GOOD LABORATORY PRACTICE (GLP)

(GLP training manual, WHO-TDR 2nd Ed, 2009)

TanZamBo Health Research Ethics Workshop

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GLP

- Born in 1979
- (US)FDA issued mandatory GLP requirements on 20th June 1979
- Why?

Historical background

- 1970s FDA investigated a number of cases of poor toxicology laboratories throughout USA
- Results from about 40 labs
  - Poorly managed studies
  - Insufficient training of personnel
  - Deliberate fraud
  - Poorly trained study directors

- Poorly designed protocols
- Raw data poorly collected, not verified, not approved by responsible person
- Lack of standardized procedures
- Poor handling of animals

- Inadequate characterization of test items
- Inadequate recourses
- Equipment not properly calibrated or qualified
- Reports not sufficiently verified, inaccurate account of study or raw data
- Inadequate archives and retrieval processes

An example

- One of the labs investigated made headline news.
- The name of the Lab was Industrial Bio Test. This big lab ran tests for big companies such as Procter & Gamble.
- It was discovered that mice that they had used to test cosmetics such as lotion and deodorants had developed cancer and died.
- Industrial Bio Test lab threw the dead mice and covered results deeming the products good for human consumption.
- Those involved in production, distribution and sales for the lab were eventually jailed

FDA decision

- Introduce a new regulation to cover non-clinical safety studies

- GLP regulations:

  - Draft USA GLP in 1976

  - An enforceable USA regulation in 1979

  - In 1981 an organization named OECD (organization for economic co-operation and development) produced GLP principles that are international standard

What is GLP

- Is Good Laboratory Practice
- It is governed by principles

- GLP principles:
  - A set of organizational requirements

  - (GLP does not assess the intrinsic scientific value of a study)

Main Goal

- To help scientists obtain Results (test data) that are:
- Quality and valid
- Valid results are:
  - Reliable
  - Repeatable/reproducible
  - Auditable
  - Recognized/acceptable by scientists worldwide

GLP Aim

- To make the incidence of False negatives more obvious
  - (results demonstrate non-toxicity of a toxic substance)
- To make the incidence of False Positives more obvious
  - (results demonstrate toxicity of a non-toxic substance)

GLP Aim

- To promote mutual recognition of study data across international frontiers

"mosquito samples will be collected in Kilimanjaro region and genotyping will be performed in CMP, Copenhagen"

Only under GLP this is possible

Benefits of GLP

- Limit waste of resources
- Ensure high quality
- Ensure compatibility of results
- Promote mutual recognition of results

GLP principles:

- Define conditions under which studies are:
  - Planned
  - Performed
  - Recorded
  - Reported
  - Archived
  - Monitored

5 Basic points addressed by GLP

1. Resources (personnel, facilities and equipment)

2. Characterization of:
   - Test article – (drug, tool, equipment etc)
   - Test system – (cell line, animal, etc)
3. Rules (protocols/study plans, procedures)

4. Results (raw data, final report, archives)

5. Quality Assurance (audit/inspection – training – advice)

1. Resources

- Resources are divided into
  A. Management
  B. Personnel
  C. Facilities

Management

Ensure:

- The principals of GLP are complied with
- A sufficient number of qualified personnel, appropriate facilities, equipment and materials are available
- Records of qualifications, job descriptions, training and experience of personnel are maintained
- Personnel understand the functions they are to perform

Personnel

- Organizational chart (important document for inspectors)
- This tells about the way the institution works
- Other important documents
  - CV of each staff (up to date) and archived
  - Training record (certificates, experience)
    - Induction to the job,
    - Future training plans
  - Job description and approval signatures
  - Who reports to who

Facilities (equipment and buildings)

- Appropriate size of facilities
  - This may affect validity of study/tests
- Establishment of defined work spaces etc/Physical separation
  - Eg: PCR set-up unit
  - Microbial culture room etc
  - Blood withdrawing room (phlebotomy unit)

Equipment

- Suitability
  - May require formal equipment qualification
  - Proof of suitability

- Calibration
  - Proof of standard working condition (documented)
  - Calibration needs use of standards
  - Calibration SOP
  - Respect calibration frequency

Maintenance

- Buildings and equipments need mentanance
- Preventive maintenance
- Curative maintenance (fix when broken)
- Back-up equipment /procedures
- Contracts with external service organizations
- Alarms

- Maintenance should be documented
  - Use standard procedures (SOPs)
  - Standardized documentation system
  - Example:

Maintenance : service/report/label
Instrument no.: _____
Date of last service _____
Next service due: _____
Name of service provide:_____
Signature/date _____

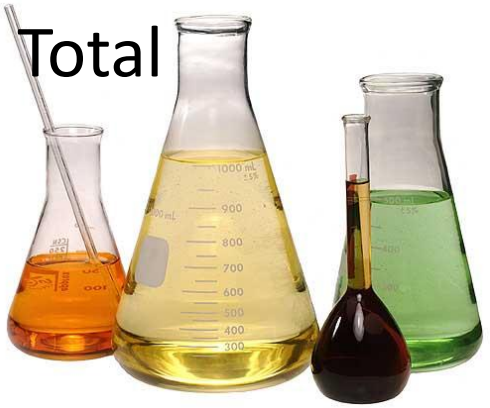
2. Characterization

Test items (and reference items)

- Test items should be clearly labeled with necessary information
  - Manufacturer's name
  - Date of dispatch
  - Number of containers or items, type of contents and quantity
  - Batch numbers
- Identity of person responsible for dispatch
- Name of transport and type of carrier

Test item containers should carry:

- Test item name, Batch number, Expiry date, storage conditions, Container number, Total weight, Initial gross weight



- Dose formulation preparation
  - Dilution
  - Reconstitution etc

Test systems

- Test system can be:
  - Animals
  - Bacteria
  - Cells
  - Plants
  - Can also be analytical equipment

- Test system characterization may involve:
  - Identification of test animals
  - Inspection and acclimatization of animal to test conditions

3. Rules

- Rules define:
  - Who does What
  - Where
  - How
  - When

- These are called prescriptive documents
- Two types
  - Study protocol
  - SOPs

  No good SOP no GLP

4. Results

- Results include:
  - Raw data
  - Study files
  - Data on environmental conditions
- Are descriptive documents
- They tell us who did what, when, where and how
- They tell us of results of the experiment

Raw data and data collection

- During the study
  - Remember lost/inaccurate data may invalidate the study
  - Collect data on prepared forms/notebooks so that they indicate:
    - “what” was done
    - “how” it was done
    - “When” it was done
    - “who” collected the data

Final report

- GLP requirement for contents:
  - Name and address of test facility/site
  - Date of study (start and finish)
  - Name of study director
  - Study objectives
  - Test article details
  - Test system details

- Dosing details – route, duration
- Results/statistics
- Summary of findings
- Discussion
- References
- Study director GLP compliance statement
- Signed/dated reports from scientists
- QA statement

Final report once signed modifications are by amendments ONLY

Archives

- This is what is left when the study is over
  - Study plan
  - Raw data
  - Specimens
  - Final report
  - QA documents
  - Personnel records
  - Facilities/equipment qualification records
  - Historical SOP file, e.t.c.

Archives function

- long-term, secure storage and fast retrieval of data
- Contains all original scientific data, master documents and reports, etc
- Endpoint for regulated work

Archives: submission form

- Department/group:
- Project name:
- Study number
- Quantity
- Description
- Comments
- Date
- Signature of submitter
- Signature of archivist

Archive: history/events form

- Date
- Event
- Authorizations

Archives: security

- Only authorized entry permitted – per SOP
- Examination in-situ of documents preferred
- Photocopies made in place if possible
- Protection against fire, flood and vandalism if possible

Storage conditions should minimize deterioration:

- Fire, flooding precautions?
- Air conditioned general environment?
- Copied made of heat sensitive papers?
- Refrigeration used where necessary?
- Blocks sealed in bags, tissues in preservatives, slides?
- computer backups maintained in security cabinet?

Indexing parameters

- Project
- Test article/reference article and lot numbers for test item and formulated material if appropriate
- Protocol/study number
- Testing facility
- Key word retrieval from comments section of master schedule (e.g. Regulatory information, dates
- department

5. Quality assurance

- Quality Assurance Unit:
- QA Programme/ Personnel
- GLP requires:
  - Document QA programme
  - Personnel who are familiar with studies
  - QAU independent from study staff
  - QAU reports to management
  - That the master schedule be supplied to QAU

QAU responsibilities (from GLP)

- Assure study plans and SOPs are available
- Ensure study plan and SOPs are followed by
  - Inspection
  - Audit
  - Record findings in writing
  - Review final reports
  - Prepare/sign QA statement
  - Review study plan/protocol (an obligation)
  - Review SOPs (a recommendation)

QA inspection / Audit

- 3 types:
  - Study based
  - Facility / system based
  - Process based

- Study based audit/inspection
  - Protocol / study plan
  - On-going (usually critical phases)
  - Report (with respect to raw data)

- Facility / system based
  - Buildings / equipment / metrology
  - Support services
  - Computer systems
  - personnel training / documentation
  - Others

- Process based
  - Inspections of processes which occur frequently e.g:
    - Slide preparation
    - Imaging
    - Measuring food consumption