Rocking the Foundation: Data Integrity Questions

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Overall Views

• What is it?

• Why does it matter?
  – Product data reliability
  – Facility data reliability

• FDA regulation

Some History

• 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
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))

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
- Consequences
  - Warning letters and enforcement actions
  - Generally deemed material
  - Harder to investigate and to remedy

Data Integrity Provisions in Decrees

- Analogous to other CGMP remedial requirements and AIP
  - Investigation with third party
  - Remedial actions
  - FDA review and verification
- Unlike other provisions in investigating past application data

Accepting or Rejecting Data

- 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
Reasons Not To Be Sanguine

• Data integrity problems are
  – Not necessarily criminal
  – Not necessarily involving many people
  – Not necessarily easy to detect and often associated with rationalization, justification or denial
  – Not necessarily easy to fix
• Such problems can be extremely damaging

Good Practices

• Reinforce rigor of procedures and unacceptability of short cut
• Accountability in systems and procedures
  – Management knows who did what when
  – Accountability in electronic data is key
• Third party involvement helps to test practices