cGMP “Pitfalls" in the QC Laboratory-
Preparing the QC Laboratory and Staff for an FDA Inspection

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Consulting
Regulations

- 21 CFR
  - Part 211, Subpart B – Responsibilities of a Quality Control Unit
  - Part 211, Subpart I - Laboratory Controls

- 21 CFR
  - Part 11
Regulations

- United States Pharmacopoeia – USP
  - Reference Standards
  - Assays
  - Test Methods
FDA Guidance

“Guidance for Industry” – Investigating Out of Specification (OOS) Test Results for Pharmaceutical Production
FDA Guidelines

- Guideline for Industry
  - International Conference for Harmonization - ICH
FDA Guidelines

- International Conference for Harmonization – ICH
  - Stability Testing of New Drug Substances and Products
  - Validation of Analytical Methods
What This Means

- The Quality Control Laboratory serves one of the most important functions in Pharmaceutical production/control
- A significant portion of FDA regulations/requirements pertain to the QC and Product Testing
Preparing for the Inspection

- Preparing the Laboratory for the Inspection
Areas to “troubleshoot”

- Laboratory Equipment
  - Calibration
  - Preventative Maintenance
  - Validation
Areas to “troubleshoot”

- Standard Operating Procedures – SOP’s
  - Laboratory Records
  - Logs
  - Data Sheets
Areas to “troubleshoot”

- Out of Specification (OOS)
  - Laboratory Errors
  - Investigations
  - Documentation
  - Investigation Timeframes
Areas to “troubleshoot”

- Training
  - Documented Program
Areas to “troubleshoot”

- Analytical Method Validation
- Reagents, Solutions and Reference Standards
Areas to “troubleshoot”

- Development “work” - GMP “work”
  - Documentation
  - Laboratory Notebooks
Laboratory Equipment

- Is all the QC equipment controlled and utilized by QC personnel
- Is there a Equipment List
- Is the Laboratory Area (with all the equipment) of a suitable size 211.42 (a)
Laboratory Equipment

- Calibration Program
  - Is it written down
  - Suitable calibration intervals
  - Provisions for remedial Action
  - Tracking capabilities
  - Is Equipment “tagged”
Laboratory Equipment

- Maintenance
  - Is there a program
  - Responsibility
  - Record Keeping
Laboratory Equipment

- Validation
  - Does the lab have equipment that requires Validation (PQ)
  - Master Validation Plan
Standard Operating Procedures – SOP’s

- SOP’s in QC Laboratory
  - Accessible to QC staff
  - Current version
Standard Operating Procedures – SOP’s

- Laboratory Records (raw laboratory data)
  - Bound or prenumbered sheets
  - Not loose or scraps of paper
  - Review of data (acceptability)
Standard Operating Procedures – SOP’s

- Laboratory Logs
  - “Sequence” dates in log – analysis dates versus manufacturing dates
  - Equipment usage logs for all equipment
  - Equipment usage logs current
Out of Specification (OOS)

- Laboratory Errors
  - Laboratory Errors should be relatively rare. Frequent errors suggest a problem:
    - Inadequate training
    - Poorly maintained equipment
    - Improperly calibrated equipment
Out of Specification (OOS)

- Laboratory Investigations
  - Analyst and Supervisor – “roles”
  - Informal Investigation
  - Formal Investigation – extending beyond the QC laboratory
Out of Specification (OOS)

- Investigation Documentation
  - Investigation or Failure Report
  - Corrective Action
Out of Specification (OOS)

Investigation Timeframes

- All failure investigations should be performed within 20 business days of the problem.
- Includes implementation time frame for corrective action
Training

- GMP’s require an “active” training program
- Documented evaluation of the training of QC analysts – “Task Training”
Analytical Method Validation

- Compendial Methods – must demonstrate that the method works under actual conditions of use.

- System suitability does not constitute method validation
Reagents, Solutions and Reference Standards

- Proper storage of
- Reuse of solutions – stability
- Appropriate identification
- Expiration “justifications”
Reagents, Solutions and Reference Standards

- Reagent and Solution preparation
  - Complete and accurate documentation
  - Highly unlikely that analysts can “accurately and consistently weigh” to the same gram or microgram
Development vs. GMP

- Use of Laboratory Notebooks
  - Documented methods
  - Documented materials
  - Traceability to equipment
Preparing QC Personnel for the Inspection

- Training the staff
Preparation for an inspection

- Clean and organize your work area
- Don’t store items on the floor
- No loose data, post-its, or writing data on your hand
- Know where SOPs, logbooks, and controlled forms applicable to your work are kept
- Clean lab coats
- Neatness counts
Conduct of the Inspection

- Inspectors are looking for issues & deficiencies, despite how they present their approach to the inspection.
- Inspectors can inspect all areas of the labs that apply to the scope of the inspection; accompanied by your QA.
- May read SOPs, review data, watch analyses, question analysts.
Conduct of the Inspection

- The inspection covers the lab, the data, and the compliance program, not the individuals in the lab
- The inspection should never be taken personally
Questions by the inspectors

- Inspectors may ask questions to learn how the lab or compliance program operates.
- May ask the same question in different ways.
- Remember: the inspectors have to learn the processes of a lab that is new to them, prior to making an assessment of the lab.
Answering the Questions

- Think before you answer
- Answer questions accurately and truthfully
- Don’t be intimidated or defensive
- Know your work and be confident of your answers
- Be professional
- If you don’t know the answer, it is acceptable to ask your supervisor
- Acceptable to reply that don’t know, but you can find out
Your role in the Inspection

◆ Things not to do:
  ★ Don’t have food in the lab
  ★ Joke with inspectors
  ★ Have clutter in your work area
  ★ Quote what the SOP says, unless you’re 200% certain you know what you’re talking about
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- Any Questions