Good Documentation Practice
Sessions 3 & 4
Good Documentation Practice

Feedback from session 2

Workshop activity:
You discussed in groups

• What practical steps do you take to ensure Good Documentation Practice?
  • Decide on top 5 for group

• What is the biggest hurdle to ensuring Good Documentation Practice?

• 20 minute discussion
Quality Culture and Cultural Excellence
Workshop activity:
Discuss in groups

- What practical steps do you take in your companies?

- What more could you do?

- 15 minute discussion

- 15 minute feedback
## Top 10 Most cited deficiency groups 2017 Jan to Jun

<table>
<thead>
<tr>
<th>Ranking</th>
<th>Groups</th>
<th>Critical</th>
<th>Major</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Quality System</td>
<td>18</td>
<td>202</td>
<td>231</td>
</tr>
<tr>
<td>2</td>
<td>Documentation</td>
<td>7</td>
<td>113</td>
<td>223</td>
</tr>
<tr>
<td>3</td>
<td>Self Inspection</td>
<td>2</td>
<td>6</td>
<td>14</td>
</tr>
<tr>
<td>4</td>
<td>Qualification/Validation</td>
<td>1</td>
<td>133</td>
<td>102</td>
</tr>
<tr>
<td>5</td>
<td>Personnel</td>
<td>1</td>
<td>16</td>
<td>47</td>
</tr>
<tr>
<td>6</td>
<td>Sterility Assurance</td>
<td>0</td>
<td>101</td>
<td>59</td>
</tr>
<tr>
<td>7</td>
<td>Production</td>
<td>0</td>
<td>75</td>
<td>153</td>
</tr>
<tr>
<td>8</td>
<td>Premises/Equipment</td>
<td>0</td>
<td>41</td>
<td>144</td>
</tr>
<tr>
<td>9</td>
<td>Complaints/Recall</td>
<td>0</td>
<td>39</td>
<td>40</td>
</tr>
<tr>
<td>10</td>
<td>Computerised Systems</td>
<td>0</td>
<td>34</td>
<td>23</td>
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</tbody>
</table>

Note – Annex 13, Major deficiencies were identified under Release of Batches
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 this 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.
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.

Think of it this way: has it EVER been acceptable to have unreliable data?
## Existing PIC/S GMP requirements

<table>
<thead>
<tr>
<th>Attributable</th>
<th>Basic Requirements for Medicinal Products (Part I): Chapter 4 (June 2011) Chapter 6 (October 2014)</th>
<th>Basic Requirements for Active Substances used as Starting Materials (Part II): Chapter 6 / Chapter 5 (Sept 2014)</th>
<th>Annex 11 (Computerized Systems) (June 2011)</th>
</tr>
</thead>
<tbody>
<tr>
<td>[4.20], [4.21, c &amp; i], [4.29, e]</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>Legible</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>Contemporaneous</td>
<td>[4.8]</td>
<td>[6.14]</td>
<td>[12.4], [14]</td>
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<tr>
<td>Original</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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<tr>
<td>Accurate</td>
<td>[4.1], [6.17]</td>
<td>[5.40], [5.45], [6.6]</td>
<td>[Paragraph &quot;Principles&quot;], [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?

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

DI failure
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?

- Breadth of scope
- Outdated control measures
- Impact to quality & patient
- Reputation
- 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
- Impact to quality & patient
- Reputation
- Fear of failure

DI 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.
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.
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