Lab GLP Refresher

Sherita's Top 10 Findings

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Seeing the Forest for the GLPs
A Lab GLP Refresher

GLP – The Forest

- Reliable data
- Preserved data
- Reconstructable studies
- Good science

GLP Study

- Any study that supports or is intended to support applications for research or marketing permits for pesticide products.
- A “study” does not include basic exploratory studies to determine if a test method is useful.
  - Method development

Facility Documents

- Floor Plan
  - Shows where things are
    - Archives
    - Sample storage
    - Reference substance storage
  - Dated
  - Archive historic versions
- Organizational Chart
  - Reporting Structure
    - Personnel conducting study
    - Study Director
    - Test Facility Management
    - Quality Assurance
  - Use position titles not university titles
  - Need all positions
  - Dated
  - Archive historic copies
- Master Schedule
  - Include Non-GLP and Non-IR-4 studies

Raw Data

Worksheets, memos, notes, or exact copies that are results of original observations and activities of a study and are necessary to reconstruct or evaluate the report for the study.

Raw Data

- Record accurately, promptly, legibly
- Permanent ink
- Who and when
- How procedure was done
  - SOPs
  - Working Method
- Changes to data
  - Who, when and why
  - Need to see original entry
- Explain unusual circumstances
  - Data not used
- Organized for easy and logical review

GLP Raw Data vs. Books and Records

- GLPs allow exact copies of data
- Books and Records (40 CFR 169) require registrant to maintain
  - All underlying raw data
  - Original raw data

Electronic Raw Data

- Unique password for each user or SOP that describes process to ensure identity
- Electronic signal is the raw data
- Backup and archive
- Software version

Study Director

Single point of control in the tudy with overall responsibility for echnical conduct, interpretation nd reporting of results.

Study Director

- Issues protocol and amendments
  - Amendments are permanent changes to the study
- Approves protocol deviations and assesses impact on the study
  - Lab generates deviations
  - Can’t just say “final impact not known until analysis”

Personnel

- Education, training, and/or experience
  - CV
  - Training records
  - Job description
  - Review regularly
- Archive
- Performance reviews in separate file

Quality Assurance is your friend!

- Separate and independent from study
- Should be able to reconstruct study from raw data
- QA audit findings are not for EPA to see without court order
- Audit each study at least once

Protocol

- Study initiation date – date Study Director signs
- Signed before start
- Supersedes SOPs
- Note out-of-the-ordinary
  - Analyze TRT 03 first
  - Residues as parent equivalent or total

Protocol Changes

- Reference methods
  - Need amendment to change
- LLMV
  - Need amendment to make higher
- Stability Study
  - Need amendment or deviation if covers <90%

SOPs

- Routine procedures
  - Everyone doing the same way
  - Reconstruct study
  - Training tool
  - Build in flexibility
- Don’t have to write step-by-step procedure each time you do something
- Review on regular basis
- Archive historic copies
  - If user manuals are referenced, need to archive those as well

Equipment

Equipment used in the generation, measurement, or assessment of data shall be adequately tested, calibrated, and/or standardized.

Equipment

- Balances
- Calibrated weights
  - Check full range of weights annually
- Thermometers
- NIST certified/traceable temperature devices
- Analytical instruments

Equipment

- SOPs
  - Maintenance and calibration
  - Remedial action in case of failure or malfunction
  - Person responsible for each operation

Equipment

- Written records of all inspections, maintenance, testing, calibrating, and/or standardizing operations

Equipment

- Use forms with prompts
  - Dates of operation
  - Routine – followed the SOP
  - Non-routine (result of failure or mal-function)
    - Nature of defect
    - How and when discovered
    - Remedial action
- Archive periodically

Reference Substances

- GLP characterized
- Certificate of analysis
- SOPs for receipt, identification, storage, handling, and mixing
  - Temperature monitored storage
    - Freezer
    - Refrigerated
    - Ambient
  - Limited access

Reference Substances

- Label
  - Name, code or CAS #
  - Batch or lot #
  - Expiration date
  - Storage conditions
- Stability of reference substance in mixture
  - Solvents
  - Storage conditions

Reference Substances

- Non-GLP reference substance
  - Test Facility Management must approve the use
  - Include on Statement of Compliance

Samples

- Maintain integrity
- Identify the crop fraction per the protocol
- SOPs for identification, transfer, and storage
  - Labeling
  - Chain of custody
  - Temperature controlled and monitored
  - Maintenance and calibration logs for temperature monitoring devices and freezers
  - Limited Access

Samples

- Sample identification maintained from time samples are generated in field to time residue results are reported
  - Includes intermediate steps in the extraction procedure

Freezer alarm

- SOP
  - What is the system
  - How tested
  - How often
  - Who tests
  - Testing Documentation

Reagents

- Proper labeling
  - Identity
  - Concentration
  - Storage
  - Expiration date

Analytical Method

- Reference method from protocol
- Allow flexibility – typically, generally, approximately
  - Elution pattern
  - Gradient
  - Standard preparation
- Need Study Director approval of method and changes

Analytical Data

- SOP
  - % Deviation between duplicate injections
  - Back calculation of standards to curve
    - Acceptance criteria
    - Just because R-squared good doesn't mean curve is good
  - Acceptable retention time variation
  - Data in spreadsheets needs to match chromatograms

Analytical Summary Report

- Experimental start date is date when test substance is applied to test system
  - Could be date stability or method validation samples fortified
- Experimental termination date
  - Last data collected –overnight run
- Correction for parent equivalence or total reported residue

Archiving Data

- SOP
  - What is archived
  - Index
  - Study records
  - Facility data
- Archivist identified on Org Chart

GLP Forest

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Sherita's

Findings

10. List of Personnel in ASR incomplete

9. Off-Scale chromatograms

8. Non-routine maintenance not properly recorded
    - Nature of defect
    - How and when discovered
    - Remedial action

7. Missing entries from instrument logs
    - Maintenance
    - Column changes

6. Working method doesn’t match what the lab is doing or did
    - Diverter program
    - Gradient
    - Temperature program
    - Preparation of standards
        - Use typically or generally or approximately
5. Incomplete documentation of unusual circumstances
    - Can’t reconstruct what happened from the notes
4. Data reported doesn’t match chromatograms

3. Reagents
   - Expired
   - Solutions prepared by ex-employee
   - Missing label requirements on reagent labels
     - Name
     - Concentration
     - Storage
     - expiration

2. Protocol amendments not issued when ASR submitted to QA

Missing dates and initials from raw data

Questions?

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