The Parenteral Drug Association presents the…

2015 PDA/FDA Joint Regulatory Conference

September 28-30, 2015 | Washington, DC

Renaissance Washington, DC Downtown Hotel

Exhibition: September 28-29 | Workshop: September 30-October 1 | Courses: October 1-2

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Data Integrity: Rocking the Foundation

Data Integrity

- Reliable for its purpose: meeting standards to assure complete, consistent, and accurate data
- Examples
- What of state of mind?

Easier to emerge than you might think . . .

- Not necessarily criminal
- Not necessarily involving many people
- Not necessarily easy to detect
- The trinity: rationalization, justification, and denial

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Why Data Integrity Matters

- Oversight in this area is foundational
- Lack of data integrity in one area raises questions about other data and records
- Inability to rely upon data raises questions about the ability to assure safety and efficacy

Internal Oversight

- A quality system should
  - prevent errors and defects
  - Assure ongoing state of control
  - Facilitate vigilance, timely action, and early warning of emerging quality issues
- Data integrity breaches undermine these abilities

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External Oversight

- Regulators rely on firm data in
  - Inspections
  - Reviewing firm correspondence
  - Application review
- Data integrity breaches undermine these reviews

Antecedents

- The Generic Drug Scandal
  - Numerous prosecutions
  - Legislation and policy approaches
    - Prosecutorial approaches
    - Looking at data integrity with CGMP
    - Application integrity policy
    - Debarment
- Data Integrity Issues Today and Tomorrow

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Prosecution

- Criminal objectives: deterrence and retribution
- Common statutory approaches
  - Title 18
    - False statements within FDA jurisdiction
    - Obstruction of agency proceeding
    - Mail and wire fraud
  - FDCA felonies: "intent to defraud or mislead" extends to FDA

Difficulties of Overseas Prosecutions

- Subpoena power in investigations
- Cooperation of foreign authorities
- Compulsory power at trial
- Evidentiary Issues
- Jurisdictional Issues
  - Extradition
  - The offense (FDASIA 718 (extraterritoriality))

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Collateral Consequences

- Debarment
  - Stems from conviction
    - Clear focus on development work in ANDAs
    - Applies more broadly as well
  - Prevents services to applicants
- Medicare exclusion and corporate integrity agreements

CGMP Issues

- Multiple provisions incorporate data collection and recordkeeping
- Process leads to inaccurate or unreliable data
- Renders product adulterated
  - Generally deemed material
  - Harder to investigate and to remedy
- Warning letters and enforcement actions

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Application Issues

- Implicit requirement of reliability
  - Not necessarily found fraudulent
  - Not necessarily found inaccurate
- FDA can reject data
- Application integrity policy – a subset
  - Applies to review (rather than rejection)
  - Applies to a pattern by applicant

Preventing and Limiting Problems

- Culture should reinforce rigor of procedures and unacceptability of short cuts
- Accountability in systems and procedures
  - Management knows who did what when
  - Accountability in electronic data is key
- Data should be attributable, legible, contemporaneously recorded, original or a true copy, and accurate (ALCOA)

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Remediation – Step One

- A comprehensive evaluation of data integrity deficiencies generally would include
  - The extent of the inaccuracy of any reported data
  - Plan to investigate deficient practices
  - Examination of management involvement, procedures, and contract agreements
- FDA expects detailed, thorough plans addressing people and systems

Remediation – Step Two

- A risk assessment of potential effect on drug product quality
- Issues
  - Affected products in marketplace
  - Potential impact on patients
  - Nature of preventative controls

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Remediation – Step Three

- A management strategy that includes CAPA
- Potential issues: customer contacts, recalls, revising procedures, implementing new controls, training, etc.
- Expectation will be for increased accountability and preventative systems in future

Inspection

- A focus on implementation of corrective actions
- Mismatch may show problems are not fully addressed

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Closing Thoughts

- Potentially high stakes consequences
- Not always easy to see
- Difficult to remediate
- Better safe than sorry: controls can prevent and limit data integrity breaches