To GLP or NOT to GLP That is the Question

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NATIONAL ALLIANCE OF INDEPENDENT CROP CONSULTANTS

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TO GLP OR NOT TO GLP THAT IS THE QUESTION?

History Timelines-What are the laws?
   GLPs, Quality Standards
Regulatory Review – 40 CFR, 21 CFR
Regulatory Review - USEPA Open Letter 2001
Regulatory Review – Quality System Series
Why do you need a QMP? What is a QMP?
What is a QAPP?
What is a T/QAP
Why GLP Is The Way?? It Is What We Know!!
GLPs Compliance is a Quality Management System
The federal Environmental Protection Agency (EPA) was created on December 2, 1970, by executive order of President Richard Nixon to permit coordinated and effective government action on behalf of the environment.

ACTs What is the Law?


CWA: The Federal Water Pollution Control Act of 1948 was the first major U.S. law to address water pollution. Growing public awareness and concern for controlling water pollution led to sweeping amendments in 1972.

The Resource Conservation and Recovery Act (RCRA), enacted in 1976

CERCLA “Superfund”; The Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), commonly known as Superfund, was enacted by Congress on December 11, 1980


1976 Toxic Substances Control Act

2016 Amended TSCA the “Frank R. Lautenberg Chemical Safety for the 21st Century Act (“Lautenberg Act”)”
REGULATORY REVIEW

Data Errors and fraud have occurred throughout history

- 1975 FDA and EPA  Industrial Bio-Test Laboratory: Naprosyn, TCC Nemacur, Sencor. 80% of 900 studies were invalid.
- 1990’s Craven Laboratories  Manipulating chromatography
- 1997 Intertek Testing Services, 59,000 projects, 250,000 test

- **1976** FDA Proposed the non-clinical GLP, approved in 1978 -1979

- **1983** GLP guidelines for pesticide toxicology and in **1989** extended to all research data for the pesticide regulations. (40 CFR Part 160)

- **2001** Inspector General Open Letter to the Environmental Analytical Laboratory Community

  Evaluate your quality system for the detection and prevention of improper laboratory activities. Prevent fraud.
To the Environmental Analytical Laboratory Community, September 5, 2001

• Letter intended to draw your attention to issues of misconduct or unethical practices

• A laboratory’s best protection against fraudulent activity is the effective implementation of strong, proactive and independent ethical practices and Quality Systems.

“There are many factors that can contribute to misconduct: poor training, ineffective ethics programs, shrinking markets for analytical services, and greater economic incentives for laboratories to implement cost-cutting measures. Nevertheless, laboratory management is responsible for maintaining effective operations.”
REGULATORY REVIEW

Reasons for Documented Quality Standards

• Careless Study Conduct
• Failure to Final Protocols
• Data was not reviewed
• All data not reported
• Untrained / unqualified personnel
• Improper lab procedures
• Sponsors failed to monitor studies
• Sponsors did not validate data or report
• Ethics Programs

1972 New Zealand

1973 Denmark

1981 OECD Principles of GLP
OECD Guidelines for National GLP
Inspections and Study Audits
The International Organization for Standardization (ISO) is an international standard-setting body composed of representatives from various national standards organizations. Founded on February 1947, promotes worldwide proprietary, industrial and commercial standards.

General requirements for the competence of calibration and testing laboratories.

ISO/IEC 17025: 1999
General requirements for the competence of testing and calibration laboratories is the main ISO standard used by testing and calibration Laboratories.
REGULATORY REVIEW – Quality System Series

EPA. Policy and Program Requirements for the Mandatory Agency-wide Quality System. EPA Order CIO2105.0  May 2000


EPA. Guidance on Environmental Data Verification and Data Validation, EPA QA/G-8  2002

EPA. EPA Requirements for Quality Assurance Project Plans. EPA QA/R-5, 2001


EPA. Records Management. EPA Classification No. 2161.  May 2009

REGULATORY REVIEW – QUALITY

EPA. Evaluation of the Verification Protocol for Low and High Speed Wind Tunnel Testing. EPA Publication No. TBD, April 2012

RTI International. Verification Testing of Air Pollution Control Technology - Quality Management Plan, Revision 2.3. March 2010


WHY DO YOU NEED A QUALITY MANAGEMENT PLAN?

Because EPA will be requesting one.

- **Pre-Award Documentation**: The offeror must submit the following quality system documentation as a separate and identifiable part of its technical proposal:

**Documentation Specifications:**

- [X] Quality Management Plan EPA Requirements for Quality Management Plans (QA/R-2) [dated 03/20/01]

- [X] Quality Assurance EPA Requirements for Issuance of Project Plan for each Quality Assurance Project statement of Applicable project Plans (QA/R-5 [dated work for the 03/20/01] applicable project
WHAT IS A QUALITY MANAGEMENT PLAN?

Key Elements in any QMP

- management and organization,
- quality system and description,
- personnel qualification and training,
- procurement of items and services,
- documentation and records,
- computer hardware and software,
- planning,
- implementation of work processes, assessment and response, and quality improvement.

Quality Management Plan through EPA Order 5360.1 A2, Policy and Program Requirements for the Mandatory Agency-wide Quality System (EPA 2000).
WHAT IS A MANAGEMENT QUALITY SYSTEM?

The Quality Management Plan specifies the general requirements necessary to carry out work activities with competence and integrity. Where these work activities produce data used to support regulatory decisions, such as environmental data, the requirements ensure that these operations produce data that is accurate, reliable and relevant for intended use.
WHAT IS A QAPP? ‘blueprint’

US EPA has developed the Quality Assurance Project Plan (QAPP) as a tool for project managers and planners to document the type and quality of data needed for environmental decisions and to describe the methods for collecting and assessing those data.

Quality Assurance Manager – the individual designated as the principal manager within the organization having management oversight and responsibilities for planning, documenting, coordinating, and assessing the effectiveness of the quality system for the organization.

Group A: Project Management
- Project Management Roles and Responsibilities

Group B: Data Generation and Acquisition
- project design and implementation
- Sampling, measurement and analysis, data collection or generation, data handling, QC activities

Group C: Assessment and Oversight
- implementation of the project and associated QA and QC activities

Group D: Data Validation and Usability
- QA activities that occur after the data collection or generation phase of the project is completed.
WHAT IS A TQAP?

Group A. Project Management
• A4 Project or Task Organization
A5 Project Definition and Background
• Background on need for new technologies, modeling results, other studies performed, test conditions
A6 Project Task Description
A6.2 Test Facility Description
• Field Testing
• Application & Process Equipment
A7 Quality Objectives and Criteria
• #Test Runs
  (EPA suggests that testing organizations use GLPs for conducting field studies due to the complexity and expense of these studies)

Drift Reduction Technology (DRT) Field Studies
Submission Review Guide

“One must not expect more precision than the subject matter allows”

Aristotle, The Nichomachean Ethics
WHAT IS A TQAP?

A8 Special Training and Certifications

• EPA compliant QA System
• Allow on-site audit by EPA
• Have an EPA approved test/QA plan
• Written Health and Safety procedures.
• Comply with EPA reporting requirements

A9 Documentation and Records

• SOPs, protocols
• Details of the test data acquisition and management
WHAT IS A TQAP?

Group B: Data Generation and Acquisition for Low Speed Wind Tunnel

- Sampling, locations
- DQIGs and DQOs for Low Speed Wind Tunnel Measurements
- Process and Application Data Collection………
- Sample Handling and Custody Requirements
- Sample Handling and Custody Requirements
- Instrument and Equipment Testing, Inspection, Maintenance, and Calibration Frequency
- Data Management and Reporting

The best place to start for information about EPA-compliant QA systems is


More generally, the EPA Quality System website (see http://www.epa.gov/quality/)
WHY GLP IS THE WAY!!! IT IS WHAT WE KNOW!!

What / How they regulate

What is the **LEGAL** Basis?
- FDA – Federal Food Drug and Cosmetic Act Public Health Services Act
- EPA/TSCA Toxic Substances Act
- EPA/FIFRA Federal Insecticide, Fungicide and Rodenticide Act
- Pesticide products

Federal, food, Drug and Cosmetic Act

What products do they regulate?

- Human food and color additives
- Animal food additives
- Human and animal drugs
- Medical devices for humans
- Biological products
- Electronic products
WHY GLP IS THE WAY!!! IT IS WHAT WE KNOW!!

What they regulate (con’t)?
EPA/TSCA

• Note: based on consent agreements and test rules – voluntary /negotiated effect of chemicals on human health and environment
  – Toxicity
  – Ecological impact
  – Ground water
  – Air monitoring
  – Degeneration in soil, water

FIFRA

• Pesticide products

What do GLP not regulate?

• Basic Research/exploratory studies
• Physical Chemical Characteristics
• Clinical work
WHY GLP IS THE WAY!!! IT IS WHAT WE KNOW!!

GLPS ARE INTENDED TO ASSURE THE QUALITY AND INTEGRITY OF THE DATA BY THEMSELVES, GLPS CANNOT GUARANTEE THAT THE WORK IS SCIENTIFICALLY SOUND

THEY ARE OF KNOWN AND DOCUMENTED QUALITY AND TRACEABLE
GLPs Compliance is a Quality Management System

DESIGNED TO ASSURAE THAT THE STUDY IS CONDUCTED:

A. By the most qualified personnel,
B. Working in the proper Facilities,
C. Using the appropriate test system,
D. Monitored by calibrated equipment,
E. Properly recorded and documented,
F. Overseen by an independent Quality Assurance Unit,
G. With raw data properly archived and retrievable for audit,
H. Complete and audited report on the conduct of the study
Responsibilities:

• Designate a Study Director (Manager).
• Replace the SD promptly, if necessary.
• Independent QAU.
• Assure test, control, and reference substances or mixtures have been appropriately tested for identity, strength, purity, stability and uniformity, as applicable.
• Assure that personnel, resources, facilities, equipment, materials and methodologies are available.
• Assure that personnel clearly understand the functions they are to perform.
• Assure that any deviations from these regulations reported by the QAU are communicated to the study director and corrective actions are taken and documented.
GLPs Compliance is a Quality Management System

STUDY DIRECTOR

The study director has overall responsibilities for the technical conduct of the study as well as interpretation.

- Analysis
- Documentation reporting of results

Responsibilities
- Protocol/amendments approval

Test systems are specified in the protocol.

- All applicable GLP regulations are followed

All raw data documentation, protocols, specimens and the final reports are transferred to the archives at the close of study.

All experimental data accurately recorded/verified unforeseen circumstances that may affect the quality and integrity of the study, noted when they occur, corrective action taken, documented.
GLPs Compliance is a Quality Management System
QUALITY ASSURANCE UNIT 160.35

WHY DO THEY EXIST?
• An objective group was needed to assure management that the facilities, equipment, personnel, methods, practices, records, and controls are in conformance with the GLPs

WHO COMPRISSES THE QAU?
• Personnel not involved in the conduct of the study’s conduct.

Functions of the QAU
• Maintain a copy of the master schedule of all studies conducted at the testing facility
• Maintain a copy of all protocols and amendments pertaining to all studies for which the unit is responsible

• Inspect each study, at intervals adequate to ensure the integrity of the study.
  – Generate inspection reports submitted to study director and management
  – Re-inspect study, if necessary
• Periodically submit to Study Director and Management written status reports (audit/inspection reports)
• Review data and procedures to determine no deviations form GLPs, protocols and/or SOPs occurred without proper authorization.
• Review the final study report.
GLPs Compliance is a Quality Management System
QUALITY ASSURANCE UNIT 160.35

• Prepare and sign a statement to be included in the final report.

• Maintain QAU SOPs

• Conduct GLP Training

• Conduct facility and subcontractor inspections
GLPs Compliance is a Quality Management System

PERSONNEL

• Each individual engaged in the conduct of or responsible for the supervision of a study shall have education, training and experience or combination thereof to enable that individual to perform the assigned functions 160.29

Training

• Study specific
• GLP
• Safety
• Cross
• Technique
• Formal education

Training Records

• Evidence of training
GLPs Compliance is a Quality Management System

PERSONNEL

What is Ethics Training?

• Ethics – Study of standards of conduct and moral judgment.

• As a result of data integrity procedural requirements, most facilities have recognized the need and have responded with an ethics program designed to prevent fraud and to inform employees of the consequences of illegal and unethical practices.
Questions?
Thank you!
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