EPA Good Laboratory Practices Standards (GLPS): An Overview

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Topics Overview

- What are GLPS and Why Must We Follow Them?
- History of GLPS
- Principles of GLPS
- Practices Supporting GLPS Principles
- GLPS Overview
- Why Are GLPS Important?
- What Are GLPS Shortcomings?
- Conclusion: Anticipated Result of a GLP Compliant Submission

What Are GLPS?

And why must we follow them?

What Are GLPS and Why Must We Follow Them?

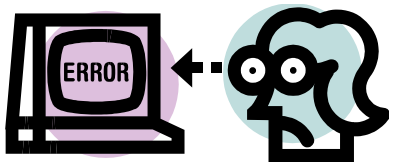
- Good Laboratory Practice Standards (GLPS) are a science management program that specify minimum practices and procedures which must be followed in order to ensure the quality and integrity of data submitted to the EPA in support of a research or marketing permit for a pesticide program.

- GLPS are mandated by law: 40 Code of Federal Regulations (CFR) Part 160, effective October 16, 1989, authorized by the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA).

History of GLPS

History of GLPS

- Throughout history, in all fields of human endeavor, errors and fraud have occurred.



- The scientific arena is no exception. In the mid 1970's Industrial Bio-Test Laboratories (IBT), a contract toxicological research laboratory, conducted approximately 40% of all U.S. toxicological testing. Due to FDA and EPA investigations of IBT that began in 1975, 75% of over 900 studies were invalidated due to deliberate fraud, and hundreds of chemicals had to be re-tested.

History of GLPS (cont.)

Some specific findings from the 1975 investigations included:

- Poor record keeping
- Data fabrication
- Dead laboratory animals were resurrected (*i.e.* lab animals were reported dead, then data was later reported on them)
- Data was too clean; in long term studies, some control animals get disease and die, yet all control animals remained healthy
- Testing was conducted by untrained, unqualified personnel, and IBT had undertaken more studies than their facilities or personnel could handle

History of GLPS (cont.)

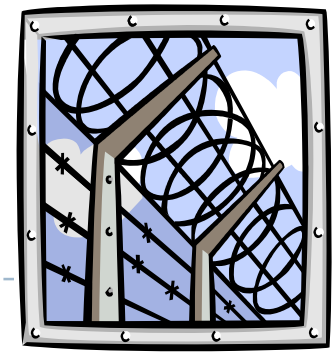
- The most significant fallout from the IBT scandal was the establishment of Good Laboratory Practice Standards regulated by the FDA that became finalized in 1978.
- In 1983, the EPA established similar guidelines for pesticide toxicology studies.
- In 1989, the EPA extended the GLPS to cover all research data, including field trial data, submitted for the purposes of pesticide registrations.

GLPS were established to assure the quality and integrity of study data, and reduce the chances of unreliability and fraud.

History of GLPS (cont.)

- After the establishment of GLPS, the first major case of fraud involved Craven Laboratories in Dallas, TX. A pesticide industry task force noted irregularities in testing to determine pesticide residues in treated crops, and alerted the EPA, and an investigation was initiated.

- In February 1994, the US Department of Justice announced the Craven company president, and 14 former employees, received punishments including fines and prison terms after being convicted of falsifying pesticide residue tests over a 10-year period.



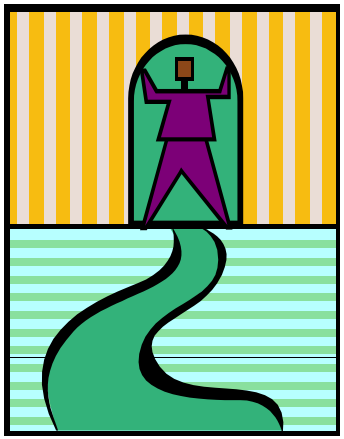
Principles of GLPS

Principles of GLPS

- Accountability
- Reconstruct-ability
- Management Commitment
- Documentation Commitment
- Planned Study Steps
- Proper Facilities
- Use of Qualified Personnel

Principles of GLPS (cont.)

- SOPs for Study Methods and Procedures
- Single Point of Study Responsibility and Control
- QAU Program – Independent QA Monitoring
- Properly Maintained and Calibrated Equipment
- Proper Data Documentation
- Creation of Strong Audit Trails



Practices Supporting GLPS Principles

Supporting Practices

Accountability:

- Protocols are signed by the study director and approved by the sponsor.
- Reports contain names of all scientists & professionals, and all supervisory personnel involved in the study.
- Study participants sign & date data entries & observation records.
- All data generated must be used & reported unless sound reasoning is provided as to why not.

Supporting Practices (cont.)

Reconstruct-ability:

- Study activities & methods used must be documented in sufficient detail and clarity to enable the study to be reconstructed at a later date from the study records.

Management Commitment:

- Management ensures trained personnel, sufficient resources, and appropriate facilities, equipment, materials, and methods are in place to conduct the study.
- Assures there is a Quality Assurance Unit to monitor study activities and facilities for GLP compliance.

Supporting Practices (cont.)

Documentation Commitment:

- Study documentation must be prompt and legible, with corrections properly made, with reasons provided for any changes or corrections - prevents data fabrication or ambiguity.

Planned, Written Study Steps:

- A well thought-out study plan (protocol) is documented in writing, signed by study director, approved by sponsor
- Changes to the protocol are documented in writing, signed and dated by the study director, and maintained with the protocol.

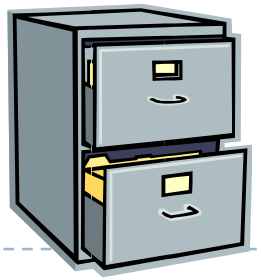
Supporting Practices (cont.)

Proper Facilities:

- Study sponsor QAU and regulatory agencies conduct GLP facility inspection audits and assess if a facility is of suitable size, location, and design to conduct required study elements.

Use of Qualified Personnel:

- Training Records, CVs, and job descriptions are kept for personnel participating in GLP studies as verification they understand their job duties, and are qualified to perform them.



Supporting Practices (cont.)

SOPs for Common Study Methods and Procedures:

- Assists in training and in maintaining consistency, and provides valid, defensible procedures with respect to science and regulations.

Single Point of Study Responsibility and Control

- Study director assures protocol is approved/followed, samples are analyzed, data is recorded, GLPS are followed, SOP deviations are noted, results are reported in a final report.

Supporting Practices (cont.)

QAU Program – Independent QA Monitoring

- Monitor each study to assure management that the facilities, equipment, personnel, methods, practices, records, and controls are in conformance with the GLP regulations.

- Inspect each study at intervals adequate to ensure the integrity of the study, and maintain written records of inspections.

- Report problems which are likely to affect study integrity to the study director and management so corrective action can be promptly taken.

Supporting Practices (cont.)

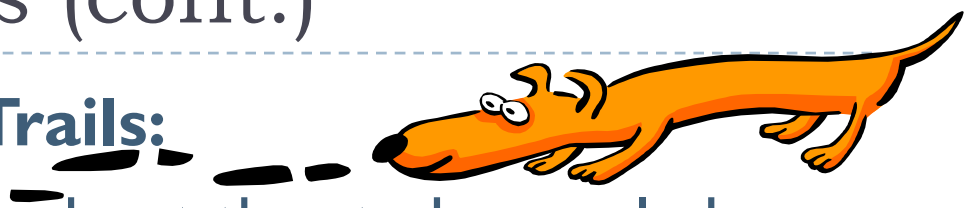
Properly Maintained and Calibrated Equipment:

- Written records are kept of all inspection, maintenance, testing, calibrating, and/or standardizing operations as verification that the equipment was working properly during study conduct.

Proper Data Documentation:

- Data recording is in ink with errors corrected so as not to obscure original entry – providing transparency to the data record.
- Data entries are to be made promptly, dated on the day of entry, and signed or initialed by the person entering the data – increases recording accuracy.

Supporting Practices (cont.)



Creation of Strong Audit Trails:

- Proper documentation throughout the study, coupled with retention/archival of the documentation records, specimens, and raw data, leaves a chronological, verified record of all study activities.
- Retention of records of quality assurance inspections, leaves a verified record that studies were monitored for compliance with GLPS.
- Retention of records and reports of the maintenance, calibration, and inspection of equipment create a verified record equipment was operating properly during study.

GLPS Overview*

*Overview Only. For complete regulations, link to:

http://www.access.gpo.gov/nara/cfr/waisidx_07/40cfr160_07.html

GLPS Overview

GLPS are divided into subparts:

- *Subpart A – General Provisions:* Defines the scope of GLPS, defines key terms, addresses the statement of compliance or non-compliance, addresses testing facility inspections by regulatory agencies, and the effects and non-compliance with GLPS.

- *Subpart B – Organization and Personnel:* Addresses the responsibilities of testing facility management, the study director, study personnel, and the quality assurance unit. Stipulates the QA must be separate from and independent of the personnel engaged in the direction and conduct of the study.

GLPS Overview (cont.)

- ***Subpart C – Facilities:*** Testing facilities must be suitable in size and construction for the conduct of the study, and there must be adequate storage space to archive specimens and data. Separate areas are needed for receipt, storage and preparation of materials.

- ***Subpart D – Equipment:*** Testing equipment must be of appropriate design and have adequate capacity in order to function and carry out requirements of the study protocol and applicable SOPs. All instrumentation must be adequately operated, inspected, cleaned, maintained, tested, calibrated and standardized. Equipment performance, use and maintenance must be documented.

GLPS Overview (cont.)

- ***Subpart E – Testing Facilities Operation:*** SOPs are required for commonly performed tasks. SOPs must be current, clearly written, immediately available to the staff, adhered to, and authorized by management; a historical file of SOPs must be maintained. Labeling requirements of reagents and solutions, and animal care requirements are specified.

- ***Subpart F – Test, Control and Reference Substances:*** Identity, strength, purity, composition and stability of test, reference and control substances must be determined and documented. Methods of synthesis for the materials must be documented. Test, reference, and control substances must be labeled with the material name, CAS number, or batch number, expiration date, and storage conditions. Test substance storage containers should be retained for the duration of the study.

GLPS Overview (cont.)

- ***Subpart G – Protocol for and Conduct of a Study:*** *A* detailed written study plan, with study objectives and methods must be used; any changes must be documented in writing. Data recording is to be done directly, promptly, and legibly in ink (excepting data generated by automated data collector systems).

- ***Subpart J – Records and Reports:*** A final report is required that includes the laboratory's name and address, key study dates, the objectives and procedures of the protocol, & protocol changes. All data, documentation, records, study-related correspondence, protocols, and final reports must be retained and archived.

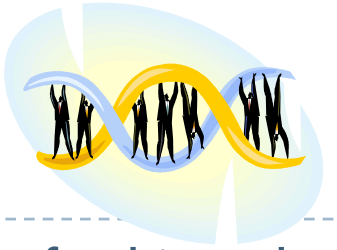
Why Are GLPS Important?

Why Are GLPS Important?

- Reduce chances of unreliability and fraud
- Help assure the quality and integrity of study data
- Increase international acceptance of data
- Mandated documentation allows for reconstruction of study years after the study is completed
- Adherence to GLPS is required by law
- Failure to conduct studies in accordance with GLPS can result in invalidation of the study

What are GLPS Shortcomings?

GLPS Shortcomings?



- Designed/written for chemical pesticides; need updating for biotech pesticides.
- Designed/written when electronic technology was in its relative infancy; need updating to address electronic records, electronic data, electronic signatures, *etc.*
- A GLPS compliant facility (in terms of a GLP facility inspection) does not necessarily equate to a GLP compliant study or trial.
- GLPS do not guarantee the quality of the study; it may be a poorly designed study, and be conducted in accordance with GLPS.
- Lack of specificity allows for numerous interpretations and a variety of ways to handle any one situation (may also be an advantage).

In Conclusion: Anticipated Result of a GLP Compliant Submission

Anticipated Result of GLP Compliant Submission

- Study Acceptance
- Registration of product
- Safe Food
- No Harm to Environment

Acknowledgements

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- Thanks to the attendees today for your attention.