Data Integrity in GXPs

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Outline

- What Is Data Integrity
- Why Is Data Integrity Important to Ensuring Medicines Quality
- Consequences of Data Integrity Issues and Why Organizations Fail to Comply
- Roadmap to Data Integrity Compliance
- Managing Data Integrity and the Data Life-Cycle
- Conclusion
USFDA: The completeness, consistency, and accuracy of data. Complete, consistent, and accurate data should be attributable, legible, contemporaneously recorded, original or a true copy, and accurate.

MHRA: The extent to which all data are complete, consistent, and accurate throughout the data lifecycle.

PIC/S: The extent to which all data are complete, consistent and accurate, throughout the data lifecycle.

WHO: The degree to which data are complete, consistent, accurate trustworthy and reliable and that these characteristics of the data are maintained throughout the data life cycle.
Data Integrity is **Not** a New Requirement

ALCOA principles first coined by **US FDA in 1980s**

**A**tttributable

[15.3] [15.7] [15.9] [15.27, d&e] [15.30 c&d] [15.43 g&h]

**L**egible

[15.2] [15.4] [15.6] [15.10]

**C**ontemporaneous

[15.8]

**O**riginal

[15.3] [15.5]

**A**ccurate

[15.2] [15.3] [15.4] [15.9] [15.11] [15.12] [17.11] [17.16]

**WHO TRS 986, 2014; GMPs for pharmaceutical products, Main principles Annex 2**
Types of Data

- Paper Data
- Electronic Data
- Hybrid Data
- Meta Data

Data Integrity

Analyst ID: JDSmith
Date: 14 Oct 2015
Time: 09:15:45
Sample Ref: B1002
Run No 1

Graph showing pH and mV signal over 60 minutes.
Data Integrity in Medicines Supply Chain

Data Integrity Is a Quality Assurance Issue!
What is data fraud?

• Unintentional issues
  – Are often the result of poorly designed processes and procedures, mistakes or lack of understanding
  – System error

• Falsification
  – Are deliberate actions to deceive or mislead, including knowingly performing manipulation, omission or deletion
  – It can be Individual or Institutional Malfeasance
Data Fraud

Changing the date/time stamp in the testing equipment used for IPC measurements

Unintentional Falsification
Data Fraud

Trial injections were performed and deleted, prior to testing “official” samples.

Unintentional Falsification
Laboratory notebook was lost

Unintentional

Falsification
Data Fraud

Analytical balance not equipped with printer showing weighing date and time.

Unintentional Falsification
Warning Letters Citing Data Integrity Issues

Cost of Data Integrity Issues

- Warning Letters, Consent Decrees, Notices of Concern, Loss of Regulatory Trust
- Import Embargos, Recalls and Seizure of Products
- Criminal Charges, Arrests and Court Trials
- Market share loss
- Drug shortage
- Patient Safety and Lives Can be Lost

Business

Patients
Why is it so hard for organizations to get Data Integrity right?!

Root Causes

- Performance & business pressure
- Lack of awareness or capability
- DI not fully integrated into our Culture
- Inadequate processes & technology
The Culture of Data Integrity

- You can fix policies
- You can fix systems
- You can fix procedures

Can you “Fix” people?
- How do you change behavior
- How do you create CULTURE?
Data Integrity Pillars

Data Governance
Training in Good Data and Record Management
Detection and Risk Mitigation
Leverage Existing Technologies
Develop and Validate Data QA Systems

Driven by Senior Management
Training in Good Data & Record Management

All Personnel
New Hires
Referesher
Self-auditing
Detection and Risk Mitigation

Follow GDRP
Should be Risk-based
Two-person verification
Leverage existing technologies; E.g. Implementing Process Analytical Technology (PAT) and other real-time measurements
Designing and validating systems to assure data quality and reliability
Roadmap to Data Integrity Compliance

Data Integrity Pillars

- Data Governance
- Training in Good Data and Record Management
- Detection and Risk Mitigation
- Leverage Existing Technologies
- Develop and Validate Data QA Systems

Driven by Senior Management
Managing DI (Data Life-Cycle)

- Design of Data Collection
- Transfer of data and meta data

- Objective Reporting
- Transparency in failures
- Tracking and Trending failures

- Objective Processing
- Handling Failures

- Source electronic data
- Re-processing events
- Failures
ALCOA principles first coined by US FDA in 1980s

- Attributable
- Legible
- Contemporaneous
- Original
- Accurate
Data Collection — ALCOA+ Principles

EMA 2010 GCPs guidelines on electronic data for clinical records

ALCOA+ Emphasis on attributes of being:

- Enduring
- Complete
- Available
- Consistent
Data Collection — Manipulation

• Regulators expect human errors

• Corrections are accepted by regulators, provided they follow appropriate procedures and controls

• Allow for corrections in
  – Paper based processes
  – Hybrid systems
  – Electronic systems
Data Processing

- Objective
- Validated method or tool
- Follow approved procedure
Data Review and Reporting

- Review of the original paper, printouts, notebooks and electronic records

- Check where data may have been stored, including locations where voided, deleted, invalid or rejected data may have been stored (Don’t forget metadata!)

- Statistically evaluate DI performance of all data – i.e. atypical, suspected, rejected, in addition to reported data
Managing DI (Data Life-Cycle)

- **Data Collection**
  - Design of Data Collection
  - Transfer of data and meta data

- **Data Archive & Retrieval**

- **Data Processing**
  - Objective Processing
  - Handling Failures

- **Data Reporting**
  - Objective Reporting
  - Transparency in failures
  - Tracking and Trending failures

- **Data Review**
  - Source electronic data
  - Re-processing events
  - Failures

• Source electronic data
• Re-processing events
• Failures

• Design of Data Collection
• Transfer of data and meta data

• Objective Processing
• Handling Failures

• Objective Reporting
• Transparency in failures
• Tracking and Trending failures
Data Storage: Archiving & Retrieval

- Don’t forget metadata
- Verify retrieval process
- Consider media lifespan
- Use validated systems
Data Storage

- Paper Record

- Electronic:
  - Offline
  - Online – Local or Cloud-based
Data Deletion (Intentional/non-fraudulent)

- SOP required
- When – periodically every quarter, every year, etc.
- What data – need to be precise and accurate
- Verification process required
  - Was correct data deleted?
  - Was other data impacted or deleted?
Data Deletion (Unintentional)

• SOP required for recovery and restoration

• Data restoration testing required
  o Multiple software
  o Multiple versions
  o Hardware changes

• Can you rebuild the data?
  o Take nto account upgrade and compatibility challenges
Data Integrity Summary

Implement DI Risk-Management: Proactively identify potential risks and remove them before they occur
• Build DI category into overall quality management system; SOPs, Training, Self-audit, Impact assessment, Root Cause Analysis, and Corrective and Preventive Action
• Incorporate DI into the self-audit program; create DI assessment checklist that accounts for systemic DI weaknesses and high-risk systems
• Encourage DI code of conduct and DI culture
• Build DI reporting into management review
References

US FDA Data Integrity and Compliance With CGMP Guidance for Industry; Draft guidance April 2016


PI_041_1_Draft_2_Guidance_on_Data_Integrity_1%20(1).pdf

WHO TRS 986, 2014; GMPs for pharmaceutical products, Main principles Annex 2 - Sections {15, 17}
Thank You
Questions