PDA is Tackling the Data Integrity Topic

Richard M. Johnson

President & CEO

Parenteral Drug Association (PDA)

Back to Basics!

- 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.

FDLI

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

FDLI

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

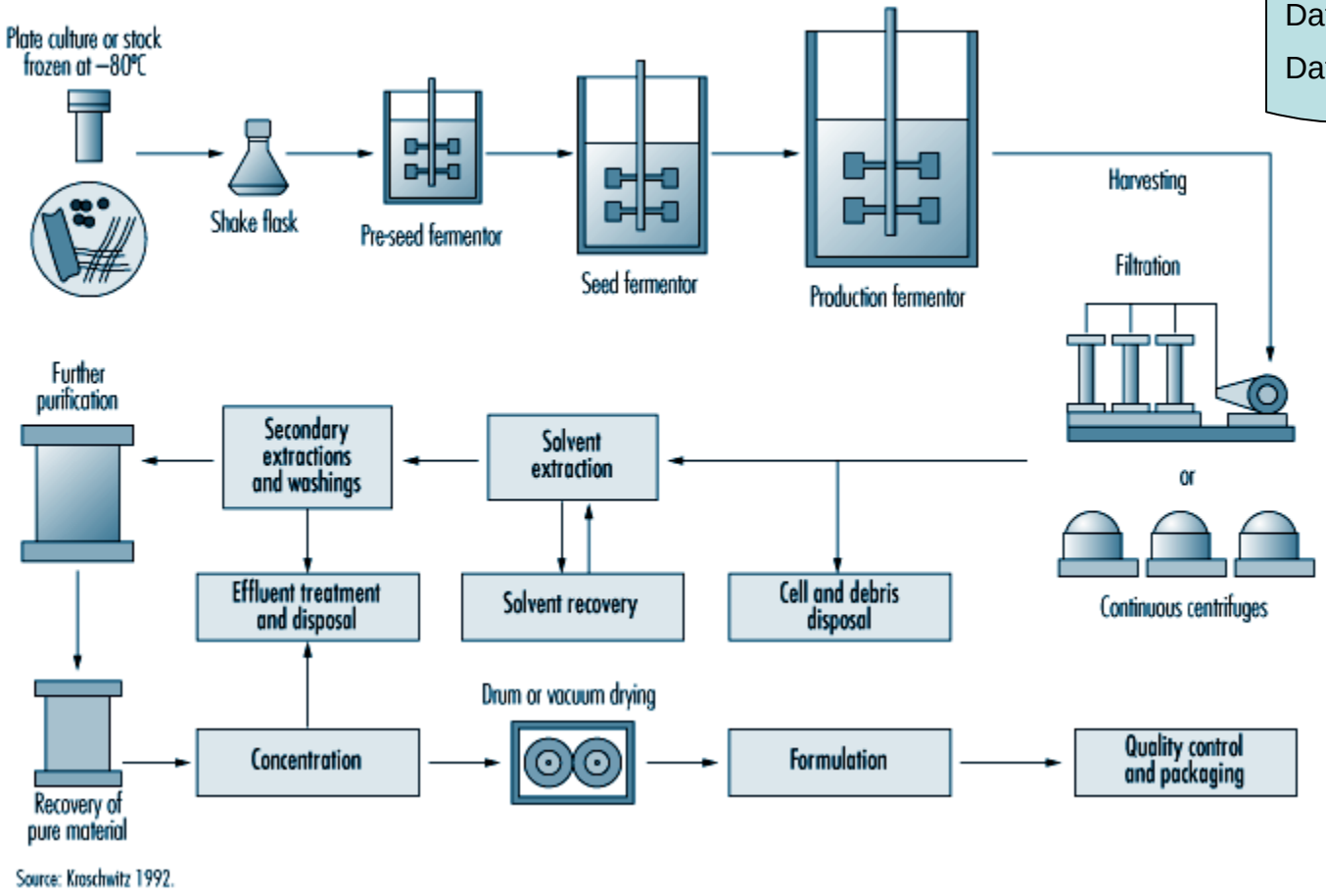
A = Accurate

FDLI

High Quality Decisions Come From High Quality Data

Every Step has Data In and

Data Out



Is this product safe and effective for the patient?

FDLI

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

Equipment Cleaning Logs
Preventive Maintenance
Sterilization Cycle Validation

Is this product safe and effective for the patient?

FDLI

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

FDLI

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

FDLI

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

FDLI

Data Integrity Continuum

System Error

Individual Mistake

Individual Malfeasance

Institutional Malfeasance

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.

Unintended Error

Deliberate Falsification

FDLI

Data Integrity: Causes & Mitigation
Task Force is Working on the following …..

Malfeasance	**Quality Culture & Code of Conduct** •Elements of Code of Conduct for Data Integrity ✓ Enforcement & Discipline built into CoC •Speak-up Culture - Quality Culture Maturity ✓ Tone at the Top
Sloppiness	**Management Controls Elements Built into DI Tech Reports** ✓ Auditing & Monitoring - ✓ Accountability & Supervision ✓ Resource Allocation
Ignorance	**Knowledge, Training, & Awareness** • Technical Reports • Workshops • Training program

FDLI

PDA Data Integrity Deliverables : Workshops, Tools & Training Courses

Date	Venue	Location
April 19-20	Millennium Gloucester Hotel	London, UK
Sept 14-15	Renaissance Washington DC, Hotel	Washington, DC
Nov 8-9	Titanic Chaussee Berlin	Berlin, Germany
Dec 7-8	Manchester Grand Hyatt	San Diego, CA

PDA Data Integrity Deliverables: Publications

Publication	Title	Status
Points To Consider	Elements of a Code of Conduct for Data Integrity in Pharmaceutical Industry	Published (>1000 downloads)
Book	Assuring Data Integrity for Life Sciences	Published
Technical Report	Data Integrity in Laboratories Systems	Q2/Q3 2016
Points To Consider	Fundamental Concepts for Data Integrity	Q2 2016
Technical Report	Data Integrity: Integration into QMS	Q4 2016
Technical Report	Data Integrity in Manufacturing Systems	Q1 2017

FDLI

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

FDLI

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

FDLI

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.

FDLI

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

FDLI