

# AMANET *Newsletter*

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## Contents

- 1 **AMANET** to Host MIM
- 2 Workshop on Malaria Vaccinology in Developing Countries
- 5 Profile: Tropical Diseases Research Centre, Ndola, Zambia
- 6 Training Course on Financial and Procurement Procedures for European Development Fund Projects
- 8 Ifakara Health Research and Development Centre Institutional Review Board Training
- 10 Workshop Training on ICH-GCP for Clinical Investigators focusing on HIV/AIDS and Malaria Vaccine Trials

### Upcoming AMANET Workshops:

Health Research Ethics  
August 2005

Data Management  
September 2005

Molecular Biology  
November 2005

## AMANET to host MIM

Imani Lwinda of KPR\*

The African Malaria Network Trust (AMANET) will host the next Multilateral Initiative on Malaria in Africa (MIM) Secretariat for five years effective next year.

Professor Wen Kilama, Managing Trustee of AMANET, said in Dar es Salaam recently, "As much as we are excited by the election, we are very much aware of the enormous challenge ahead, the AMANET Secretariat will do everything to make sure that the MIM Secretariat has a good start, and carries on the good work of our predecessors".

AMANET is a pan-African not-for-profit organization based in Dar es Salaam, Tanzania. Professor Kilama noted: "We will of course need the continued support of all the MIM stakeholders and all those of good will."

Stockholm University and Karolinska Institute in Sweden have been hosting the secretariat since January 2003. It will now be placed at the AMANET Secretariat in Dar es Salaam between 2006 and 2010.

MIM is an international alliance of organizations and individuals concerned with malaria, and seek to maximize the impact of scientific research on malaria in Africa through promoting capacity building and facilitating global collaboration and coordination.

The alliance was launched in 1997 at the First MIM Pan-African Malaria Conference in Dakar, Senegal. Following the founding conference, The Special Programme for Research and Training in Tropical Diseases (TDR) was charged with the task of bringing together stakeholders with an interest in supporting capacity building research.

According to the current MIM Secretariat Coordinator Dr Andreas Heddini, MIM transfer will take place shortly after the fourth MIM Pan-African Malaria Conference to be held November 13-18, 2005 in Yaoundé, Cameroon. "AMANET, as the new secretariat, will officially assume its role from January 2006," said Dr Heddini recently.

Prof Kilama noted that as the mandate for the current secretariat comes to term in November this year, a fair and transparent transfer mechanism for a successor was employed.

"A call for applications was released. Having reviewed the functions and activities of the MIM Secretariat, AMANET decided that it has adequate infrastructure, institutional organization, skills and personnel to effectively run the secretariat for the next five year period," he noted.

He added that a large group of eligible voting representatives composed

\*Kabula Public Relations and media adverts agency

of MIM's major partners, including the World Health Organization, the US National Institute for Allergy and Infectious Diseases, Roll Back Malaria Partnership, government agencies, scientific institutions in Europe, the Americas and Africa and several malaria organizations voted for AMANET as the next host of the MIM Secretariat.

AMANET's mission is to promote capacity strengthening and networking of malaria research and development in Africa. Since its inception several years ago, AMANET has advanced essential human capacity for undertaking research and development of new malaria interventions, particularly malaria vaccines across Africa. Over 500 researchers across sub-Saharan Africa have participated in short-term AMANET training workshops.

Professor Kilama stated that the current AMANET Network Director, Professor Charles S. Mgone will head the new MIM Secretariat as Director.

"Initially, the Secretariat was being hosted for a duration of three years. The mandate period has been extended to a period of five years following recommendations of the external

review that MIM underwent in 2002 and by input from the MIM Strategic Advisory Board," Prof. Kilama said. Besides the MIM Secretariat and MIM-TDR the MIM alliance is also constituted of MIMCom, and MR4 which are based in the USA. These two evolved as constituents of the initiative to address other specific needs.

MIMCom, created by the National Library of Medicine at the US-NIH in partnership with institutions in Africa, USA and Europe, is an electronic malaria research network which has promoted electronic connectivity and therefore enhanced communication and collaboration between malaria researchers; by installing communication equipment MIMCom has facilitated scientific literature searches across Africa especially at remote research institutions.

MR4 on the other hand has been in the forefront of provision of laboratory reagents, exchanging research materials and conducting training in molecular biology and Good Laboratory Practice.

The MIM Secretariat maintains cohesion and ensures good communication between all constituents of the initiative. The Secretariat also organizes

the biannual Pan African Malaria Conference as well as periodic courses, symposia, stakeholders' meetings and workshops.

AMANET has been in the forefront of major institutional capacity strengthening. Institutions identified for AMANET strengthening besides being prioritised in short-term training in workshops, they receive capacity strengthening grants, which cover long-term professional training, provide essential equipment, upgrade infrastructure and support site characterization.

Institutions currently benefiting from AMANET capacity strengthening grants include the Centre National de Recherche et de Formation sur le Paludisme in Burkina Faso, the Amani Medical Research Centre in Tanzania, and the Tropical Diseases Research Centre in Ndola, Zambia.

AMANET sponsors clinical trials aimed at development of malaria vaccines, currently AMANET is funding a malaria vaccine trial in Burkina Faso; other institutions recently selected for developing malaria vaccines under AMANET sponsorship are in Gabon, Mali and Ghana.

## Report on the Workshop on Malaria Vaccinology in Developing Countries

Josephine C. Ocran, Ngandwe Kalungwana, Jane Maina and Charles Wanga

### Introduction

AMANET organized a five-day training workshop on "Malaria Vaccinology in Developing Countries" in Bagamoyo, Tanzania, from 14 to 18 March 2005. The aim of the workshop was to update participants with recent advances in research and development

of malaria vaccines and also, among others, discuss malaria vaccine research problems in Africa.

Secondly, the workshop aimed at equipping the participants' capacity to influence decision making towards the acceleration of malaria vaccines as viable intervention tools.

Thirty four (34) participants from Burkina Faso, Cameroon, Ghana, Kenya, Malawi, Nigeria, Sudan, Tanzania, Zambia, and Zimbabwe attended the workshop.

Facilitators came from AMANET, European Malaria Vaccine Initiative (EMVI), Gates Malaria Partnership-LSHTM,

GSK Biologicals, Tanzania Commission for Science and Technology, Tanzania National Institute for Medical Research, Rooster Training Solutions, Radboud University, Nijmegen Medical Centre, Statens Serum Institut, MRTC Bamako and MacNaughton Limited (representing AstraZeneca) The workshop was divided into five themes, one for each day. The following is a summary of the proceedings.

### Immunity in malaria

The history of immunoprophylaxis dates as far back as 1000 AD, in China, where some form of smallpox variolation was practiced as a method of disease prevention. Parenteral variolation spread from the Indian sub-continent to Europe in the 1700s and this progressed to culminate in eradication of smallpox in 1977.

There are six vaccine targets or approaches that can be adopted in searching for a workable malaria vaccine; two each against infection and disease, one against transmission and a live attenuated parasite vaccine. Transmission blocking agents have been successfully used against Lyme disease.

The ideal malaria vaccine candidate against blood stage should have antigens that are recognized by human antibodies acting through biological mechanisms that are effective only in clinically immune individuals, that are highly conserved because an antigen that constantly changes its sequence is a major challenge to vaccine development, and when used will generate the same response as was used in its identification in the first place.

Different vaccine targets require induction of different immune mechanisms, a prior knowledge of this is required to allow careful design of combinations, avoiding potential problems of interference or suppression.

On the current state of affairs of malaria vaccine candidates, there is a clear need for a public-private partnership. A few vaccine candidates have undergone phase Ia up to phase II trials; some of the lessons learnt are the following: there is the need of a clear definition of roles and responsibilities of all the players including sponsor, investigator, regulatory authorities and other stakeholders; insurance and indemnification, personal and institutional liability; need for validated assays including challenge and surrogate markers; and many small phase I trials may be needed.



*Participants in a group discussion*

### Evaluation of malaria vaccines and experiences in vaccine trials in Africa

In general the development, execution and orderly termination of a clinical trial is often complicated and time consuming; requiring significant resources in personnel, funding, facilities, equipment and supplementary support activities. The take home message was that there should be a manual of procedures and there should be systematic back up of equipment and personnel and remember that "if it is not written it

did not happen!"

Some of the experiences and lessons learnt from the DNA ME-TRAP/MVA vaccine trial in The Gambia were that, there should be established criteria for moving a candidate malaria vaccine from phase I to phase IIb field trials. Study designs should be more robust i.e. clearly defined as to whether the study looks at clinical disease or parasitaemia as the end point.

Length of post trial follow up, data management issues and clinical trial monitoring roles should be clearly defined.

Other lessons from the AMA-1 vaccine trial in Mali were that, there is a need

for intense continuous learning and capacity building and that sites need to have a vision of their own development in discussions with potential sponsors and product manufacturers. Investigators should also build a long term relationship with their study populations.

### Regulatory and ethical issues

The important issues that came out of this discussion are the need for Africans to have clear guidelines for the ethical and regulatory approval process for vaccine trials,

increased capacity for ethical and regulatory review and common agreements to decrease "IRB shopping".

An important part of ethical considerations is the informed consent process, which involves disclosure of all necessary information to a competent potential research subject or acceptable legal representative. Potential subjects should be given enough time to consider the information provided and understand it before giving their consent. Decision making must be completely voluntary and information must be updated whenever necessary.

The need for regulatory control in the production of biologicals has to a large extent been prompted by tragedy. Tragedy can occur anywhere down the supply chain from manufacture to the use of the product and hence regulatory control is necessary at all these stages. The regulatory body keeps an eye on all the processes an investigative drug or vaccine goes through, from concept through clinical trials, it facilitates the availability, accessibility and desirability of the product.

African countries need to harmonize their regulatory requirements so that they can have mutual recognition agreements among themselves and with other countries. There was a call for AMANET to act as the driving force to facilitate such an achievement through the African Union (AU), NEPAD and WHO.

On Intellectual Property Rights (IPR) the importance of contractual agreements was emphasised to be critical especially in research and development. It was learnt that intellectual properties were not only in a finished product, but could also be in the process. The advantages and disadvantages of patents in medical prod-

ucts and their implications were discussed. It was recommended that research institutions participating in product development need to articulate their own IPR policies to guide them in collaborative work. The subject of Material Transfer Agreements (MTA) was also discussed as a potential source of problems in research if the issues are not well articulated.

### Conducting Malaria Vaccine Trials

There are many guidelines which direct the evaluation of malaria vaccines in endemic areas. Good Clinical Practice (GCP) was presented as the international scientific and ethical standard of designing, conducting, documenting and reporting clinical trials. Compliance with this standard provides public assurance that the trial participants were not abused and that the data collected are credible.

Generally safety is evaluated in all trial phases. The profile of the candidate is compared to other vaccines/known data in terms of frequency and nature of adverse events, serious adverse events. Efficacy measures are widely varied depending on the perceived mode of action of the vaccine and may include: time to infection, parasite density, clinical episodes, time to clinical episodes, disease severity, overall mortality, etc. The crucial issue is to carefully standardise all definitions so that data are consistent and comparable.

The role of the principal investigator was emphasised especially in collection of accurate data, reporting and record keeping. Completeness of the investigator file with all essential documents for the conduct of a clinical trial was said to be central to GCP and product development research. Adverse events following the immunization process must be reported

according to a pre-determined protocol criteria.

During the Private-Public partnerships in malaria vaccine development session, it was noted that the perceived lack of profitable market is a major hindrance to malaria vaccine development. Solutions to this under-investment in product development for poverty related diseases depend on increased research funding by the public/not for profit sector. Private enterprise would be attracted by mechanisms that minimise their investment into the process i.e. streamlined regulatory and ethical processes, capacity for GCP trials in disease endemic countries, commitment by government to improve absorption capacity for the product and partnerships with the public sector.

### Vaccine delivery and logistics

The search for a malaria vaccine is an enormous task. But even when an effective vaccine is found there are still problems related to mechanisms of introducing the vaccine and the public finding it acceptable. Information dissemination is very important in research as well as public health as it is the means to improved service/product utilization. In a general sense, scientists may not be the best publicists. It is thus important whenever possible that expert advice is sought for transmitting information to the public. It is desirable that institutions have publication policies that guide information dissemination. In collaborative research, it is also important to develop publication strategies right at the beginning of the work, so that appropriately packaged information is disseminated in a targeted and controlled manner.

# Profile: Tropical Diseases Research Centre, Ndola, Zambia

Violet Siachinji

## Historical Background

The World Health Organization established the Tropical Diseases Research Center (TDRC, fondly called the Centre) at Ndola, Zambia in 1975. In January 1981, the Centre became a national institute under the Zambian Government. The first stage of this transformation was a shift in emphasis from a WHO Regional Centre towards a national institution aiming at strengthening capacity for epidemiological research. The second phase of this transformation was to establish TDRC as a viable national and regional research and training centre.

Presently, the Centre operates under the provisions of the TDRC Act of 1982 of the laws of Zambia. There is a Board of Directors appointed by the Minister of Health which is the policy making body for the institution. The Director who is assisted by a Deputy Director and Board Secretary heads the management team, which is responsible for the day-to-day running of the Centre.

In the period 1975 to 1981, the research activities of the Centre were tailored to the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR). The major thrust was on epidemiology of malaria, trypanosomiasis and schistosomiasis. Since the Centre became a national institution, the research agenda has expanded to include research in micronutrient deficiency disorders, tuberculosis, HIV/AIDS and other sexually transmitted infections. The

types of studies carried out by TDRC include epidemiology, entomology, and clinical trials of anti-malarial drugs, social science and the search for herbal remedies for malaria.

## Staffing

The TDRC currently employs 74 staff.

Of these, 34 are scientific and technical while the rest are administrative and auxiliary staff.

## The TDRC Location and Infrastructure

The Centre is housed on the two top-most floors of the Ndola Central Hospital; a tertiary care facility in the Copperbelt Province of Zambia. The 6th floor has Administrative Offices, the Public Health Department, the Fee Paying Clinic and a mosquito proof Clinical Trials Ward with 20 beds and 6 paediatric cots.

The laboratories are situated on the 7th floor and are demarcated into eight units namely: Biochemistry, Haematology, Microbiology, Parasitology, Immunology, Molecular Biology, Nutrition and Vector Biology.

The most recent addition is the cross cutting Molecular Biology unit which deals with the confirmation of mosquito species and their infectivity and the determination of drug resistant micro-organisms such as *Plasmodium falciparum*, tuberculosis and the human immune virus using state of the art equipment.



*Participants for a Training Workshop on Laboratory Diagnosis recently organized by TDRC*

The Center has telephone, facsimile. There is a reliable internet connection which links the institutional computers through a local area network. There is a fleet of institutional vehicles which are used for research operations acquired mostly through project funding.

## Mission

The mission of TDRC is to contribute to socio-economic development through targeted research leading to prevention and control of diseases.

## The Vision

The vision of TDRC is to be a center of excellence in the promotion of health through research and training in the Region.

## Achievements

Tropical Diseases Research Centre has strength as the leading malaria research institution in the country, and supports the National Malaria Control Centre as a resource for information to be used in the formulation

of evidence-based national malaria policy. A case in kind is the changing of the malaria treatment policy from Chloroquine® as first line drug to Coartem®. In collaboration with the National Malaria Control Centre, TDRc spearheaded the introduction of insecticide treated bed nets in Zambia.



*The TDRc Molecular Biology laboratory*

Over the years TDRc has developed an internationally recognized capacity for conducting clinical trials and has successfully conducted several phase I, II & III clinical trials under Good Clinical Practice (GCP) guidelines.

TDRc was instrumental in the drastic reduction of human and animal trypanosomiasis incidences in Isoka district in the northern part of the country.

It was the research results from TDRc that led to confirmation that the high prevalence of blindness in Northern Zambia was due to micronutrient deficiency. And TDRc championed the fortification of sugar with vitamin A in Zambia. It continues to play a role in the evaluation of the impact of the food fortification programme on the micronutrient status of Zambia children. TDRc further confirmed the efficacy of Praziquantel on *Schistosoma mansoni* and *S. haematobium* at community level in Zambia.

Recently, a new TDRc TB reference laboratory has been opened to serve the Northern part of Zambia so that TB can be diagnosed early and managed effectively.

### STC and Ethical Committee

The TDRc has a policy whereby all research proposals are passed through the Scientific and Technical Committee for assessment of scientific merit before any study can be initiated. After being passed by the STC, proposals are then submitted to the Ethical Committee to ensure that the proposed research upholds the

fundamental international ethical guidelines.

The TDRc Ethical Committee is an independent body that consists of members from different institutions including the church, legal fraternity, ordinary community members, scientific and medical personnel. It is presently chaired by an army General who is also a Neurologist.

### Future Plans

TDRc wishes to continue assisting in the development and evaluating of techniques, methods, tools and strategies to solving health related problems. There are plans laid out to evolve into:

- (i) a reference resource for malaria diagnosis for Zambia;
- (ii) an institution with capacity to participate in testing vaccines for malaria, HIV and other diseases affecting Africa.

With the excellent laboratory facilities at the institution, the TDRc is also beginning to work with traditional healers on rediscovering the herbal remedies for the treatment of malaria and those for HIV/AIDS.

## Report on the Training Course on Financial and Procurement Procedures for European Development Fund Projects

Badru B. Amri

### Introduction

One of the major donors to AMANET is the European Aid Co-operation Office (AIDCO) of the European Commission. Projects funded by AIDCO have to be accounted for in accordance with the special European Commission guidelines. Thus AMANET decided to work with the MDF Management &

Consultancy BV of the Netherlands as an AIDCO accredited firm to organize and host a four-day Training Workshop on "Financial and Procurement Procedures for EDF funded Projects".

The target participants were financial personnel in African health research institutions that are recipients of AMANET capacity strengthening grants

received through AIDCO funding.

MDF Management and Consultancy BV is a sole AIDCO-commissioned consultant that conducts these trainings. The workshop was held on 09-12 May 2005 at Moivaro Coffee Lodge in Arusha, Tanzania.



Thirteen participants in attendance were drawn from AMANET strengthened institutions in Burkina Faso, Ghana, Gabon, Mali, Tanzania, Zambia and Zimbabwe.

### Objective

The aim of the workshop was to acquaint accountants and procurement officers responsible for managing AMANET capacity strengthening and site development grants with AIDCO accounting standards and procurement procedures. The four-day long training included ten lectures and eight practical exercises covering:

1. Afro-Caribbean Pacific-European Union Cooperation
2. Organization of Europe Aid Cooperation Office
3. Project financing
4. Procurement procedures
5. Programme estimates (budgeting)
6. Internal controls and auditing
7. AMANET accounting procedures
8. International accounting procedures
9. Payments
10. Financial reporting and auditing

The participants were taken through all stages in a project cycle. From its planning, initiation to evaluation.

Emphasis was put on the involvement of all professionals throughout all stages of the project cycle. It was

noted that most scientific project proposals are written without inputs from accountants or finance officers. African research institutions must therefore learn to involve them as they are critical partners in the project cycle especially that they involve accountability and reporting back to the donors.

In any of the stages in a Project Cycle, participants were urged to comply with financial and procurement procedures of the different donors, in particular those of the European Development Fund (EDF 9).

Recipients of project funds need to invest time and personnel in understanding these requirements in order to avoid non-compliance which jeopardizes the prospect of further fund releases. The need for efficiency, economy and effectiveness were emphasized throughout with practical examples highlighted.

### Contracts

The course paid particular attention to contracts. The participants were taken through the various types of contracts supported by EDF namely Works, Supply, Services and Grants. It was however noted that most of the research work is undertaken through Service and Grant contracts.

For these the following issues were expanded on:

- Preliminary provision to contracts: language, documents, supervision etc.
- Obligations of the contracting authority.
- Obligations of the contractor.
- Commencement and delay.
- Materials and workmanship.
- Payments, acceptance and maintenance.
- Breach of contracts and termination.
- Settlement of disputes.

*“The aim of the workshop was to acquaint accountants and procurement officers ...with AIDCO accounting standards and procurement procedures.”*

### Feedback

The overall feedback from participants and facilitators was positive. Various aspects had to be ranked from 4 (very good) to 1 (poor) with highest being given to the criteria ‘quality of lectures’.

Participants responded particularly well to the practical sessions where they shared their knowledge and experiences. Wherever possible, facilitators encouraged application of knowledge learned to real-life. All participants were successful at the final course test.



*Congratulations!*

# Report on the Ifakara Health Research and Development Centre Institutional Review Board Training Workshop

Sally Mtenga and Roma Chilengi

The Ifakara Health Research and Development Centre (IHRDC) which was founded in 1957, is a not for profit, independent, district based health research and resource centre. The IHRDC is established to carry out research on topics perceived to be local priorities, to support those planning health systems, and to help members of the local community to achieve better health.

Over the years the main activities have included basic, laboratory, clinical, health systems and social anthropology research in malaria, tuberculosis, schistosomiasis and other infectious diseases of public health importance. Of recent, the increased number of activities at the institution has necessitated improvement on the operational strategy.

One of the areas that required revamping is the Institutional Review Board (IRB), charged with responsibility of ensuring ethical conduct of research. In this regard, IHRDC requested the African Malaria Network Trust (AMANET) for technical assistance in the process of reconstituting the IRB. This is the report of the three-day IRB training workshop that was organized and hosted at the IHRDC Dar es Salaam office from 29 to 31st March 2005.

## Day 1

The session was officially opened by Dr Salim Abdulla, standing in for the IHRDC director Dr Hassan Mshinda. He welcomed participants and asked them to give a brief introduction of themselves. This was followed by a

brief background about the Center with an aim of letting the new participants to know what IHRDC has been doing in the area of health research and interventions. He explained that the aim of this workshop was to have a common understanding on guiding principles with regards to research ethics and empower all the IRB members so they participate fully in the reviewing of the research protocols.

Another major objective was to improve the existing standard operating procedures to be able to meet national and international guidelines of research ethics. Further, to accommodate physical and professional expansions that IHRDC is currently undertaking.

The first topic was on history of research ethics & major ethical guideline codes.

Dr Chilengi began by giving a justification for biomedical research. Distinction was made between research and medical practice in that research is not routine treatment but rather experimentation and involves human subjects. Though there is need to accept research as important to human kind, it is also important to safeguard the welfare of the human research subjects.

The historical background was followed by sessions on guidelines for operations of ethics committees. The WHO guideline for operations of ethics committees was presented as a sample guide. Under this section the facil-

itator argued that there are many important international guidelines (ICH, GCP, FDA, EMEA etc), but it is also important to have consideration for the national guidelines without overlooking different local and cultural aspects.

However in developing SOPs, it is critical to integrate the fundamental international principles so as to be comprehensive in catering for collaborative research.

The group worked on improving their current IRB SOP by integrating impor-



*IHRDC-IRB Training in session*

tant elements from the WHO ethical guideline. This led to a number of modifications, which would be submitted to the national committee for approval after the IHRDC administration ratifies them.

## Day 2

Mrs. Ikingura from National Institute of Medical Research (NIMR) started the day with sharing experiences of national ethics committee in its composition, election process and the execution of different ethical issues. It was learnt that all research involving non-Tanzanian collaborators need

to obtain national approval, which involves authorization permit for the external collaborators through the Tanzania Commission for Science and Technology.

Valuable information was discussed on how the national ethics committee would interact with IRBs, what can be done to improve inter-IRB communication, examples of “IRB shopping” and matters pertaining to the legal mandate of ethics committee. It was learnt that the national committee was handling in excess of 20 proposals monthly and lessons learned in meeting the challenges were discussed.

The session continued with looking at establishing a system of ethical review; it was emphasised that the critical pathway of the protocols needs to be streamlined. The IRB needs to clearly stipulate in the SOP what kind of expertise it will need and how they will be engaged; how the investigators would get relevant information on the procedures to follow, establish a communication strategy that respects the set timelines and estimate the cost implications for their operations so that resources are appropriately allocated.

It was emphasised that the IHRDC ethical committee needs to have a strong collaboration with other ethical committees especially the national committee. The need for independence was also raised in that the IRB should not suffer undue pressure from administration or the scientists, but rather should adhere to guidelines once established. However, the IRB procedures should also be flexible, being responsive to demands of expedited review when appropriate.

The discussion on informed consent emphasised the fact that it should be a process and not a one off event.

There is therefore need to have a mechanism of providing feedback to the participants whenever new information comes up or if there is a change in the research procedure. The IRB members need to make sure that, the information given in the informed consent is comprehensive enough and is in the language, which can be understood easily by the research participants, especially uneducated ones. Obtaining “true informed consent” was presented as the greatest challenge for investigators, and the IRB needs to evaluate that information package before approving the research.

The elements of informed consent according to GCP were discussed, highlighting that it must all be in a language to be understood by the participant, and adequate time must be allowed for information, comprehension and decision making. It is particularly important the participant knows that this is research, appreciate the risks involved, understand the benefits, accept the expected responsibilities and volunteer to participate without undue coercion. Beyond this, the question of the IRB responsibilities, and how can it ensure that they are fulfilled was addressed.

The cardinal obligation being that the participant’s rights, safety and well being are protected. It was pointed out that ethical approval should not be seen as a “blank cheque” to the investigators, but rather an approval of only activities strictly stipulated in the protocol. The IRB therefore should have a way to ensure that the investigators are actually doing only what they approved, and this is the need for procedures to address the question of ethical oversight.

Strategies to help follow up on approved activities were discussed, and they would include:

- Requirements for regular progress reports, and penalties for non compliance;
- Requirements that all clinical trials be monitored by independent experienced clinical monitors;
- Requirements for Data Safety and Monitoring Boards (DSMB) to be set up for all randomised controlled trials;
- Random unannounced inspection checks by IRB;
- Feedback information from the participant community;
- Obtain institutional backing to follow up with disciplinary measures if needed.

The discussion was followed by further review of the SOP and again relevant amendments and proposals were made in the light of the topics discussed.

### Day 3

The third day began by an overview on the topic on the “IRB’s meeting and decision-making process”. There is need for well-coordinated communication to the IRB members with regard to documents to review, meeting place and time. The schedule should preferably be drawn ahead of time, logistics prepared and quorum requirements considered to avoid time wastage. The secretariat needs to have basic office facilities to allow for printing, communication, filing, and a secure meeting room.

Full decisions on protocols should only be made during meetings, and other earlier decisions otherwise made through conference calls or mail should be reviewed. Elements of the protocol to be considered were presented beginning with the statement “bad science is unethical” therefore scientific review should also be adequate. In reviewing research protocols it is important to pay particular

attention when special groups of vulnerable populations are targeted.

The IRB must adopt a mode of reviewing protocols which must be followed. The decision making process should also be preset; whether by consensus or voting, but it must be clearly written in the procedures and adhered to. It is important to take time for other business including the time to assess the progress of the IRB, reviewing all operational costs and welfare of the IRB members besides making decisions on protocols.

The issue of dealing with ethical misconduct was discussed starting with the various definitions: "Misconduct means fabrications, plagiarism or any

serious deviation from accepted scientific practices in proposing, conducting or reporting research". The IRB needs to understand the environment, under which misconduct happens, and this may include excessive personal financial incentives for subjects; overworked investigator or study team; excessive work demands for staff or investigator and previous successful fraudulent behaviour. Other important issues to look out for include high staff turnover, complex protocols, extremely slow subjects accrual, rapid subject accrual and inadequate investigator qualification. Approaches to prevention were discussed in a stepwise manner from primary, secondary and tertiary prevention.



*Certificate presentation*

The final activity was to come up with a plan of action for the next steps in order to complete the SOP revision exercise, steps to improve the composition of the IRB, and draw an annual schedule of the meeting dates to be included in the SOP.

## Report on the Training Workshop on ICH-GCP for Clinical Investigators focusing on HIV/AIDS and Malaria Vaccine Trials

Josephine Ocran, Mark Kaddu Mukasa, Samson Gwer and Charles Wanga

### Introduction

The WHO Initiative for Vaccine Research (IVR) in collaboration with AMANET and African AIDS Vaccine Programme (AAVP) hosted a five-day Training Workshop on "International Conference on Harmonization (ICH) of Good Clinical Practice (GCP) for Clinical Investigators Focusing on HIV/AIDS and Malaria Vaccine Trials" in Zanzibar, Tanzania from 25-29 April 2005. The 31 Participants were drawn from Botswana, Burkina Faso, Ethiopia, Gabon, Ghana, Kenya, Mali, Sudan, Tanzania, Uganda, Zambia and Zimbabwe. Facilitators came from WHO-TDR, WHO-IVR, AMANET, AAVP and Tanzania Food and Drug Authority (TFDA).

The aim of the workshop was to acquaint participants with:

- The roles and responsibilities of investigators doing research according to ICH-GCP standards;
- Current international ethical/regulatory guidelines for clinical research ;
- Requirements for HIV/AIDS and Malaria clinical studies;
- Developing of field Standard Operating Procedures (SOP's) and;
- Basics of data management and documentation skills.

Hon. Mussa Ame Silima, Zanzibar Minister for Trade, Industry, Marketing & Tourism, officially opened the workshop by pointing out that malaria is Africa's public health enemy number one, and the situation is deteriorating

despite intensified efforts at containing it. As if that were not enough, the plague of the HIV infection and its deadly consequence, AIDS, is haunting Africa, especially in the sub-Saharan region where it is claiming many lives daily. The challenges facing Africa are real and require adopting workable strategies. The aim should be at training scientists so that they are empowered to actively participate in setting the research agenda for Africa, and contribute to development of appropriate intervention tools.

**GCP** is an international ethical and scientific quality standard for the designing, conducting, recording and reporting trials that involve participation of human subjects

## Overview of product development and principles of GCP

The development of a new drug or vaccine can be summarized into 3 stages: (i) Target discovery when a gene or protein link is found; (ii) drug discovery and (iii) development which includes pre-clinical testing and clinical trials in humans.

The primary aim of Good Clinical Practice (GCP) is to produce credible data in research while protecting the dignity and safety of trial participants.

GCP is an international ethical and scientific quality standard for the designing, conducting, recording and reporting trials that involve participation of human subjects.

International Conference on Harmonisation (ICH) guidelines for GCP gives a set of international recommendations on the harmonised requirements for drug registration. They should be followed when generating clinical trial data that are intended to be submitted to regulatory authorities.

The basic principles of GCP ensure that the rights, safety and well-being of trial subjects prevail over the interest of science and society. The second basic principle is to have credible trial data and by following GCP guidelines, one ensures that data is accurate and verifiable.

## Regulatory Authorities

National Regulatory authorities have a key role to play in protecting subjects in clinical trials. They oversee the importation and use of the investigational product. In developing countries especially Africa, regulatory authorities are only now beginning to be familiar with their role in clinical trials. In many countries there are no regulatory authorities, and where they

exist, often do not have regulations regarding clinical trials. The Tanzanian Food and Drug Authority was presented as a case for the role of regulatory authorities in Africa. The process and requirements of clinical trial drug importation was presented and practical implications for the investigators discussed. It was learnt that the regulatory authorities within the Eastern and Southern African region are in the process of harmonising their requirements as per ICH.

The need to work with and comply with regulatory authorities is cardinal in product development as they hold the key to the registration and public use of the product.

## The Role of a sponsor

During the workshop, the definition and responsibilities of a sponsor was clearly outlined. A sponsor was described as a person or institution who takes the responsibility for initiation, management and financing of a clinical trial. A financier may not necessarily be a sponsor if his/her interests do not go beyond that of philanthropy. It is the sponsor's responsibility to select the appropriate site, to appoint a qualified investigator, to delegate other roles outlined in the protocol and to provide the investigational product and all the information pertaining to it.

The sponsor should also be committed to providing indemnity to the investigator and compensation of the trial participants in case of a trial related injury. Overall, the sponsor should

ensure that the trial is conducted in accordance with sound scientific principles and good clinical practice standards and that the operations are within existing legal and regulatory bounds.



*Session during the ICH-GCP workshop*

## Investigator responsibilities

For this topic, participants were allocated the various responsibilities to present with practical examples from their own experiences. An investigator was defined as the person responsible for the conduct of the clinical trial at the trial site. S/he plays an important role from the initiation of the study till the end. Sufficient time and availability during the trial was emphasized.

Adequate knowledge of GCP and understanding of the SOPs by the investigator and his team is essential. The investigator should ensure adherence to the SOPs, communication with the community as well as safety of participants. Recruitment and enrolment of participants should be according to the protocol.

Case report forms completion should be done by the investigator immediately so that errors can be identified and rectified as soon as possible. Source documents should be kept by the investigator and confidentiality maintained.

Drug accountability with emphasis on storage, labelling, prescription should be followed as per protocol. While labelling is a sponsor responsibility, the investigator must ensure that storage or the cold chain is maintained as stated in the investigator's brochure. The personnel handling drugs should be qualified and trained for the job and proper accountability kept.



*Dr J. Karbwang supervising an interactive session*

Essential documents were listed and said to individually or together allow evaluation of the conduct of the study and the quality of the data produced. These should be filed and be readily available. They include investigator's brochure, study protocol, informed consent, patients information sheet, signed agreements between the investigator and sponsor, approval from the

IEC/IRB, CVs of the investigators, signed, dated and completed CRF, administrative and communications with the sponsors to mention some.

### Monitor responsibilities

Monitoring is the act of overseeing the progress of a clinical trial, and of ensuring that is conducted, recorded and reported in accordance with the protocol, SOPs, GCP and applicable regulatory requirements. Monitoring of a trial is a sponsor responsibility, but while the monitor is the eyes and ears of the sponsor, the monitor is also there to help the investigator and ensure the success of the trial.

The monitor is not there only to fault find but he is also there to identify

sources of errors that may not have been apparent to the investigator and suggest solutions in order to ensure that trial data are credible. In order to achieve this, monitors must be appropriately trained and should have the scientific and / or clinical knowledge needed to monitor the scientific trial adequately.

The extent and nature of monitoring

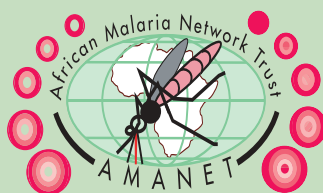
is determined by the sponsor and should be commensurate with the level of technical detail involved.

The trial monitoring is an integral component of trial quality assurance process and critical for GCP fulfilment.

### Role of the Institutional Review Board (IRB) or Independent Ethics Committee (IEC)

An overview of ethics in research was given where participants were given the history of ethics in clinical trials with classical examples such as the thalidomide tragedy, the Tuskegee study, the Nuremberg doctors' trial of 1946. Declarations such as the World Medical Association's Helsinki Declaration, CIOMS and others currently provide acceptable guidelines on health research ethics.

The role of the Institutional Review Board (IRB) or Independent Ethics Committee (IEC) is to provide guidance, public assurance in protecting the rights, dignity and well-being of the trial participants. To do this an IRB/IEC needs to be competent in its composition and operations. Unfortunately, most IRBs in Africa are still struggling to attain that level of proficiency, and therefore, investigators must participate in ensuring that their IRBs are up to date with current issues relating to biomedical research.



### African Malaria Network Trust

Tanzania Commission for Science and Technology Building  
Ali Hassan Mwinyi Road  
P. O. Box 33207  
Dar es Salaam, Tanzania.

Phone: +255 22 270 0018  
Fax: +255 22 270 0380  
Email: [info@amanet-trust.org](mailto:info@amanet-trust.org)

[www.amanet-trust.org](http://www.amanet-trust.org)