Data Integrity: TGA Expectations

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Presentation Overview

- What is Data Integrity?
- Global/Australian/US FDA Environments
- Data Integrity General Examples
- Basic Data Integrity Expectations
- ALCOA Principles
- TGA Licensed Manufacturers Expectations
- Conclusions
What is data integrity?

• The extent to which all data are complete, consistent and accurate throughout the data lifecycle

• From initial data generation and recording through processing (including transformation or migration), use, retention, archiving, retrieval and destruction.

(MHRA Guidance March 2015)
## Why so much interest now?- Global Environment

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<thead>
<tr>
<th>Manufacturer 1</th>
<th>Manufacturer 4</th>
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<tbody>
<tr>
<td>Overwriting of electronic raw data until acceptable results were achieved</td>
<td>Chromatographic software was not validated to ensure re-writing, deletion of data prohibited</td>
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<td>OOS not initiated</td>
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<tr>
<td>Falsification of data to support regulatory filings</td>
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<td>Stand alone GC systems without adequate controls</td>
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<tr>
<th>Manufacturer 2</th>
<th>Manufacturer 5</th>
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<tr>
<td>Falsification of batch records (re-writing clean records)</td>
<td>IPQC performed without batch record present</td>
</tr>
<tr>
<td>Non-contemporaneous recording of lab data</td>
<td>Unexplained ‘trial’ samples run before analysis</td>
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<tr>
<td>Recording of sample weights on scraps of paper</td>
<td>Deletion of HPLC data - lack of data security</td>
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<tr>
<td>Missing raw data</td>
<td>Missing stability samples</td>
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<th>Manufacturer 3</th>
<th>Manufacturer 6</th>
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<tbody>
<tr>
<td>Unofficial testing of samples (trial samples)</td>
<td>Lack of records demonstrating who performed analysis</td>
</tr>
<tr>
<td>OOS results not investigated</td>
<td>Raw data not recorded contemporaneously nor by the performing analyst</td>
</tr>
<tr>
<td>Retesting completed but not justified</td>
<td>Failed injections of QC standards (SS) deleted, repeated and inserted into the analytical sequence without explanation</td>
</tr>
<tr>
<td>No restriction/protection of electronic data</td>
<td></td>
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Objective 3: Data Integrity

Objective 2: Conformance to Application

Objective 1: Readiness for Commercial Manufacturing

1a: Investigations/Trends
1b: Material Handling
1c: Contamination
1d: Procedures
1e: Process feasibility

PAI Objectives (Sections 3.3 – 3.4 CPGM)
Australian Environment: Inspection report

• DEFINITIONS

• Critical Deficiency
• A deficiency in a practice or process that has produced, or may result in, a significant risk of producing a product that is harmful to the user. Also occurs when it is observed that the manufacturer has engaged in fraud, misrepresentation or falsification of products or data.
Data Integrity: General Examples

• Human errors
  – data entered by mistake
  – ignorance (not being aware of regulatory requirements or poor training)
  – Wilfully (falsification or fraud with the intent to deceive)

• Selection of good or passing results to the exclusion or poor or failing results

• Unauthorised changes to data post acquisition

Need to know the difference between falsification and poor/bad GMP/practice
Data Integrity: General Examples

• Errors during transmission from one computer to another

• Changes due to software bugs or malware of which the user is unaware

• Hardware malfunctions

• Technology changes making an older item obsolete – old records may become unreadable or inaccessible
Basic Data Integrity expectations – *Manufacturing Principles*

- **PIC/S Guide PE009-8:**
  - Chapter 4
  - Annex 11
- **Australian Code GMP human blood, blood components, human tissues and human cellular therapy products**
  - Sections 400 – 415
- **ISO 13485**
  - Sections 4.2.3, 4.2.4
Basic Data Integrity expectations

• Regulator responses
  – MHRA notifications to industry: December 2013 & March 2015
  – FDA
  – Health Canada

• Influencing factors:
  – Organisational culture, risk awareness and leadership
  – QMS design of systems to comply with DI principles
    ▪ “ALCOA” principles
  – Company processes for data review and system monitoring
ALCOA Principles

A - Attributable
  • Clearly indicates who recorded the data or performed the activity
  • Signed / dated
  • Who wrote it / when

I - Legible
  • It must be possible to read or interpret the data after it is recorded
  • Permanent
  • No unexplained hieroglyphics
  • Properly corrected if necessary

C - Contemporaneous
  • Data must be recorded at the time it was generated
  • Close proximity to occurrence

O - Original
  • Data must be preserved in its unaltered state
  • If not, why not
  • Certified copies

A - Accurate
  • Data must correctly reflect the action / observation made
  • Data checked where necessary
  • Modifications explained if not self-evident
TGA Licensed Manufacturers Expectations

• Manufacturers should:
  – Understand their **vulnerabilities** to DI issues
    ▪ Not just about your site –
      Contractors (outsourced activities)

  – Assess risks relating to data integrity- QRM Approach
TGA Licensed Manufacturers Expectations

• Manufacturers should:
  – Design systems to prevent DI issues
    ▪ Ensure the data is authentic and retrievable
  – Train staff and encourage correct behaviours and practices
    ▪ Open communication
    ▪ Encourage feedback
  – System for ongoing DI review
Conclusions

• GMP requirements already include provisions for DI- inspection report definitions, PIC/S Guide to GMP for medicinal products

• Existing systems should be able to ensure data integrity, traceability and reliability-Understand your vulnerabilities to DI issues
  – The inability of a manufacturer to detect and prevent poor data integrity practices = lack of quality system effectiveness

• QRM approach to prevent, detect and control potential risks
Conclusions continued

• Where data is generated and used to make manufacturing and quality decisions, ensure it is trustworthy and reliable

• Increased regulator focus on DI

• Remember it’s the responsibility of the manufacturer to prevent and detect data integrity vulnerabilities