Risk Based Quality Management, Quality Risk Management, Quality by Design, Associated Tools & Challenges in a Clinical Trial Setting

JMP Discovery
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Risk Based Quality Management (RBQM), Quality Risk Management (QRM)

- **Risk Based Quality Management (RBQM)**
  - RBQM provides a **framework for managing the overall quality of a clinical trial** by identifying critical processes and critical data to ensure resources are focused on those areas. The purpose of Risk Based Quality Management is to ensure that risks are identified and managed proactively and systematically throughout the clinical trial process

- **Quality Risk Management (QRM)**
  - Quality Risk Management, is a systematic process of evaluating, assessing, controlling, and communicating **risks that could affect the quality** of a clinical trial. The purpose of QRM is to identify potential risks to quality and implement appropriate measures to mitigate those risks. QRM is a vital component of a comprehensive quality management system and is essential for ensuring patient safety and regulatory compliance. Quality Risk Management focuses on all processes and potential risks
- **Why is this Important?**
  - RBQM and QRM are both essential components of a comprehensive quality management system in clinical trials. While they have different focuses and methodologies, they are complementary approaches to managing risk and ensuring trial quality. Implementing both RBQM and QRM is crucial for ensuring patient safety, data integrity, and regulatory compliance

Quality by Design

- Quality by design (QbD) is a framework for embedding quality into the design, conduct, and monitoring of clinical trials e.g Standard Protocol Templates, Standard electronic case report formss, incorporation of prior knowledge, design of experiments utilized.
- **Main Components**

PEOPLE

Skilled professionals in Risk Management

PROCESSES

End-to-end process for clinical trial QbD and Quality Risk Management

TOOLS

Electronic system to ensure consistent approach across the enterprise

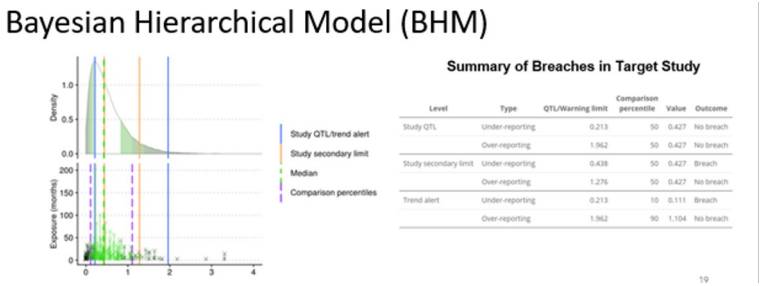
CULTURE

Clinical trial quality OWNED by the study team

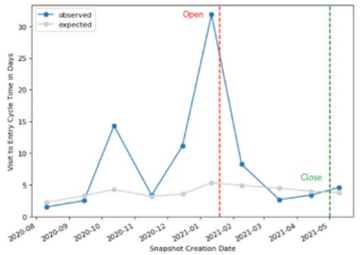
ICH Guidelines. What are they?

- The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) is unique in bringing together the regulatory authorities and pharmaceutical industry to discuss scientific and technical aspects of pharmaceuticals and develop ICH guidelines.
- There are 14 guidelines covering four elements:
  - Quality, Safety, Efficacy and Multidisciplinary
- RBQM are governed by ICH E6 R2 and the soon to be coming ICH E6 R3
  - Recommended risk-based approach to quality management
- Quality by Design is governed by ICH E8 R1 & Quality by ICH Q9
  - Aims to Design Quality into Clinical Trials
- Efficacy are governed by ICH E9
  - The principles outlined in ICH E9(R1) for Estimands are relevant "**whenever a treatment effect is estimated, or a hypothesis related to a treatment effect is tested, whether related to efficacy or safety**"

Tools/Metrics used in RBQM



- **Quality Tolerance Limits (QTLs) and Key Risk Indicators (KRIs)** are key metrics of risk-based quality management systems
  - QTLs are planned to identify systematic deviations at study level
  - KRIs typically trigger risk mitigation actions at site performance level.
    - e.g average data entry cycle time at site



- **Statistical Monitoring**
  - Statistical Monitoring is the use of complex statistical algorithms to discover data outliers and anomalies across the trial, the results of which will inform various monitoring, escalation or communication actions
- **Data Quality Oversight Tools**
  - A range of other tools built to detect anomalies or data outliers e.g Query Management: Are some sites querying more than other sites, do those queries lead to changes in the data, are the queries on only critical data.

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Implementation - What are the challenges?

- Methodology
- Historic Data access
- Study Design
  - Small studies / Platform Studies/ Basket Studies/ Cohort Studies
  - Complex Designs (Seamless, Adaptive Designs)
  - Decentralised Trials
- Parameters to use
- Even with Statistical underpinning, they are not an exact science

- Senior Leadership support
- Complex to implement and comprehend – Unlike manufacturing processes
- Tools & Processes
- Ability to embed
- Lack of belief they are meaningful

Doing now what patients need next

JMP Clinical Overview

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What is JMP Clinical?

Overview

- JMP Clinical is a focused and specialized product for Clinical Trial data review.
- We give users “straight out-of-the-box” functionality to do thorough reviews of clinical trials at the study, site, and subject level
- Utilized across the pharmaceutical industry and regulatory agencies
- Focused on
  - Safety Review
  - Medical Monitoring
  - Study Monitoring

JMP Products

- JMP –desktop statistics and data visualization tool
- JMP Pro – JMP + advanced predictive analysis tools
- JMP Clinical – an extension of JMP using JSL, for clinical trial safety analysis and study monitoring
- JMP Live – web-based publishing platform

Data Standards Enable Solutions

JMP Clinical Utilizes the CDISC Data Models

- JMP Clinical utilizes Clinical Data Interchange Standards Consortium (CDISC) data standards
  - Study Data Tabulation Model (SDTM)
  - Analysis Data Model (ADaM)
  - These data standards are mandated for new drug product submissions to regulatory authorities in the US and Japan, and recommended in many other regions
- Having a well-defined data model allows us to develop standardized approaches for analyzing and visualizing clinical trial results.
- JMP has been deeply involved with CDISC for many years and we have contributed to the development of these standards
- Recent article highlighting CDISC Standards and JMP Clinical: https://www.jscdm.org/article/id/169/