GOOD LABORATORY PRACTICES

BP606T

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GLP (Good laboratory practices)

- ***Good laboratory practice*** or **GLP** specifically refers to a quality system of management controls for research **laboratories** and organizations to try to ensure uniformity, consistency, **reliability**, reproducibility, quality, and integrity of chemical (including pharmaceuticals) non-clinical safety tests; from physio-chemical properties through acute to chronic toxicity tests.

  •Medicines and Healthcare products Regulatory Agency-UK which defines GLP as:

  "Good Laboratory Practice (GLP) embodies a set of principles that provides a framework within which laboratory studies are planned, performed, monitored, recorded, reported and archived".

- GOOD LABORATORY PRACTICE applies to nonclinical studies conducted for the assessment of the safety or chemicals (including pharmaceuticals). effi cacy of

- GLP helpsassure regulatory authoritiesthat the data submitted are a true

HISTORY

- The term GLP was first used in New Zealand in 1972.
- GLP was instituted in US following cases of fraud generated by toxicology labs in data submitted to the FDA by pharmaceutical companies. As a result of these findings, FDA promulgated the Good Laboratory Practice (GLP) Regulations, 21 CFR part 58, on December 22, 1978 (43 FR 59986). The regulations became effective June 1979. Assure the quality and integrity of safety Nonclinical laboratory studies
- In 1981 an organization named OECD (organization for economic co-operation and development) produced GLP principles that are international standard.

Reason behind GLP creation

- In the early 70's FDA became aware of cases of poor laboratory practice all over the United States.
- FDA decided to do an in-depth investigation on 40 toxicology labs.
- They discovered a lot fraudulent activities and a lot of poor lab practices.
- Examples of some of these poor lab practices found were

  1.Equipment not been calibrated to standard form , therefore giving wrong measurements.

  2.Incorrect/inaccurate accounts of the actual lab study

  3.Inadequate test systems

Reason behind GLP creation

- One of the labs that went under such an investigation made headline news.
- The name of the Lab was Industrial Bio Test. This was a big lab that ran tests for big companies such as Procter and 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 eventually served jail time

OBJECTIVES OF GLP

- GLP makes sure that the data submitted are a true reflection of the results that are obtained during the study.
- GLP also makes sure that data is traceable.
- Promotes international acceptance of tests.

Basic elements in GLP

- Personnel
  - Sponsor
  - Management
  - Study director
  - Quality Assurance
- Facility
  - Laboratory Operation
  - Animal care
  - Equipment
  - Reagents Storage
  -
- Documents
  - ✓ Standard Operating
  - ✓ Protocols
  - ✓ Reports
  - ✓ Archiving
- Test and Control Articles
  - ✓ Characterization
  - ✓ Handling
  - ✓ Storage

Personnel

- Qualification of personnel:

  The assumptions is that in order to conduct GLP studies with right quality a couple of things are important;

  1)There should be sufficient .

  2)The personnel should be qualified. Sponsor:

- Sponsor: person who initiates & supports nonclinical laboratory study, a person who submits nonclinical study to FDA or testing facility that initiates & conducts the study.

  Facility management:

- Responsibilities of facility management is well defined. They designate a study director, as well as assure quality assurance unit is available, test and control articles are characterized.

- Study director:

  He has overall responsibilities for technical conduct safety studies, as well as interpretation, analysis, documentation and reporting of results.

- Quality Assurance unit:

  The quality assurance unit (QAU) serves an internal control function. It is responsible for monitoring each study to assure management that facilities, equipment, personnel, methods, practices, records, controls, SOPs, final reports (for data integrity), and archives are in conformance with the GLP/GALP

Maintenance & Calibration of Equipment

- Equipment shall be adequately inspected, cleaned & maintained
- Equipment used for assessment of data shall be tested, calibrated and/or standardized
- Scales & balances should be calibrated at regular intervals (usually ranging from 1-12 months)

Reagent/ Materials Certification

- This policy is to assure that reagents used are specified in the standard operating procedure.
- Purchasing and testing should be handled by a quality assurance program.
- Requirements:
- Reagents and solutions shall be labeled
- Deteriorated or outdated reagents and solutions shall not be used
- Include Date opened
- Stored under ambient temperature
- Expiration date

Standard Operating Procedures (SOP)

- Written procedures for a laboratories program.
- They define how to carry out protocol-specified activities.
- Most often written in a chronological listing of action steps.
- They are written to explain how the procedures are suppose to work
- Routine inspection, cleaning, maintenance, testing and calibration.
- Actions to be taken in response to equipment failure.
- Analytical methods
- Definition of raw data
- Keeping records, reporting, storage, mixing, and retrieval of data

Statistical Procedures for Data Evaluation

- Statistical procedures are not simply chosen from a text book
- Practitioners in a particular field may adopt certain standards which are deemed acceptable within that field.
- Regulatory agencies often describe acceptable statistical procedures.

Test and control articles

- Control articles or reference substances as they re-called in the OECD principles are of utmost importance as they are commonly used to calibrate the instrument.
- Main requirements for control articles are: the identity, strength, purity, composition and other characteristics should be determined for each batch and documented.
- The stability of each test and articles should also be determined.
- Certified reference standards can be purchased from appropriate suppliers. If standards are not available , the recommendation is to take a lot of your own material and analyze, certify and use it as the standard.

Analyst Certification

- Some acceptable proof of satisfactory training and/or competence with specific laboratory procedures must be established for each analyst.
- Qualification can come from education, experience or additional trainings, but it should be documented
- Sufficient people
- Requirements of certification vary

Laboratory Certification

- Normally done by an external agency
- Evaluation is concerned with issues such as
  - Adequate space
  - Ventilation
  - Storage
  - Hygiene

Documentation and Maintenance of Records

- Maintenance of all records provide documentation which may be required in the event of legal challenges due to repercussions of decisions based on the original analytical results.

- General guidelines followed in regulated laboratories is to maintain records for at least five years

- Length of time over which laboratory records should be maintained will vary with the situation

IF WORK PLACE DOESN'T COMPLY WITH FDA GLP STANDARDS

Disqualification of a Facility

- Before a workplace can experience the consequences of noncompliance, an explanation of disqualification is needed
- The FDA states the purpose of disqualification as the exclusion of a testing facility from completing laboratory studies or starting studies due to not following the standards of compliance set by the Good Laboratory Practice manual

Possible Violations

- Falsifying information for permit, registration or any required records
- Falsifying information related to testing~ protocols, ingredients, observations, data equipment, etc.
- Failure to prepare, retain, or submit written records required by law

Consequences of Noncompliance

- The FDA states the following consequences of noncompliance:
  - ➢The commissioner will send a written proposal of disqualification to the testing facility
  - ➢A regulatory hearing on the disqualification will be scheduled
  - ➢If the commissioner finds that after the hearing, the facility has complied, then a written statement with an explanation of termination of disqualification will be sent to the facility
  - ➢Thus, if it can be shown that such disqualifications did not affect the integrity and outcome of the study itself, or did not occur at all, then the study may be reinstated at the will of the commissioner

Upon Disqualification…

- If the commissioner finds that the facility was noncompliant on any of the grounds after the hearing, then a final order of noncompliance will be sent to the facility with explanations
- If a testing facility has been disqualified, any studies done before of after the disqualification will need to be determined as essential to a decision (acceptable or not)
- If the study is determined unacceptable, then the facility itself may need to show that the study was not affected by the noncompliance that led to the disqualification
- Once finally disqualified, the facility may not receive or be considered for a research or marketing permit and the study is rejected.

- The commissioner may notify the public and all interested persons, including other federal agencies the facility may have contacted
- The FDA may ask the other agencies to consider whether to support the facility or not under the disqualification
- The FDA may turn it over to the federal, state or local law enforcement
- The facility's sponsor may terminate or suspend the facility from doing any non- clinical study for a permit
- The sponsor is required to notify the FDA in writing within 15 working days that the facility is to be suspended or terminated and why

Reinstatementof a Disqualified Facility

- The testing facility may be reinstated as acceptable non-clinical study to be turned into the FDA if the commissioner can be certain that future studies will be conducted in compliance with the Good Laboratory Practice standards and that any current studies integrity have not been severely harmed by the disqualification
- The disqualified facility will be required to put in writing to the commissioner reasons why it should be reinstated and any actions the facility will take or have taken to assure any disqualification problems will not happen again

- The commissioner will inspect the facility and determine if it shall be reinstated
- If it is reinstated, the commissioner is required to notify all persons that were notified of the disqualification including the facility itself