Data Integrity: TGA Expectations

Stephen Hart
Senior Inspector, Manufacturing Quality Branch, TGA

PDA conference July 2015
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

<table>
<thead>
<tr>
<th>Manufacturer 1</th>
<th>Manufacturer 4</th>
</tr>
</thead>
<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>
</tr>
<tr>
<td>OOS not initiated</td>
<td></td>
</tr>
<tr>
<td>Falsification of data to support regulatory filings</td>
<td></td>
</tr>
<tr>
<td>Stand alone GC systems without adequate controls</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Manufacturer 2</th>
<th>Manufacturer 5</th>
</tr>
</thead>
<tbody>
<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>
</tr>
<tr>
<td>Recording of sample weights on scraps of paper</td>
<td>Deletion of HPLC data – lack of data security</td>
</tr>
<tr>
<td>Missing raw data</td>
<td>Missing stability samples</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Manufacturer 3</th>
<th>Manufacturer 6</th>
</tr>
</thead>
<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>
</tr>
</tbody>
</table>
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

Ref: “Data Integrity”
pharmauptoday@gmail.com
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

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

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

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

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

**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