CONSEQUENCES OF POOR GMP INSPECTIONS

■ Voluntary product recalls, alerts, temporary cessation of manufacture or distribution
■ Increased FDA oversight
  ■ re-inspection
  ■ inspection of other sites
  ■ heightened attention to ADEs and other reports
■ FDA regulatory action
  ■ Significant inspectional observations
  ■ Warning letter
  ■ “Compliance hold” on pending NDAs and supplements, and exports
  ■ Disruption of clinical research
  ■ Withdrawal of NDA
  ■ Seizure, injunction, criminal prosecution
ADDITIONAL IMPACTS

- Revised processes and procedures
- Adverse government contract decisions
- Disruption of contractual obligations
- Reassessment by the business/investment community
- Strains on employee morale
- Adverse publicity
- Increased product liability exposure
- Shareholder suits
- False Claims Act suits (implied certification)
THE REASONS FOR POOR GMP INSPECTIONS

- Inadequate QA
  - QA authority and resources
  - Training
  - Supervision
  - SOPs and document control
  - Shared understanding of quality objectives
  - Performance
  - Financial support

- Inadequate management controls over operations and quality
  - Establishing the corporate compliance culture
  - Communicating the corporate compliance culture
  - Enforcing accountability
  - Clearly identified responsibility
Ineffective auditing and monitoring
Unclear or inadequate documentation/inadequate change control
Poor validation
Failure to recognize indicators of manufacturing or quality system problems
Weak mechanisms of preventive and corrective action
Unresolved cGMP deficiencies (“repeat violations”)
Inadequate preparation for FDA inspection
FDA GMP Inspections

- Bottom-up inspections
  - recalls/alerts
  - OOS findings
  - OOS/manufacturing error investigations and reports
  - QA release decisions
  - QA/manufacturing changes
  - environmental excursions
  - CAPA

- Top-Down Inspections
  - management controls
  - quality reports and reviews
  - quality unit authority/quality system infrastructure
  - quality manual/documentation
  - training processes
  - validation/process control system
FDA GMP INSPECTION REALITIES

- Demonstrating a “state of control”
- Your GMP compliance is what it is
- Performance often lags behind system controls
- Documents speak for themselves

- Exercising good communication
- Being responsive to investigator requests
- Daily meetings/daily reports
- Avoiding 483 surprises
FDA GMP INSPECTION ISSUES

- Perceived failure to fully correct previous observations or fully meet prior commitments
- Perceived lack of candor
- Perceived lack of compliance with SOPs
- Perceived superficial or inadequate quality operations (e.g., failure to identify and resolve root causes)
- Perceived lack of alignment between manufacturing/shipment decisions and quality data
- Perceived lack of understanding of quality processes
- Investigator expectations exceeding cGMP
MORE QUESTIONS?

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