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Good Laboratory Practices

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Overview

- What are Good Laboratory Practices (GLPs)
- Background
- Requirements

Good Laboratory Practices

- Standards for the conduct of nonclinical laboratory studies
  - Quality and integrity of the data
  - Study reconstruction
  - Accountability for study conduct and data

Good Laboratory Practices

- Scope
  - FDA 21 CFR Part 58
    - First version 1979
    - Food and Color Additives
    - Cosmetics
    - Animal Food Additives
    - Human and Animal Drugs
    - Medical Devices for Human Use
    - Biological Products
    - Electronic Products
    - Tobacco Products
  - EPA 40 CFR Part 160
    - First version 1984
    - Pesticides
    - Fungicides
    - Rodenticides
  - EPA 40 CFR Part 792
    - First version 1984
    - All Other Chemicals

Background

- Industrial Bio-Test

  - Late 1960s to mid-1970s conducted estimated 35-40% of Tox studies in U.S.
  - FDA performed inspection in 1976
  - Identified numerous issues
    - Poor animal care
    - Replacement of dead animals with animals that had not been dosed
    - Fabrication of data
    - Concealing administration of the wrong test compound
    - Destruction of records
    - Only 214 of 1205 pesticide studies were deemed to be of acceptable quality
- Other Examples – G.D. Searle

GLP Requirements - Staff

- Personnel
  - staff shall have education, training, and experience
- Testing Facility Management
  - Assign Study Director
  - Make sure sufficient resources are available for study conduct
- Study Director
  - Single point of control for the study
  - Responsible for the protocol, interpretation of data, and reporting of data.
  - Ensures unforeseen circumstances (e.g., deviations) that may affect quality are noted and corrective action taken
- Quality Assurance
  - Separate and independent from staff conducting study
  - Monitors study for conformance with GLPs

GLP Requirements - Facilities

- Animal Rooms
  - Separation of species
  - Isolation of studies
- Facilities for Test Compound and Control Articles
  - Separation to prevent contamination
- Laboratory Areas
  - Necropsy
  - Clinical Pathology
  - Histology
- Storage Area
  - Specimens
  - Raw Data (paper and electronic)

GLP Requirements - Equipment

- Maintenance and Calibration
- Validation of Equipment Prior to Use
  - IQ – Installation Qualification
  - OQ – Operational Qualification
  - PQ – Performance Qualification
- Standard Operating Procedures
  - Methods
  - Schedules for cleaning, maintenance, testing, calibration
  - Remedial action in the event of failure or malfunction
- Written Records of Maintenance and Calibration

GLP Requirements - Operations

- Standard Operating Procedures
  - Animal care
  - Receipt, identification, storage, handling, mixing of test and control articles
  - Observation of animals
  - Lab tests
  - Handling of moribund animals
  - Necropsy procedures
  - Histology procedures
- Reagents Must be Labeled and Have Expiration Date
- Animal Care Procedures
  - Housing
  - Feeding
  - Handling

GLP Requirements – Test and Control Articles

- Characterization
  - Identity
  - Purity
  - Composition
  - Method of Synthesis
  - Stability
- Formulations in Carriers
  - Homogeneity
  - Stability
  - Concentration

GLP Requirements – Protocol and Study Conduct

- Protocol
  - Objective
  - Test Article Identification
  - Number of Animals, Species, Source, Sex, Strain, Substrain, Age
  - Detailed Description of Experimental Design
  - Dose Levels
  - Statistical Methods
  - Date of Approval by Study Director and Sponsor
- Study Conduct
  - Labeling of Specimens
  - Data Recording - ALCOA
    - Attributable
    - Legible
    - Contemporaneous
    - Original
    - Accurate

GLP Requirements – Records and Reporting

- Description of Methods
- Statistical Methods
- Description of Circumstances that May have Affected Study Quality
- Signed and Dated Report
- Archiving Data
  - All Raw Data – paper, electronic, specimens
- Retention of Records
  - 2 years following marketing permit approval by FDA
  - 5 years following submission to FDA
  - If not submitted to FDA, 2 years following study completion

GLP Inspections

- FDA Surveillance Inspections Approximately Every 2 Years
  - Unannounced
  - Last a few days to weeks
  - Review facility records and several studies
- For-Cause Inspections
  - Quality Problems
  - Follow Up on Complaints
  - Evaluation corrective actions to previous violations
- Application-Based Inspections
  - Review process for drug submitted for approval
- FDA Form 483
  - Inspector identified a condition or practice in violation of FDA requirements

GLP Inspections

- FDA Form 483
  - Inspector identified a condition or practice in violation of FDA requirements
- Response not required but typically respond in 15 business days
- FDA Warning Letter
  - 483 responses not accepted
  - Serious violations
  - Corrective action need to be completed in 15 working days
- Disqualification
  - Exclude consideration of completed studies from a laboratory

GLP Conclusions

- The FDA reviews nonclinical data to determine if a drug can move into clinical trials or be approved for sale.
- On December 22, 1978 the FDA published the first GLPs in the Federal Register to ensure the reliability and integrity of safety data in response to concerns over fraudulent and inaccurate reporting of results.
- Although some individuals have taken GLP compliance to extremes, these regulations have significantly improved data quality