Rocking the Foundation: Data Integrity Questions

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Connecting a World of Pharmaceutical Knowledge

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