Introduction to Data Integrity

IPA Advanced GMP Workshops, India, November 2017
The guidance is out there. So why are companies struggling?
Data integrity:

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

- Publicised data integrity failures date back to early 2000’s
- 2013: increased focus on data integrity
  - Increasing failures identified
  - Change in regulatory approach.
Has increased focus solved the problem?

- No....

- In 2015:
  - 35% EU ‘statements of non-compliance’ for Data Integrity
  - Significant number of USFDA Warning Letters
  - MHRA inspection findings*:
    - 121 Major, 218 Other deficiencies had references relevant to DI
    - 20 Major DI deficiencies in regulatory action cases
    - 10 Major DI deficiencies under compliance management.

(* Dosage form inspections Jan-Oct 2015)
Why is data integrity still an issue?

- Nothing new
- Requirements in place for many years
- No change in basic data expectations
  - Attributable
  - Legible
  - Contemporaneous
  - Original
  - Accurate.
## Existing PIC/S GMP requirements

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<tbody>
<tr>
<td><strong>Attributable</strong></td>
<td>[4.20], [4.21, c &amp; i], [4.29, e]</td>
<td>[6.14], [6.18], [6.52]</td>
<td>[2], [12.4], [15]</td>
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<td><strong>Legible</strong></td>
<td>[4.1], [4.2], [4.7], [4.8], [4.9], [4.10]</td>
<td>[5.43] [6.11], [6.14], [6.15], [6.50]</td>
<td>[7.1], [9], [10], [17]</td>
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<td><strong>Contemporaneous</strong></td>
<td>[4.8]</td>
<td>[6.14]</td>
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<td><strong>Original</strong></td>
<td>[4.9], [4.27], [Paragraph &quot;Record&quot;]</td>
<td>[6.14], [6.15], [6.16]</td>
<td>[8.2], [9]</td>
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<td><strong>Accurate</strong></td>
<td>[4.1], [6.17]</td>
<td>[5.40], [5.45], [6.6]</td>
<td>[Paragraph “Principles”], [5], [6], [10], [11]</td>
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Historical expectations

PIC/S GMP Guide 1972:

- ‘[copies of master documents]….which avoids transcription error….’
- records enabling recreation of batch history
- ‘all records shall be legibly written….and traceable’
- ‘dated signature of the persons who performed each activity’
Historical expectations

EU GMP January 1989:
- “…entries made in clear indelible handwriting….”
- “[alterations]…signed and dated….permit reading of original….reason recorded”
- “…records completed at the time each action taken...”
- “…accuracy of records should be checked…”
- “…name of persons carrying out activities…”. 
Why is data integrity still an issue?

- Breadth of scope
- Out-dated control measures
- DI failure
- Impact to quality & patient
Impact to quality and patient

- Important daily decisions regarding safety, efficacy and quality of medicines are based on data
- Unreliable data is a significant barrier to providing safe and effective medicines
  - “Precision guesswork”
- Safety / efficacy risks from substandard or falsified medicines.
Why is data integrity still an issue?

- **Out-dated control measures**
- **Breadth of scope**
- **Impact to quality & patient**
- **Reputation**

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**DI failure**
DI failure vs defect: reputational impact

Alleged falsification of emissions data

- €26bn (~20%) loss in share value
- 4.8% global reduction in 2015 sales; first drop in 11 years
- (General Motors increased 8%)
- €1bn cut in investment

Software fault: engine stops and all electrics fail while vehicle in motion

- 59,000 cars recalled in 40 markets
- Transient impact to share price (-3%)
- Share price continues upward trend.
Why is data integrity still an issue?

- Breadth of scope
- Out-dated control measures
- DI failure
- Impact to quality & patient
- Reputation
- Fear of failure
DI failure: Fear of failure

- Causes the wrong behaviour
  - Panic
  - Disproportionate management action: ‘zero tolerance’

- Complexity of proposed remediation
  - Aspirations vs action

- Quality Risk Management approach
  - Risk identification, mitigation and communication
  - Balanced with other GMP priorities
  - Perfection is a barrier to progress.
International regulatory collaboration
International data integrity collaboration

- PIC/S
- EU
- WHO
- National regulators
- Industry groups
International data integrity collaboration

- International convergence in data integrity standards
- Inspectorates better equipped to:
  - Identify data integrity failures
  - Manage post-inspection actions and remediation plans
- Cooperation between international regulators
  - Shared / common training
  - Exchange of information
  - Joint inspections
  - Coordinated market actions.
MHRA actions

- Continuing work
  - Inspections
  - Training (Inspectorate)
  - Regulatory capacity-building with PIC/S, WHO
  - Education and guidance documents (Industry)
    - Blog
    - GMP guidance published Q1 2015
    - GxP guidance in draft
  - Encouraging a reporting culture between Industry and Regulators.
Data Integrity in the Global Supply Chain
Supply chain: Influence of others around me

- Data Integrity failure
- Supply chain reputational damage
- Shortage, poor quality medicine
- Health impact

- Patients
Supply chain: data integrity considerations

- Global supply chain requires a global approach to data governance
  - Interaction between contract giver and acceptor
  - Verifying equivalence of data management systems
  - Challenges of remote data verification.
Supply chain: can we trust summary reports?

• Audit / self inspection scope - focus on data integrity
  • Summary documents can be reviewed off line
  • Capacity vs output
  • Where contracts permit, perform horizontal checks
    – Across batches, across products

• What is the company’s approach:
  • Data lifecycle and risk management
  • Data governance.
Regulators are also affected…….

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