THE ACTIVITIES AND FUTURE DEVELOPMENT OF GCP INSPECTIONS IN TANZANIA

Godwin D. Ndossi, PhD
Chairman
Tanzania National Health Research Forum
Formerly, Managing Director
Tanzania Food and Nutrition Centre
gndossi2@yahoo.co.uk

Outline of Presentation

1. Clinical Trials Inspection in Tanzania: Definition and Legal framework
2. Types of Clinical Trial Inspection
3. Qualification of Clinical Trial Inspectors
4. Inspection activities
5. Major Clinical Trial Sites in Tanzania
6. Challenges
7. Future Development of GCP Inspection in Tanzania

Clinical Trials Inspection in Tanzania: Definition and Legal Framework

Definition:

- According to ICH E6, 1.29 "an inspection is the act by a regulatory authority(ies) of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority(ies) to be related to the clinical trial and that may be located at the site of the trial, at the sponsor's and /or contract research organization's (CRO's) facilities or at other establishments deemed appropriate by the regulatory authority(ies)." The purpose of such inspection is to determine whether research was conducted in compliance with national/local laws and regulations for the conduct of research and the protection of human subjects.

Clinical Trials Inspection in Tanzania: Definition and Legal Framework (cont…)

Legal Framework:

- In the case of Tanzania, Section 69 of the Tanzania Food, Drugs and Cosmetics Act No. 1, 2003 provides for the Tanzania Food and Drugs Authority (TFDA) to monitor clinical trials from the beginning to the end in order to ensure adequate protection of the general public against any risks or adverse effects.
- The law further requires the Authority to satisfy itself that all specific and general conditions subject to which the trial was authorized are being strictly observed by the person conducting the trial and that to all intents and purposes the trial achieve its aims and objectives.

Clinical Trials Inspection in Tanzania: Definition and Legal Framework (cont…)

Objective of CT Inspection:

- The overall objective is to ensure that the trial is conducted in accordance with the study protocol, standard operating procedures (SOPs), good clinical practice (GCP) and TFDA requirements. The ultimate goal is to ensure the safety of trial participants and validity and credibility of data
- Check patient's compliance with study medication
- Regulations and rules are being followed
- Violations verified
- Providing suggestions for improving medical care

Clinical Trials Inspection in Tanzania: Definition and Legal Framework (cont…)

Bottom line:

- Inspections – an opportunity for improvement of quality of performance of CTs including assisting investigators to comply with GCP and other requirements and taking measures to correct any specific deficiencies.

Types of Clinical Trial Inspection

There are two types of inspection;

- Routine inspections – carried out before or after approval of a trial. Such inspections are announced and are carried out in accordance with TFDA requirements, ICH-GCP, study protocols and SOPs

- Investigative or "For cause" inspections – undertaken to deal with specific complaints received about lapses or non-compliance with standards. Such inspections are unannounced

Qualification of Clinical Trial Inspectors

CT Inspectors should have the necessary qualification in terms of:

- Academic qualification – degree in medicine, pharmacy, CTs, epidemiology, pharmacology, toxicology, biochemistry, and other related fields
- Training – GCP and CTs inspection, on-job training from senior inspectors, continuous training to keep pace with new developments in the field

Qualification of Clinical Trial Inspectors (cont…)

- Experience – through involvement in or exposure to CT inspection activities. An inspector will be deemed experienced if
  - has conducted at least 3 inspections;
  - has reviewed at least 3 trial protocols and other related application documents
  - Has demonstrated competence in communication skills and report writing

Inspection Activities

- Planning and preparation
  - Annual schedule and budget
  - Site selection
  - Notice of inspection (14 working days in advance, await confirmation)
  - Pre-inspection meeting of inspectors to review objectives and task order
  - Pre-trial inspection where applicable (**Pre-trial Inspection Checklist** available: **Appendix 2**) and if not feasible request for pre-trial monitoring report
  - Familiarize with/review GCP principles, study protocol, trial site profile, Investigator's Brochure, applicable local regulatory requirements, review report of previous inspection or any records such as complaints
  - Prepare list of actions and aspects to be checked

Inspection Activities (cont…)

- Conducting the Inspection
  - Opening interview or pre-inspection briefing
  - Actual inspection: Inventory of Essential Documents
  - Clinical Data Audit
  - Elements of Data Quality/Data Integrity
  - Facilities Tour; Additional Interviews
  - Check presence and validity of essential documents in the trial master file (TMF) **(See Checklist for Conducting Inspection – Appendix 3)**

Inspection Activities (cont…)

- Post-inspection Briefing
  - Convey inspection findings in brief to inspectees
  - Provide both positive and negative findings
  - Suggestions for improvement
  - Inspector and inspectee should sign the **Clinical Trial Inspection Observation Form – Appendix 4**

Inspection Activities (cont…)

- Documenting and Reporting the Inspection
  - Report should be submitted within 10 working days after completion of inspection **(See Clinical Trial Inspection Report Format – Appendix 5)**
  - The report should be balanced i.e. not an inventory of non-conformances

Inspection Activities (cont…)

- Classification of Clinical Trial Inspection Observations
  - Clear distinction should be made between ‘positive’ and ‘non-conformances’
  - Situations involving fraud, misrepresentation or falsification of source data or records linked with CTs will result in non-conformance rating
  - Deficiencies or deviations should be noted during inspection and confirmed in writing in the Inspection observation form

Inspection Activities (cont…)

Non-conformance observations can be classified as 'critical', 'major', and 'minor'

- Critical non-conformers – include observations describing a situation that result in fatal, life threatening or unsafe conditions for study participants

Inspection Activities (cont…)

- Major non-conformers – include observations describing a marked deviation or deficiency, other than a critical one that may result in undue health risks to the CT participants or other persons or could invalidate the data **(See Major Observations List – Appendix 7)**

Inspection Activities (cont…)

- Minor non-conformers – include observations that are classified as not critical or major, but which indicates a deficiency and/or deviation **(See List of Minor Observations – Appendix 8)**

Inspection Activities (cont…)

- Recommended list of regulatory actions

Category of non-conformers	Regulatory action(s)
Minor	•Recommend corrective action within given time frame •Follow-up inspections to verify implementation
Major	•Issue warning letter •Recommend corrective action within given time frame •Recommend temporary withdrawal or suspension of trial authorization •Follow-up inspection to verify implementation
Critical	•Recommend permanent withdrawal of trial authorization •Take matter to court of law

Major Trial sites in Tanzania

- Sites with Clinical Trial Labs
- Mbeya (Walter Reed)
- KCMC (KCRI)
- Bagamoyo (IHI)
- Mwanza (NIMR)
- Muhimbili (MNH & MUHAS)

Major Trial sites in Tanzania

- Currently TFDA has zonal offices in Arusha, Mwanza, Mbeya, Dodoma, & Dar es Salaam. Offices for Kigoma and Mtwara are under consideration.
- Ideally the zonal offices should be able to provide Inspection oversight in sites located in those zones but this is currently not the case.
- Available tools include: *Clinical Trials Inspection Manual (2008), Guidelines for application to Conduct Clinical Trials in Tanzania (Second Edition, 2009)*
- *Regulations for Conducting Clinical Trials in Tanzania* is awaiting signature and release
- Clinical Trial Registry is being developed

Challenges

- It is estimated that on average 25 clinical trials per year are in progress (10 new + 15 ongoing) in Tanzania. TFDA has a core staff of 4 on clinical trials and pharmacovigilance. Although 8 staff have received relevant training in-country and abroad and another 15 have received in-house training on CT inspection, the number is not enough considering that they have to work in teams (to gain skills and experience) and, moreover, they have other tasks as well.

Challenges (cont…)

- The research infrastructure in Tanzania is not in tune with modern developments in science and medicine and this acts as a barrier to scientific innovations.
- Regulations to guide implementation of CTs in the country are not yet in place and this situation might compromise the regulatory functions of TFDA.
- Oversight structures such s IRBs/IECs are still lacking or not functional in research institutions

Challenges (cont…)

- The budget for carrying out GCP inspections is limited
- Opportunities for inter-institutional collaboration not adequately utilized.

Future Development of GCP Inspections in Tanzania

In order to address the challenges cited above the research and regulatory environment in Tanzania has to be improved with respect to the following considerations:

- Attract more researchers in the medical field so that we can have 'home grown' clinical trials
- Increase the human resource capacity in terms of numbers and skill to perform CT review and GCP inspections
- Improve research facilities e.g. laboratories in centres that participate in CTs. Currently some sites transfer material to be analyzed abroad

Future Development in Tanzania (cont…)

- Formulate laws and regulations that will guide implementation of CTs in the country as well as facilitate the inspection function
- Ensure that institutions that participate in CTs have well constituted IRBs/IECs
- Timely and thorough CT inspections are constrained by lack of adequate financial resources hence efforts should be directed at finding adequate funds

Future Development in Tanzania (cont…)

- There is need to form a network/forum of researchers to share experiences in conducting CTs and to foster inter-institutional collaboration

THANK YOU FOR YOUR ATTENTION

Question

Which of the following three statements is **not** correct?

A) Monitoring is the act of overseeing the conduct of a clinical trial while it is in progress

B) Inspection is the act of reviewing documents, facilities, records, and any other resources related to the clinical trial. It is carried out by the drug regulatory authority of a country

C) Auditing is like monitoring and is conducted while the clinical trial is in progress.