Culture of Quality
Data Integrity at the Center of
Patient-Focused Generic Drug Development

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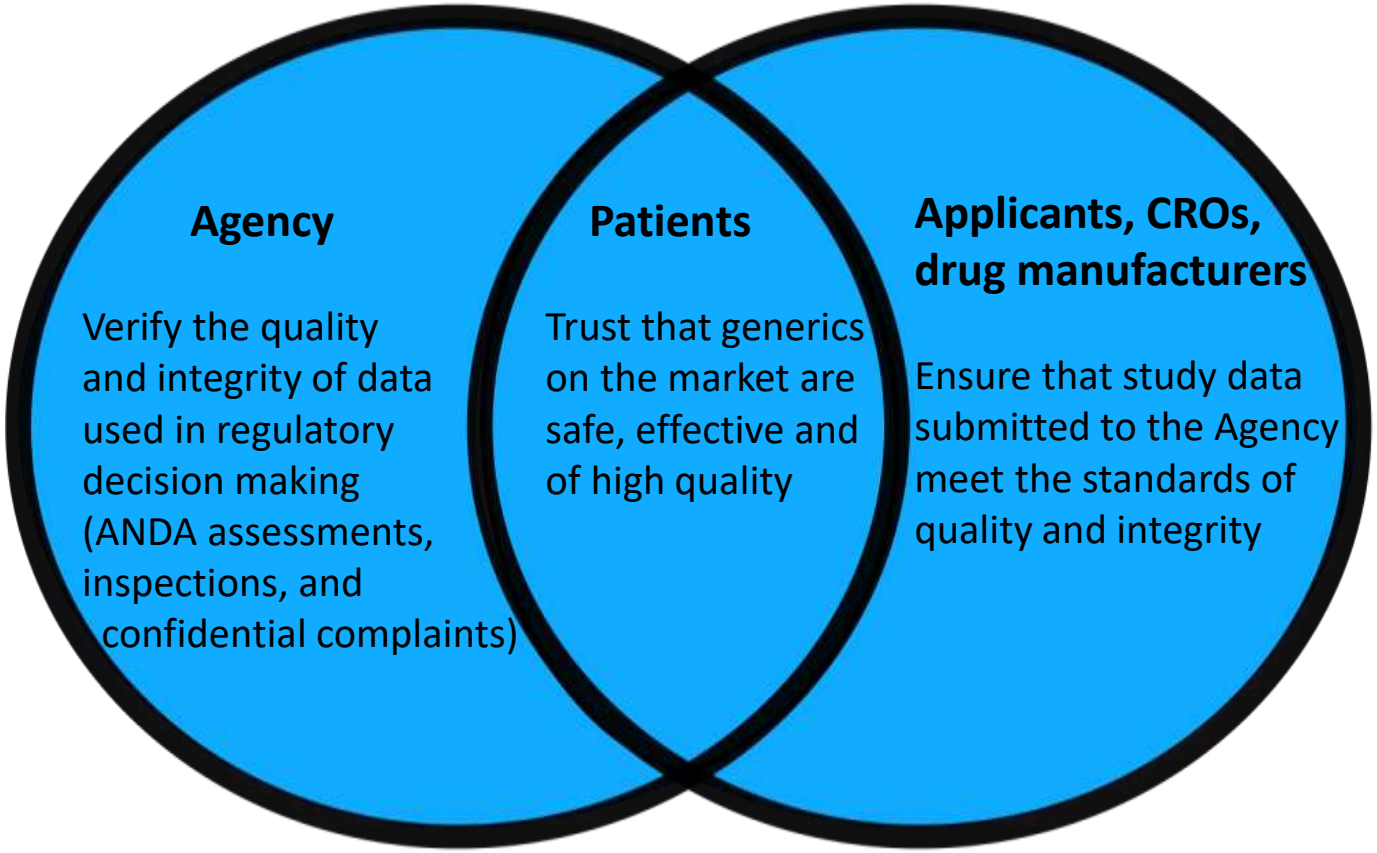
Outline

- Discuss the importance of data integrity and quality in a patient-centric approach and the Agency's experience with the data integrity issues
- Provide an overview of the key tools for ensuring data integrity
- Provide an understanding of how each entity can meet the responsibility of ensuring data integrity

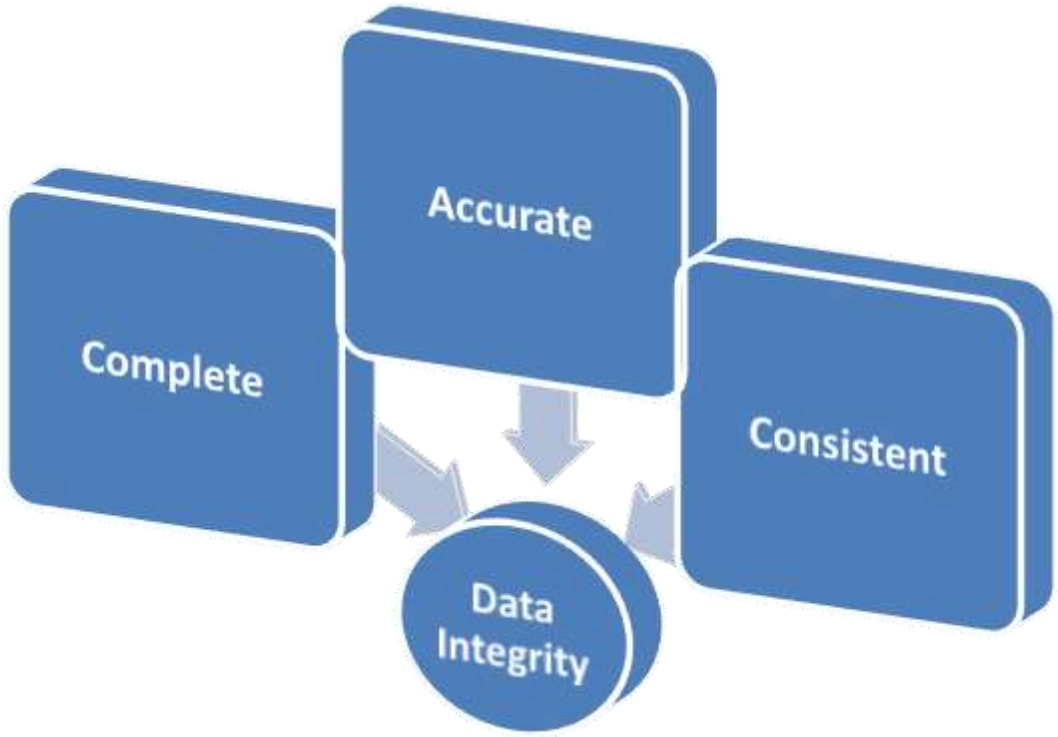
Patient-Centric Approach



CRO: Contract Research Organization

Cornerstones of Regulatory Decisions

Data Integrity*



Applicable to clinical, bioanalytical, and non-clinical studies and drug manufacturing

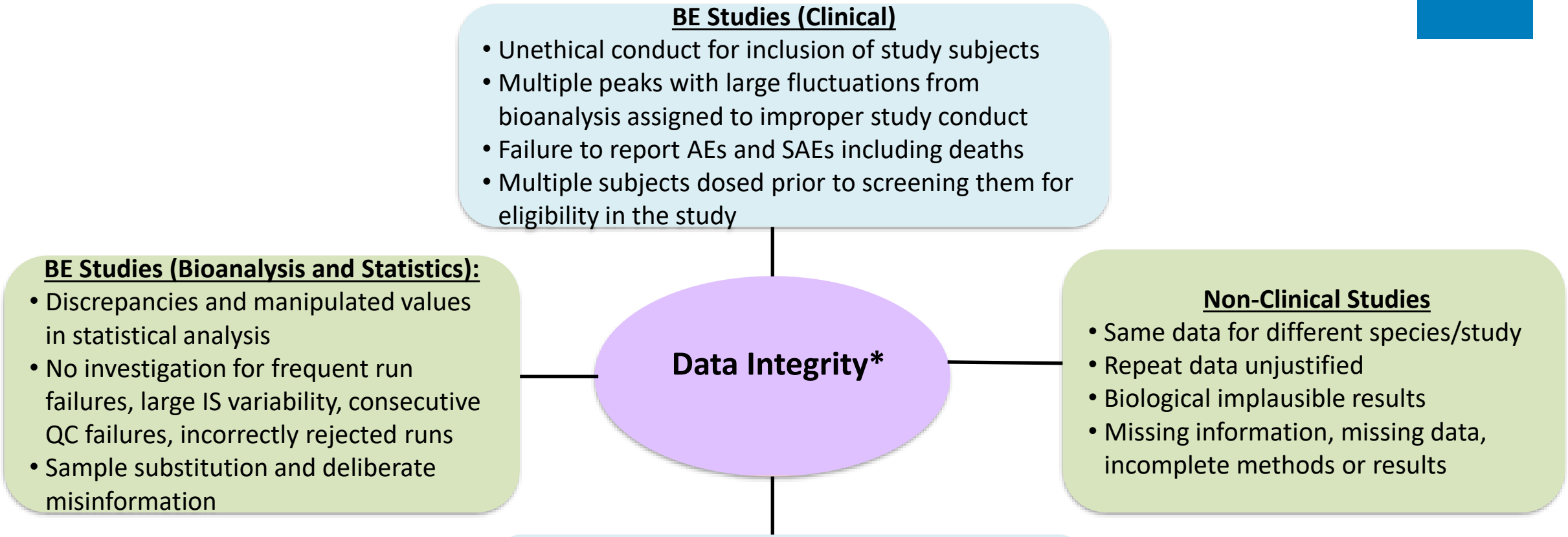
*Data Integrity and Compliance With Drug CGMP: Questions and Answers; Guidance for Industry https://www.fda.gov/media/119267/download

Data Quality

- Assurance that data are generated in compliance with applicable standards
- Data are fit for their intended use

https://www.oecd.org/env/ehs/testing/DRAFT_OECD_Advisory_Document_on_GLP_Data_Integrity_07_August_2020.pdf.

Data Integrity Observations Related to Generic Drugs



BE: Bioequivalence
IS: Internal standard
AEs = adverse events
SAEs = serious adverse events
OOS = out of Specification

* Increasingly observed data integrity during assessments, inspections, and follow-ups to complaints

A Case for Ensuring Data Integrity and Quality

Benefits to patients

- Ensures safe, effective, and high-quality generics
- Provides access to new drug treatments and affordable generic drugs

An asset for businesses (applicants, CROs, and manufacturers)

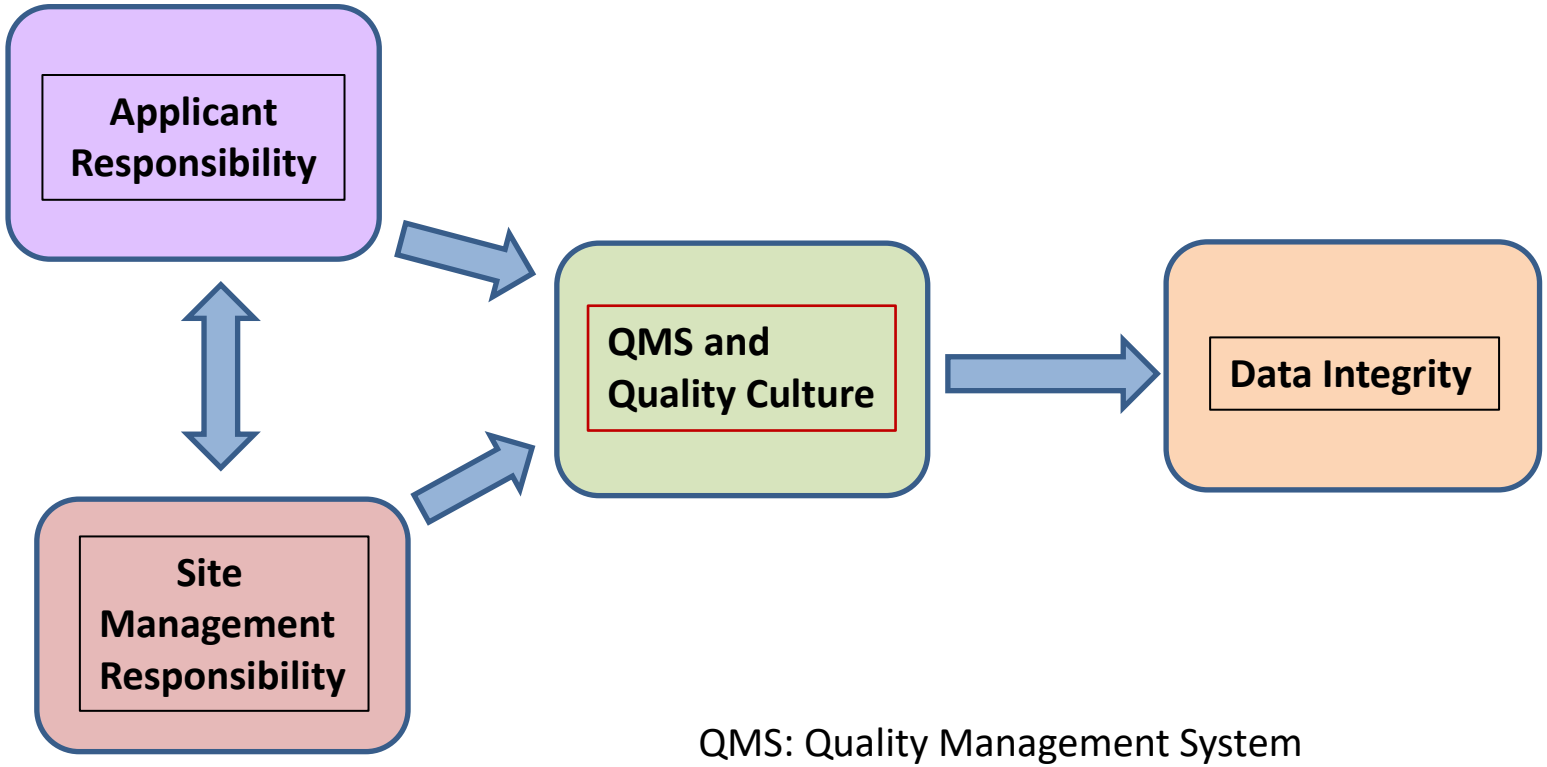
- Provides a competitive edge for the business
- Minimizes loss of revenue from recalls, change in TE codes, repeating studies

Reduced regulatory risk for the Agency

- Allows for regulatory decisions are based on reliable and quality data
- Ensures efficient use of Agency's limited resources

TE = Therapeutic equivalence

Data Integrity Tools

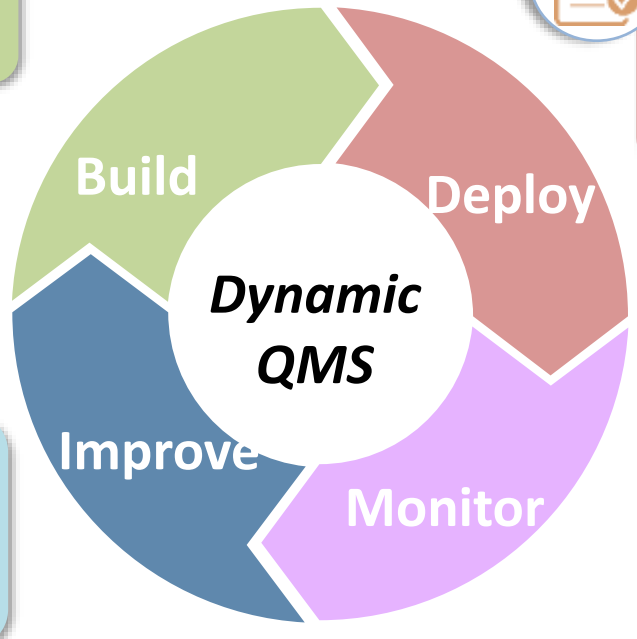


QMS: Quality Management System

Quality Management System

Build to minimize potential risks to data integrity

Implement robust policies, operating procedures, processes and controls to manage the risks



Refine the QMS to correct and prevent similar breaches in future

Monitor the effectiveness of the QMS (program-level and study-specific) to detect breaches in data integrity and identify the cause(s)

Corporate Quality Culture

Leadership is committed to promoting a work environment that supports integrity and quality of the work product

- develops detail policies regarding the standards of ethical conduct
- establishes procedures and programs for implementation
- encourages open and transparent communications between personnel at all levels, for reporting errors, deviations, etc.
- supports continued training for reinforcement of corporate culture
- underscores integrity and quality of data as everyone's responsibility

Applicant's Role for Outsourced Studies

Applicant is accountable for assuring the integrity of all outsourced study related activities

- provide CROs a full understanding of study risks (study subjects and data) and regulatory requirements
- provide monitoring and oversight for the activities, independent of the site's Quality Assurance
- document the monitoring and communications with site management in sufficient detail to allow verification, if needed
- confirm the reliability of the data submitted to the Agency

Approach by the Office of Bioequivalence

Multi-disciplinary approach

- Assessors and investigators alike are sensitive to the possibility of inaccurate, withheld, or otherwise false data in submissions and work collaboratively on these issues
  - request 'For-cause' inspections for individual ANDAs
  - perform investigative analysis if data manipulation is suspected to be systemic in nature
  - assess complaints and information received from external sources*

- Initiated efforts for enhanced analytics to verify the integrity of study data during assessment of ANDAs

- Plans to publish a guidance, in future on 'ANDA and NDA Submissions: Data Integrity for BA/BE Studies at Testing Sites'

* Mailbox: genericdrugs@fda.hhs.gov
* Mailbox: DrugInfo@fda.hhs.gov

Key Takeaways

- FDA expects that all data submitted in Abbreviated New Drug Applications be reliable and accurate
  - ensures that generic drugs meet FDA's standards of interchangeable, high-quality medicines

- Applicants are accountable for assuring the integrity of all outsourced study related activities

- Leadership at the testing site should proactively invest in tools and policies to enhance data integrity compliance
  - QMS and corporate quality culture are not one time and done deals