



**REPORT
OF
THE HEALTH RESEARCH ETHICS WORKSHOP
FOR MEMBERS OF ETHICS REVIEW COMMITTEES
AND NATIONAL REGULATORY AUTHORITIES
OF CENTRAL AFRICA**

**Organized by
CANTAM-
with support of
AMANET-Tanzania
CAMBIN-Cameroon**

[Hôtel Mont-Febe, Yaounde, Cameroon,

September 27- October 1 2010]

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English Version

Translation made by the Amanet Sub-Hub Translation Unit

HEALTH RESEARCH ETHICS WORKSHOP FOR MEMBERS OF ETHICS REVIEW COMMITTEES AND NATIONAL REGULATORY AUTHORITIES OF CENTRAL AFRICA

From September 27 to October 1, 2010, a workshop on Health Research Ethics for Members of Ethics Review Committees and National Regulatory Authorities of Central Africa was held in Yaounde, Cameroon, at the Mont Febe Hotel. This workshop was co-organised by AMANET (African Malaria Network Trust) and CAMBIN (Cameroon Bioethics Initiative) within the framework of the CANTAM (Central Africa Network on Tuberculosis, HIV/AIDS and Malaria) project, which aims at building capacities and promoting health research in Central Africa.

There were 35 people in attendance including 29 participants from Gabon, Congo and Cameroon, and 4 facilitators from Mali, Tanzania and Cameroon.

DAY ONE: MONDAY, SEPTEMBER 27, 2010

The workshop began on Monday, September 27, 2010. First, there was the registration of participants at 8 a.m.; then the workshop documents were distributed. The opening ceremony followed with Professor Marie Thérèse Abena Obama, Minister of Women's Empowerment and the Family as guest of honour.

After preliminary remarks by Dr. Odile Ouwe Missi Oukem, Prof. Godfrey Tangwa discussed the purpose of the workshop. The keynote speech was made by the Administrator of the Chantal Biya International Research Centre (CIRCB), Dr. Pierre Joseph Fouda, who wished that the workshop should be the starting point of a long-term collaboration amongst participants. Afterwards, volunteers to be rapporteurs and daily time keepers were identified; then everybody gathered for a group photograph.

Identified volunteers to be rapporteurs and daily time keepers were:

- Day 1 :
 - o Rapporteur : Mrs. Elisabeth Dibantsa
- Day 2 :
 - o Rapporteur : Mrs. Patricia Elisabeth Fayette
 - o Time keeper : Dr. Abdouramani Lamaro
- Day 3 :
 - o Rapporteur : Dr. François Zambou
 - o Time keeper : Dr. Abdouramani Lamaro
- Day 4 :
 - o Rapporteur : Dr. Mathieu Ndounga
 - o Time keeper : Mrs. Merline Nouboussi
- Day 5 :

- Rapporteurs : Mr. Thomas Michel Anana Betilene and Dr. Marceline Djuidje Ngounoue. These two were also in charge of writing the general report of the workshop.

The first workshop session was opened by Dr. Pierre-Blaise Matsiegui with a general introduction on ethics.

Then, Prof. Godfrey Tangwa gave a presentation on the history of health research ethics. He stressed the importance of this discipline by discussing its contribution to biomedical research which aims at improving the health and ensuring the well-being of human beings.

A speech by Pieter Botha, the former South African President, was read out by Dr. Awa Keita as a prelude to a discussion that yielded the following recommendations:

- Researchers should be watchful so as to avoid being corruptible;
- Every government should elicit legal provisions regulating research on human subjects;
- Ethics committees should see to it that directives that are harmful to a human subject are not applied.

Then, Prof. Tangwa's second intervention focussed on the fundamental principles of health research ethics and on the protocol review process. He cited four such fundamental principles which are:

- autonomy
- beneficence
- non-maleficence
- justice

In the afternoon, a presentation was made by Research Ethics Committees (RECs) from various countries as follows:

- CERSSA (Congo-Brazzaville) by Prof. Honoré Ntsiba;
- NEC (Gabon) by Dr. Sylvain Patrick Enkoro;
- NEC (Cameroon) by Dr. Marceline Djuidje Ngounoue;
- EC CIRCB (Cameroon) by Prof. Jacques Philippe Tsala Tsala.

The problem of the lack of accommodation faced by all Ethics Review Committees was identified and discussed. The issue of the absence of a systematic monitoring of approved research projects was raised in almost all the presentations by representatives of Ethics Review Committees.

Presentations by representatives of National Regulatory Authorities (NRAs) from various countries followed in this order:

- NRA of Congo by Mrs Elisabeth Dibantsa

- NRA Gabon by Dr. Stéphane Germain Iloko Bousseguie
- NRA Cameroon by Dr. Abdouramani Lamaro.

Dr. Rose Ngoni, Adviser at the WHO-Cameroon also presented a complementary paper on NRAs in Cameroon, in which she provided a review of their constitutional framework.

DAY TWO: TUESDAY, SEPTEMBER 28, 2010

On day two, activities started at 8:45 a.m. with the review of the proceedings of day one, which was adopted subject to the addition of the various modifications suggested by participants.

The first presentation of the day titled *“Types of Health Research: Overview of experimental designs and various players involved”* was given by Dr. Odile Ouwe Missi Oukem. She listed the different types of health research as well as the various experimental methods.

From her presentation, participants learnt that some terminologies are specific to clinical trials and are keywords for NRAs and ERCs. These include ‘randomised study’, ‘multicentre study’, ‘single or double blinding’, ‘therapeutic study’, ‘superiority-of-product trial’, ‘non-inferiority-of-product trial’, ‘witness case study’.

In conclusion to her presentation, she said that players involved in health research are participants, the community, researchers, sponsors, research institutes, regulatory authorities, Ethics Review Committees, the Data Safety and Monitoring Board, ministries in charge of health and research, communicators, etc.

Dr. Aceme Nyika presented a paper titled *“Clinical Trials: Phases, randomization, blinding and other technical terms.”*

He defined a clinical trial as a study in human beings in order to determine the safety or the efficacy of a new drug, combination of existing drugs, vaccine, medical device, or medical procedures. He cited different types of them including ‘treatment trials’, ‘prevention trials’, ‘diagnostic trials’, ‘quality-of-life trials’.

He cited different indispensable steps in a new drug production process.

At the end of that presentation, participants asked several questions and sought further details about pharmacovigilance, phases I-a and I-b of clinical trials, the importance of insurance in those trials, the role and importance of Data Safety and Monitoring Boards (DSMB).

After a tea break, participants were divided into three groups for case studies on: 1/Trovan trial in Nigeria, 2/ Research on orphans, 3/ Tenofovir trial in Cameroon.

After lunch, each group presented its report and discussions followed. It came out from these discussions that increased vigilance and active collaboration between ERCs, NRAs and researchers is more than ever necessary.

DAY THREE: WEDNESDAY, SEPTEMBER 29, 2010

Activities for day three opened with the presentation of the proceedings of day two by Mrs Elisabeth Fayette.

Then Dr. Awa Keita presented a paper titled “*Types of Ethical Review in Health Research*”. In that presentation, she explained that there exist three types of ethical reviews (the centralised system, the decentralised system and, the private commercialised ECs); each of them has advantages and disadvantages.

In order to avoid double submissions, it was suggested that Institutional Review Boards (IRBs) should send a copy of their evaluation to the National Ethics Committee (NEC). Some participants believed it would be preferable to set up a stratified system in which the NEC would serve as the channel between the IRBs and the Ministry of Health.

Other participants thought it would be good to specify the types of protocols to be evaluated by IRBs and those to be evaluated by NECs. Facilitators believed that in creating IRBs or regional ethics committees in a country, the availability of human resources should be considered. They said that the three types discussed by Dr. Awa Keita were reliable and believed that the most appropriate would be the one in which a NEC does not evaluate protocols but has the following prerogatives:

- Recognise and grant official recognition to IRBs freely created by institutions if these IRBs have an expertise which is deemed reliable;
- coordinate the activities of IRBs;
- grant research authorisations on the basis of the ethical clearance issued by the IRBs.

Each country chooses its type freely; however, whatever the type, researchers should not submit their projects both to the NEC and the IRBs.

Whatever the type selected in a given country, its efficiency depends on the degree of collaboration between Ethics Review Committees within this country.

The second activity of day three was exercises to present the mandates and roles of Ethics Review Committees and National Regulatory Authorities. These exercises were based on three research protocols. They were aimed at enabling participants to agree on the structure (Ethics Review Committee and/or National Regulatory Authority) entitled to evaluate the various submitted projects. At the end of this exercise, it was noticed that participants were able to tell the role of each of the structures in charge of the review of research projects.

In order to complement this achievement, Mrs Awa Keita presented another paper on the specific and common roles of ECs and NRAs.

Specifically, it was seen that the main role of Ethics Committees is to protect research participants, populations, researchers and their institutions and to follow up the conduct of approved research projects. As far as the interests of researchers and institutions are concerned, carrying out research in line with ethical requirements protects and promotes the career of the researcher. The protection of the well-being of participants preserves the popularity and the brand image of the institution carrying out the research. It is therefore necessary for institutions to make sure that Ethics Committees function efficiently by giving them adequate funding as they fulfil their lofty mission.

Ethics Committees and National Regulatory Authorities share some common objectives such as:

- The review of clinical trial protocols;
- The passive supervision of approved clinical trials;
- The active supervision of approved clinical trials by visiting the sites of clinical trials;
- The protection of participants in a clinical trial.

It was mentioned that each country should set up a system to avoid conflicts of competence between Ethics Committees and National Regulatory Authorities.

Participants were also given synthesized copies of the report of the activities of AVAREF (African Vaccine Regulatory Forum). As a matter of fact, since 2006, the WHO has been organizing AVAREF meetings in countries selected for clinical trials (case of vaccines). The aim of these meetings is to provide pieces of information to countries targeted by the clinical trials of vaccines and to encourage and reinforce collaboration between Ethics Committees and National Regulatory Authorities in these countries. There have been 5 AVAREF meetings since 2006.

Afterwards, participants were divided into three groups in order to reflect on the following case studies:

The SAN people and their traditional knowledge

This case study enabled Dr. Rose Ngono, the representative of the WHO, to discuss the four types of drugs that can be obtained from medicinal plants. These are unrefined essences, essences or fractions with a complex chemical composition that are directly tapped from a medicinal plant: oils or fixed or essential resin, pure active constituents. The Ethics Committee should carry out the ethical review of clinical trial protocols if the traditional drug belongs at least to category 2, that is, an improved drug.

Dr. Rose Ngono recommended that Ethics Committees should read the WHO's document on the categorisation of traditional drugs.

The Virodene P058 controversy

This case study showed some unethical methods that some researchers opt for in conducting their projects. This is a case where the researcher seeks authorisation from the government or from the parliament thereby bypassing Ethics Committees and NRAs.

Plague samples from Tanzania land American researchers in court

This case study showed the absolute necessity for ECs, in case of collaborative research, to closely examine as many aspects of the projects as possible submitted to them for review. As a matter of fact, poorly designed or unfair and imbalanced contract specifications cause prejudice, especially to poor countries. Thus,

- During protocol review, ECs should pay attention to Material Transfer Agreement (MTA) and to access to scientific data or Data Sharing Agreement (DSA).
- Biosecurity standards should be respected in case the protocol indicates that there will be biological sample transfer. This will pre-empt any misuse of the sample for bioterrorism.
- ECs must insist on the traceability of biological samples that are collected in poor countries and studied in developed countries' laboratories.
- Researchers in poor countries should avoid acting as mere sample collection agents and should actively participate in collaborative research.

Day three ended with the projection of the film "***The Constant Gardener***", which showed some of the unethical practices used by some researchers and pharmaceutical industries during clinical trials. It was agreed that viewers would comment on the film the following day.

In the evening, members of the National Regulatory Authorities were awarded their attendance certificates during a diner at Bois Sainte Anastasie, downtown Yaounde.

DAY FOUR: SEPTEMBER 30, 2010

Activities began with the review of the proceedings of day three. This was done by Dr. François Zambou.

Prof. Tangwa then asked participants to comment on the film "***The Constant Gardener***" which they had watched the previous day. Basically, everybody seemed to agree that wealth, misery, and corruption can have a negative impact on ethics, undermine research and lead to illegal and violent practices. Consequently, it was

agreed that while evaluating projects, members of ECs should pay attention to what participants risk or stand to benefit from the study.

For purposes of illustration, 2 case studies were proposed.

a- A protocol on a new anti-malaria drug

Lessons from the case study:

- Basically, risks and benefits should be explicitly stated in the protocol
- All players in the research should stand to benefit something: the participant in the clinical trial (an individual), the community, the country, the researcher and his institution
- If risks and benefits are not explicitly stated, members of ECs should reject the protocol

b- A study on the sexual habits of adolescents

Lessons from the case study:

- The risk/benefits analysis should be carried out for every participant as an individual, for the community/population, the researcher and his institution.
- The risk/benefits analysis should not be limited to participants and the duration of study; it should include other people/community or population and the duration should go well beyond that of the project
- Such an analysis can be determined by technological advancements as well as by sundry other factors such as new diseases
- Benefits could be material/financial compensations; the EC should assess these compensations

Afterwards, Dr. Awa Keita gave a presentation on informed consent, which was further elaborated upon during group discussions.

The last theme was on privacy and confidentiality. It was discussed in a presentation by Dr. Awa KEITA. The following recommendations ensued from her presentation:

- The ethics committee should protect the privacy of research participants
- A researcher should not use information from/about a participant, elements of his body (which are part of his privacy), without seeking his prior consent
- The researcher must have genuine reasons for collecting private information about the participant
- It is the duty of the researcher to blind and keep collected data confidential

DAY FIVE: OCTOBER 1, 2010

Day five began with the presentation of the proceedings of day four. This was done by Dr. Mathieu Ndounga.

Immediately after, Dr Odile Ouwe Missi Oukem presented a paper on Good Participatory Practices (GPP). In the presentation, she identified some 19 key guiding elements for a clinical trial. These elements grapple with the evolution of prevention standards, access to health care, women and adolescents' participation in clinical trials, informed consent, the involvement of the community, etc.

Moreover, she identified 10 fundamental principles that govern Good Participatory Practices in clinical trials. It was said for example that patients involved in a study must be informed of the results of, and benefits from the study. These benefits may include access to treatment solutions arrived at at the end of the study or to any other appropriate treatment or benefits.

Participants were then asked to reflect on the involvement of minority and vulnerable groups like the albinos and pygmies in clinical trials.

The next presentation was given by Dr. Aceme Nyika. Its theme was *"Collaborative Research: Ethical and Practical Issues."* It appears data sharing may be contentious in international collaborative research. Signing a contract is clearly not enough, since the contract can be unethical. Similarly, giving informed consent of unspecified duration is like signing a blank cheque. Generally, researchers in poor countries are given protocols and collaboration contracts skilfully designed by researchers from developed countries. They hastily sign these contracts because of the potential accruing benefits, without getting acquainted with their specifications. Most often, such actions trigger serious consequences.

Yet another crucial problem is that of biological sample transfer to developed countries. It should be recalled that genomic studies span many years. To avoid acting as a mere data collector and in order to actively participate in the design of the contract specifications for a better sharing and use of data, 4 tips were given:

1. First, researchers and members of ethics committees need a good training and capacity building for them to be even more watchful;
2. Conceptual work should start well in advance through exchanges, discussions amongst the various actors involved, the putting together of issues raised etc., write-up of the contract per se;
3. At each stage, fundamental ethical principles governing health research should be respected. All the principles are applicable here;
4. Every country should have a health care policy, a health research policy, which is the basis of all negotiations. In other words, governments should be highly involved.

The next presentation was on controversial research. The overview of controversial research was presented by Dr. Aceme Nyika. He discussed the following aspects:

- Cloning research with the case of Dolly the cloned sheep that survived from 1996 to 2003. The idea of reproductive cloning of human beings is highly

- controversial. However, therapeutic cloning is acceptable. For example, thanks to biotechnology, synthetic insulin was developed and is used in the area of public health care today.
- Research on Genetically Modified Organisms (GMO). It can help improve agricultural production in a hunger-stricken country or continent. However, although only plants are involved in this case, such manipulations can have a negative impact on humans, the ecosystem, and the environment since their impact is hardly known. That is why such projects must also seek ethical approval from ECs.
 - Stem cell research. This has helped find treatment for some diseases such as cancer, diabetes, stroke, Alzheimer. However research on embryonic stem cells is controversial.
 - Research on human embryos. Ethical concerns are involved when it comes to determining at what moment an embryo becomes a human being. In other words, is a human embryo a human being?
 - o If it is a human being, then using it in research is murder
 - o If it is not a human being, then its use in research could be acceptable
 - Good research, bad purposes. Sometimes, findings from a good research can be used by the powers that be for unethical purposes. Example: manufacturing biological weapons.

Most countries do not have any clear-cut position or policy on this type of research. Consequently, this makes it very difficult for ECs and NRAs to perform their task of ensuring the protection of populations. It is very important to be watchful when projects are being carried out and to remain watchful even after the project has ended. ECs should operate within the policies or laws of their own countries.

Finally, the logical steps in protocol review were discussed. Through this discussion, participants came out with a non-standard method that members of ECs could use. Although everyone has their preferred procedure, these identified steps are of crucial importance.

After lunch, the closing ceremony was organised. A brief summary of the reports of the 5-day workshop on health research ethics was prepared by Dr. Odile Ouwe Missi Oukem.

It was recommended that every EC should create a database, and that funding should be sought from such organisations as AMANET and EDCTP, to reinforce the functioning of ECs in Central Africa. Then the representative of participants, Dr. Marceline Djuidje Ngounoue, was given the floor to give the general impressions of participants.

After her, the representative of AMANET, Dr. Aceme Nyika, and then Prof. Godfrey Tangwa, the president of CAMBIN, took the floor to thank all the participants at the workshop.

The workshop ended with the distribution of certificates to participants and facilitators, and then another group photograph was taken.



Appendices

- 1- Workshop programme
- 2- List of participants and facilitators
- 3- Group photograph