Regulatory Inspection Readiness for Pharmacology Laboratories

Edward P. Acosta, Pharm.D.

Professor/Director, Division of Clinical Pharmacology

University of Alabama at Birmingham

School of Medicine

Regulatory Readiness

- FDA Audit Expectations and Realities
- Previous Experiences
- Requirements
  - Immediate and continual
- Getting there, and staying there

Expectations and Realities

- Expectation
  - Everything will be scrutinized
  - Full GLP laboratory audit
- Reality
  - Generally study specific, focus on daily activities of data generation, work flow
  - Lab is the focus
    - PK results/analyses rarely audited

Previous Experiences

- Lab personnel are key to the process
  - Must be well-trained, focused individuals
- Organization is critical
  - Data/information needs to be recalled efficiently
- Data Integrity
  - Intact, sufficient, supporting documentation

Previous Experiences

- Fall, 2017
  - We received a 483
  - Lab manager at the time did not:
    - Follow our own SOPs
    - Write SOPs that were needed
    - Document daily assay activities
    - Properly document assay validation
    - Maintain sufficient organization

Previous Experiences

- Following the audit
  - Remaining lab staff worked 28 days straight to address 483 observations
  - All observations were addressed to FDA satisfaction within the required response period, sNDA approved
- Lab has been restructured and all previous deficiencies have been resolved
- Lab is fully GCP/GLP compliant

Elements of FDA Compliance

- Safety
- Organization and Personnel
- Facilities and Equipment
- Laboratory Information Systems
- Verification of Performance Specifications
- Standard Operating Procedures
- Quality Management
- Specimen Management and Tracking
- Records and Reports

Requirements

- Organization and Personnel
  - Org. chart, training files,
- Facilities and Equipment
  - Controlled access, Installation, Operational & Performance Qualifications (IQ/OQ/PQ), maint. records
- Laboratory Information Systems
  - Software validation, disaster recovery plans
- Verification of Performance Specifications
  - Assay validation, external proficiency testing

Requirements

- Standard Operating Procedures
  - SOP for everything, even how to write an SOP
- Quality Management
  - Data reviews/checks, CPQA
- Specimen Management and Tracking
  - Primarily LDMS
- Records and Reports
  - Folders for study data, equipment records (pipette calibrations, freezer temps, balances)

Getting there and staying there

- Any lab wishing to become FDA compliant should:
  - Find an outside audit source (e.g., industry, CPQA)
  - This can initially be done electronically, but site visit is useful
  - Make a list of every deficiency. Start with small ones and work up to larger ones
    - Small (SOPs, training, documentation)
    - Large (disaster recovery plans, software validation, emergency power redundancy)

Getting there and staying there

- Basic building blocks
  - Is your facility (lab) adequate (space, security)?
  - Develop organizational structure
  - Assign staff to SOP development (we have ~25)
    - Governs how the lab operates
  - Make sure all are trained to perform their responsibilities (internal vs. external)
  - Instrumentation compliance (e.g., IQ/OQ)
  - Software validation (Cost us 15K for external consultant)

Getting there and staying there

- Basic building blocks
  - Ensure proper data back-up
    - Redundancy is key
  - Validate your assays
    - FDA guidance on bioanalytical method validation
    - CPQA
  - Run study samples
    - Daily assay worksheet, supporting documentation (e.g., QC/mobile phase preps, curve preps)

Getting there and staying there

- Data review/check by others
- Report Data
  - Enter into LDMS
  - Bioanalytical report (BAR) for submissions
- Data Maintenance and Archival
  - Ability to access old data
- Oftentimes companies want to use old data for sNDA – so best to be consistently compliant

Conclusions

- Becoming FDA compliant is a top down decision
- Takes time and considerable costs
- Once over the initial start-up, process becomes standard and easy to maintain
- Significantly increases value of laboratory output