Rx-360 2023 CONFERENCE

DATA INTEGRITY MANUAL AND FUTURE PLANNING

Jim Henderson, Eli Lilly & Company

TOPICS

- Charter
- Data Integrity Work Group Members
- Data Integrity Survey
- Rx-360 GMP Audit Manual; Data Governance and Data Integrity – March 2018
- Selection and GMP Auditing of Software and Hardware Vendors – December 2022
  - Rx-360 Vendor Questionnaires:
    - Quality System
    - Software
- Data Integrity Library
- Rx-360 Data Integrity Work Group Newsletter

DATA INTEGRITY WORK GROUP CHARTER

Statement

- Failures in data governance and data integrity have plagued the industry for over 15 years. The US FDA, European inspectorate, and WHO have enforced such actions in the US and Europe as well as countries such as India, China and Japan. The industry does not appear to have fully met the data integrity requirements and expectations.
- The Rx-360 Data Integrity Work Group will work to develop processes, tools and training to incorporate data integrity best practices for our Rx-360 partners.

Goal

- Improve Data Integrity Governance by assisting members and third-party auditors to:
  - Develop processes, guides, and tools establish policies, procedures and best practices.

DATA INTEGRITY WORK GROUP MEMBERS

Jim Henderson, Eli Lilly & Co

Dan Ewald, Boehringer Ingelheim

Luc Sergile, Eli Lilly & Co

Bobby Stein, Eli Lilly & Co

Thomas Craig, Amgen

Zalini Bhagroo, American Regent

Parthiv Chauduri, PTC Therapeutics, Inc.

Leigh Ann Greenwald, TCR² Therapeutics Inc

Abner Vasquez, Biogen

Sonal Rana, Bristol Myers Squibb

Jason Chattoo, Merck

Tanya Sandino, Eli Lilly & Co

Nneka Eltinor, Millipore Sigma

Cara Fowler, Eli Lilly & Co

DATA INTEGRITY SURVEY

Data Integrity Work Group developed a Data Integrity Survey to better understand the level of understanding and compliance. 65 Responses

Within Life Sciences which best describes your organization or division?

ANSWER CHOICES	RESPONSES	
Small Molecule Manufacturer	18.46%	12
Large Molecule Manufacturer	18.46%	12
Medical Devices	6.15%	4
Clinical Research	1.54%	1
Testing Lab	1.54%	1
Other (please specify)	53.85%	35
TOTAL		65

DATA INTEGRITY SURVEY

Does your organization have a DI governance program which includes top level management commitment and training at all levels of the organization, which emphasizes a holistic understanding of the data lifecycle?

ANSWER CHOICES	RESPONSES	
Yes	85.94%	55
No	14.06%	9
TOTAL		64

What is the maturity level of your data integrity governance program?

ANSWER CHOICES	RESPONSES	
Green - Complete (Assessment and Remediation) - identified risks remediated accordingly with identification of accepted risk.	36.92%	24
Yellow - In progress (remediation) - in the process of performing remediation activities. Assessment performed, significant issues identified, and interim measures have been implemented.	49.23%	32
Red - Not started/in progress and no remediation of significant issues.	13.85%	9
TOTAL		65

DATA INTEGRITY SURVEY

Who in your organization is responsible for overall data governance?

ANSWER CHOICES	RESPONSES	
Dedicated Data Integrity Team	23.08%	15
Individual Data Owners	20.00%	13
Quality Assurance/Quality Control	43.08%	28
Other (please specify)	13.85%	9
TOTAL		65

DATA INTEGRITY SURVEY

What tools does your organization use to detect data integrity gaps/risks?

ANSWER CHOICES	RESPONSES	
Data integrity risk assessment	38.46%	25
FMEA	7.69%	5
Simple checklist	3.08%	2
Incident management	3.08%	2
Self-inspection	12.31%	8
Other (please specify)	35.38%	23
TOTAL		65

DATA INTEGRITY SURVEY

What percentage of your GxP records are:

ANSWER CHOICES	RESPONSES	
Paper Based?	81.03%	47
Electronic?	91.38%	53
Hybrid (Paper and Electronic)?	68.97%	40

DATA INTEGRITY SURVEY

Were you aware of the Rx-360 GMP Audit Manual?

ANSWER CHOICES	RESPONSES	
Yes	41.27%	26
No	58.73%	37
TOTAL		63

If "yes", have you used the manual to improve any aspects of your data Integrity program at your organization?

ANSWER CHOICES	RESPONSES	
Yes (Please use comment field to explain how)	15.00%	9
No (Please use comment field to explain)	23.33%	14
N/A as you answered "no" to Question 15	61.67%	37
TOTAL		60

DATA INTEGRITY SURVEY

Based on the survey outcome, the team identified the following as potential deliverables

- Leverage the results to determine how we could better support Rx-360 colleagues
- Update and Rebrand the GMP Audit Manual
- Incorporate Data Integrity references into the Rx-360 Audit Checklists
- Publish Quarterly Data Integrity Newsletter
- Update the DI Library

Rx-360 GMP AUDIT MANUAL 2018

- Provides approach for Auditing and Self-Assessment
  - Computer System Validation
  - Quality Control laboratory and Manufacturing Systems
  - Management of Suppliers
- Should be used in conjunction with FDA, PIC/S, MHRA, WHO, and ISPE GAMP 5
- Not a checklist or meant to explain concepts and requirements
- Written for Pharmaceutical GMP Operations: APIs, Key Intermediates, Drug Products, Excipients, Raw Material Providers
- Excludes vendors of hardware and software

Rx-360 GMP AUDIT MANUAL REBRAND

Original plan, update based on new and updated regulations and guidance: ISPE DIbD, GAMP 5 2nd Addition, PDA, USP <1058>

Based on feedback that 35 (54%) responded “Other” to describe your Organization / Division, we decide to have a broader approach to the Data Integrity and Data Management guide

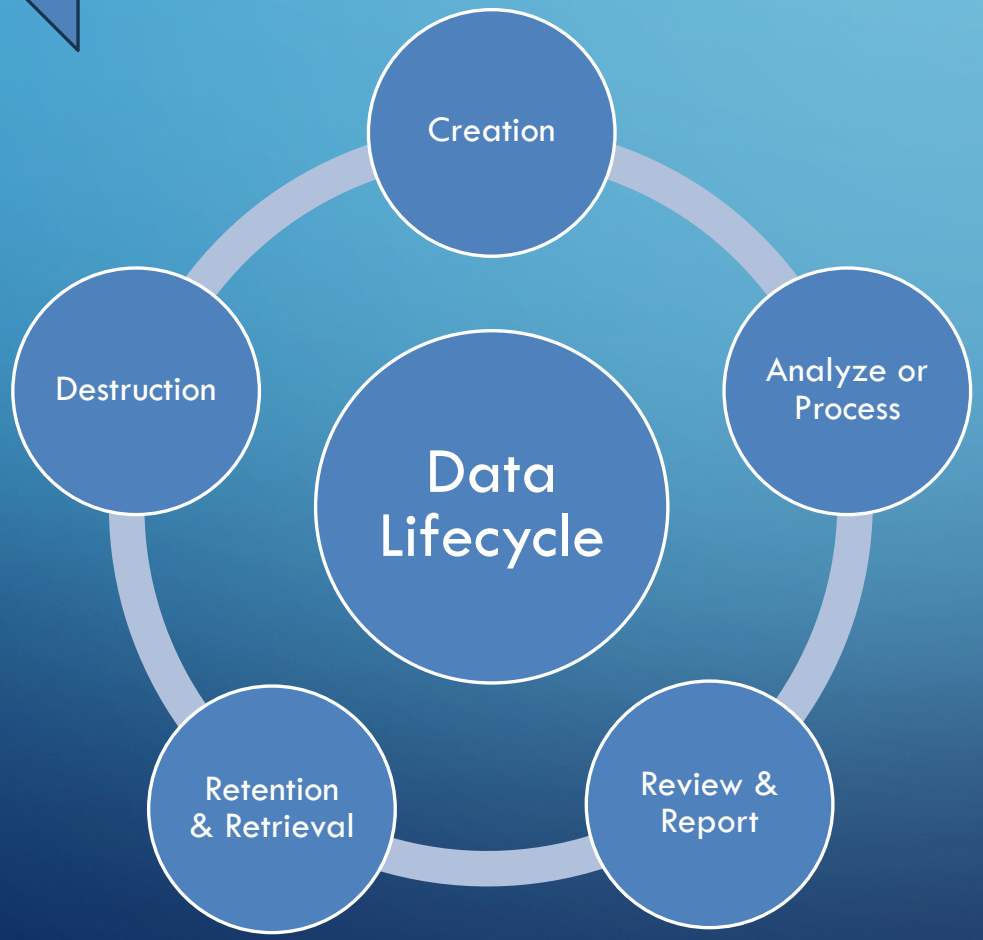
Based on the intended use and risk

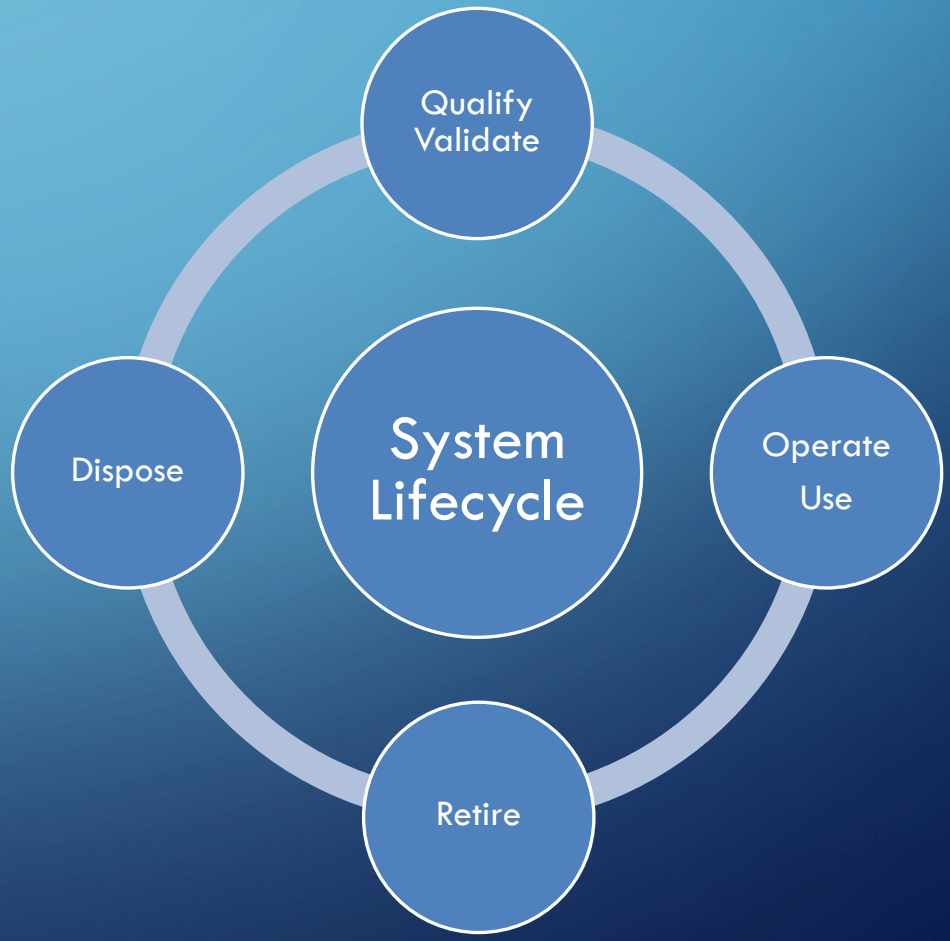
- Drug Substance and Drug Product Commercial Manufacturing
- Quality Control Laboratories
- Excipients
- Raw Materials

Rx-360 GMP AUDIT MANUAL REBRAND

Data Governance MHRA

The arrangements to ensure that data, irrespective of the format in which they are generated, are recorded, processed, retained and used to ensure the record throughout the data lifecycle





Rx-360 GMP AUDIT MANUAL REBRAND

DI Guide Organization

- Provide the expected DI practices
  - Add details based on regulation and guidance
  - Provide additional guidance where it doesn’t exist within the manual or other publications
  - New concepts to help provide additional guidance to Rx-360

Rx-360 GMP AUDIT MANUAL REBRAND

The survey showed that 69% of the systems were Hybrid Systems

MHRA / PIC/S: likely to require increased data review due to vulnerable to non-attributable data changes

ISPE DIbD: Business rules must be automated to be practical. Hybrid processes are difficult, if not impossible, to implement in an efficient manner.

Warning Letter:

- While your firm retained a static copy of laboratory records for review (i.e., paper record), they were inadequate as they did not preserve the dynamic record format of the test to support the results
- You did not retain all original, dynamic records, obtained during the course of testing

SELECTION AND GMP AUDITING OF SOFTWARE AND HARDWARE VENDORS

Addendum to the Rx-360 Audit Manual

- Applicable to GXP systems and software vendors
- Provides an approach for selecting vendors and performing quality system, data governance, and data integrity of computerized systems
- Provided a process flow diagram based on:
  - System Purpose
  - User Requirements
  - System Criticality
- Guidance: audit prep, performing, acceptance/rejection/post audit activities
- Goal: Rx-360 Vendor Audit Program

Rx-360 AUDIT PROGRAM

Data Integrity Work Group and Audit Operations Group Collaboration

- Provide a copy of the Rx-360 DI Guide to auditors and auditees
- Provide as a resource for CAPA
- Add a Data Integrity Guide reference to the to Rx-360 Audit Checklist
- Add DI principles and references to the Audit Checklist where they are not present
- Develop data integrity training for auditors

DATA INTEGRITY LIBRARY AND NEWSLETTER

Data integrity regulations have changed over the years

- Organize based on topic and date
- Update references, publications, and guidance
- Add new Warning Letters and 483

Data Integrity Work Group Newsletter

- Share Warning Letter trends
- Associated regulations
- What controls should be considered for that topic

DATA INTEGRITY NEWSLETTER EXAMPLE

Access Control: FTIR instrument did not have access control, audit trail, electronic signatures

Access: FDA 211.69 B. Appropriate controls shall be exercised over computer or related systems to assure that changes in master production and control records or other records are instituted only by authorized personnel.

Audit Trails: 21 CFR Part 11, EU Annex 11, ISPE DIbD, MHRA

The audit trail provides for secure recording of life-cycle details in the form of metadata containing information of related actions; creation, modification or deletion of GXP records.

Electronic Signature: 21 CFR Part 11, ISPE DIbD, MHRA

Digital form equal to handwritten signature

- Unique to an individual, two components – username and password
- Meaning associated with the e-sig: review, approve, author, etc.,

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