Good Laboratory Practice

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Good Laboratory Practice

- Good Laboratory Practice (GLP) is a quality system concerned with the organizational process and the conditions under which a study is planned, performed, monitored, recorded, archived and reported.

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Quality Assurance in Analytical Chemistry – Training and Teaching (2nd ed.)

History of GLP

- First in US after irregularities in pharmaceutical companies
- Other countries followed
  - To increase trust
  - To be able to export to US
- OECD (Organization for the Economic Cooperation and Development)
  - First decision in 1981
  - Binding guidelines in 1989

Why GLP?

- Development of quality test data
- Mutual acceptance of data
- Avoid duplication of data
- Avoid technical barriers to trade
- Protection of human health and the environment

Scope

- Non-clinical safety testing of test items contained in
  - Pharmaceutical products
  - Pesticide products
  - Cosmetic products
  - Veterinary drugs
  - Food and feed additives
  - Industrial chemicals

The European Commission Directive 2004/9/EC

- EU Member States shall verify the compliance with GLP of any testing laboratory within their territory claiming to use GLP in the conduct of tests on chemicals

Inspection and Audit

- The authorities of the EU Member States shall inspect the laboratory and audit the studies in accordance with the provisions laid down in Annex I of the Directive 2004/9/EC

Directive 2004/9/EC Annex I, Part A

- Guides for compliance monitoring procedures for good laboratory practice

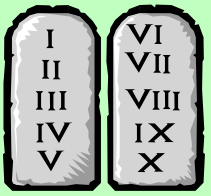
Directive 2004/9/EC Annex I, Part B

- Guidance for the conduct of test facility inspections and study audits

The Commission Directive 2004/10/EC

- The harmonisation of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of their applications for tests on chemical substances

The GLP Principles



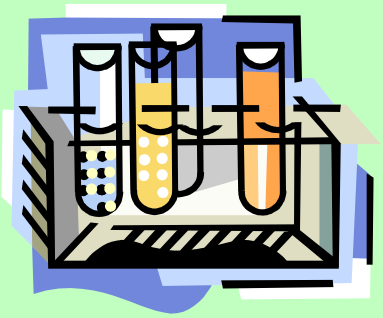
1. Test facility organization and personnel
2. Quality Assurance (QA) program
3. Facilities
4. Apparatus, materials and reagents
5. Test systems
6. Test and reference items
7. Standard Operating Procedures (SOP's)
8. Performance of the study
9. Reporting of study results
10. Storage and retention of records and materials

Terms Concerning the Organization of a Test Facility

- Test facility
- Test site
- Test facility management
- Test site management
- Sponsor
- Study director
- Principal investigator
- Quality assurance program
- Standard operating procedures
- Master schedule

Terms Concerning the Study

- Non-clinical health and environmental safety study
- Short term study
- Study plan
- Study plan amendment
- Study plan deviation
- Test system
- Raw data
- Specimen
- Experimental starting date
- Experimental completion date
- Study initiation date
- Study completion date



Terms Concerning the Test Item

- Test item: the article that is subject of a study
- Reference item
- Batch
- Vehicle

1. Test Facility Organization and Personnel

- Test facility management's responsibilities
- Study director's responsibilities
- Principal investigator's responsibilities
- Study personnel's responsibilities

1. Test Facility Organization and Personnel
Test Facility Management's Responsibilities

- The management should ensure that
  - The principles 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

1. Test Facility Organization and Personnel

Test facility Management's Responsibilities

- Appropriate and valid SOP's are established and followed
- A Quality Assurance Program is in place
- A Study Director and a Principal Investigator, if needed, is designated
- Documented approval of the study plan
- The study plan is available to quality assurance personnel

1. Test Facility Organization and Personnel

Test Facility Management's Responsibilities

- A document control system is in place
- Purchased materials meet specified requirements
- Test and reference items are appropriately characterized
- Clear lines of communication exist
- Computerized systems are suitable for their intended purpose

1. Test Facility Organization and Personnel

Study Director's Responsibilities

- Has the responsibility for the overall performance of the study and the final report
- Approves the study plan and amendments and communicate them to the QA personnel
- Ensures that SOPs, study plans and their amendments are available to study personnel
- Ensures that the SOPs are followed, assess the impact of any deviations and takes appropriate corrective and preventive action

1. Test Facility Organization and Personnel

Study Director's Responsibilities

- Ensures that
  - Raw data are documented and recorded
  - Computerized systems are validated
  - SOPs are followed
  - Deviations are acknowledged
  - Records and data are archived
- Sign and date the final report to indicate acceptance of responsibility

1. Test Facility Organization and Personnel

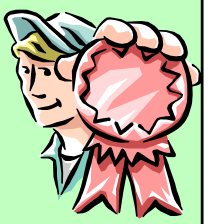
Study Personnel Responsibilities

- Knowledge of the GLP principals
- Access to the study plan and appropriate SOPs
- Comply with the instructions of the SOPs
- Record raw data
- Study personnel are responsible for the quality of their data
- Exercise health precautions to minimize risk
- Ensure the integrity of the study

2. Quality Assurance Program

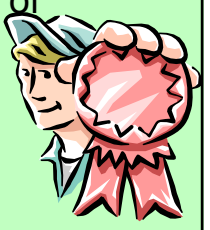
General

- Documented Quality Assurance (QA) Program
- Designated individuals as members of the QA team directly responsible to the management
- QA members not to be involved in the conduct of the study being assured



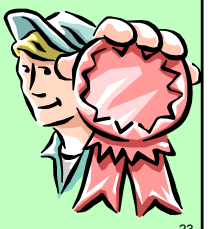
2. Quality Assurance Program
Responsibilities of the QA Personnel

- Access to the updated study plans and SOPs
- Documented verification of the compliance of study plan to the GLP principals
- Inspections to determine compliance of the study with GLP principles. Three types of inspection
  - Study-based inspections
  - Facility-based inspections
  - Process-based inspections



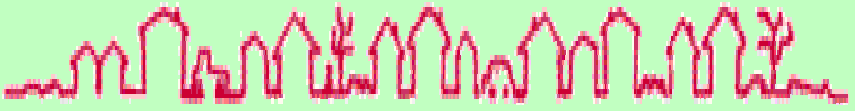
2. Quality Assurance Program
Responsibilities of the QA Personnel

- Inspection of the final reports for accurate and full description
- Report the inspection results to the management
- Statement



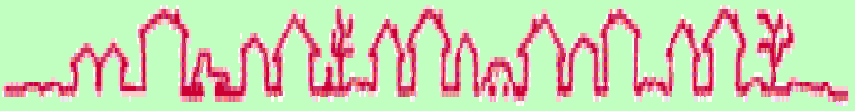
3. Facilities

- Suitable size, construction and location
- Adequate degree of separation of the different activities
- Isolation of test systems and individual projects to protect from biological hazards
- Suitable rooms for the diagnosis, treatment and control of diseases
- Storage rooms for supplies and equipment



3. Facilities

- Separate areas for receipts and storage of the test and reference items
- Separation of test items from test systems
- Archive facilities for easy retrieval of study plans, raw data, final reports, samples of test items and specimen
- Handling and disposal of waste in such a way not to jeopardize the integrity of the study



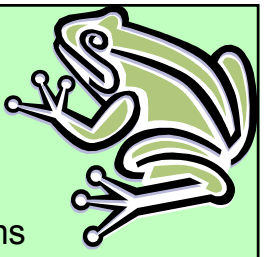
4. Apparatus, Materials and Reagents

- Apparatus of appropriate design and adequate capacity
- Documented inspection, cleaning, maintenance and calibration of apparatus. Calibration to be traceable to national or international standards
- Apparatus and materials not to interfere with the test systems
- Chemicals, reagent and solutions should be labeled to indicate identity, expiry and specific storage instructions.

5. Test Systems

- Physical and chemical test systems
  - Appropriate design and adequate capacity of apparatus used for the generation of data
  - Integrity of physical/chemical test systems
- Biological test systems
  - Proper conditions for storage, housing, handling and care
  - Isolation of newly received animal and plant test systems until health status is evaluated
  - Humanely destruction of inappropriate test systems

5. Test Systems



- Records of source, date of arrival, and arrival conditions of test systems
- Acclimatization of biological systems to the test environment
- Proper identification of test systems in their housing or container or when removed
- Cleaning and sanitization of housings or containers
- Pest control agents to be documented
- Avoid interference from past usage of pesticides

6. Test and Reference Items

- Receipt, handling, sampling and storage
  - Records for date of receipt, expiry date, quantities received and used in studies etc.
  - Handling, sampling and storage procedures to ensure homogeneity and stability and avoid contamination or mix-up
  - Identification information on storage containers

6. Test and Reference Items

- Characterization
  - Identification of each test and reference item
    - Code, CAS number, name etc.
  - Identification of each batch of the test or reference items
    - Batch number, purity, composition, concentration etc.
  - Cooperation between the sponsor and the test facility
    - Verification of identity of the test item

6. Test and Reference Items

- Known stability of test and reference items
- Stability of the test item in its vehicle (container)
- Experiments to determine stability in tank mixers used in the field studies
- Samples for analytical purposes for each batch

7. Standard Operating Procedures

- Approved SOPs to ensure the quality and integrity of the laboratory data
- Immediately available current SOPs relevant to the activities being performed
- Deviations from SOPs to be acknowledged by the study director

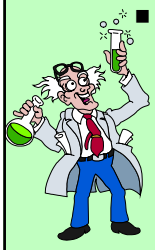
7. Standard Operating Procedures

- SOPs for
  - Test and reference items
    - Receipt, identification, labeling, handling, sampling, storage
  - Apparatus
    - Use, maintenance, cleaning, calibration
  - Computerized systems
    - Validation, operation, maintenance, security, change control, back-up
  - Materials, reagents and solutions
    - Preparation and labeling

7. Standard Operating Procedures

- Record keeping, reporting, storage and retrieval
  - Coding system, data collection, preparation of reports, indexing system, handling of data
- Test system
  - Room preparation, environmental room conditions, receipt, transfer, identification etc., test system preparation, observations etc.,
- Quality Assurance Procedures
  - Operation of QA personnel

8. Performance of the Study



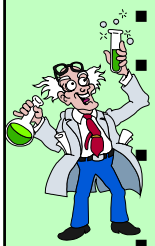
- Study plan
  - Written plan, verified for GLP compliance, approved by the study director and by the management
  - Approval of amendments by dated signatures
  - Deviations to be explained and acknowledged

8. Performance of the Study

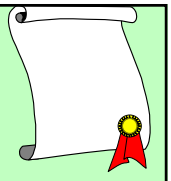
- Content of the study plan
  - Identification of the study
    - Title, nature and purpose of the study, test item identity, reference item used etc.
  - Information concerning the sponsor and facility
    - Names and address (sponsor, test facility, study director)
  - Dates
    - Approval dates of the study plan, estimated starting and completion dates etc.
  - Reference to test methods
  - Records

8. Performance of the Study

- Conduct of the study
  - Identification of each study
  - The study to be conducted in accordance with the study plan
  - Data generated to be recorded directly and accurately
  - Changes in the raw data not to obscure the previous data
  - Identification of electronic data

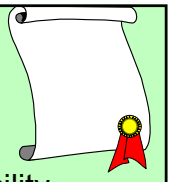


9. Reporting of Study Results



- General
  - Final report for each study
  - Scientists to sign and date their reports
  - Approval by the Study Director
  - Corrections, additions, amendments to be signed and dated by the study director
- Content of the final report
  - Identification of the study
    - Descriptive title, identification of the test and reference item, purity, stability

9. Reporting of Study Results



- Information on sponsor and test facility
  - Name and addresses of the sponsor, test facility, study director, the scientists involved to the study etc.)
- Experimental starting and completion dates
- A Quality Assurance Program statement
- Description of materials and test methods
- Results
  - Including uncertainties, level of significance
  - Evaluation discussion and conclusions
- Storage (of samples, reference items, raw data, final reports etc.)

10. Storage and Retention of Records and Materials

- What to retain in archives
  - The study plan, raw data, samples
  - Inspection data and master schedules
  - Qualification, training experience, job description
  - Maintenance and calibration data
  - Validation data
  - SOPs
  - Environmental, health & safety monitoring records

10. Storage and Retention of Records and Materials

- Retention period to be defined
- If any study material is disposed of before expiry the reason to be justified and documented
- Index of materials retained in the archives
- Controlled access to the archives
- In case that the laboratory goes out of business the archives are transferred to the relevant sponsor(s)

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Summary

- GLP v/v ISO 9000 and ISO 17025
- Non-clinical health and environmental safety studies
- Physical and chemical test systems
- Biological test systems
- OECD
- EU Directive 1999/11/EC

Where to Get More Information

- Commission Directive 2004/9/EC and Commission Directive 2004/10/EC
  - http://eur-lex.europa.eu
- http://ec.europa.eu/enterprise/chemicals/legislation/glp/index_en.htm
- http://www.oecd.org under environment/chemical safety