



AFRICAN MALARIA NETWORK TRUST

The Advanced AMANET Training Workshop on Clinical Data Management in Malaria Vaccine Trials

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Workshop Report

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Opening Ceremony:

Following on the basic course on clinical data management in malaria vaccine trials offered in 2005, the African Malaria Network Trust (AMANET), in collaboration with the Malaria Research and Training Centre (MRTC) of the University of Bamako in Mali, organized a five-day advanced workshop on Clinical Data Management in Malaria Vaccine Trials. The Workshop was held on 17-21 July 2006 at MRTC in Bamako. The 22 participants for this workshop came from Gabon, Ghana, Kenya, Mali, Nigeria, Senegal, Tanzania, Uganda, and Zambia, representing a network of centres that are currently or intending to participate in malaria vaccine trials. The goal of this advanced course was to further enhance the capacity of data managers at trials sites to be able to create and manage data processing units with little or no external assistance. Like in the previous course, this course used Microsoft ACCESS as software of choice for the creation of a GCP compliant trial database(s).

Day one

Opening remarks were given by the MRTC Director, Prof. Ogobara K Doumbo who emphasised on the urgent need for Africa to build its own capacity and create a pool of experts in this field. Prof Doumbo said that this and previous workshop are like a dream come true; seeing an all-African team conducting a full vaccine trial and at international standards, in which data managers play a crucial role.

Dr Chilengi on behalf of AMANET gave a summary background of AMANET and its objectives. He expressed his concern about the lack of an efficient mentorship programme for young scientists. The role being played by AMANET in building capacity for African scientists was highlighted with emphasise that knowledge gained through such workshops should be utilised to promote good data management in Africa. He urged participants to fully utilize this opportunity and pass on what they have learned to their colleagues in their respective institutions.

A pre-workshop test was then offered to ascertain the level of knowledge of participants on clinical trial data management

Workshop overview:

Introducing the course, Dr Issaka Sagara presented the sample completed database that participants would be building during the workshop. He discussed the features of the database including security levels which ensured that different users had different access levels to the

system depending on their roles. He also demonstrated how the reconciliation function worked. Afterward he explained the audit trail function which traced and recorded all activities done on the data and finally discussed the automatic back-up of the system.

The workshop was then effectively underway with facilitators taking turns to walk through the participants on the various stages of building the database system as well as underlining theories on data management for clinical trials.

Quality Assurance And Quality Control (QA/QC) in clinical data management

In this presentation Dr Alassane Dicko talked about the importance and the purpose of quality assurance and quality control. It must be noted that QA/QC is a responsibility of each member of the team. Dr Dicko said that data management begins at the time of protocol development through database designing and data capture to the end of study and all the way through to and after product licensure.

In discussions that followed, Dr Chilengi read a short note of the GCP requirements and further emphasized the need for QA/QC. Further discussions on this topic covered the various types of double data entry; role of clinical monitors; making changes on the database and source documents; pilot testing databases; protocol adherence and source document verification.

Data management Standard Operation Procedures

Dr Mahamadou Thera presented a talk on clinical data management standard operating procedures (SOPS). SOP's writing was said to require team work and should be written by the whole team in that section i.e. data managers, entry clerks, lab or clinical staff etc. SOPs also require an official framework through which to operate. It was said that SOPs are written to ensure that the same procedures are adhered to and these should be detailed and clear enough. Sample SOP's were presented and it was stated that some required details may be given as appendices to avoid crowding the SOP and allow SOP's to be actionable documents.

Discussions following this talk included ways of streamlining the SOP's, identifying kinds of SOPs required in data management; procedures for amending SOPs; communications and training on SOPs; Sponsor approval of SOPs; and the need for training and retraining of staff on relevant procedures. .

Form Processing/Entry and filing

Dr Sagara took the participants through the various forms used in data management and their processing.

Batch Receipt form

This covered procedures to be followed when case-report forms (CRFs) arrive at the data management unit. The key procedures emphasized include receipt of CRFs; review of forms for discrepancies; completing batch flow charts; tracking the CRF pages; filing; stamping arrival date on CRFs; process and resolution of queries; creation of working copies; observation of QA/QC steps; and a review of the "blind Verification" (Second person does not see errors – a third person should review errors and do "interactive verification", a second entry would see errors made and decided on correct entry)..

Reconciliation

Reconciliation is a process of checking the database to make sure that all batches of forms are stored in the database. Reconciling with a database that captures dates when records were entered was emphasised as essential for audit trail.

Filing of forms

Storage and maintenance of study records and forms is important. Where there is more than one site, each centre should have their assigned area for filing of forms; and this must be accessible only to authorised study personnel. The filing system must observe the rules of confidentiality especially with regards to participant identifying information. Answered queries should be filed together with their corresponding forms. Once study is complete, an internal audit should be done to ensure that no forms are missing.

Creating tables: Practical session

This was the first practical session for the day given by Mr. Ismaila Thera. Participants were taken through the process of creating a new Microsoft Access table for storing CRF data using the design view. Key points in this tutorial included how to name columns, choosing data type for the columns and giving description of what data would be stored in each column. In addition participants learned how to control the value that would be stored in the column by using validation rules.

As homework participants were asked to create more columns on their database tables based on the provided CRF templates.

Day two

This day's work consisted entirely of hands-on practical activities which were facilitated by Mr. Ismaila Thera and Mr. Saye Soumaila. The day began by a review of the homework for the previous day and addressing all difficulties encountered. Participants were then taken through the process of creating a form in MS Access for entering and displaying data stored in the table that had been created. The use of the wizard function to quickly link all table fields with controls on the form and then manually arrange the controls to exactly match the CRF was demonstrated.

Creating the double entry system

Later in the afternoon, participants were taken through the process of creating a double entry system said to be the hallmark in data management. The double entry system was created by duplicating all tables and data entry forms in the database and then each set of forms and tables would be made accessible to specified data entrants. During this process Drs Chilengi and Sagara drew the attention of the participants to important concepts of data management such as primary keys, labelling of controls, and relationships within the database.

More homework was given to the participants for them to continue the practice of creating a double entry system.

Day three

This day also began with practical work facilitated by Ismaila and Saye, and had one lecture presentation later on. Day 2 homework was reviewed and participant queries explained before going on into the day's exercises.

Reconciliation of forms

This is a very important activity in data management, designed to compare data entered by each entrant in the double entry system and address wrong or missing data. Participants were then shown how to reconcile the forms by two separate entrants and on how to create reconciled forms. The importance of documenting the process was highlighted and also utilising this process to identify any systematic errors and weaknesses of particular data entrants. These may be used for identifying areas for focussed retraining of data entrants.

Discussions on this subject included clarification on the role of reconciliation in the clinical trial; internal and external audits and quality checks on sampled CRF's.

Role of data management in malaria vaccine Development

In this presentation, Dr Chilengi reviewed issues surrounding diseases of poverty such as malaria. He explained the lack of a promising market to be one of many reasons why pharmaceutical companies do not invest much on malaria vaccine development. He then discussed the steps that any vaccine in development should follow and highlighting on the time and costs involved. He also emphasized the critical role of data management in this process in ensuring that all studies provide credible data that adds to the product dossier for licensure. Data managers need to have an understanding in order to contribute effectively and insist on the quality and integrity of the data from each trial which is only a piece of the bigger picture.

The question and answer aspects of this talk covered explanations of exactly how the safety and efficacy of a vaccine can be evaluated, ethics of vaccine trials, GCP definitions of adverse/serious events, and statistical considerations for each protocol. Further, discussions on phase IIa malaria vaccines included explanations of how they are conducted and ethics of administering an artificial infection to volunteers.

Creating the database switchboard

The afternoon practical session took the participants through the process of creating the switchboard for the system. Although Microsoft Access comes with its automatic switchboard, data managers need to be able to create or adapt one to tailor suit their situation. This was also the focus of the homework for the day.

Day four

The day began with a continuation of previous work. This day was also full of practical hands on exercises that taught the participants the procedures of creating

- **Start form.** This form allows entry into the database once the people submit an acceptable password.
- **Audit trail system-** The audit trail system shows the changes made on the dataset, who made it, and reason for making changes, the new and old values on the affected variables.
- **How to secure data base.** This activity taught participants how to hide the database forms and tables, minimizing the chances of unauthorized person from viewing or changing the data.
- **Conversion to MDE.** This showed the process of converting a Microsoft access database to an MDE file.
- **Back ups.** How to make an automatic backup system using Visual Basic (VBA) codes. This is essential for prevention of loss of data in case of any anomalies.

Day five

This day also began with technical assistance to participants on their databases, followed by a lectures and discussions.

Internal & external audit queries

Dr Sagara began this session by exploring on the steps that follow the double entry system. He then demonstrated on a programme that can be used to track discrepancies in the data set, internal audit system and perform quality checks on sampled CRFs. Dr Sagara said that checks are performed to ensure integrity of the data. This was particularly emphasised as it has a serious bearing on the interpretation of the vaccine safety or efficacy. Moreover, a study may be terminated on the grounds of safety issues, and so, the data management needs to be as accurate as possible.

Resolving data queries

This topic was covered in the basic course. However, the emphasis this time was on the application of an efficient system for resolving queries. Changes must never be made on the database before the queries are resolved and reflected in the relevant forms. Dr Sagara emphasized the importance of generating a Data Clarification Form (DCF) for each query; even if one CRF has more than one question, a separate DCF **should be generated** for each question. Everything on the database should be supported by a verifiable source document. The process of cleaning the data should be well planned with adequate time allocated. The analytical plan for the study should accommodate the fact that once the database is locked, no changes can be made. This was said to be a critical regulatory requirements in vaccine trials.

Post course test.

A post test was undertaken by the participants, and it was immediately marked by the facilitators. There was a major improvement in performance by the participants with a mean gain of two marks, which was statistically significant.

Closing ceremony

Two participants spoke on behalf of the others. Both expressed their gratitude to the organizers and facilitators of the workshop on their high competence, dedication, and on how they made every participant to feel part of trial data management team! On behalf of the facilitators, Mr. Ismaila Thera thanked participants for the full attention and dedication to the course. He also thanked them for the opportunity to network and share experiences from different countries. On behalf of the sponsor, Dr. Chilengi also thanked participants for coming all the way to Mali to participate in this workshop. He encouraged the participants to initiate and maintain networks among themselves as African professionals.

Prof. Doumbo concluded that he was grateful that AMANET chose MRTC to host this and the previous workshop on Data management. He also stressed on the significant role data management plays in clinical research. He finally thanked the participant for taking the workshop seriously and was joyous to see a new generation of Africans being raised up in the scientific research field. He closed by extended another invitation to AMANET to come back to Mali for a Data Management workshop in the near future. .