KEMRI Bioethics Review

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Ethics and Change

Contents

Production Team

Editor In Chief:

Prof Elizabeth Bukusi

Editor

Daisy Kadenyi

Production and Design

Timothy Kipkosgei

The **KEMRI Bioethics Newsletter** is published every 3 months on the KEMRI website. We publish articles by KEMRI affiliated authors and from other contributors from all over instituitions within and outside Kenya. The scope of articles ranges from ethical issues in biomedical science, healthcare, technology, law , religion and policy.

The chief editor encourages submisssion of articles as a way of creating awareness and discussions on bioethics. Please get in touch by writing to seru@kemri.org

From the Outgoing Editor in Chief

Prof Elizabeth Bukusi

A New Year, and new opportunities and changes that is the cycle of life. Welcome to the first issue of 2018 of the KBR.

As an obstetrician, one of the greatest joys is ushering a new baby into the world. It is important that obstetricians and midwives alike realize their job is to help the baby into the world, but that the baby is not theirs. The child belongs to the parents and it is their responsibility to nurture and grow it into adulthood.

The KEMRI bioethics review which has been part of the tools for improving research regulation at KEMRI represents a birthing process for me. It has been an immense privilege to have been part of the process of change in the research regulation at KEMRI. To work alongside KEMRI management and scientific and administrative staff to see the changes that have been the effort of many 'parents'.

This is the last issue of the KBR where I am the Editor in Chief. And as a good obstetrician / midwife I hand over the baby into the very capable hands of the parents knowing it will be nurtured to full maturity.

The SERU which houses the KBR has only grown from strength to strength and with the new leadership, I can anticipate even better processes and more efficient systems.

Thank you for the privilege of having served you all and I wish you all Godspeed and every blessing as you continue in your quest for improving the lives of Kenyans and indeed others all over the world on a back bone of sound ethics that maximizes s research opportunities while protecting human subjects.

Prof Elizabeth Bukusi

Chief Research Officer

CMR, KEMRI

A word from the Director, KEMRI

Dr Yeri Kombe
Ag, Director, KEMRI

A warm welcome to the year 2018 and to this first issue of 2018 of the KEMRI Bioethics Review newsletter. This being a transition period at the institute, Scientific and Ethics Review Unit (SERU) has also witnessed changes from the re-organization that the institute continues to undertake so as to better achieve our mandate. The SERU is a key department at the institute owing to the research regulatory role it plays. There has been a surge of protocols submitted for review both from within the institute and from outside. It is therefore critical that the unit functions optimally to effectively handle the continued increasing workload.

SERU has faced challenges of staffing with staff on short term contracts for a long time, however we have now placed a substantial number of staff on long-term employment terms. The Unit is now headed by Dr. Mercy Njeru.

The increase in human resource at the unit has allowed for allocation of dedicated contact persons to specific Institute centres who can handle day to day regulatory concerns that centre staff may encounter while preparing their submission for review. We urge researchers to accord the unit necessary support so that it delivers on its mandate effectively.

The restructuring of the regulatory system from a single three tiered system to a two-tiered system with multiple committees has had a positive impact, and has contributed significantly to increased efficiency in review and approval of submission received at the Institute.

KEMRI remains committed to continue transforming and strengthen SERU into a one stop shop for research regulation that will serve not only KEMRI researchers but also researchers from other institutions and contribute towards increasing capacity in research ethics in the country. We look forward to the continued improved performance of SERU under the leadership of Dr. Mercy Njeru.

Wishing you all a productive year in 2018 as you work towards better health for all.

Dr Yeri Kombe, MBChB, MPH, PHD

Ag. Director, KEMRI

A word from the Deputy Director, Research and Development

Dr Evans Amukoye
AG DDRD, KEMRI

Welcome to this issue of the KEMRI Bioethics Review. This newsletter has been instrumental in providing vital information on research ethics and other related topics There have been several changes that have been made at the SERU in bid to strengthen and increase its efficiency in regulating research at the Institute.

Research regulation and administration is the heart of the research activities at the institute. The restructuring of the regulatory system in KEMRI that began in 2010 has born fruits, researchers are now experiencing a faster turnaround time in review and subsequent approval of submissions received at the SERU. There has been an increase in e capacity of SERU office is more robust and the systems in place are working more efficiently. The Institute is committed to continue transforming to its maximum efficiency by improving communication infrastructure that will allow for teleconferencing especially during committee meetings. This will ensure that the burden of travel for some of our committee members who are located outside Nairobi is reduced, but still they are able to attend a meeting and give their contribution. In addition we would like to eventually transition to an online based system submission and review of applications.

KEMRI recognizes the importance of a well-functioning research regulatory system and its role in ensuring responsible conduct in research, the Director recently appointed a unit head to steer the operations of SERU. As a result, various changes have been witnessed which includes implementation of a devolved system in its operation that has allowed allocation of dedicated members of staff which will improve service delivery and efficiency of SERU. Scientists can now concentrate on churning out proposals with a surety of timely and quality review. Enjoy reading

Interview with Dr Mercy Njeru (KEMRI SERU Ag Head), conducted in August 2017

Dr. Mercy Karimi Njeru holds a PhD in International health with a focus on health systems, from the university of Bergen in Norway. Her PhD thesis title is "HIV testing services in Kenya, Tanzania and Zambia: Determinants, experiences and responsiveness". She has extensive experience in the application of mixed methods and her work has recently received global recognition as one the best resources in mixed methods applications in health research. She is involved in various research projects mainly from a health systems perspective and has also been involved in mentoring and supervising graduate students. Dr. Njeru has participated in the developments of national guidelines as well as research involving other countries in sub-Saharan Africa. Her research focus is mainly on health systems and policy research. She was appointed as the acting unit head of KEMRI SERU from May 2017

1. Congratulations on your appointment as head SERU. What was your reaction towards this appointment?

This was a pleasant and challenging Surprise!

It is indeed a challenging position as it requires balancing the needs of many people with diverse backgrounds including: the research scientists, committee members, the secretariat team and the KEMRI management.

2. What are some of the milestones and challenges within SERU?

Milestone

The establishment of an independent scientific and bioethics center within KEMRI has addressed the several challenges on research regulation. For instance SERU boasts of robust multiple review committees. The committees are composed of members with diverse backgrounds including medicine, research scientists, statisticians, lawyers, and the clergy among others. The multiple committees have strengthened and enhanced the Institute's bioethics capabilities and transformed the review process at KEMRI for use by all KEMRI researchers and affiliated collaborators.

There is capacity to conduct ethics based research although this is hindered by the lack of funds and inadequate personnel. The Unit has certified IRB professionals and experienced personnel who are well equipped to address research regulatory issues. The secretariat team within, has enabled the unit to attract clients from within and outside KEMRI, enabling the institute to foster collaborations.

Challenges

The greatest challenge that SERU faces is inadequate funding. I would urge the institute to increase the funds allocated to the unit. The unit is responsible for oversight, regulation, capacity building, approvals as well as monitoring and evaluation of the scientific and ethical aspects of all research activities. The budgetary allocations to the unit should be enough to support and sustain its functions.

Additionally, there are challenges with the infrastructure. The office space is inadequate for staff, some of the staff members use the board room as their work station because they do not have a space to use.

Finally our protocol tracking system is purely paper based and is prone to many risks. An online based tracking system would not only make it easier for researchers

to submit their protocols from the comfort of their work stations, but also help the secretariat in tracking protocols, flagging those that need renewal, sending reminders to investigators who delay to respond to letters that need their attention. Plans are underway to develop an electronic system that will be well suited for our use.

3. What plans to you have for SERU going forward?

We intend to improve on the visibility of SERU in and out of the institute. We have begun this process through creation of a SERU webpage[https://www.kemri.org/index.php/blog/2015-07-06-18-01-18] on the KEMRI website, where researchers can visit and get information about the processes in SERU. With support from the KEMRI management, we plan to establish an automated submission and review system which will ease the protocol submission process for the Principal Investigators and review of submissions by the committee members. We wouldn't want principal investigators to be bogged down by inefficiencies either at submission or review levels.

Finally, we intend to continue with capacity building activities for the secretariat, scientists and the reviewers to enhance high quality proposals and ultimately achieve a reduced turn-around time of review and increase the efficiency of SERU as a whole.

4. What plans are in place to make sure the unit continues to provide stellar services to researchers within and outside the institute

Our plan is to bring SERU services closer to the scientists. We have now allocated center contact persons from within our secretariat staff to the various KEMRI centers. In addition we have one of our staff dedicated to handling all applications from all our affiliated collaborators (non-KEMRI submissions to SERU). We envision a SERU that is interactive and not a stand-alone. We will continue to engage with the research scientists, committee members and the KEMRI management team to know how best we can serve them. Additionally we plan to provide regular capacity building sessions to the researchers, committee members and the SERU secretariat.

5. Any suggestions on the future of the. The KEMRI Bioethics Review Newsletter

The newsletter is a powerful resource tool. The goal is to make it more visible within and outside the institute so that it can address the information needs of the scientists, reviewers and the public in matters to do with Bioethics.

Interview with Ag Head Grantmanship office.

Dr Beatrice Irungu

Beatrice Irungu is a Research Scientist at Centre for Traditional Medicine and Drug Research (CTMDR), Kenya Medical Research Institute, Nairobi Kenya. She holds a Doctorate in Chemistry from the University of Nairobi. Her research interests are in drug discovery and development (synthetic and natural products) for management of communicable diseases. She has attracted a number of Research grants as a Principal Investigator from International Foundation for Science (IFS), National Council of Science Technology and Innovation (NACOSTI) and WHO/ TDR. She is a member of CTMDR Centre Scientific Committee (CSC) and was recently appointed to be a member of KEMRI's Scientific and Ethics Research Unit (SERU) for a period of three years effective 1st March 2015. Dr Irungu was recently appointed as the acting head of the grantmanship office.

1. Congratulations on your appointment as head of the Grants office. What plans do you have to improve the operations of the office?

As a department, with the support of the management we are buiding the capacity of the Grants office to enable the active monitoring and evaluation ongoing research projects. In addition, we have funding from the National Institute of Health through a project titled UWEZO: Developing a KEMRI Office of Sponsored Research (OSR). The overall goal of UWEZO is to build capacity for KEMRI for an office of sponsored research, learning from University for California San Francisco's (UCSF) experience. We would like to benchmark with UCSF's OSR transition over the last 4 years and develop an office of sponsored research for KEMRI. Funds from this grant will provide an excellent opportunity for capacity building within the grantmanship office. This will enable the department to provide support for KEMRI scientists for Pre and post-award management including reporting and financial oversight of sponsored research within the institute.

2. Health research ethics is a key area in research but not many scientist have ventured into research on ethics. Are there any initiative from your office to fund research that focuses on improving research ethics in KEMRI?

The Grantmanship office provides funding for research to the Institute scientists through the IRG. We fund research that focuses in several areas including ethics. SERU has a representative in the IRG committee which provides funding even for ethics based research. The committee meets regularly and representatives from various departments are encouraged to inform their departmental staff and urge them to apply for funding. The representatives should highlight the possible gaps in different or any research that is of benefit to the funding from KEMRI. We also have a call for the inter-center grants which require collaboration between investigators from KEMRI centers with some specific conditions. We therefore expect calls even for those with inclinations to research ethics

3. What is your office doing to encourage and stimulate research and generation of knowledge in Research ethics?

Grants office provides funding opportunities for all KEMRI Scientists. We therefore encourage people interested in ethics to apply whenever calls are made. I urge scientist interested to visit the Grants office to find out more details on the available opportunities and the timelines.

4. What are the current funding opportunities in research ethics that young scientist should consider applying for?

We had a call for the Internal Research Grants for young scientists. These scientist should have attained their PhD not more than 5 years from the time of the call. However, a PhD is not a requirement to apply, one can apply with a Bachelors or a Master's degree. The call is open and thus people interested in research on ethics can apply. The award is up to one million Kenyan Shillings and is open for application for anyone interested.

Interview with Dr Peter Mwitari (CTMDR Director) on Research Ethics Knowledge management and dissemination

Dr Peter Mwitari is a Principal Research Officer and Director of the Centre for Traditional Medicine and Drug Research (CTMDR) at the Kenya Medical Research Institute (KEMRI). Dr Mwitari holds a PhD in Pharmacology from Tianjin University of Traditional Chinese Medicine. He joined KEMRI in 1998 and has over 15 years' experience in the field of traditional medicine. His career interests are on application and development of plant medicines in the management of communicable/non-communicable diseases, drug quality control, analysis and development and training & technology transfer. He is currently a Co-principal investigator in the pyrethrum as well as a co-investigator in the khat study funded by the Government of Kenya. He is a member of the Committee B KEMRI Scientific and Ethics Review Unit. Dr. Mwitari has published widely in the area of plant medicine and pharmacology.

1. Ethics is a key component of research. What is your view on the current attitude of researchers towards ethics in research?

Personally, as researcher and a reviewer of proposals at the center level and a committee member at the SERU, I appreciate the need to employ ethics and follow laid down ethical procedures and standards when dealing with human subjects and animals. I regularly engage in research studies and clinical trials that involve animal bioassays. Research ethics is important, and as a SERU reviewer, I fully appreciate the fact that researchers, especially those undertaking clinical trials need to ensure they adhere to ethical standard when conducting their research. I also believe researchers in KEMRI now understand the importance of ethical conduct in research since most of them also serve as reviewers either at the centre level where they are based or as SERU committee members.

Being a reviewer is a learning process, I am not a clinician but being a reviewer has taught me a lot in field of bioethics. In clinical trials for instance, we cannot do without ethics, There is need to treat the human subjects with the dignity they deserve and ensure that the risks or harm are minimal in the studies they participate in.

The Collaborative Institutional Training Initiative (CITI) course that is being sponsored by the Institute is very important. Some of the graduate students who I supervise have reported the positive impact that CITI training has had on them. They find the training applicable even beyond ethics to the basics of biomedical research. Scientists are also benefiting from CITI because as they take the course they also learn about other things in research.

2. Do you think KEMRI is playing its part in creation and dissemination of knowledge on research ethics

In my opinion the issue of ethics and training on ethics is still a new field. I would suggest that when KEMRI recruits new scientist, research ethics should be included in their induction to the Institute. I am not aware if most of the local Universities offer training to graduate students on ethics in research. It is important that KEMRI takes the initiative to provide training to the scientists rather than waiting until a scientist is ready to submit their first proposal for them to learn that ethics certification is required as part of the documentation for their

submissions. They need to have undertaken basic ethics training. KEMRI to a small extent is doing something to pass ethics information through the bioethics newsletter. I am confident KEMRI can do more, which may include making ethics training part of the requirements for new scientists joining the institute. The SERU should make it mandatory for scientist doing research in KEMRI to undergo in house training in research ethics may be though certificate course periodically.

3. Apart from of the online ethics training, do you think face to face training may be important in imparting knowledge on ethics?

There is need for some formal ethics training. For instance, researchers using animals in studies should be taken through demonstration on how treat these animal during research. Scientists should also be exposed to clinical trials so that they get firsthand experience on how they should handle research participants. In addition to undergoing the theoretical trainings, the practical aspects would also be important. This will ensure that ethics become ingrained in one's mind in that whenever they are undertaking research, they are aware of the norms in research involving either animals or human subjects. It is also important for the researchers to understand the consenting process and how to ensure the process is clear to participants to know that they are free to withdraw from a study anytime when they feel uncomfortable.

4. Ethics Knowledge utilization is important to ensure ethical conduct in research. What do you think are the key strategies that the SERU and KEMRI management can adopt to ensure available knowledge on health research ethics is utilized and applied to enhance the quality of research?

As I pointed out, there is need for orientation for new scientist in order for them to have basic knowledge on ethics and how to utilize it in real life situations. We have a few scientists joining KEMRI at any one time hence it will not be costly to intensively train them on research and research ethics for a few weeks in active field engagement.

I would like to appreciate the initiative of the SERU in allocating officers in charge of specific centers. At some point we hope the officers will be able to continuously train scientists on research ethics. There is still room for improvement so that we avoid receiving proposal submissions that do not meet the threshold of scientific and ethics standards, this will shorten the time it takes to approve some studies because most of the issues that delay approval border on ethical considerations. For instance , when using animals, investigators need to justify the uses of animals, the number of animals and the various aspects involved, But if scientist are aware of alternative to animal models, then they can avoid delays involved.

5. KEMRI Bioethics Review has been in production for the last five years with an objective of communicating knowledge on research ethics to KEMRI scientist. Do you think the newsletter has helped in knowledge dissemination

The expectation is that a newsletter or any important literature that a scientist interact with helps in building knowledge. But the question is when the newsletter is published, do the scientist have time to read? how is the volume? For my case I download and put it aside for reading later but I rarely do get sufficient time and I end up receiving the next issue before I read the previous one. I suggest we can have some seminars on ethics where we invite experts in ethics to make presentations. This is to complement the information on the newsletter. The good thing is that once the newsletter is out, we can always refer to at our own convenient time. But when there is an interesting topic, it can be presented during the KASH monthly seminars. This will help disseminate informa-

tion to wide audience and also in a timely manner. An example is the outbreak of cholera in the country last year, there were serious ethical issues around food handling and preparation that had ethical ramifications that can be dealt with in a seminar.

6. Do you have suggestions for improvement of the newsletter?

Whenever I get a newsletter I always feel I do not have sufficient time to read hence I put it aside and find time to read later, but if it was a few pages maybe I could read it immediately. We can therefore think of ways of summarizing the information in a few slide animations for those who may not have time to go through the full issue which can be in form of a short video presentation. We can also print some hard copies which will be placed strategically in the office waiting areas.

Final remarks

SERU has helped plug the gap which existed in research ethics. In the former two tiered system (SSC-ERC), Ethical Review Committee (ERC)was viewed as an unnecessary hurdle for scientists who felt once Scientific Steering Committee (SSC) approved their research, there was no need to raise more questions. But the SERU has demystified ethics and scientists now appreciate the importance of ethics in research. I am now fully aware of the importance of complying with the ethical guidelines to ensure the wellbeing of participants.

CASE CHALLENGE: Short-course AZT to prevent mother-to-child transmission of HIV

Adapted from WHO CASEBOOK ON ETHICAL ISSUES IN INTERNATIONAL HEALTH RESEARCH, 2009, Case 12, pg 63

The risk of vertical transmission of HIV during pregnancy and delivery has been estimated at 15-30%, depending on several factors, including the stage of the mother's illness and whether it has been treated. In the mid-1990s, the bestknown method for prevention of maternal HIV transmission was the "076 regimen", or long-course AZT treatment, in which a pregnant HIV-positive woman received zidovudine (AZT) five times a day orally from weeks 14 to 34 of the pregnancy and intravenously at the time of delivery. The infant would also be given AZT orally four times a day for 6 weeks after delivery. This regimen reduces vertical transmission of HIV by about 68%, provided that breastfeeding does not occur.1 However most public health experts in sub-Saharan Africa at the time that the study was designed considered that the "076" long-course regimen was impractical, because:

- prenatal visits do not begin until just before delivery;
- most deliveries do not occur in hospital, and of those that do, intravenous infusion during labour is not viable for most; and
- the cost of AZT for the long-course treatment is not affordble for most patients in most countries in sub- Saharan Africa.

To address these barriers, researchers proposed a series of Multisite, placebo-controlled trials in sub-Saharan Africa and the Asia-Pacific region to evaluate the efficacy of a short course of AZT for the prevention of vertical transmission of HIV. Participating mothers would begin treatment with AZT or a placebo 2 days before delivery; infants would also receive the drug (or placebo) for 2 days postpartum. The researchers were uncertain whether the short course would be as effective as the long course; however, a short course of treatment would be much less expensive than a long course and could increase access to care because it would be more in accord with delivery patterns in these two regions. Even if the shortcourse regimen proved less effective than the long-course regimen, the researchers hoped the short course would be adopted as standard preventive therapy in the absence of other feasible alternative regimens.

The researchers proposed to use a placebo control, since: the clinically relevant comparison was with the treatment that pregnant women were receiving at the time, which was no treatment at all; due to the practical and financial barriers, the longcourse regimen would not be widely implemented,and thus local public health officials in the study countries found it unethical to provide it to the control groups in the clinical trials; and because the short-course regimen requires less time to complete, the study countries could adopt the short course much sooner if it proved effective. Critics, mainly in the West, argued that the control groups should be given the "076" regimen rather than a placebo,

because: the decision to use a placebo, rather than long-course treatment in the control groups, violated the explicit provisions of the Declaration of Helsinki;

1 WHO recommends that HIV-infected women should use exclusive breastfeeding for the first 6 months of a child's life unless replacement feeding is acceptable, feasible, affordable, sustainable, and safe for them and their infants before that time. If those criteria are met, avoidance of all breastfeeding by HIV-infected women is recommended. WHO HIV and Infant Feeding Technical consultation. Consensus Statement. Geneva,Switzerland: Inter-agency Task Team (IATT) on Prevention of HIV Infections in Pregnant Women, Mothers and their Infants, 2006.

In June 1964, the World Medical Association (WMA) adopted the "Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. Although the original version did not address the issue of placebos, the issue emerged in subsequent revisions. Paragraph 32 in the 2008 version (based upon paragraph 29 in the earlier 2004 version)states that "The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best proven current method, except in the following circumstances: The use of placebo, or no treatment, is acceptable in studies where no proven current method exists; or Where for compelling and scientifically sound methodological reasons the use of placebo is necessary to determine the efficacy or safety of a method and the patients who receive placebo or no treatment will not be subject to any additional risk of serious or irreversible harm."
For more information, visit http://www.wma.net/e/policy/b3.htm (accessed 5 June 2009).

- the researchers were using a double standard since they would not be permitted to run a placebocontrolled trial in their own countries, on the ground that an effective therapy existed; and
- even though results would take longer – and be more expensive – to achieve with active rather than placebo controls, trials could be designed that excluded placebo controls.

Questions

1 If the health authorities in the African and Asia-Pacific countries declared the proven effectiveness of longcourse treatment irrelevant and impractical to their needs, should research ethics committees in the donor institutions still insist on long-course treatment for the controls?

2 If the researchers believed that short-course AZT would be effective but less so than long-course treatment, should the short course have been tested at all (even if the control group received the long course)?

3 If the test could not be conducted in a high-income country, would this, by definition, lead to a double standard for therapeutic intervention?

The first correct response will receive a prize.
Answers should be submitted to seru@kemri.org by 28th February 2018