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

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

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

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

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)

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

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

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