

AMANET *Newsletter*

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Contents

- 1 Editorial
- 2 Announcing the AMANET web-based health research ethics course
- 3 Profile: National Institute for Medical Research (NIMR), Tanga Medical Research Centre
- 4 AMANET participation at the VI FAIS International Congress
- 5 AMANET Workshop on Molecular Biology and Immunology in Malaria Vaccine Development and the Makerere University-University of California at San Francisco (MU-UCSF) Malaria Symposium
- 11 Fifth AMANET Biennial Conference: First Announcement and Call for Abstracts

Upcoming AMANET Activities:

Management for Research Leaders Workshop
September 2006

Pilot Workshop:
Web-based HRE Training
September 2006

Fifth AMANET Biennial Conference
February 2007

Editorial

Wen Kilama

I am once again honoured to communicate with you all in this special newsletter editorial. For those who have followed our evolution closely, you would agree with me that we have come quite a long way. Though it seems like only yesterday, I am pleasantly surprised that this is actually the nineteenth issue of the AMANET newsletter.

Our quest to take the role of sponsoring trials for malaria interventions was faced with severe discouragements from within and without. We have steadfastly fought the sceptics and are glad to say that we are now more confident than ever before in this regard. During the past year we have seen our leading malaria vaccine candidate MSP3 undergo phase Ib testing in Burkina Faso. We are very optimistic with our encouraging results which have fulfilled the "go criteria" set up in its clinical development plan. We are now preparing to age de-escalate toward infants and toddlers with this vaccine. We are also bracing ourselves for the phase Ib trial of AMA1 vaccine planned to start around the end of this year in Mali. For our GMZ2 vaccine, plans are also advanced for its trials early next year in Lambaréné, Gabon.

In our eighteenth issue we announced one of AMANET's landmark successes in becoming the first African host institution for the MIM Secretariat. This dream is now a big reality as the new Secretariat is steadily finding its feet. The Secretariat has since enjoyed the company of Professor Joas Rugemalila as the new MIM Coordinator and Mr Saad Ramadhan as Information Technology Officer. As the transition settles in, we are looking forward to great challenges and greater impact of our contribution to the global fight against malaria. At the fourth MIM pan African Malaria Conference in Yaoundé, AMANET was classified as one of the major donors as it brought to the conference over 70 participants, 35 of whom were young African scientists. We remain grateful to the outgoing Secretariat at Stockholm for the invaluable support during our teething period.

We believe the drums are sounding so loud that even the deaf will hear; "the child AMANET is now man". We look forward to contributing more to strengthening capacity on the continent. Our latest approach is to provide web-based health research ethics training. In this newsletter issue, we are announcing our fresh course to be released soon on the AMANET website.



*Prof. Wen L. Kilama
Managing Trustee, AMANET*



*Prof. Joas B. Rugemalila
MIM Secretariat Coordinator*



*Mr. Saad W. Ramadhan
Information Technology
Officer*

Reaching more through new system of teaching

Announcing the AMANET web-based health research ethics course

Roma Chilengi

In June this year, AMANET was awarded a grant by the European Developing Countries Clinical Trials Partnership (EDCTP) through which a web-based course on basic health research ethics will be created for Africans. This development comes in the light of the successful training workshops that AMANET has conducted in the past.

Our experience has been frustrating when we try to match the supply of training opportunities against the huge demand out there. It has been sadly noted that during the preparation of each workshop, eligible candidates apply in their hundreds, when in fact each course could only take up to thirty candidates. Health research ethics in Africa is emerging to be an important field, owing to the sharp increase in the number of research projects and particularly in clinical and field trials taking place on the continent, and these, largely involving the poor rural communities which are inadvertently vulnerable.

Moreover, the ethical review framework in Africa is still poor in most cases depending on very few researchers who dedicate part of their time as volunteers on ethics review committees. Besides, ethics as a subject is in general, poorly covered in most academic institutions to the effect that most of our scientific professionals on the continent do not have adequate understanding of the fundamental principles of health research ethics. The lack or poor funding of the ethics review

committees, where they exist, further makes the field unattractive to young Africans to take up the field as a career. Thus, we end up with ethics committees which are reviewing complex research protocols without the necessary training background. Moreover, opportunities for specific training in ethics remain prohibitive to those who need it because of cost and the time required.

In this background, AMANET has reached advanced stages in developing a web-based programme that will make available, free of charge, teaching in basic health research ethics. With increased internet access across Africa, we believe that this resource will be available to many individuals. Unlike most of the currently available web-based teaching resources, efforts have been made to minimise “western government” laws and regulations while maintaining the fundamental principles. The lecture type slides will contain links to other additional resource materials such as guidelines, declarations and codes which can also be downloaded and printed out.

To ensure that the participants have actually learned, a test will be set at the end of each of the teaching modules. There will be ten modules in all, but to meet the requirement for basic knowledge, a minimum of seven successfully completed modules will earn the AMANET certificate. The students will have to score at least 70% in the module test to be able to proceed to the next module. Five of



*Dr Roma Chilengi,
AMANET Clinical Trials Coordinator*

the modules will be compulsory, and then there will be a free choice of another two from a list of five, in order to meet the requirements for a certificate.

The following are the learning objectives set out for this course:

- Understand the evolution of health research ethics citing a few historical events that influenced the discourse;
- Have an understanding of the fundamental ethical principles and interpret their applications in research practice;
- Identify the major international guidelines and codes of ethical research conduct when human participants are involved;
- Define an ethical review board, describe its membership requirements, identify their responsibilities and understand the operations of an ERB;
- Have an understanding of potentially vulnerable research

participants and issues surrounding their consideration in research ethics, particularly in Africa;

- Define informed consent and describe the elements of the process and a good informed consent document, emphasizing the African context;
- List the criteria a study must meet in order to be approved by an ERC;
- Understand some ways of ensuring protection of human

participants throughout the conduct of a study;

- Orientation on trans-cultural and international research ethics with a focus on some African issues.

This basic course has been developed as a pilot project, which if successful will lead to development of an advanced course and possibly attend to other clinical research disciplines. Deliberate efforts are being made to ensure that the course is very user

friendly with help options. The programme in development is intended to have capacity for handling up to 1000 students simultaneously. What is more, one may proceed at their own pace as long as they can complete the modules within three (3) months. When the course is set in the near future, we will invite every ethicist, researcher, laboratory scientist, clinician, or scholar is invited to visit the AMANET website and consider this course.

Profile: National Institute for Medical Research (NIMR), Tanga Medical Research Centre

Martha Lemnge

Background

Following the collapse of the East African Community (EAC) in 1977, the National Institute for Medical Research (NIMR) was established by Act of Parliament No.23 of 1979 and became operational in October 1980. Tanga Medical Research Centre (NIMR Tanga), is one of the Centres of the Tanzania National Institute for Medical Research (NIMR). NIMR Tanga Centre had been operating as a Field Station and then Research Station known as Bombo under the NIMR Amani Centre until August 2005. Bombo Station, which had been researching on filariasis during the EAC as Tanga Centre, continued to work under the supervision of Amani Centre until it became fully operational in September 2005, when most research activities were shifted from Amani to Tanga.

The Centre is situated next to Bombo regional hospital. Most of the laboratory activities are carried out at the Amani Biomedical Research Laboratory (AMBRELA). Tanga Centre

is managed by a Director appointed by NIMR Council.

Mission: To conduct health research to alleviate disease burden in Tanzania.

Vision: To be a Centre of Excellence in clinical research and clinical trials in northeastern Tanzania.

Staff: Tanga Centre has a total of 58 staff members of whom 14 are research scientists, 8 laboratory technicians, 4 laboratory assistants, and 8 laboratory attendants. The Project staff working in Korogwe, Muheza, and Tanga total 62.

Departments: The Centre has five



Amani Biomedical Research Laboratory (AMBRELA): Front view

scientific departments: Biochemistry, Immunology, & Molecular Biology; Epidemiology & Clinical Research Trials; Medical Parasitology & Microbiology; Information Technology & Medical Documentation; and Health System & Policy Research.

Research Projects

In 2005, the NIMR-Tanga Centre was awarded a 250,000 Euros grant by AMANET. The two year grant aims at strengthening the center's infrastructure, human resource and

research capacity; establishing a demographic surveillance system and carrying out epidemiological surveys in areas with different malaria transmission intensities in preparation for malaria vaccine trials.

Other ongoing research activities at the Centre include: Epidemiology of Malaria, TB, HIV/AIDS, and lymphatic filariasis; Clinical trials (efficacy of antimalarials at EANMAT sentinel sites (NMCP) , IPTi with short and long acting antimalarials (BMGF), Lapdap

and Coartem pharmacovigilance and effectiveness (WHO/TDR); malaria morbidity and immunity in pregnant women and children (RUF-ENRECA); human genetics and immunity (MalariaGEN, Oxford University)

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NIMR Tanga Centre Laboratory

AMANET participation at the Sixth FAIS International Congress

Daniel Dodoo

The Federation of the African Immunological Societies (FAIS) in collaboration with the Senegalese Society for Immunology (SSI) and other partners organized an International Congress on 20-23 March 2006 in Dakar, Senegal.

The theme for the Sixth Congress was "Immunology; a tool against diseases related to poverty". Sub-themes included host-pathogenic interactions, infectious diseases, cancer, immunotherapy and vaccination, autoimmune and allergies, homeostasis and immune system, innate and adaptive immunity, lymphocytes

development, cytokines, vaccine trial practices in Africa and strategies for vaccine design in Africa.

During the Congress, eight scientific presentations were made from AMANET's Afroimmunoassay (AIA) network sites. These presentations included the AIA standardized ELISA assay systems, Assessment of the relationship between antibody responses against AMA1, MSP1-19, MSP3, GLURP and protection from clinical malaria and the role of antibodies against GLURP and MSP3 in malaria parasite resistance to Chloroquine and Fansidar.

The AMANET and Netherlands Ministry of Foreign Affairs (DGIS) sponsored Afroimmunoassay network.

The project has developed standardized and validated ELISA assays for immuno-epidemiological assessment of asexual stage malaria vaccine candidate molecules. The standardized ELISA assays are for isotype and IgG subclass determinations and enable comparison of data from studies conducted at different places. Standardization of immunological assays have become increasingly important as quite a number of putative malaria vaccines are in

various stages of Clinical Trials in different endemic regions of Africa and the assessment of vaccine immunogenicity that afford comparability of data should involve African scientists and Institutions.

Subsequent to the FAIS congress, a 3-day AIA publication workshop was held where issues regarding centralized data analysis and publication of site specific data were discussed.

In the next phase, AIA will expand to include additional African partners and establish additional immunological assays including the functional parasite growth inhibition, ELISPOT, multiplex and IFA assays. Such expertise will be made available to the African scientific community through GLP-compliant hands-on training workshops.

The AIA standard operating procedures (SOPs) for immuno-epidemiological assessment of asexual stage malaria vaccine candidate molecules, will be posted at the AMANET website. The ELISA SOP will include quality assurance procedures, quality assurance of equipment, personnel, a Microsoft Excel based curve-fitting and ELISA data merge

program. The standardized AIA ELISA will enable validation of promising malaria vaccine candidate antigens, provide essential baseline information for clinical trials and enhance quality assured laboratory capacity and capability.

Also presented were results from phase Ib trial of the candidate malaria vaccine MSP3 by the Principal Investigator, Dr Sodiomon Bienvenue Sirima who was given a Recognition Award for successful completion of the study. The MSP3 trial was done at

Centre National de Recherche et de Formation sur le Paludisme (CNRFP), Ouagadougou, Burkina

The FAIS sixth congress offered scientists, experts in the field of immunology, junior and senior researchers and students from Africa and the rest of the world, an opportunity for publication of their research findings and for networking. The Congress elected Ahmed El-Gohary as the new FAIS President. The next FAIS Congress will be hosted by Egypt in November 2009.



AMANET-funded AIA delegation at the Sixth FAIS Congress

Report on the AMANET Workshop on Molecular Biology and Immunology in Malaria Vaccine Development and the Makerere University-University of California at San Francisco (MU-UCSF) Malaria Symposium

Brenda Okech, Jane Achan, Charles Wanga, Nnaemeka Iriemenam

Introduction

The Faculty of Medicine, Makerere University and the African Malaria Network Trust (AMANET) held a five-day malaria conference at Hotel Africana, Kampala, Uganda on 26-30 June 2006. The conference comprised

of a two-day Symposium on Malaria organized by Makerere University-University of California at San Francisco (MU-UCSF), Malaria Collaboration and Uganda Malaria Surveillance Program (UMP). This was followed immediately by a three-day AMANET workshop on Molecular

Biology and Immunology on Malaria Vaccine Development.

The MU-UCSF/UMP symposium focused on malaria treatment, control and research priorities while the AMANET workshop discussed current state-of-affairs vis-à-vis immunological aspects

of malaria vaccine development. Over 100 individuals participated in the event. Thirty-four (34) of these participants were sponsored by AMANET representing Burkina Faso, Cameroon, Gabon, Gambia, Ghana, Kenya, Mali, Nigeria, Sudan, Tanzania, Uganda, Zambia, and Zimbabwe.

Also present were various partners and stakeholders in the field of malaria control including officials from the Uganda Ministry of health, Researchers from Universities/Institutes, Malaria Consortium, World

of malaria in Uganda and Africa at large. He also encouraged useful deliberations between researchers and policy makers in view of promoting research policies that will translate into better control tools.

Official opening of the workshop was followed by introductory remarks from the MU-UCSF Director, Dr Moses Kanya, and presentations by Drs Albert Kilian (*Malaria burden and control*) and Phil Rosenthal (MU-UCSF Results and ongoing studies). In his presentation, Dr Kilian revealed the

highlighting current projects, the presentations discussed published data on malaria drug resistance in Uganda. The data showed increasing resistance to Chloroquine as well as Fansidar with a conclusion that risk of treatment failure with CQ + SP was unacceptably high at all sites. It was also noted in this talk that a combination of Amodiaquine (AQ) + SP was much more efficacious than CQ + SP. It was further revealed that artemether/lumefantrine and artesunate/amodiaquine have been found to be more efficacious than other drug combinations. The presentation concluded that for ACTs to have maximum desired effect, a combination with other malaria control measures for reducing transmission intensity is vital.

An overview of the Malaria Consortium activities was presented by Ms Nakanwagi. The vision of Malaria Consortium is to become a recognized international resource, creating regional centres of expertise in malaria endemic areas, working together with partners to control malaria and other diseases to achieve better health. The consortium was said to be actively involved in operational research, malaria control through indoor residual spraying (IRS) and long lasting treated nets research, and research in other diseases like leishmaniasis, diarrhoeal and pneumonia.

Subsequent presentations were on *malaria drug policy in Uganda* (JB Rwakimari); *the challenges in making drug policy changes* (Kato), *home based management of fever strategy* (HBMF, by Sarah Staedke); *update on the US President's Malaria Initiative* (PMI, by Linda Quick), and an



Official opening of the MU-UCSF/UMSP Malaria Symposium

Health Organization, US President's Malaria Initiative (PMI), the US National Institutes of Health (NIH), and Epicentre (France).

Day 1

The workshop was officially opened by the Dean of the Faculty of Medicine, Makerere University who was represented by Professor Elly Katabira, also standing in for Vice Chancellor. Prof Katabira welcomed all participants from the various parts of the world and highlighted the plight

increasing trend in the malaria cases in Uganda over the years with more than 70,000 children dying from malaria every year. Dr Rosenthal talked on MU-UCSF achievements in research, training and capacity building as evidenced by the number of papers published and individuals trained both in Uganda and the U.S.

The Symposium continued with more presentations by Dr Wabwire Mangen and Dr Adoke Yeka on MU-UCSF Results and ongoing studies. Besides

overview of malaria research priorities in Uganda (Grant Dorsey).

Day 2

Day two kicked off with a presentation by Dr Ambrose Talisuna on *Training Health Workers, Operational Research: from policy makers to good medical practice using ACTs*. This talk discussed the need for training, the process and time it takes to change policy comparing and contrasting Uganda's experience to that of other countries in Africa.

Dr Rosenthal then presented and discussed preliminary findings from a study that compared *combination antimalarial therapies among Ugandan children*. As part of these findings, Dr Njama Denise looked at *presumptive anti-malarial treatment of febrile episodes among children*, a practice widely advocated in Africa. Recommendations from this study were that in the era of ACT, resources to expand the use of microscopy or other validated diagnostic methods may provide a cost effective measure for promoting rational use of anti-malarial therapy.

Two presentations focused on *HIV-Malaria interactions*. The first talk was given by Dr Gasasira Anne who reviewed the current literature in this field. Dr Achan Jane then discussed findings of a study on *interactions between HIV and malaria in children*. The study shows that the use of ITNs and septrin prophylaxis is effective in lowering the incidence of malaria in HIV positive patients. The findings also hinted on the fact that providing integrated interventions in areas heavily infected by malaria and HIV is crucial for reducing the burden of the two diseases.

The afternoon session covered topics

on molecular biology and malaria vaccine immuno-epidemiology. A series of presentations were made each with a key take home message. Dr Dorsey presented a paper on the *use of molecular genotyping to improve estimates of anti-malarial treatment*. Dr Hakim Ssendagire gave an *overview of molecular studies done to monitor levels of resistance to Chloroquine and Fansidar* at a site in central Uganda. Dr Sam Nsobya discussed the *molecular markers for drug resistance* and concluded that studies of molecular markers may complement in vivo studies by helping policy makers in the planning of anti-malarial treatment guidelines.

Other presentations in this session were on *chemokine biomarkers and polymorphisms in falciparum malaria in Ugandan children* (Dr Tom Egwang), and *immuno-epidemiological studies of natural IgG responses to P. falciparum vaccine candidates in Apac* (Dr Brenda Okech).

The final session had two presentations; Dr Heidi Hopkins discussed the *increasing importance of RDTs in the diagnosis of malaria* especially in rural areas. Dr Gisela Schneider presented an *Overview of the Joint Malaria Training Programme (JMTP)*, detailing the goal, objectives and envisaged contributions of the programme in the fight against malaria in Uganda through improved case management and effective use of intervention tools such as ACT, IPT, ITN and IRS.

The MU-UCSF symposium was wrapped up by Dr Kanya who reviewed the presentations made over the two days and emphasized the need for continued research to guide policy.

Day 3

The AMANET workshop on Molecular Biology and Immunology in Malaria Vaccine development began with the introduction of all participants and facilitators. Dr Roma Chilengi then briefly explained the goal and objectives of the workshop and the scope of activities being undertaken by AMANET. This was followed by a lively discussion with the participants calling on AMANET to extend its activities to include other sites. After the warming introduction, Professor Mats Wahlgren (Karolinska Institute, Sweden) presented an *overview of malaria immunity*.

Dr Adrian Luty (Radboud University, Netherlands) then gave a talk on *T-cell immunity*. T-cell immunity was said to play an important role in the elimination of exo-erythrocytic parasites via CD8+ T-cells with help from CD4+ T-cells. CD4+ T-cells were also said to be effective in controlling asexual blood stage parasite multiplication possibly through cytokine mediated hyper-regulation of phagocytic cell activity.

A presentation on *B-Cell immunity* was then given by Dr Fred Kironde (Makerere University, Uganda). Dr Kironde said that the degree of immunity is believed to be correlated with antibody titres and IgG subclasses. The mechanisms behind this action was said to involve blockage of merozoite invasion, enhancement of parasite clearance through opsonisation, parasite toxin neutralisation, inhibition of cell attachment (cytoadherence), antibody dependent cell mediated cytotoxicity (ADCC) and inhibition of rosetting of parasites. Success in the development of malaria vaccine was said to be hampered by parasite ability to evade and suppress immune

response (immunesuppression/immunomodulation) through antigenic diversity, variation, sequestration, etc.

Later on, Prof. Wahlgren discussed *Malaria immunity to severe and pregnancy malaria*. It was noted that pregnancy reduces a woman's immunity to malaria, making her more susceptible to severe malaria than other adults and that malaria is a significant contributor to anaemia in pregnancy. Malaria infection of the placenta and anaemia were said to be major contributors to low birth weight and premature delivery.

The lecture on *Malaria vaccine development strategy* was given by Dr Qijun Chen (Karolinska Institute, Sweden). Dr Chen said malaria vaccine strategies are targeted to the prevention of infection, prevention of anti-disease manifestation and transmission blocking. The working hypothesis is to block parasite invasion pathways, disrupt parasite development process, neutralise parasite toxin, and inhibit adhesion. Several vaccine candidates were said to be undergoing some form of trials at different stages and these included attenuated parasite-irradiated sporozoites, recombinant proteins with AMA-1, MSP-1, 2, CSP, synthetic peptide (Sp66, LSP), virus-like protein particles, DNA – (plasmid, virus) and RNA (virus particle).

The first evidence of the protective role of sickle cell trait against severe malaria was by Allison in 1954 as described by Dr Francine Ntoumi (EDCTP, Netherlands) in her talk on *Host genetic factors and protection from malaria: Sickle cell*. The sickle cell trait was said to result from a mutation of the β -chain of the globulin due to a single gene base

pair mutation (A to T) in haemoglobin genome sequence. The talk further reported that this results into reduced solubility of the deoxyhemoglobin molecule and erythrocytes assume irregular shapes. The sickled erythrocytes become trapped in the microcirculation and cause damage to multiple organs resulting in HbSS (homozygote) having a high mortality rate and HbAS (heterozygote) having a selective advantage against mild and severe malaria. The mechanism behind the conferment of protection, as she said, with sickle cell trait is still unclear although higher levels of cellular and humoral immunity to crude or neo *P. falciparum* antigens in carriers of haemoglobin AS have also been shown with contributions to protective effects.

Day 4

Day four started with a talk by Dr Ntoumi on *Characterization of malaria parasites*. Dr Ntoumi said that parasite diversity has been described by two phenomena; Allelic polymorphism - polymorphism within a gene (number and/or size of repeats), and Antigenic

variation – which occurs during the course of an infection where the parasite expresses different forms of the same gene, for instance the var genes used to escape human host immune responses. – Importance in evaluation of malaria vaccines. It was further revealed that the malaria parasite *P. falciparum* exhibits the largest polymorphism in chromosome structure. This calls for a need to characterize parasite genetic markers.

The talk concluded that interpretation of genotyping markers has to take into account the study design and the fluctuations of parasite populations. Relationships between infecting genotypes and malaria control interventions also need to be further investigated.

Dr Michael Theisen (Statens Serum Institut, Denmark), in his talk on the *Development of candidate malaria vaccines: Experience with synthetic peptides*, mentioned six candidate malaria vaccine targets: anti-sporozoite stage vaccines, anti-hepatic stage vaccines, anti-



Group photo, Participants for the AMANET Workshop on Molecular Biology in Malaria Vaccine Trials

erythrocytic stage vaccines, antitoxic vaccines, anti-gamete ookinete stage and live attenuated stage. The peptide synthesis vaccine approach was said to be relatively inexpensive and convenient from a regulatory point of view, it lacks contamination by irrelevant foreign proteins or DNA and improves the focus of the immune system upon specific domains. Issues on purification by RP-HPLC, fast sequence analysis by mass spectrometry, improved chemistry; scaling up production, antigenicity and immunogenicity were also discussed as challenges in the process.

In his second presentation on *Development of candidate malaria vaccines: Experience with recombinant proteins*, Dr Thiesen said that recombinant proteins are used for the assessment of antigenicity using ELISA, T cell assays; Immunogenicity in mice, rabbits, monkeys; can be demonstrated for purification of specific antibodies and in clinical trials. Clinical development plans for the recombinant candidate malaria vaccine GMZ2 were also presented, as an example of a vaccine based on recombinant technology.

Dr Chen then examined *PfEMP1 as an anti-severe malaria vaccine*. *Plasmodium falciparum* erythrocyte membrane protein 1 (PfEMP1) was said to be the parasite's virulence factor associated with severe malaria. It was also noted that PfEMP1 molecules are both functionally specialised and differentially recognized. Dr Chen then discussed research on var genes responsible for the production of mediators that bind the infected red blood cells to CD36 domain of endothelial cells of blood vessels. It was also noted that research in Aotus monkeys has shown promising results as the monkeys developed only severe

anaemia after infection with *P. falciparum* but not cerebral malaria. Even better results have been shown with Rhesus monkey which developed no *P. falciparum* infection.

In a presentation on *Assays for Evaluating Immune Responses*, Dr Adrian Luty discussed the importance, methods and timing of immunoassays in malaria vaccine development. Dr Luty said that the stage- and antigen-specificity of vaccine-induced responses will determine the choice and design of immunoassays. Vaccines targeting pre-erythrocytic stages of *P. falciparum* may be designed to induce both antibody (anti-sporozoite) and CMI (anti-liver stage) responses while vaccines targeting asexual or sexual stages may be designed primarily to induce antibody responses. It was also said that assays may need to take account of functional attributes of specific 'protective' responses. Regarding time, Dr Luty said that immunogenicity is usually assessed at least once after each immunization e.g. 2 or 4 weeks later and/or on the day of each subsequent boosting, as well as some months after the last boost to assess longevity of responses. Qualitative and quantitative assays and their evaluation methods were also discussed.

In his presentation on *Immunological correlates in the evaluation of malaria vaccines* Dr Daniel Dodoo (Noguchi Memorial Institute for Medical Research, Ghana) presented lessons learnt from passive transfer of IgG experiments which have shown IgG to play an important role in protection against *P. falciparum* blood stage infection. It was also said that studies have unequivocally supported a crucial role for antibodies in naturally acquired protection, the specificities and mechanism(s) of

action of these protective antibodies remains largely unknown.

Professor Wen Kilama talked on the *Role of public-private-partnership (PPP) in malaria vaccine development*. He mentioned that progress in malaria control has been achieved elsewhere but not in Sub Saharan Africa, and as of late, malaria morbidity and mortality is on the increase. The problem has been associated with drug and insecticide resistance, weakened health systems and poor environmental management to mention but a few. Malaria vaccine research and development was said to be a lengthy and costly exercise attracting no interest to current market forces. It was also noted that recently there has been increase in funding malaria R&D from governments, bilateral and multilateral donors, philanthropy and NGOs. This now calls for a careful and determined public-private partnership throughout, and the involvement and recognition of responsibilities by all stakeholders (scientists, politicians, the media, funders, pharmaceutical agent, NGOs, etc) and at all stages.

Day 5

Day five kicked off with lectures towards human use. In his lecture on *Clinical evaluation of candidate malaria vaccines*, Dr Chilengi said that basic pre-clinical guidelines should aim at defining the characteristics, safety and immunogenicity of the product in appropriate animal models. He further said that adequate animal studies should be done and there must be close collaboration between pre-clinical and clinical teams. Good manufacturing practice (GMP) principles were also discussed. Regarding evaluation of malaria vaccines, Dr Chilengi said that the current convention is to take the

products through a series of phases to assess safety first in non immune populations, then to endemic-areas followed by assessment of immunogenicity and efficacy. Clear go-no-go criteria must be set up. The vaccine development roadmap was also presented and said to be a long and costly process.

epidemiological studies and vaccine trials. To address this, the AMANET sponsored Afro-immuno Assay (AIA) develops standardized assays using the same reagents and statistical tools to assess the relationship between acquisition of malaria specific antibody responses to four potential malaria vaccine candidate

MF59, oil-in-water emulsion, component of Chiron's flu vaccine, comprising squalene & surfactants-Tween 80/Span85) and Europe (Virosomes; reconstituted influenza virosomes, IRIV, Berna Biotech and Cholera toxin B subunit-used in a cholera vaccine licensed by PowderJect, UK) were presented and discussed. Their mechanism of action were also presented and discussed. The following adjuvants were said to be currently in use for malaria vaccines in development; Alum (alhydrogel, various commercial suppliers e.g. Superfos, Denmark); ASO2 (GSK proprietary adjuvant; oil-in-water with MPL (Corixa Corp) & QS-21 (Antigenics Inc.); ISA 720 (SEPPIC, Montanide); water-in-oil with vegetable oil & emulsifier [mannide monooleate]; ISA 51 (SEPPIC, Montanide); water-in-oil with mineral oil & emulsifier [mannide monooleate]; CpG (manufactured by Coley Pharma); different types of CpG for stimulation of e.g. plasmacytoid DC, B cells, NK cells, etc.



Session during the AMANET Molecular Biology Workshop

In a presentation on *Standardized assessment of immunogenicity/immune responses in preclinical studies and vaccine trials in Africa* Dr Daniel Doodoo said that the primary goal of malaria vaccine development is to reduce morbidity and mortality caused especially by *P. falciparum* among children in Africa. It was said that traditional techniques exist for the evaluation of specific immunological responses i.e. ELISA, IFA, Cytokine CTL assay, ELISPOT assay, etc. In many studies/trials today, there have been differences in methodologies. These differences in immunological assay protocols have made data comparison difficult hence the need for standardization of antibody and T-cell assays to enable comparison of immunological measurements in immuno-

antigens. The objectives of AIA were also presented and these included development and introduction of standardized immunological assays that could form part of a set of criteria for the validation of promising malaria vaccine candidate antigens, provision of essential baseline information for clinical trials and enhancement of quality assured laboratory capacity and capability.

Dr Luty later gave a lecture on *Adjuvants: giving the right boost to malaria vaccines*. In this talk an adjuvant was said to be a substance that, in combination with a specific antigen, produces more immunity than the antigen alone i.e. an immuno-potentiating agent. Examples of licensed adjuvants used in the US (Aluminium salts [AlOH; AlPO₄],

The last presentation was made by Prof Kilama who discussed *Ethical perspectives on malaria research for Africa*. Prof Kilama said that research is needed to sharpen existing blunt antimalarial tools, to discover, develop and deploy new antimalarial tools, and to bridge the 10/90 gap. However, research must answer to the health needs of study populations. It was further said that historically researchers have abused research participants hence the need to protect research them. The presentation then discussed the three pillars in health research ethics which are informed consent (in the African settings), standards of care and its dilemmas, and benefits and risks.

Fifth AMANET Biennial Conference

First Announcement and Call for Abstracts



Date: 26 February 2007 - 1 March 2007
Venue: Zanzibar Beach Resort, Zanzibar, Tanzania

Deadline for Abstract Submission: 30 November 2006
Deadline for Attendance Confirmation: 31 December 2006

Background and scope

The African Malaria Network Trust (AMANET) in March 2002 became the legal successor to the African Malaria Vaccine Testing Network (AMVTN). The mission of AMANET is to strengthen the capacity and expertise of African malaria R&D institutions in intervention trials and networking in order to facilitate the development of cost-effective malaria intervention tools. In accordance with its constitution AMANET holds biennial conferences. Presentations and discussions at the 3rd and the 4th Conferences, which addressed theme 'Malaria Vaccines in the Pipeline for Africa', and "Experiences of Organizing Malaria Intervention Trials"; respectively, highlighted not only the problems, corrective actions needed, results obtained so far and the way forward with regard to intervention trials. The two conferences also underscored the need for further capacity strengthening.

The Fifth AMANET Biennial Conference will bring together scientists,

researchers and other experts in the malaria field from different areas in Africa and elsewhere to present new research results, findings and perspectives on recent and future developments in malaria R&D, intervention and control, capacity building and funding.

Location

The Fifth AMANET Biennial Conference will be held at Zanzibar Beach Resort on 26 February 2007 to 01 March 2007, in Zanzibar, Tanzania.

About Zanzibar

Zanzibar is an archipelago made up of Zanzibar and Pemba Islands, and several islets. It is located in the Indian Ocean, about 25 miles from the Tanzanian coast, and 6° south of the equator. Zanzibar Island (known locally as Unguja, but as Zanzibar internationally) is 60 miles long and 20 miles wide, occupying a total area of approximately 650 square miles. It is characterized by beautiful sandy beaches with fringing coral reefs, and the magic of historic Stone Town - said to be the only functioning ancient

town in East Africa.

Conference Theme and Sub-Themes

The theme for the 5th AMANET Conference is:

Results from Clinical Development and Trials of Malaria Interventions;

and the sub-themes will be:

1. *Candidate Antimalarial Drugs in Pre-Clinical Development;*
2. *Candidate Malaria Vaccines in Pre-Clinical Development;*
3. *African Experiences on Site Characterization for Malaria Intervention Trials;*
4. *Capacity Strengthening for Development of Malaria Interventions;*
5. *Clinical Trials of Antimalarial Drugs;*
6. *Clinical Trials of Malaria Candidate Vaccines;*
7. *Developments in Intermittent Preventive Treatment Initiatives;*
8. *Developments in ITNs and other Vector Control Tools;*
9. *Trial Site Development;*
10. *Who is Who in Malaria Intervention Trials in Africa.*

Satellite Meetings

1. AMANET Scientific Coordinating Committee
2. AMANET Board of Trustees
3. AMANET General Assembly

Call for Papers

Papers are invited on the above sub-themes. Paper abstracts must be submitted electronically by 30 November 2006. The text should not exceed 300 words and where applicable should highlight the research or review rationale, objectives, methodology, results, conclusions and recommendations. The accepted abstracts will be compiled in the Conference Book to be distributed at registration. Each oral presentation including discussion time must not exceed 20 minutes.

Audiovisual Facilities

There will be projection facilities for transparencies, and PowerPoint.

Scientific panel

Saurwein, Robert (Chairman, Netherlands)
 Kironde, Fred (Vice Chairman, Uganda)
 Kilama, Wen (Secretary, Tanzania)
 Akumu, Achidi Eric (Cameroon)
 Chilengi, Roma (Tanzania)
 Diggs, Carter
 Druilhe, Pierre (France)
 Elhassan, Ibrahim (Sudan)
 Hall, Lee (USA)
 Jepsen, Søren (Denmark)
 Kreamer, Peter (Germany)

Lemnge, Martha (Tanzania)
 Malenga, Grace (Malawi)
 Manyando, Christine (Zambia)
 Marsh, Kevin (United Kingdom)
 Mshinda, Hassan (Tanzania)
 Ntoumi, Francine (Gabon)
 Penali, Louis (Côte d'Ivoire)
 Sirima, Sodiomon (Burkina Faso)
 Sukwa, Thomas (WHO/AFRO)
 Tesfaye Mengesha (Ethiopia)
 Vincent, Robert (France)
 Thor, Theander (Denmark)

Social Events

Local operators will be invited to arrange for paying participants to visit various cultural and tourist sites in Zanzibar. Social events will be organized for Conference participants.

Registration for the Conference

Pre-registration is necessary for the participants requiring special arrangements to be made for them and for timely estimation of the conference requirements. However, registration for the Conference will be free and will also take place at the conference venue from the evening preceding the start of the Conference.

Sponsorship

There is limited funding for sponsorship of deserving participants. Priority will be given to members of AMANET governance bodies, some institutional representatives, and needy participants whose papers are accepted for presentation.

Accommodation

Most of the participants sponsored by AMANET will be booked at the Zanzibar Beach Resort. Delegates will be required to confirm their participation by 31 December 2006. All other participants are expected to make their own accommodation arrangements.

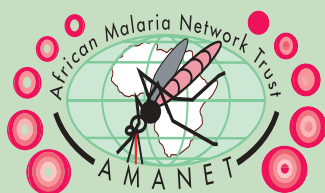
Contact Addresses

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Venue

Zanzibar Beach Resort
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 Tel: +255 24 2330208/
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 Fax: +255 24 2230556/ 2233957
 Email: znzbeachresort@zanlink.com
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