



## REPORT OF THE FIRST AMANET ADVANCED HEALTH RESEARCH ETHICS TRAINING WORKSHOP FOR INVESTIGATORS IN AFRICA, 23-27 JUNE 2008.

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### **Day 1; June 23, 2008**

The first in series of five workshops on advanced health research ethics for Africa investigators was held in Regency Hotel, Dar Es Salaam, Tanzania from 23<sup>rd</sup> to 27<sup>th</sup> June 2008. A total of 28 participants from ten countries attended the workshop. The countries that were represented include Cameroon, Somalia, Ethiopia, Ghana, Kenya, Malawi, Nigeria, Sudan, Tanzania, and Zambia. The workshop was officially declared open by the Director of Preventive health in the Tanzanian Ministry of health who represented the permanent secretary of Tanzania Ministry of health at an organised opening ceremony under the chairmanship of Prof. James Oloo. In the speech of the permanent secretary, the heavy burden of malaria on African and Tanzania in particular was highlighted and a call to conduct dedicated and ethically sound research was made. He also pointed out that “the workshop will facilitate sharing of experiences, constraints, challenges and strengths among researchers from different institutions in different countries and sub regions of Africa.” He anticipated that the interactions at this workshop will promote networking of researchers at national and continental levels.

The first presentation was given as part of the opening ceremony by Wen Kilama, the AMANET managing trustee. The title of the presentation was ‘Health Research Ethics Come to Africa’. He gave an overview of research ethics and its evolution in Africa. He mentioned important landmarks such as the 1900 Prissian directives,

Reich Council Regulations (1931), Nazi Germany experiments, Nuremberg Doctors' Trial (1946 –47), Nuremberg Code of Medical Ethics (1948), Helsinki Declaration (1964), Tuskegee Study, BELMONT REPORT (1979) and CIOMS (2002) that prompted development of research ethics. Unethical abuses of human subjects occurring in other parts of the World were also highlighted. After questions and answers, the participants and the guest at the opening ceremony had a group photograph and then proceeded into the hall for the morning session.

During the morning session, the participants introduced themselves before the series of presentations for the day. The first presentation for the session was titled 'from research to disease control: what challenges for Africa?' given by Prof. Wen L. Kilama. The Professor used the example of malaria to explain the role of researches in the control and prevention of diseases and other health related problems. He also highlighted some of the current and past problems encountered in malaria control programmes. Health research is necessary in order to set priorities, to accelerate application of knowledge to solving problems, to develop new tools and fresh strategies. He went further to explain AMANET procedures and rules for selection of vaccine(s) trial site in Africa. He concluded his presentation by emphasising to the participants that basic health research is mainly sponsored by the public and there is the need to develop more trial sites in Africa with more sponsorship from governments in African.

Prof. Paul Ndebele from Centre for Bioethics, College of Medicine, University of Malawi, Malawi gave the second presentation on Research with Vulnerable Persons, Groups and Institutions. He explained that "Vulnerable persons are those who are relatively (or absolutely) incapable of protecting their own interests. More formally, they may have insufficient power, intelligence, education, resources, strength, or other needed attributes to protect their own interests" (CIOM, 2002). Vulnerability may be applied to animal, man and Africa countries and developing countries in general. Individuals who could be vulnerable to abuses include institutionalised persons, minors, mentally handicapped, desperately ill, politically powerless, drug users, homeless, commercial sex workers and may others. It was also noted that

researchers and Institutional Review Boards (IRB) members may be vulnerable. Issues of informed consent, confidentiality, subject remuneration and involvement of children in research were highlighted.

During the afternoon session, the participants were divided into two groups in order to discuss the case studies. Case one centred on ethical issues surrounding research and development of bed nets. The two groups resolved that provision of bed net during and after trials should be the responsibility of both public and private partners in long term. However the sponsor of the research is obliged to provide ITN's/LLINs to the population that participated in the study as one of their benefit (Beneficence). The government and private partners should strive to meet the demand of the population by having strategies to reduce the burden of Malaria through the provision of ITN's/LLINs to the population, especially those in the low socioeconomic status. Since social-economic growth works better with healthier population, reducing the burden of Malaria will contribute to promotion of healthy living. Implementation steps in the provision and sustenance of treated bednet use should include; initial free ITN's/LLINs supply for a short term, followed by a period of subsidy on the ITN's which would further improve health and understanding of the efficacy and value of ITN's/LLINs use by the population. During the last phase, ITN's/LLINs could be sold at full price to the population as they would have now known their values and uses in order to achieve better health and increased economic production, and also understood the importance of ITN's/LLINs. All the above should be accompanied with continuous health education on the relevance and importance of using ITN's/LLINs. The ITN's/LLINs should be made available soonest after the nets have been approved to be safe and effective. It was also noted that guidelines do not address well the issue that sponsor should cover so as to meet the initial cost for implementing the intervention once found to be effective after clinical trials. All participants agreed that it is the duty of the ethic committee to request for the implementation of the intervention from the study sponsor. However the challenges are decision on how long would the sponsor offers the intervention and also the total cost for implementation may be too exorbitant for the sponsor to bear. Overall, all participants opined that there should be no reason sufficient to

delay implementation of research findings, and it is against the principle of beneficence and justice to market ITNs in the urban areas only because the population in the rural areas could not afford to buy whereas the actual research took place in rural and poor settings.

Case study two was on the delay in change of anti-malarial drug policy in Tanzania despite availability of sufficient evidence. The two teams resolved that the delay in implementation was unjustifiable and costly, which was “man made.” The pros for delaying such implementation include having enough time to review evidence about the efficacy of new intervention, having more time for consultation and interaction with end users and more time for effective planning and budgeting for implementation. The cons for delaying are the inestimable effects of increasing morbidity, probably mortality as a result of the failure of the existing drugs and increase in the burden on health system. The translation of health research findings into interventional policy is the responsibility of all stake holders viz sponsors, investigators, regulatory authorities, CAB and policy makers (the government). Overall, investigators are obliged to use the data to solve the situation by making results available to the responsible bodies (policy maker) for implementation. The discrepancies in the relationship between health research and policy formulation could be addressed through early submission of findings to policy makers, efficient communication and feedback systems, and publication of findings in both scientific and non-scientific media in the language that people concern understood. The need for re-orientation of investigators towards problem-solving approach rather than building career was identified. The involvement of other parties such as NGO’s, advocacy groups and media crew in research may go a long way in improving the situation.

## **Day 2; June 24, 2008**

The day started by review of the previous day that was shared by Estomih, a member of the reportour team. Thereafter, the Chairman of the day took over the

coordination of the programme; Prof. Francis Crawley was the first to give his lecture. He spoke on “Real and potential impacts of health research”. The highlights of his presentation include sources and levels of research funding, ownership of the good of health research and distinctions among the role of the public (government) and commerce. He discussed the concept of health research and good clinical practice (GCP).

The second presentation was given by Prof. Paul Ndebele on “Inducement, coercion, deception and debriefing”. He explained with examples the meaning of exploitation, inducement, vulnerability and emphasised distinction among use of the various terminologies such as compensation, reimbursement, inducement, undue inducement, motivation and coercion. It was noted that poverty promotes vulnerability and power differences increase the role of coercion in research. The IRBs can do more to minimise undue inducement and coercion while educating the community can assist in making research participation voluntary.

Dr George Shemdoe gave the third presentation titled “Introduction to intellectual property (IP)”. He defined and discussed the concept of IP and its relevance in health research and product development. He emphasised the importance of registration or patenting products and the risk of doing otherwise.

The fourth presentation for the day was on “Ethical issues in social and behavioural researches”. It was given by Prof. Paul Ndebele. He highlighted the mode of data collection – surveys, interviews, questionnaires, educational testing/psychology, observation in social science research. Ethical principles in the conduction of these types of studies are the same as in biomedical research but with focus on the sensitive nature of these categories of study. He concluded by saying that we need to take caution, be conversant with methods, reduce exposure to risk and remember that social science research can damage socially and/or physically.

The presentation on Ethical issues in genetic research was also given by Dr Aceme Nyika. He gave an overview of genetic research and differentiated between genetic

and genomic studies. He further discussed the controversies of genetically modified organisms, research involving stem cell with reference to embryonic stem cell. In the light of international collaborative genetic research in Africa, ethical and legal frameworks are critical for protection of participants and community.

Discussions on Case studies were held in two groups. Group I discussed the case study on “Tenofovir trial stopped in Cameroun.” The participants resolved that though it was necessary to conduct the study, several ethical issues arose. These include conflict of interest; the IRB might have been weak and influenced during the review of protocol and that the IRB failed in their oversight functions. All stakeholders have roles to play in making such drugs available and affordable after the completion of trial. Case study four was on research on Orphans. It was noted that all principles of research ethics were violated in the conduct of this study. The consensus at the group level was that IRB and investigator have the responsibility to protect the welfare of the Orphans but during the discussion Prof. Francis opined that it is the sole responsibility of the investigator. The study should have been carried out in non-vulnerable population since conducting this study among the orphans is tantamount to exploitation of defenceless minors. The fifth case study was on practical challenges encountered in the field. It was noted that the conduct of study particularly the timing of informed consent procedure was wrong as there was no hurry in blood sampling and as such the investigator should have delayed the process till patient recovered. In the word of Prof. Francis “Medicine and research should have been separated.”

### **Day 3; June 25, 2008**

The day started by recap of the previous day that was shared by Adebola, a member of the reportour team.

The first presentation was given by Prof. Kilama. It was on the ethics of vector control studies. In his presentation he talked about the need for research to identify and set priorities, to guide and accelerate the application of knowledge, to develop new tools and fresh strategies and to advance basic understanding and the frontiers

of knowledge on vectors and diseases. He further drew our attention to the urgent need for highlighting ethics in epidemiological, public health research and implementation of research findings,.

The presentation on Models and practicalities of community consultation was delivered by Dr. Aceme Nyika. It was noted in the presentation that community consultation should involve interaction with ordinary members of the community of interest and that it should be planned upfront, otherwise there will be no time and funds to do it. The importance of involving the community from the initial stage was to raise awareness and instil sense of community ownership of the study. Some challenges in research could be minimized or circumvented through community consultation. The importance of involving the community to the end of the research was also mentioned as in most cases after sample collection, researches do cut communication!

The presentation on intellectual property in health research and commercialization of research results was delivered by George. He emphasised the significance of intellectual property rights (IPR) to research and the need for instrument to guide the stakeholders and Institutional intellectual property (IP) Policy in Africa

Data Monitoring in Clinical trials was taught by Ramadhani. He explained the needs for data monitoring in health research and pointed out the essence of building capacity in this area as there is shortage of appropriately trained and experienced personnel. The role of data and safety monitoring board (DSMB) was discussed. Dr. Roma Chilengi gave a presentation on responsibilities in research to round up the day four presentations.

The case Studies for the day centred on ethical issues involved in researches on traditional materials and knowledge. One of the cases discussed was on the Communal traditional knowledge and IPR; the San people and their traditional knowledge. The consensuses from the group on the questions following the discussion were as follows;

1. Scientists could temper with traditional knowledge as there is the need to establish scientific basis of the use of medicinal products
2. Local communities participating in research and/or providing leads to scientific findings should be considered partners. In this particular case, because the San people gave (contributed) the lead and they need to enjoy the fruit of the research.
3. Local individual peoples and companies are obliged to plough back to the community concerned, because of the principle of beneficence and justice
4. Regulatory authorities are mandated to regulate all medical products that are marketed to the people because they are to regulate anything that is consumed

Group 2 discussed the case study about the different Protocol Review outcomes

1. The various EC were concerned about different aspect and different interest areas in the proposal
2. No. The measures were inadequate to address the concerns raised by the ECs
3. No. The local EC was more concerned about the immediate benefits from the project. They fail to think through what can happen to the data after the project has ended.

The other case study discussed was the Trovan Studies in Nigeria, and both groups were involved.

Discussion on the third case study was anchored by Roma and the consensuses reached were:

- Illiteracy does not justify failure to obtain consents

- The local health personnel who collaborated with Pfizer researchers were to be blamed for unethical recruitment of children into the Trovan trial, they were to ensure the protection of the welfare of health research participants.
- The conduct of the Trovan study was unethical from the design to the conclusion
- The design was not appropriate to address the research objectives
- There was existing local legal mechanism to address the case in Nigeria. However, opinions differ on why they went to the US. There may be some other reasons.
- It is unethical to conduct trial on drugs whose efficacy is not known in a devastating epidemic situation

Local investigator should be responsible wholly for ensuring the protection and safeguard the welfare of the research participants from the stage of protocol development to the day to day conduct of the research

#### **Day 4; June 26, 2008**

Dr Shemdoe Georges chaired the session.

The day started by recap of the previous day that was shared by Selorme, a member of the reportour team.

Dr Nyika Presented the topic on Animal Research Ethics;

The session started by emphasizing the importance of research in the context that although sometime it may not be done in human being, it may have effects on human. For this reason the importance of having insight in both animal and human research was stressed.

Overview of the presentation from the perspective of applied aspect of animal research (and not philosophical point of view) involved:

- Relationship between human and animals
- Use of animals in research
- Potential abuse of animals in research
- The 3Rs, and
- Animal research Ethics committee

It was mentioned that, there is a feeling that human are more important than animals and this is the reason why most studies starts by exposing animals to investigational products to learn the preliminary information about the safety and efficacy to help decide whether to move to human beings or not. Thus using animal in research is critical for the benefit of both human and animals; however, there should not be potential abuse of animal.

The concept of the 3Rs stands for;

- Replacement- (involving lower organism or non-biological/alternative methods where possible).
- Refinement – (refining scientific procedure to reduce suffering, discomfort or pain endured by animals).
- Reduction – (minimizing the number of animals to use as per scientifically justification or need).

It was also mentioned that the Legal ethics framework for the protection of animals does not exists in Africa at this point, but seen as an advantage to abuse animals in conduct of research.

Second session:

Presenter Prof. Tangwa Godfrey

Topic; Applying Ethical Principles in Health Research and Ethical review process

Presentation started by drawing our attention to the comment that “some of the animal has increased capacity than certain group of human being e.g. babies, mentally retarded people etc”. However, this may not be the case since the analogy

is that if we are to be careful with animal, we should be more careful with human beings!

Back to the subject, it was mentioned that ethics has no univocal definition and can be defined in various ways, and an easy description is that “ethics is a branch of philosophy which deals with the morality of human actions or behaviour”

The concept of “thinking and Logic” was further used to clarify ethics in the sense that “thinking” is for everyone where as “logic” comes in when there is justification of thinking.

The question of ethics being science or not was also explained at length. In the narrower sense it is not science since there is no descriptive method to justify, but on the broader side it is science since “*ethics is a normative science which is prescriptive rather than descriptive in its intention*”.

Natural allies of ethics were then mentioned including; Law, human right theory, Civics, Religion, Customs and tradition. However, it was mentioned that ethics is separable from each of all of them with the fact that ethics is limited to acts, action and behaviour that are free, purposive, intentional, and liable to impact to others. The natural challenges of ethics were then mentioned to be; amoralism, egoism, psychological egoism, and morality. Further, the fundamental principles of ethics were mentioned to be

- Autonomy; responsible for self action
- Justice; fairness, human beings are morally equal thus should be treated equally, unless there is justification.
- Beneficence; Non-malificence; usually used together meaning doing good and avoiding bad/evil.

The scope of the four fundamental principles of ethics was said to be equally relevant and important in medical ethics, clinical ethics, bioethics, and morality, generally within all possible contexts and perspectives. The importance of these

principles was said that they stand as the bedrock, foundation, anchor, support and referral points of the ethics of our actions and behaviour. They spread through life and not only in the research context. The presentation was ended by sharing the practicability and value systems of the principles. These essential values are:

- Honesty (truth)
- Responsibility (accountability)
- Respect (tolerance)
- Fairness (justice) and
- Compassion (love, empathy and caring)

The three resolution principles to meet the goal were then mentioned to be:

- Rules based thinking (deontological)
- Ends based thinking (teleological, consequential)
- Care based thinking (sympathetic, impartiality)

Paradigms of right versus right i.e. short term vs long term, justice vs mercy, truth vs loyalty, and individual vs community. And right versus wrong i.e. smell test, parent test and front-page news these were looked at to end the session.

Second session: involved group work where both groups had opportunity to discuss the same case study and later shared their views.

The case study was “Data sharing in an international collaborative research project”

The consensuses to the questions were as follows:

1. Both groups agreed with Prof. Kabisa that all sites should have access to the data since the consortium shared the same amount of work in terms of sample collection. In this context, it was not fair for one group to have access to the data and others not. There must be equity.
2. About data sharing policy, there should be a practical plan or agreement within the consortium. However, the implementation mechanism goes back to multiple aspects such as protocol and informed consent (IC). The issues if intellectual property (IP) also comes in as to who should own the data? These issues must be iron out.

3. The ethical principles to support the argument were said to be; Justice and beneficence
4. Regarding who to involve in determining an appropriate data sharing policy, the agreement was the Investigators (PI), as they are the one who ultimately oversee the right of the site such as the institution, study participant etc.

Afternoon session:

*The session was lead by Dr Nyika Aceme.*

Introduction involved the history of vaccinology where Edward Jenner tested cowpox in young boy in a poorly designed research, which was unethical. Preceding working to the questions and discussion, groups went through the case study about Gambia expels UN report over AIDS cure grills [Afro News, 2 Feb 08]. This was aimed at fuelling the interaction and to enhance understanding of the subject. The following consensuses were reached by the groups regarding the questions:

1. Traditional medicines are more affordable and accessible to the majority of African population.
2. The burden of diseases were said to be increasing, thus indicating that there is no improvement of traditional medicine, as are the one widely used as mentioned in Q1.
3. There is no improvement in traditional medicine (TM), and the reason given was that there is no investment in science aiming to improve them
4. Improvement of TM need changing of attitude, imposing science on TM thus making them sounder.
5. Process to improve TM involves several stages. These are; separation and discrimination of traditional healers to identify the genuine one and work in partnership with them.
6. The issues to overcome the challenge were mentioned as being; how to modernize TM? How to decolonize our minds (scientists) to have a systematic standardized process to improve the TM

The last presentation for day 4 was from Prof. Jerome Amir Singh and was about the Interface between Health Research Ethics, Law and Human rights

In the Introduction, among what was shared were the growing disparities in health and wealth both within and between countries which presents formidable challenges to research ethics, public health ethics and human right.

The overview of bioethics was then shared which involved; defining ethics, bioethics and research ethics, and the way they help health care professional to identify and respond to moral dilemmas in their day to day work. Research ethics and biomedical Principles of ethics (Autonomy, Beneficence, Non-maleficence and Justice) were shared at length. Challenges that impose deviating from the principles ethics in the interest and safety of the public health research were also emphasised. The area where the application of the principle move to benefit the public rather than individual is where there is increased risk of spreading the disease (especially airborne) e.g. MDR TB, XDR TB, Ebola etc. Here public health looks more to the threat to population rather than the right of the individual.

The next part involved Public health and public health ethic; Prior to embedding in public health, the difference between medicine and public health were outlined as; PH identify and measures threat to the health of population while medicine work with individuals, PH develops government response to these concerns, and seek to assure certain benefits.

The principles of PH were then outlined as:

1. Principle of Harm, prevention and necessity (PH goals of a proposed project)
2. Principle of Effectiveness ( how effective is the project to reach the stated goal)
3. Principle of burden identification (Known or potential burden of the project)
4. principle of least infringement/restriction/coercion (looking for alternatives or minimizing the burdens)
5. Principle of proportionality (fair implementation of project)
6. Principle of public justification and transparency (balancing the benefit and burden of the project)

7. Principle of reciprocity (individual affected by PH initiative should be adequately supported and/or compensated)

The concern of PH ethics vs Human rights were outlined to be; application of principles of PH ethics which raises human right concern with question such as:

- Are PH ethics compatible with human rights?
- While human being has a right to health, can a researcher or state restrict a research participant's rights in the name of science?
- Is the restriction ethical or compatible with human rights?

He mentioned that Public health importance may be invoked as a ground for limiting certain rights in order to allow a state to take measures to deal with a serious threat to the health of the population or individual members of the population. These measures was said to be specifically aiming at preventing disease or injury or providing care for the sick and injured.

In conclusion, when conducting public health research, it was mentioned that one must take into account more than just the principles of biomedical ethics in weighing the ethical merits and risk-benefit ratio of a proposed study. Thus PH research should also take into account the human rights and the Siracusa principles which allow for a restriction of rights if doing so is in the interest of public health.

### **Day 5; June 27, 2008**

The day started by recoup of the previous day that was shared by Estomih, a member of the reportour team

Professor Jerome Amir Singh presented on "Legal liability of research ethics committees and researchers". The report of the US Commission in 1978 on protection of human subjects of biomedical and behavioural research drew attention to the discourse on REC/IRB and legal liability. In the report of the Commission it was stated that *"On the principle that one who undertakes to protect others must act responsibly, IRB members could be liable if they did not exercise reasonable care in*

*carrying out their review. This might occur if their approval led to a research activity and injuries that would not have occurred if a reasonable person, confronted with the same information, would have placed conditions on the research that would have prevented the injury*". Thus, an injured subject could allege negligence by IRB members in assessing the risks and benefits of proposed research, or in approving consent procedures not reasonably likely to assure legally effective consent.

It was also noted that IRBs members may be personally liable for their or be completely protected by their institutions for their actions. However, most IRBs in African countries are not legally protected. 'They have no liability indemnity'. IRB members might be liable, legally or ethically, if they cannot demonstrate a good faith effort to show that they attempted to determine whether subjects would really want to know the information. Members of IRBs take on enormous responsibility usually with little or no compensation, and usually with great stress and inconvenience. If members are expected to do their job properly, they should be free of the threat of legal action. They should be protected just for taking on their duties. Two case studies namely; Nigeria's Trovan and Gelsinger cases were discussed to illustrate the legal issues that may arise from researches with respect to IRB members' responsibilities.

The group discussion for day five centered on professional ethics. Cases of neglect of principles of ethics in researches and practices of therapeutics misconceptions were cited and discussed. The ethical, practical and the legal issues of plagiarism, exploitation of subordinates such as trainees, unmerited authorship and participation of investigators in the conduct of researches just for the purpose of personal gains were discussed. These were considered to constitute serious professional ethical misconducts that must be borne in mind at the level of investigators and IRBs' meetings.

The group then looked at the issues of "Brain drain in Africa" from ethical and practical perspectives. Discussion referred to the case study "ethical issues

surrounding brain drain in the health sector”. Among the factors that may lead to brain drain were said to be lack of required infrastructures and poor motivation. It was noted that while the mass movement of African health professionals to developed countries is unethical and detrimental to the well being of the people, it is necessary that governments of African nations rise up to the needs of the people. The professionals also have responsibility to the nation that invested resources in them. Prof. Wen L. Kilama drew the attention of the participants to the occurrence of an attitude he described as “brain in the drain”. This refers to people who do not utilize their opportunities and time at work to enhance productivities in spite having sufficient facilities and prerequisite skills to do so.

The last presentation was on the AMANET web-based courses given by Charles Wanga, the communication officer for AMANET. These courses include Basic Health Research Ethics (HRE) in English and French languages and Good Clinical Practice (GCP). Participants at the advanced HRE were encouraged to enroll and finish the course on GCP.

The second session ended, and the group was given opportunity to visit Kariakoo a famous place centrally located in Dar Es Salaam with peak business activities. The group was to meet in the evening at the Msasani coral beach club for closing session.

During the closing session, the group was led by the chairperson of the AMANET trustee Prof. Kilama and his wife, and this was in line with African traditional culture where the elder led the ceremony, or traditional healer tested medicine on their own or family members before providing to others! The trustee chairperson then introduced the guest to the group who were mostly the AMANET team both working in Dar Es Salaam and Ifakara.

The guest were then introduced to the team of facilitators that included Dr Nyika Aceme, Prof. Oloo James, Prof. Tangwa Godfrey from Cameroon, Prof. Jerome Singh from South Africa, Prof. Ndebele Paul from Malawi and Mr George Shemdoe.

Next part involved presentation of certificate of participation to all the workshop participants and facilitators to mark the end of the most exciting, educative, and memorable opportunity, which most probably decolonized brain of each investigator who attended, as each was looking forward to practice all that was learned.

We believe that AMANET has started a new history of ethical health research in Africa!