingdom
Strub Wourgaft, Nathalie	Drugs for Neglected Diseases Initiative (DNDi)	Switzerland
Uwamwezi, Marie-Chantal	GlaxoSmithKline Vaccines	Rwanda
Van Loggerenberg, Francois	The Global Health Network, The University of Oxford	United Kingdom
van Niekerk, Christo	TB Alliance	South Africa
Verdonck, Tine	Prince Leopold Institute of Tropical Medicine (ITM)	Belgium
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Colophon

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