Regulatory Capacity Building Workshop Report

Effective collaboration between National Regulatory Authorities & Research Ethics Committees in the Ethical Review of Clinical Trials

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Sincere gratitude is extended to the Health Canada Canadian HIV Vaccine Initiative (CHVI) workshop organizing team.

The Council on Health Research for Development (COHRED; www.cohred.org) through the MARC (Mapping African Research Ethics Review and Medicines Regulatory Capacity: (www.researchethicsweb.org) project is indebted to CHVI for funding and according MARC the opportunity to participate at the International Regulatory Forum and regulatory capacity building workshops. Most importantly, for awarding MARC the honour to conduct and facilitate the satellite workshop on building effective collaboration between National Medicines Regulatory authorities (NMRAs) and Research Ethics Committees (RECs) in the ethical review of clinical trials.

Sincere appreciation is extended to all participants, facilitators and translators who greatly enriched the workshop with their enthusiastic participation.

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Acronyms

AVAREF	African Vaccines Regulatory Forum
CSO	Civil Society Organization
COBRA	Consortium Study on Benefit / Risk Analysis
CTD	Common Technical Document
COHRED	Council on Health Research for Development
DSTS	Drug Submission Tracking System
eCTD	Electronic Common Technical Document
EDCTP	European and Developing Countries Clinical Trials Partnership
FBHP	Food Branch and Health Products
GFHR	Global Forum for Health Research
HR Web	Health Research Web
IMS	Information Management System
ICH	International Conference on Harmonization
LMIC	Low and Middle Income Countries
MARC	Mapping African Research Ethics Review and Medicines Regulatory Capacity
NMRAs	National Medicines Regulatory Authorities
PAHO	Pan American Health Organization
RECs	Research Ethics Committees
SARETI	South African Research Ethics Training Initiative
SOPs	Standard Operating Procedures
RHInnO	Research for Health and Innovation Organizer

Key Messages

1. **Inadequate communication and collaboration between the National Medicines Regulatory Authorities (NMRAs) and Research Ethics Committees (RECs)**
   Participants recognized the fact that clinical trials may only be undertaken once approved by a REC/IRB. Hence, effective communication and closer collaboration between RECs and NMRAs is a prerequisite for effective and efficient HIV clinical trials oversight, reaching a consensus on ethical review, and supporting compliance.

2. **Lack of clearly defined roles for the NMRAs and RECs**
   Although participants strongly agreed that RECs and NMRAs should operate autonomously, the need for clearly defined roles and responsibilities in the clinical trials review process was strongly emphasized. The latter could enable quality review for scientific merit as well as integrity and ethical considerations as requirements for best practices and decision making.

3. **Lack of resources**
   Lack of resources such as infrastructure, financial resources/funding and information management systems were reported to have a negative impact on the effectiveness and efficiency of NMRAs.

4. **Training**
   Participants reiterated the importance and need for capacity building in terms of short-term and long-term training opportunities, training in research ethics – both basic and advanced and annual consultative forums involving both RECs and NMRAs.

Executive Summary

Health Canada's fourth annual Health Products & Food Branch (HPFB) International Regulatory Forum and regulatory capacity building satellite workshops were held on September 22 – 29, 2012 in Ottawa, Canada. The forum hosted over a hundred participants from at least forty countries.

The core program provided a comprehensive and detailed overview of Canadian regulatory processes for biologics, pharmaceuticals and medical devices, throughout the pre and post market product lifecycle. To align the program with the Canadian HIV Vaccine Initiative (CHVI) regulatory capacity building objectives, a two day course was offered during the Forum on vaccine and clinical trial regulation along with case studies on lot release as a special topic.

The two satellite workshops were CHVI-sponsored and targeted specific audiences. One workshop was held in partnership with the Pan American Health Organization (PAHO) and discussed considerations for implementing the Common Technical Document for vaccines in the Latin American region. The other was delivered by the Mapping African Research Ethics Review and Medicines Regulatory Capacity (MARC) project from the Council on Health Research for Development (COHRED), with focus on building effective collaboration between NMRAs and RECs in the ethical review of clinical trials. The focus of this report is on the latter.

Under the CHVI, Health Canada sponsored 40 participants from 24 NMRAs to attend the Forum and satellite workshops, of the CHVI-sponsored participants, 23 participants attended the MARC workshop. Delegates included members of the African Vaccines Regulatory Forum (AVAREF), the Pan American Network for Drug Regulatory Harmonization Vaccine Working Group, the Pharmacy, Medicines and Poisons Board of Malawi as part of the ongoing CHVI Regulatory Capacity Mentorship Program, as well as other countries whom have demonstrated a commitment to building regulatory capacity via interactions with CHVI at the Developing Country Vaccine Regulators' Network.

The workshop aimed to leverage collaboration and strengthen vital links between NMRAs facing similar challenges regarding the ethical review of clinical trials with focus on HIV clinical trials. It also served as an engaging platform for open dialogue through discussions and exchange of best clinical trials regulatory oversight processes. It became evident that many African, Latin American and Asian countries are still faced with huge challenges regarding the type of products regulated, quality control and regulations. Most countries only regulated drugs; a few regulate food products and diagnostics, and lacked regulatory guiding documents. Major challenges highlighted included lack of consensus on ethical review of research between the NMRAs and RECs, poor or lack of communication and collaboration between the NMRAs and RECs, lack of clearly defined roles for the NMRAs and RECs in the clinical trial review process and lack of best practices for NMRAs and RECs to follow for ethical review decision-making.

Health Canada's initiative in recognizing the lack of ethics regulatory capacity among NMRAs and organizing an ethics-based workshop to link the NMRAs and RECs in ethical review decision making, was highly appreciated. Future meetings with focus on strategies for capacity building and strengthening clinical trials regulatory systems to improve the quality of clinical trials ethics review and the throughput of NMRAs and RECs in LMICs were recommended.

Key Words: Medicines regulatory authorities, clinical trials, HIV, ethical review, research ethics committees.

1. Introduction

Currently, there is an urgent need to speed up development of new medical treatments that are effective, safe, accessible and affordable as well as building evidence, support innovations and create new solutions, technologies and drugs for populations in low and middle-income countries.[1] Ethical development of new drugs calls for building sound and sustainable ethical review systems in form of RECs and NMRAs to oversee the process. Experience gained from national regulatory systems worldwide indicates that many countries face challenges in fully implementing effective clinical trials regulation, making many of them unable to guarantee the necessary quality, safety and efficacy of marketed products and the availability of appropriate information for use.[2]

The WHO 2010 assessment[2] concluded that although the majority of LMICs, particularly in Africa, had provisions in place to control ethical aspects of the conduct of clinical trials, there was lack of capacity to enable quality ethics review and throughput of NMRAs and RECs. Therefore, NMRAs are continually challenged by the rapid development and sophistication of medicinal products, new technologies and health care techniques. Such developments pose a heavy demand on regulatory control systems, an inability for NMRAs to respond adequately. Furthermore, with the enlargement of distribution and access channels, growing use of the internet and penetration of substandard and counterfeit medicines into many markets, the regulator's task has become even more daunting. Therefore, there is a need to collaboratively build and strengthen NMRAs' and RECs' capacity in LMICs to promote and improve the quality of their ethical review and throughput systems. This will be particularly important since most of the efforts to address the issue appear to have been sporadic and would benefit from more coordination.

2. Objectives

1. To identify key challenges faced by NMRAs arising from ethical review conducted by RECs and identify strategies to facilitate better communication between NMRA and RECs.
2. To discuss existing models/best practices currently used for scientific and ethical reviews by NMRAs and RECs in various LMICs and suggest an ideal model.
3. To introduce the Research for Health and Innovation Organizer (RhinnO) - an information management solution that oversees and automates the entire life-cycle of the research process, and manages data.

3. Proceedings of the workshop

An "open space"[3] approach was used during the first morning sessions to identify challenges in the review of clinical trials regarding the scientific design, methodology and safety focusing on HIV clinical trials. The workshop covered various topics on the ethical review of clinical trials (Annex 1). Presentations were given on key ethical issues in the review of clinical trials by research ethics committees and RHinnO as a solution to information management. Group discussions were also held to discuss existing models/best practices, used by NMRAs and RECs in the ethical review of clinical trials, and to propose an ideal model for implementation. Participants presented summaries of their group discussions.

4. Key concerns identified

- Lack of training opportunities in research ethics for MRAs.
- Lack of consensus by NMRAs and RECs on ethical review of protocols.
- Lack of communication and collaboration between the NMRAs and RECs.
- Lack of clearly defined roles for the NMRAs and RECs in the clinical trial review process.
- Best practices for the NMRAs and RECs to follow for ethical and NRA decision-making.
- Lack of accountability by investigators/research teams.
- Poor quality assurance systems like inspections and auditing.
- Lack of infrastructure including poor and lack of information management systems. RHInnO was deemed a timely solution, which can capacitate both RECs and NMRAs, replace the current complex paper based system and speed up the review processes.
- The need for annual consultative forums like this workshop was strongly emphasized.
- Other common challenges regarding ethical review of clinical trials addressed by all represented countries included: shortage of reviewers, very short time frame allowed reaching a reviewer decision and increasing workload coupled with the increase in complexity of clinical trials (science, types of products and treatment of disease, gene therapies, product combination, nanotechnology, vaccines and radiopharmaceuticals).
- Developing and implementing tools to manage documents and information submitted by sponsors.

5. Conclusion

The workshop increased participants' awareness about the importance of building and strengthening capacity of NMRAs and collaboration with RECs to ethically review clinical trials. There seemed to be a consensus among the participants regarding the existence of gaps in the clinical trial regulatory oversight systems including the need for more training in research ethics and establishing/improving NMRA information management systems and creation of networks. Participants committed to working together towards sensitizing their institutions, governments, clinical trial sponsors and other donor agencies about the importance of investing more into strengthening the capacity of NMRAs to enable the integration of ethics.

Lastly, the forum served as very engaging platform through open dialogue among both emerging and established regulators; it enabled very fruitful discussions and sharing of best regulatory practices. The forum also acted as a gateway to new and future collaborations between COHRED/MARC Health Canada and many Latin American, African and Asian countries that participated.

6. Recommendations

Due to time constraints participants strongly felt that in future longer meetings involving more countries and experts should be planned to continue the dialogue and create new networks, to improve regional, sub-regional, national and ultimately sharing of information and best practices related to NMRAs and RECs interaction and clinical trials regulatory oversight systems.

7. Evaluation of the workshop

Participants evaluated the workshop as satisfactory and well delivered despite the short time availed. The topics presented met their expectations especially the insight on ethical issues in conducting HIV clinical trials and Research for Health Innovation Organizer (RHinnO). Recommendations included: use of case study to illustrate theory, conducting longer trainings in research ethics and future involvement of REC members to enhance communication and collaboration. Participants found RHinnO a very good idea and felt it could improve the efficiency of their NMRAs and if funds were available they would suggest it be implemented in their institutions.

References

1. IJsselmuiden C., Marais D., Wassenaar D., Mokgatla-Moipolai., B. Mapping African Ethical Review Committee activity onto capacity needs. The MARC initiative and HRWebs interactiveness database on RECs in Africa: *Developing World Bioethics 2012;* 1471-8847.
2. World Health Organization (WHO) at: www.who.int/medicines .
3. Open Space at : http://en.wikipedia.org/wiki/Open_Space_Technology

Annex 1: Workshop Program

Time	Item	Presenter / Facilitator
08.00-08.15	Welcome Remarks & Introductions	Anita /Bobby
08.15-08.30	Open Space. What to expect	
08.30-09.15	Review of the design, methodology and safety of clinical trials by NRAs with a focus on HIV clinical trials (open space forum)	Mary
09.15-09.45	Group Feedback	Boitumelo
09.45–10.30	Key ethical issues in review of clinical trials by RECs with a focus on HIV clinical trials	Boitumelo
10.30-11.00	Group Discussion: Strategies to link NRA and REC decision making regarding approval of clinical trials	Mary
11.00–11.30	Group Feedback	Marzelle
12.30-13.30	LUNCH	
14.00–14.30	Group Discussion: Existing NRA/REC review models in comparison with the participants' country models (Africa, Asia, Latin America)	Mary
14.30-15.00	Group Feedback	Boitumelo
15.00–15.20	General Discussion: Ideas on the optimal model/process of review	Mary/ Marzelle
15.20–15.40	Summary of recommendations of suggested model/process	Marzelle
15.40–16.45	MARC Project and Research for Health and Innovation Organizer (RHInnO)	Boitumelo
16.45–17.00	Wrap up & Closing Remarks	Boitumelo/ Anita / Bobby

Annex 2: Participants List

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Health Canada	Norman Viner
Health Canada	Christina Bellotti

Special Guests

We sincerely thank Dr. Robert Cushman for graciously officiating the workshop and welcoming the participants, and Dr. Gregory Hammond for participating in the workshop on behalf of the Canadian HIV Vaccine Initiative Advisory Board."

Organization	Name
Health Canada, Director General, Biologics & Genetic Therapies Directorate	Robert Cushman,
Director, Canadian HIV Vaccine Initiative Alliance Coordinating Office	Gregory Hammond