EDCTP Stakeholder Meeting on Regulatory Affairs

Online Consultation Feedback

1 Introduction

In preparation for the meeting, EDCTP has set up an online consultation to gather views from stakeholders. The end result is expected to be a concrete set of recommendations through an open consultative process that involves a broad range of stakeholders from academia, industry, foundations, non-governmental organisations, civil society, governments and other interested parties working in the field of regulatory affairs.

The comments and recommendations will inform discussions at the respective meetings and where appropriate contribute to EDCTP strategy in this field. The feedback from the online consultation is presented in this document as they have been submitted. These will also feature in the final meeting report.

2 Online Consultation Feedback

Ms. Loren Becker
Global Health Technologies Coalition at PATH, United States

Current status of the field

- Limited human resources to manage both technical and administrative aspects of review
- Lack of established and enforced timelines for review
- Lack of incentives for efficiency in review of clinical trials, particularly where reviewers are not professional staff or have outside positions
- Lack of incentives for trained regulators to remain in public service
- Lack of coordination among capacity building and harmonization initiatives.

Future Directions

- Increase support for mechanisms for collaborative review of new protocols by NRAs across countries
- Develop and implement a common training curriculum to be used across capacity building initiatives
- Develop sustainable financing approaches for supporting NRA activities.

The role of EDCTP

- Support/ facilitate mechanisms for joint reviews among NRAs. Partners for this would include the WHO, existing harmonization/collaboration initiatives (AMRH, AVAREF) product developers, relevant NRAs
- Support coordination and alignment across NRA capacity building initiatives in Africa. Key aspects of this could include building curriculum consensus, tracking training delivered and who participates. Key partners for this would be major deliverers of capacity building, including so-called stringent regulatory authorities (FDA, EMA, etc.), WHO, US Pharmacopoeia.

Professor Christian Burri
Swiss Tropical and Public Health Institute, Switzerland

Current status of the field
A multistep registration process has to be achieved for new products today: marketing

authorisation in one or more reference countries, pre-qualification at the WHO and marketing authorisation in the target countries. The process can take between two and seven years depending of the type of product and the target market which is unacceptable from the access point of view. As like ethics committees which received major attention in the past 10 years regulatory authorities need to be strengthened, the regulatory review and registration process rendered more efficient and international exchange and communication fostered.

Future Directions
The African Medicines Regulatory Harmonization initiative, AMRH, was launched by NEPAD and the African Vaccine Regulatory Forum, AVAREF, were recently founded in order to harmonize and facilitate registration of novel medicines in Africa. Substantial funding will flow into those initiatives and other bilateral or multilateral projects. Given the shortfall of some countries or regions the task is formidable and will need major support from the private and public sector including Northern regulatory authorities.

The role of EDCTP

The EDCTP may:

- Finance or facilitate selected trainings published competitively by calls similar to the mechanisms in the ethics arena
- Financially support preparation of registration dossiers (particularly the contacts with Southern competent authorities) of products in Phase III receiving major finances from the EDCTP
- Finance regional meetings of drug authorities (maybe along the geographic delineation of the networks of excellence).

Mercè Caturla (PhD),
Janssen Infectious Diseases, Belgium

Mr Bertrand Fournier
Janssen Research & Development, The Netherlands

Current status of the field
Even though guidelines are generally available for many countries, challenge is usually that these guidelines tend to be very generic/non-specific/ambiguous...They are sometimes not well adapted to Pharma-type (global) trials. Timelines are also not clear (may impact enrolment period on global trials). Local agent/CRO to be the applicant in certain countries, but few CROs with expertise in Sub-Saharan Africa. The clinical trial applicants also need to do some background search/homework prior to applying - ensure their understanding with the regulatory environment in the African situation.

Future Directions
An attempt at direct engagement with the respective regulatory authorities needs to be made to somewhat standardise regulations/requirements per ICH-GCP or some other agreed upon international standards.
Sharing expertise and review reports between NMRAs. Rely on SRA (reference to SRA-CTA approval (do not fully review in this case), in some cases, reference also to EU SmPC (instead of asking for the full IMPD). Go to parallel health authorities /Ethics Committee review processes in all countries.

The role of EDCTP
Make awareness of what is happening in the EU and see how this can be customized to the African environment (e.g. EU going forward to have the health authorities review focused on scientific documentation (centralized review) and the Ethics Committee review focused on legal/financial/ethical documentation (this would avoid duplication).
Alignment of Pan African and EU registries.

Dr Nditonda Benno Chukilizo
Tanzania Food and Drugs Authority, Tanzania, United Republic

Current status of the field
Lack of weak laws, inadequate availability of personnel with adequate education, training and experience in scientific assessment of study protocols and study products and inspection of clinical trials.

Future Directions
Conduct situation analysis to find out what is the current situation in countries and support programmes to address the identified gaps.

The role of EDCTP
Provide support for training of regulatory officials and members of national ethics committees.

Mrs Emer Cooke
European Medicines Agency (EMA), United Kingdom

Current status of the field
Clear identification of needs, challenges and priorities.

Future Directions
Streamlining of existing initiatives to ensure principles are addressed.

The role of EDCTP
Preparation of an inventory of existing initiatives with regulatory capacity goals either as primary or secondary objectives.

Dr Joachim Doua
University of Antwerp, Belgium

Current status of the field
The issues, challenges and limitation of regulatory capacity in Africa can be summarized by the financial resources limitation of the countries, the limited regulatory awareness of political leaders and decision makers, and the dispersion of African scientific resources due to migration.

Future Directions
Sustainably support the African Medicines Regulatory Harmonization of the NEPAD. That will raise the awareness of political leaders and strengthen the regulatory capacity building of the African countries. Organize and actively involve scientists in drug regulation of the African diaspora in the AMRH programme. Based on my previous a role as clinical assessor at the Dutch Medicines Evaluation Board of the Netherlands and thereby for the European Medicines Agency (EMA) I have established a pool of scientists in drug regulation from the African diaspora in Europe. The aim of this pool of experts is to actively contribute to the drug regulatory capacity building on the continent and accompany NEPAD in the AMRH programme.

The role of EDCTP
EDCTP could encourage research in drug regulation by giving fund to universities and other research organizations. EDCTP could also support operational and capacity building activities in drug regulation with emphasis on clinical safety and pharmacovigilance, drug quality, and pharmacokinetics that are the key regulatory skills for health authorities for generic products assessment as these are increasing in the African countries.

Mrs Valérie Faillat-Proux
Sanofi Access to Medicines, France

Current status of the field
Despite 20 years of work by the ICH, the regulatory review and approval times in various parts of the world have not decreased. On the contrary, they seem to be increasing. In addition, drug lags appear more pronounced in several of the major emerging markets. Furthermore, as the need for harmonization grows, so do the number of organizations involved. The industry's coordination efforts themselves have yielded a new layer of complexity in the form of more bodies working toward the objective of harmonization. The ICH has spawned several initiatives serving regions in Asia, Africa and the Americas, while regulatory agencies from different nations have developed programs to recognize the rules of others. Industry groups have gotten into the game as well. Worst of all, these dozens of harmonization efforts often work independently, rather than coordinating their agendas or even communicating with each other. The harmonization process shows also some weaknesses:

- The environment is sometimes inconsistent: on one side, efforts are made for harmonization (ICH, ASEAN, African initiatives…), but on the other side, the complexity of the processes and the number of stakeholders increase leading to multiple rules which have a great impact on the regulatory environment
- The gap between the field reality and the gold standards requirements leads to difficulties (i.e. Risk Management Plan, stability data and supply chain, etc.)
- The increased complexity to be handled is one of the reasons to develop harmonization but in the same time it may jeopardize the harmonization for countries far from the current gold standards.

Future Directions
Now more than ever, the various stakeholders need to act together to harmonize harmonization. Perhaps it is time to establish an umbrella body that will provide a forum for regulators and industry to help harmonize harmonization. This body would focus our efforts toward collaboration, cooperation, mutual recognition, technical standardization, uniformity and partnership. If we succeed in this, we will have reduced the delays and confusion on the roadways that deliver rapid—and possibly simultaneous—access to medicines for patients worldwide.

The role of EDCTP
Be part of the umbrella body

Dr Søren Jepsen
Statens Serum Institut, Denmark

Current status of the field
It seems that there are a limited number of highly qualified R.A. professionals in a fair number of African countries. Regional collaboration, which could alleviate this problem, is hardly functioning. Some African RA officials claim that the salary structure is prohibitive and that carrier possibilities are lacking.

Future Directions
Political recognition of the importance of a well functioning RA. Appropriate salary structure. Sandwich programmes that provide for update training and alignment at EMA and/or European National RA. This could be developed in consultation with WHO.

The role of EDCTP
EDCTP could support regional RA collaboration, and insist on that EDCTP funds for clinical trials only will be allocated to partner countries with a well functioning RA body.

Mrs Mary Kasule
Council on Health Research for Development, Botswana

Current status of the field
Lack of capacity by research ethics administrators to manage research ethics committees due to lack of training, guidance and tools to strengthen REC information management systems.

Future Directions
Improve the research ethics committee's information management systems by providing web-based tools for administration of research ethics committees. Sponsor accredited agencies to train research ethics stakeholders to keep pace with advances in clinical trial research e.g. genomic studies.

The role of EDCTP
Efficient and effective research ethics (REC) administration by research ethics committee administrators remains a challenge in sub-Saharan Africa due to lack of guidance, weak information management systems and harmonized regulatory systems. This has led to Governments and research institutions losing scarce resources and research grants, especially for multi-center studies that depend on efficient and timely review of proposals by RECs in countries competing for grants. Therefore, EDCTP needs to invest more in the strengthening of Research Ethics Committee Administrators by providing training and web-based tools to improve the ethics review process. Therefore the areas of strengthening capacity of research ethics committee administrators and providing web-based tools that can automate the ethics review process.

Dr NE Khoma
Medicines Control Council, South Africa

Current status of the field
Challenges: very few health practitioners know about regulatory affairs. Skills shortages in NRAs force the authorities to rely on practitioners on full time academic appointments and delays approval of applications.

Future Directions
1. Formal training of healthcare practitioners and scientists in regulatory affairs
2. Informal (short term) training of current evaluators to upgrade their skills.

The role of EDCTP
Communicate with the NRAs for needs assessment.

Mr Bather Kone
African Union Commission, Nigeria

Current status of the field
Put in place a real regional coordinated/standard approach towards continental dynamic.

Future Directions
Work to connect all the existing initiatives for more efficiency and maximize funds utilisation.

The role of EDCTP
Face specific issues to Africa without re-inventing the wheel, transfer of experience.

Dr Bocar Amadou Kouyate
Ministry of Health, Burkina Faso

Current status of the field

Access to safe, effective and quality biologics, including vaccines, is an important element in the delivery of health care. Although these biological medicines, including vaccines, are manufactured and tested in developed and developing countries in recent years, there has been an increased interest in manufacture and test these products in the countries of the African Region. Several public- private partnerships (PPP) are actively engaged in supporting clinical trials of drugs, including vaccines, in countries in the African Region.

African countries have always relied heavily on ethics committees (EC) and the national regulatory authorities (NRAs) in developed countries for the control of ethical and regulatory aspects of clinical trials. In addition, the countries of the African Region have long relied on RNA developed countries for the registration of new drugs and vaccines. This is mainly due to the weak, inadequate or lack for NRAs and the EC of most countries in the region, the ability to perform the required functions.

Future Directions
Building capacity and sharing best practices in a network of NRA would be beneficial and could accelerate product design. So far African Vaccines Regulatory Forum (AVAREF) is one this network where RNA and EC are working together to strengthen the capacity of regulatory bodies in Africa.

The role of EDCTP
The lessons learnt from the transformation of ATM to PACTA as well as the financial support from EDCTP to EC can be shared and improved.
Support capacity building of national regulatory bodies and/or network of regulatory bodies e.g. AVAREF.

Mr Belgharbi Lahouari
World health organisation (WHO), Switzerland

Current status of the field
Political: lack of commitment from government to monitor and follow up their initial support for this area.
Technical: lack of national expertise or skills/competencies in some emerging technical issues (regulatory sciences agenda, good regulatory practices, e-governance for speeding registration of products, Good Manufacturing Practices for all medicinal products specially the biotechnology products, the biological products, etc.).
Resources: funding allocated by donors does not allow major changes as it is not institutionally sustained and has limited term.

Future directions
Increasing capacity building of elites in regulatory system to lead, programme manage and spend more time in focusing in one or two areas and raise it before they are recruited or diverted by international organisation, foundations or NGOs, attrition of staff is one issue and the lack of resources to train and develop, limited use of IT technology to invest in E-governance, limitation of harmonization of regulations, investment in transparency and anti-corruption mechanisms to avoid to divert main resources to other areas, curriculum that can help to build the capacity. One single country institutional development plan and road map to assist countries to develop institutions in charge of the regulation or affiliated to the national regulatory system.

The role of EDCTP
- Support in country activities that help to enforce institutional development plan (IDP) recommendations
- Support training capacity and promote in-country or in-region learning experience and dissemination of the tools
- Investment in e-governance to assist countries to develop and modernise their

regulatory system and provide training in this area or in development of best practices
- Promote good regulatory practices to assist countries to use harmonised and coherent approaches to develop their national regulatory system
- Invest in exchanges, transparency, or sharing information about national system
- Promote and support accountability of system through efficient Quality Management System (QMS) and transparency
- Coordination with international organisations and support funding which is coherent with institutional development plan.

Dr Diagne Madicke
Director of Pharmacy and Medication, Ministry of Health, Senegal

Current status of the field
Lack of training on clinical trials and BPC inspections.
(Manque de formation concernant les essais cliniques et la formation en inspections BPC).

Future Directions
Support and follow up of action points elaborated at country level but with no funding secured.
(Appui et un suivi des plan d'actions qui sont élaborés dans les pays mais qui ne trouvent pas de financement).

The role of EDCTP
Support and capacity building for pharmacy and ethical committee stakeholders.
(Appui et renforcement de capacité des acteurs direction pharmacie et comité éthique).

Dr Wilfred Mbacham
University of Yaoundé, Cameroon

Current status of the field
The regulators are not trained, the regulators are very temporal and get moved often, need to be in constant knowledge of current developments and this can be through seminars.

Future Directions
1. To train, train and train
2. To have some of the regulators incubate in Europe
3. To provide funds for them to be semi independent.

The role of EDCTP
Organise seminars and webinars and on line courses and debates over topical issues.

Dr Paul Ndebele
Medical Research Council of Zimbabwe (MRCZ), Zimbabwe

Current status of the field
Limited technical expertise and manpower due to unattractive working conditions and brain drain.

Future Directions
Continuing to build capacity of the Drug Regulatory Authorities to ensure that they have more confidence in regulating medical products and clinical trials.

The role of EDCTP
EDCTP can provide resources and facilitate partnerships with European Drug Regulators so that junior staff from African countries can be mentored.

Dr Opokua Ofori-Anyinam

GSK, Belgium

Current status of the field

- Exposure to different kinds of development for vaccines, drugs, biologicals and devices
- Trained personnel
- Audit and supervisory capacity
- Exposure to different worldwide regulations.

Future Directions

- Train regulatory personnel especially in CMC
- Develop a training programme and a certification programme for regulatory personnel already in service
- Although regulatory is sovereign - develop a communication programme between regulatory agencies to fight fraud.

The role of EDCTP

- Train personnel
- Broker training sessions with established regulatory agencies
- Develop awareness training programmes with like minded institutions so that this can be introduced early into training programmes on regulation of research.

Ms Raffaella Ravinetto
ITM, Belgium

Current status of the field

There is clearly a strong need to give structural support for strengthening regulatory capacity in Sub-Saharan Africa. Training is an important part of such strengthening but it will not be sufficient, if regulatory bodies lack sufficient personnel, sufficient administrative support etc. In sub-Saharan Africa, clinical research mostly involve socio-economical vulnerable populations. Regulatory rules and supervision cannot therefore be just copy-pasted from affluent contexts, but they should focus on those elements that are specifically needed to protect disadvantaged individuals and communities from possible exploitations. At the same time, regulation should prioritize research in neglected fields, to serve at best the interests and health needs of neglected populations.

Future Directions

- Structural support, beyond ad hoc training
- Developing special attention for protection of socio-economically marginalized populations.

The role of EDCTP

- Promote South-South and North-South regulatory networks, for mutual learning
- Promote structural support to regulators in the South
- Provide concrete support for Southern research sponsors (e.g., guidance on clinical trials insurance).

Mr Gordon Katende Sematiko
National Drug Authority, Uganda

Current status of the field

Old laws not covering current challenges, none availability of qualified human resource and retaining the few available.

Future directions

- Review legislations and harmonizing them in the region
- Training

- Regional cooperation.

The role of EDCTP
- Availing training opportunities and attachment of specialists
- Information sharing on regulatory issues
- Supporting regional regulatory harmonization initiatives.

Mrs Margareth Ndomondo Sigonda
African Union NEPAD Agency, South Africa

Current status of the field
Lack of unified approach to address regulatory capacity limitations in Africa.

Future Directions
i) Take stock of partners and regulatory capacity building initiatives being carried out on the African continent; ii) streamline efforts and develop a partnership platform to address regulatory challenges on the continent and ensure accountability; iii) promote regional integration initiatives with a view to harmonize regulatory standards and practice; iv) institute mechanisms that will ensure efficiency and transparency in the provision of regulatory services; v) support institutional capacity development, governance and management mechanisms; vi) institute robust monitoring, evaluation and impact assessment frameworks; and vii) benchmark national medicines regulatory agencies.

The role of EDCTP
Support the proposed future direction with focus on R&D, clinical trial oversight and post market safety surveillance.

Mr Hiiti Sillo
Tanzania Food and Drugs Authority, Tanzania, United Republic

Current status of the field
Availability and accessibility to safe, efficacious and quality medicines.

Future Directions
Capacity to regulate quality, safety and efficacy of medicines including effective clinical trials control and post-marketing surveillance programmes.

The role of EDCTP
EDCTP could interact with national medicines regulatory agencies and help build their capacities to effectively control the products.

Mrs Thania Spathopoulou
European Medicines Agency, United Kingdom

Current status of the field
My personal opinion is that main issues include: limited resources, a need for specialised training and networking.

Future Directions
Explore collaboration possibilities, maintain and update contact points for regulators in Africa, invite African regulators to international workshops, organise on the field training activities.

The role of EDCTP
EDCTP could provide funding for building of networks, training opportunities with specific objectives e.g. on inspections.

Mrs Marie-Chantal Uwamwezi
GlaxoSmithKline Vaccines, Rwanda

Current status of the field
Lack of political will is one of the key issues when relatively wealthy countries such as Gabon do not have fully functional medicine regulatory agencies overseeing clinical trials.

Future Directions
- Advocacy at higher levels of political and governmental institutions in African countries
- Enhance collaboration through pooling of experts (e.g. Medicines regulatory harmonization initiative NEPAD)
- Twining of NRAs.

The role of EDCTP
Not in a position to comment.

Dr Francois Van Loggerenberg
The Global Health Network, The University of Oxford, United Kingdom

Current status of the field
More pragmatic, investigator initiated trials in LMIC countries should be encouraged.

Future Directions
N/A

The role of EDCTP
The EDCTP could leverage the free and open access resources of The Global Health Network to support research training and professional development.

Dr Christo van Niekerk
TB Alliance, South Africa

Current status of the field
Lack of opportunity to meet with regulators/reviewers to discuss issues; moving goal posts for protocol reviews and approvals; unresponsiveness to emails and calls; unpredictable and long approval time lines.

Future Directions
Develop clear guidelines/requirements for approval of protocols; define agreed time lines for approval of protocols. Create a platform and the opportunity to discuss protocol design, etc. with regulators.

The role of EDCTP
Assist in the development of guidelines/SOPs for the evaluation and approval of protocols. Work with different members states i.e. SADC, East Africa and West Africa Forum to have a unified process and mutual recognition between member states through harmonisation. Coaching and training of reviewers in the scientific and procedural processes needed to review protocol.

Dr Tine Verdonck
Institute of Tropical Medicine Antwerp**,** Belgium

Current status of the field
- The regulatory culture coming from high-income countries may be inappropriate for the sub-Saharan setting (e.g. excessive emphasis on written rather than on verbal agreements, on documents rather than on human attitude)

- By putting too much emphasis on regulatory issues, we may miss the purpose of the regulation. Regulation is a means, not an end in itself!
- If in fragile, non-democratic settings, the regulatory authority falls in the hands of the wrong people, it is very unlikely that the objectives of regulation will be reached.

Future Directions
- Harmonize and simplify regulatory issues everywhere in the world
- Get to know different settings very well. Where possible and relevant: adapt regulation to different contexts
- Never lose track of the final objectives of regulation.

The role of EDCTP
- Promote dialogue. Avoid creating a caste of "professional" regulators that loses contact with the rest of the world
- Train regulatory staff from high-income countries in Africa
- Involve people from Africa as key teachers of regulatory affairs.

Mr Jef Verellen
Institute of Tropical Medicine, Belgium

Current status of the field
Limitations:
- Many countries have no clear or no legislation on the conduct of clinical trials or biomedical research in their country. Often only approval from the national EC is required, but the quality of the national EC is substandard and follow-up of the trial by the EC is unclear
- No pan-African directive/legislation/guidance is in place for entire Africa like there is in Europe with the Clinical Trial directive and Eudralex volume 10. A pan-African directive or guideline could be a minimum requirements for those countries not empowered enough to work out (on a foreseeable timeline) their own specific legislation
- No requirement for entry in public registry prior to recruitment
- Usually no requirement for study-specific insurance (GCP refers to the local legislation and European requirements only necessary for trials in the EU) or specific pharmacovigilance measures.

Challenges:
- Regulatory inspections for CT's are increasing in sub-Saharan Africa, but the quality of the inspections is low. The findings and recommendations are often not to the point and may have an adverse effect on the clinical trial climate and willingness of sponsors to continue doing trials. Conducting trials should be encouraged, not discouraged, yet attaining to GCP standards. Capacity building aspects in CT's could become a formal regulatory requirement.

Future Directions
- Emphasis and consciousness on the importance of clinical trials: highly sophisticated thereby increasing local know-how and autonomy, importance of public health affairs, etc. This will allow politicians to invest more time, money and know-how in setting up a good framework for CT's and the regulatory aspects
- Networking and capacity strengthening initiatives, involving all or most of policy makers in sub-Saharan/pan Africa. North-south poles with regulatory officers sharing knowledge and knowhow + setting up African minimal guidelines and requirements for conduct of clinical research. Simultaneously, Ethics/scientific Committees should be strengthened and at least 1 well-performing EC should be present in each country, having sufficient staff and knowledge to perform its duties
- Regulatory affairs for CT's should become more integrated, sharing experiences and data. Significant investment in IT platforms for storing, archiving and sharing data

(public or MoH shared registries, databases for pharmacovigilance and generally sharing experiences on review and approval mechanisms which would multilaterally enforce regulatory affairs in involved countries
- Sharing information on a broad basis, like good websites with easy to retrieve information and good contact points and service delivery towards sponsors, health institutions, investigators, EC's, pharma companies, etc.

The role of EDCTP
See above.

Ms Claire Ward
Swiss TPH/IBMB, United Kingdom

Current status of the field
- Independence of Ethic Review Boards - financial pressures persist
- Understanding and guidance on vulnerability - ERBs' ability to protect participants against vulnerability of depravation. Better understanding of the issues related to limits in the medical services and poverty need support. Rather than the traditional focus of interventions with higher risks of harm
- Compliance to ERB requests and conditions
- Ability to access and retain control of data and health feedback.

Future Directions
- Educate Community Advisory Boards and Community networks
- Develop ERB monitoring capacity
- Develop feedback mechanisms for data use and integration to present healthcare systems.

The role of EDCTP
- ERB training and development of assessing fair benefits, data feedback and monitoring capacity
- Community Advisory Board development and training.