Developing a Robust Quality System to Assure Data Integrity

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Data Integrity

Facts or information generted and used to calculate, analyze or plan,

possess the qualities of being truthful, honest, complete, accurate and uncorrupt

Data Integrity

Data Integrity must be honored, not only to the letter of the law…

but in principle.

In as much as we strive to develop a Quality Management System (QMS) that assures data integrity, we must strive to develop a culture that values and understands the critical role of data integrity in ensuring patient safety, and forging a trusting bond with clients and Regulators.

Regulatory Guidance & Trends

Regulatory Agencies have increased their focus

on Data Integrity, including issuing guidance documents and taking consistent action in regards to compliance gaps related to Data Integrity requirements and expectations

A key cornerstone for the integration of Data Integrity into a robust Quality Management System (QMS) capable of preventing, detecting, and remediating Data Integrity issues will require keeping pulse on Regulatory guidance and trends to ensure both; knowledge of the requirements, as well as how the requirements continue to be interpreted.

Regulatory Guidance & Trends

Stay Current!

- ❖ MHRA Guidance, March 2015; Draft Revision, July 2016
- ❖ FDA Draft Guidance, April 2016
- ❖ WHO Annex 5, June 2016
- ❖ PIC/s Draft Guidance, August 2016

Regulatory Guidance & Trends

- Warning Letters/Untitled Letters

- FDA 483 Observations

- Import Alerts

- EU Non-Compliance Reports

- WHO De-Certification

Data Integrity: Code of Conduct

Company Officers and Chief Executives should establish a written testimony outlining the company's ethical and practical commitment to Data Integrity.

This commitment is the foundation for integrating Data Integrity principles and requirements throughout the QMS

Values

Code of Conduct

Policies/Standards

Standard Operating Procedures

Values

Values
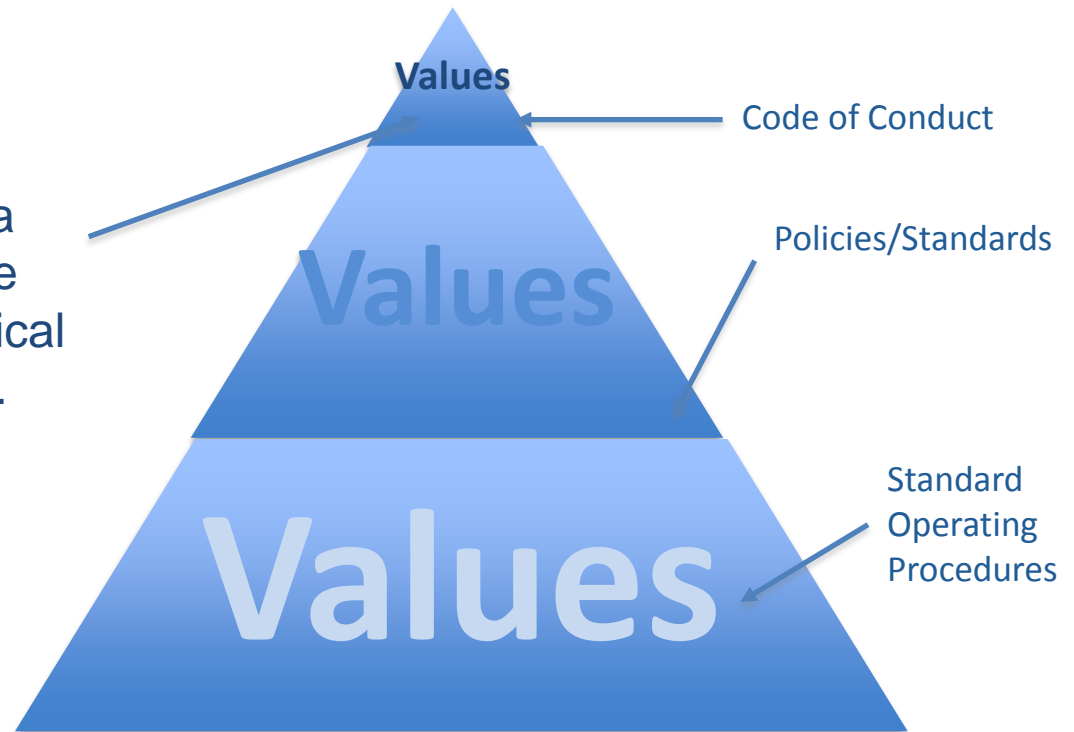
Code of Conduct

The Code of conduct should apply to all officers, management and employees of a company, including suppliers and contractors, engaged in the development, manufacture, testing and distribution of drug products, and as such, responsible for operations required to adhere to GxP practices in accordance with applicable laws, regulations and directives of regulatory authorities.

Code of Conduct

The Code of Conduct should establish a process for reporting Date Integrity issues, including clearly defining what constitutes a breach and the consequences that will be enforced

Code of Conduct

Code of Conduct

Policies/Standards

Standard Operating Procedures/Process
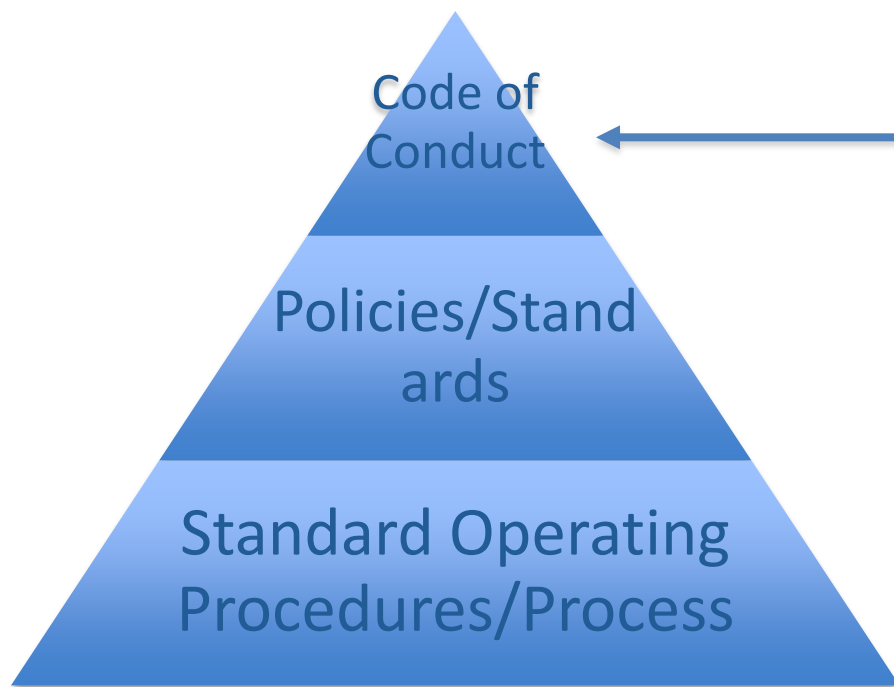
The company should outline high level expectations and requirements for management to develop standards, policies, processes and procedures to ensure the QMS establishes the harmonized and comprehensive organizational and technical control of data.

Organizational Structure

Consideration should be given to the structure of the organization:

Departments specifically designed to ensure compliance across functional areas is recommended
•Increased expertise and governance is required to meet regulatory expectations for compliance
•Increased complexity throughout the supply chain, coupled with the call for automation and computerized systems to ensure security and control of data

Data Governance

Management should develop and implement a Data Governance System to ensure Data Integrity principles, requirements, definitions and supporting processes are clearly defined, and that Data is managed in accordance with applicable

regulations, guidance and best practice throughout the Data Lifecycle

Risk management principles should be applied when developing and assigning resources for Data Governance, ensuring an acceptable level of control is in place based on the criticality and risk to data

Data Governance: Key Attributes

- Management should be responsible for the design, implementation, monitoring and maintenance of the data governance system to ensure systems and processes are compliant with data integrity requirements and principles.

- Appropriate resources should be in place to demonstrate support for the data governance system, and to ensure compliance with data integrity principles, procedures, and applicable regulations.

- Roles, responsibilities and the ownership of data should be established throughout the data lifecycle

- Procedures and controls should be established to ensure data integrity, including such that define accountability for individuals who breach such requirements

Data Governance

- Effective process and product monitoring provide early warning of emerging quality issues

- Training should be established in data integrity principles, elements and practices for all individuals responsible for data in the testing and manufacturing of drug product

- Data integrity issues should be communicated and/or escalated commensurate with criticality – to include establishing appropriate timelines to address Data Integrity compliance gaps

- Data integrity principles should be applied to outsourced activities, including contract givers and suppliers

- Self inspection should include a review of the effectiveness of the data governance system

Quality Culture

- Management controls should be established, communicated and followed to:
  - Promote transparency and timely escalation of possible data integrity gaps
  - Provide incentives and amnesty for communication of possible gaps
  - Provide a no-retaliation environment to allow for individuals to raise and investigate concerns without fear of retaliation

Remember…

Data Integrity applies to manual, hybrid and electronic systems

The processes that generate and manage data throughout the product lifecycle MUST meet regulatory requirements and expectations.

Integration

Successful pharmaceutical product development and manufacturing are contingent upon the reliability of supporting data generated at each phase of the product lifecycle.

Integration

A robust and effective QMS is intended to integrate
the objectives and requirements (systems/processes/programs)
of GMP regulations and Data Integrity principles throughout the QMS and
its associated systems

Based on FDA's Six System Inspection Model, the QMS consists of the following systems:
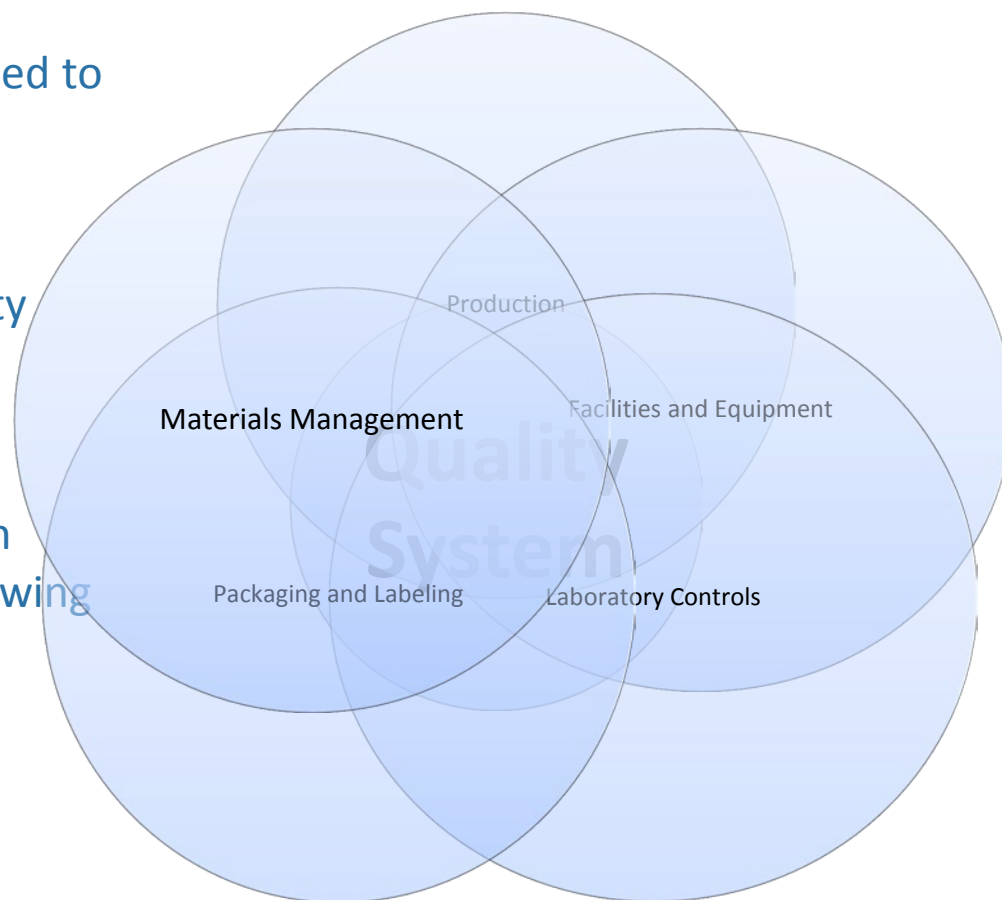
Quality System
Production System
Facilities and Equipment System
Laboratory Controls System
Materials System
Packaging and Labeling System

Integration

Quality Management System DATA INTEGRITY PRINCIPLES					
DATA INTEGRITY PRINCIPLES	Quality System	Production System	Laboratory Control System	Materials Management System	Facilities and Equipment	Packaging and Labeling
Management Review						
Change Management						
CAPA Management						
Deviation Management						
Training Program						
Audit Program						

Mapping out programs/processes and systems against the QMS may be useful in planning integration…

Integration

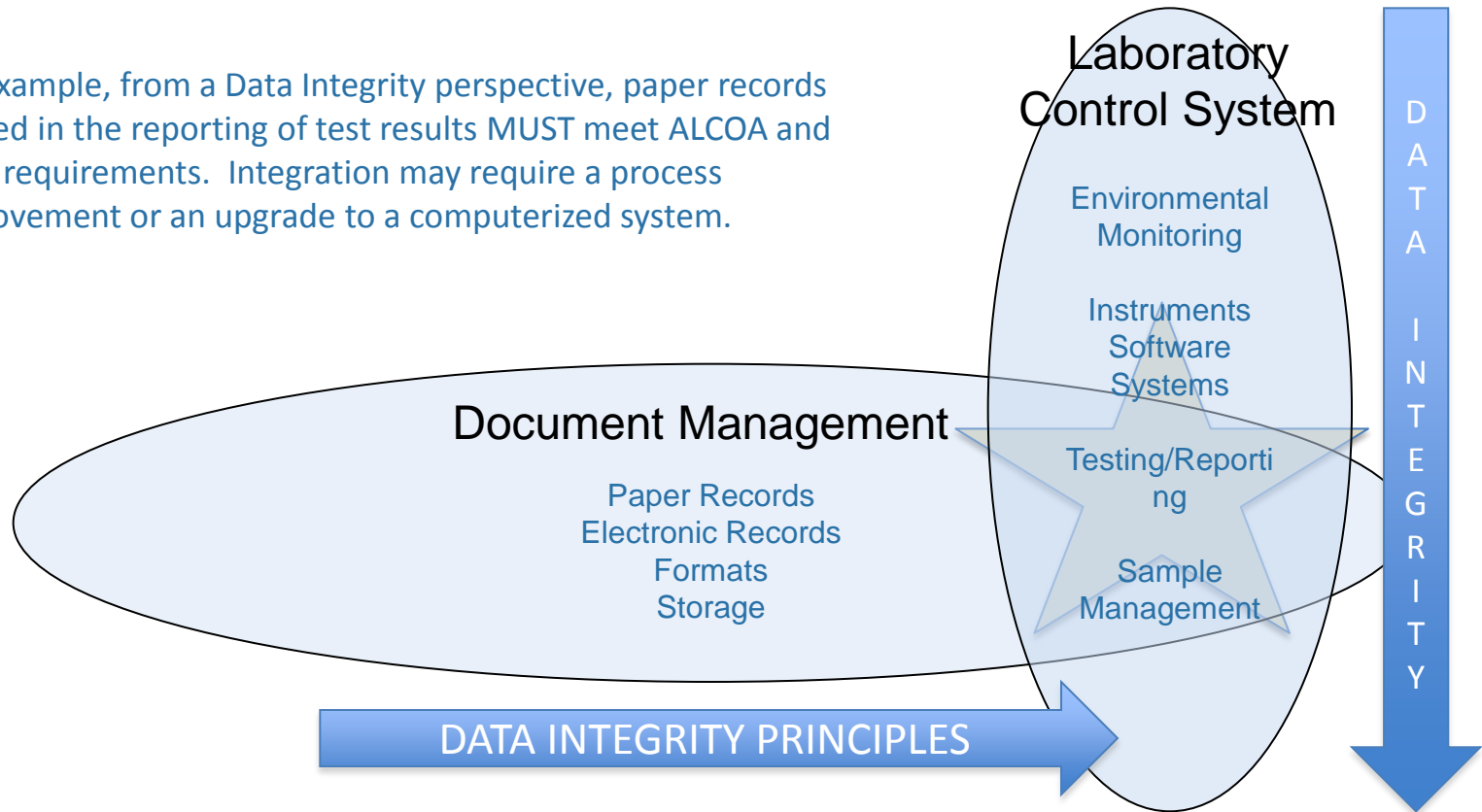| DATA INTEGRITY PRINCIPLES	Quality Management System DATA INTEGRITY PRINCIPLES					
	Quality System	Production System	Laboratory Control System	Materials Management System	Facilities and Equipment	Packaging and Labeling
Management Review						
Change Management						
CAPA Management						
Deviation Management						
Document Management						
Audit Program						

> Integration can be visualized from the point of the QMS foundation, across quality systems, programs and processes, down to the elements and actions wherein the principles, programs, processes and actions intersect.

Integration

For example, from a Data Integrity perspective, paper records utilized in the reporting of test results MUST meet ALCOA and GMP requirements. Integration may require a process improvement or an upgrade to a computerized system.

Laboratory Control System

- Environmental Monitoring
- Instruments Software Systems
- Testing/Reporting
- Sample Management

Document Management

- Paper Records
- Electronic Records
- Formats
- Storage

DATA INTEGRITY PRINCIPLES

DATA INTEGRITY

Integration

Some key integration strategies across quality systems and programs/processes may include:

	Quality System	Production System	Laboratory System	Materials Management	Facilities and Equipment	Packaging and Labeling
Deviation	Requirement for DI category : Define types					
Audit Program	Specialized training for auditor qualification in identifying DI compliance gaps		Procedures and forms to ensure tracking of DI specific related laboratory incidents			
CAPA						
Management Review						

Integration

- Data Integrity principles (ALCOA) are considered the foundation of the QMS, and are to be integrated into each system within the QMS

Integration

- Data integrity policies defining the requirements and expectations for data management, monitoring and reporting, will provide for a consistent approach to processes and practices across all systems within the QMS.

- Requirements are further defined in standard operating procedures and associated process records and controls.

Integration

- Data Integrity Breaches may occur in any system and/or phase of the product lifecycle.

- Examples of Data Integrity Breaches include:
  - Not recording and/or reporting data accurately
  - Manipulating data
    - Misrepresenting facts
    - Copying (Recreating) existing data as new data
    - Backdating/adding or modifying data after the fact
  - Fabricating data
  - Discarding data
  - Omission of material facts
  - Events may be attributable to mistakes and/or deliberate misconduct.

Remediation

- FDA requires Data Integrity Gaps be fully investigated to determine scope, root cause, impact and to define immediate, corrective and preventative actions.

  - When determining scope, consider if this issue has the potential to occur in other areas, systems and/or with other individuals.

  - Root cause should determine not only how the deviation occurred but also assess any factors which may influence, promote or motivate the error, as well as factors that allowed for the deviation to go undetected

Remediation

- Investigations should determine the impact of deficient documentation practices on the quality of the drug products produced
    - Were adulterated and/or OOS drugs shipped?
        - If yes, what is impact on patients?
    - How was the data impacted?
        - Did the data integrity gaps alter material facts which would have impact on decisions made using that data?

Remediation

- Investigations into data integrity gaps should be documented and tracked within the QMS.

- It is common for firms to have a separate repository for certain confidential information, especially when the investigation is in-process.

  - This will allow for individuals performing the investigations to conduct their reviews in a confidential manner as facts are being gathered.

Remediation

- Individuals performing these investigations and/or audits must be impartial and qualified to perform data integrity reviews for the type of systems and process under evaluation

- FDA Warning Letters may be used as a guide to confirm FDA expectations when a specific type of deficiency is identified.

  - Excerpt from recent Warning Letter:

    - *"…a* comprehensive evaluation *of the extent of the inaccuracy of the reported data. As part of your comprehensive evaluation, provide a detailed action plan to investigate the extent of the deficient documentation practices. . ."*

    - Even if no OOS drugs were shipped, it is important to maintain appropriate preventative controls.

Indicators of Potential Data Integrity Gaps

- Discrepancies between Workload, Capacity and Output
  - Equipment
  - Materials Management
  - Resourcing
- Quality Metrics show delays in closure of quality records
- Lack of documented deviations/incidents/OOS reports/Data integrity issues
- Separate quality system or laboratories for "other" markets
- Lack of detailed procedures for review of electronic data
- Computerized and automated system risks not well understood/identified and tested to confirm controls and configuration are appropriate
- Documents not submitted to Quality in timely manner (no time limits or monitoring of this timeline)
- Documents found in trash/recycle/shredder bins (location of bins in areas where documents should not need to be discarded)

Summary

- Establish a QMS with management controls that define your company values and expectations with regard to Data Integrity

- Create a culture and environment fostering the detection, reporting and management of Data Integrity issues.

- If you are aware of, discover or witness a practice that is a breach of Data Integrity, regulations or policy, follow your quality system.

- Awareness of the issues is key and prompt action will reduce your risk of regulatory sanctions and consequences.

Questions?