PDA is Tackling the Data Integrity Topic

Richard M. Johnson
President & CEO
Parenteral Drug Association (PDA)
A **basic principle** of assuring the quality of healthcare products is the **review of data**: by industry of data from their partners, of manufacturing and testing data by an independent quality function, and of all of this data by regulators who are responsible for monitoring the products for the public.

The **accuracy and trustworthiness** of the data, the integrity of that data, **must not be in question**, or all of the checks and balances, control measures, and quality agreements will not be effective.
Key themes from PDA-FDA 2014 Brainstorming Meeting on Data Integrity

- Culture—quality and local -- issue is huge. Good quality culture can counterbalance weak systems. Culture can influence understanding or definition of “integrity”
- Data Integrity is a disease with a spectrum like cancer; proper diagnosis is needed to identify appropriate treatments.
- Data Integrity is really a design issue. Fear or desire to make a batch pass leads to DI problems. A lifecycle problem.
- All levels and parts of the organization need to understand importance of DI and their individual roles: C suite, IT, operator level, etc. First level supervision is key.
- Natural tendency to bias and assume a root cause rather than make a thorough analysis. Assumption the equipment is broken etc.
- Companies to consider whether rewards are based on outcomes or behaviors
Data Integrity: Increased Focus of Regulatory Agencies Worldwide

Increasing trend in Health Authority Observations and Actions related to Data Integrity.

- US FDA Warning Letters & Import Alerts
- EU Non Compliance Reports
- WHO Notices of Concern and De-certification

Data integrity refers to the quality and accuracy of data over the entire data lifecycle

A = Attributable
L = Legible
C = Contemporaneous
O = Original
A = Accurate
High Quality Decisions Come From High Quality Data

Is this product safe and effective for the patient?
High Quality Decisions Come From High Quality Data

Operator Training Records
Quality Control Checks
Media Fill Results

Raw Material Identity
Filter Integrity Testing
Potency Assay
Particulate Inspection

Is this product safe and effective for the patient?

Equipment Cleaning Logs
Preventive Maintenance
Sterilization Cycle Validation
Examples of Data Integrity Problems

- Security Breaches of physical plant or information systems
- Site access without secure ID.
- Uncontrolled and unrecorded access to restricted rooms such as data centers, manufacturing suites, and document storage centers
- Access to GxP computer applications not limited to authorized personnel.
- Sharing of passwords and logon IDs
- Employees logged in to unattended computer terminals.
- No requirements for periodic password updates
Examples of Data Integrity Problems

- Lack of employee ownership and accountability
  - Improper data manipulation
  - Adjustment of time clocks
  - Backdating of information
  - Creating records after the fact
  - Excluding adverse information
  - Discarding or destroying original records
- Data systems not accurate, reliable, nor fit for their intended use.
  - Uncontrolled or haphazard backup/restore, copying, and archiving of data
  - No review of electronic record by supervisory personnel
  - Audit trails not maintained nor reviewed
  - Poor process flow inhibits access to documentation systems
  - Floor operators lack access to document process exceptions
Recent FDA Inspection Findings

• Poor Documentation Practices
  • Batch records found in the trash which don’t match “official” records
  • Photocopied labels with information filled out in advance of activity occurring
  • Data recorded for a microbial test with no sample plates found in the incubator
  • Microbial contamination recorded in an unofficial notebook but not found in any GMP documentation
  • Lack of second person verification of data

• Poor laboratory practices.
  • Manipulation of integration settings to achieve passing results
  • Retesting samples outside the quality system until a passing result is achieved.
  • Using multiple “trial/setup/training injections” before recording a single result.
  • Use of analytical methods not validated
  • Results can not be reproduced on subsequent aliquots

• Security Breaches of physical plant or information systems
  • Using Administrator access to override analyst results
  • Deletion of raw data or unfavorable results
  • Inspector denied access to view data recorded on a thumb drive
GMP regulations do not require determining intent while assessing Data Integrity, however companies should determine intent. Even with deliberate falsification of records, companies must understand the dynamics that drove and allowed the individual to do this if companies are to truly fix the issue and prevent its reoccurrence.

Without an understanding of the true root causes for human misbehavior, companies may be forced to take widespread actions that may not be indicated, especially when factored with the preventive data integrity measures already in-place.
Data Integrity: Causes & Mitigation
Task Force is Working on the following …..

<table>
<thead>
<tr>
<th>Malfeasance</th>
<th>Quality Culture &amp; Code of Conduct</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Elements of Code of Conduct for Data Integrity</td>
</tr>
<tr>
<td></td>
<td>✓ Enforcement &amp; Discipline built into CoC</td>
</tr>
<tr>
<td></td>
<td>• Speak-up Culture - Quality Culture Maturity</td>
</tr>
<tr>
<td></td>
<td>✓ Tone at the Top</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sloppiness</th>
<th>Management Controls Elements Built into DI Tech Reports</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>✓ Auditing &amp; Monitoring -</td>
</tr>
<tr>
<td></td>
<td>✓ Accountability &amp; Supervision</td>
</tr>
<tr>
<td></td>
<td>✓ Resource Allocation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ignorance</th>
<th>Knowledge, Training, &amp; Awareness</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Technical Reports</td>
</tr>
<tr>
<td></td>
<td>• Workshops</td>
</tr>
<tr>
<td></td>
<td>• Training program</td>
</tr>
</tbody>
</table>
## PDA Data Integrity Deliverables: Workshops, Tools & Training Courses

<table>
<thead>
<tr>
<th>Date</th>
<th>Venue</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>April 19-20</td>
<td>Millennium Gloucester Hotel</td>
<td>London, UK</td>
</tr>
<tr>
<td>Sept 14-15</td>
<td>Renaissance Washington DC, Hotel</td>
<td>Washington, DC</td>
</tr>
<tr>
<td>Nov 8-9</td>
<td>Titanic Chaussee Berlin</td>
<td>Berlin, Germany</td>
</tr>
<tr>
<td>Dec 7-8</td>
<td>Manchester Grand Hyatt</td>
<td>San Diego, CA</td>
</tr>
</tbody>
</table>

### TOOLS AND TRAINING

- Root Cause/Risk Assessment Matrix
- PDA Education Course
<table>
<thead>
<tr>
<th>Publication</th>
<th>Title</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Points To Consider</td>
<td>Elements of a Code of Conduct for Data Integrity in Pharmaceutical Industry</td>
<td>Published (&gt;1000 downloads)</td>
</tr>
<tr>
<td>Book</td>
<td>Assuring Data Integrity for Life Sciences</td>
<td>Published</td>
</tr>
<tr>
<td>Technical Report</td>
<td>Data Integrity in Laboratories Systems</td>
<td>Q2/Q3 2016</td>
</tr>
<tr>
<td>Points To Consider</td>
<td>Fundamental Concepts for Data Integrity</td>
<td>Q2 2016</td>
</tr>
<tr>
<td>Technical Report</td>
<td>Data Integrity: Integration into QMS</td>
<td>Q4 2016</td>
</tr>
<tr>
<td>Technical Report</td>
<td>Data Integrity in Manufacturing Systems</td>
<td>Q1 2017</td>
</tr>
</tbody>
</table>
Elements of a Code of Conduct for Data Integrity

Scope and Purpose

- Developed by a team of quality and regulatory experts with input from attorneys.
- Ready to use language that can be incorporated into existing company codes of conduct or supplier quality agreements.
- Written to apply to GXP activities for drug and biological products
Elements of a Code of Conduct for Data Integrity

Key Elements and Sections

• Senior Management must establish quality standards and requirements.
• Every employee has a duty to engage in conduct which results in data that are accurate, truthful and complete.
  • Data Collection, Analysis, Reporting and Retention
  • Electronic Data Acquisition Systems and Access Security
  • Auditing and Investigations
  • Internal Reporting Responsibility and Disciplinary Actions
  • Notifying Regulatory Authorities
  • Outsourced Services and Purchased Raw Materials
  • Employee Training
  • Glossary of Terms
Data Integrity Task Force: Expected Outcomes

- Harmonized standards to comply with regulatory expectations for maintaining data integrity,
- Defining mechanisms for detecting non-compliance and outlining a clear methodology for remediating gaps.
- Serves both industry and regulators in creating and defining solutions for the increasing number of failed inspections where firms lack the needed controls to ensure data integrity and lack the expertise to detect and resolve non-compliance
- Methodology for restoring confidence in a system and organization to avoid revenue loss and regulatory impacts.
Questions?

• Richard M. Johnson
• E: johnson@pda.org
• P: +1.301.656.5900

• More Info.:
  https://www.pda.org/scientific-and-regulatory-affairs/regulatory-resources/data-integrity