Paper RM02

Operationalizing ICH E6 R3: A Risk-Based Blueprint for Data Management

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ABSTRACT

The release of ICH E6 (R3) represents a fundamental shift in regulatory expectations for clinical trial quality oversight. Risk-based approaches, previously focused primarily on site monitoring, are now expected to extend across all functional review thought the entire lifecycle, including data management, medical review, monitoring, safety review and other.

This paper examines the impact of ICH E6 (R3) on expansion of risk-based approaches and outlines a practical framework for enabling an integrated risk-based management strategy across planning, execution, and oversight.

INTRODUCTION

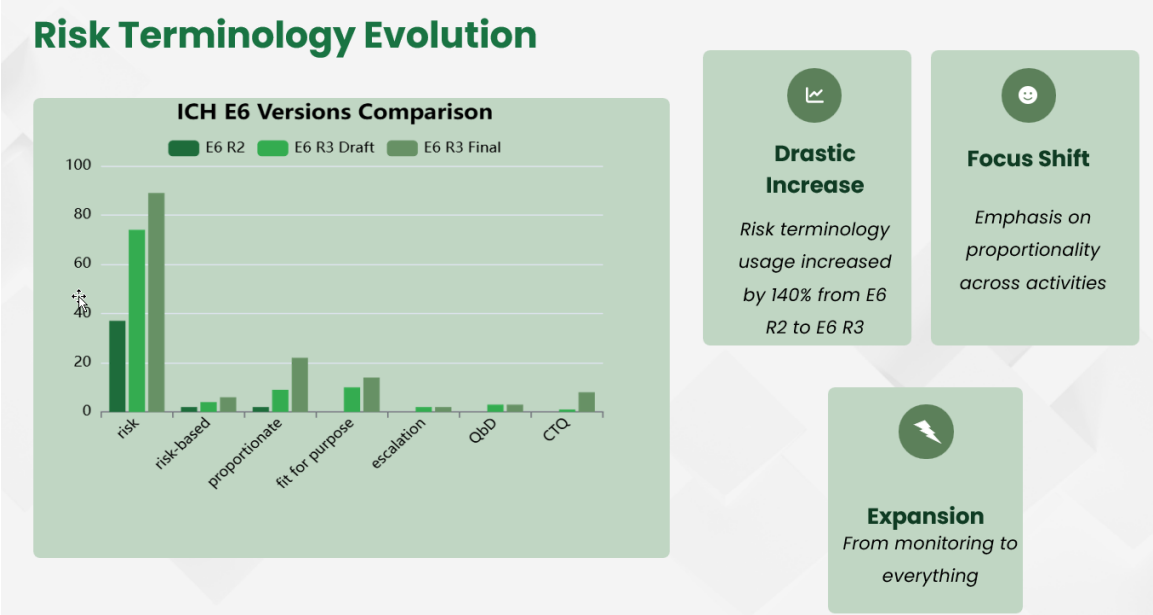
Over the past decade, risk-based approaches have become an integral component of clinical trial oversight. However, their implementation has often been fragmented, with individual functions such as monitoring or data management operating independently. The introduction of ICH E6 (R3) reinforces the importance of integrated, holistic risk management framework.

For the pharmaceutical industry, this shift has significant implications for how risk-based data management is designed, executed, and governed. This paper explores the evolving regulatory expectations introduced by ICH E6 (R3) and their impact on RBDM and proposes an integrated, technology-enabled approach that supports entire lifecycle.

REGULATORY EVOLUTION AND ICH E6 (R3) EXPECTATIONS

The evolution from ICH E6 (R2) to ICH E6 (R3) reflects a substantial increase in regulatory emphasis on risk-based approaches. Risk-related terminology has expanded significantly, reinforcing expectations that trial activities should be planned and executed proportionate to their impact on subject safety and data integrity.

In 2015, Transcelerate published a white paper describing IQRMP (Integrated Quality Risk Management Plan) concept. However, adoption in the industry remained low for many years until new HA updates reinforced the importance of this direction.



Health authorities including the FDA, EMA, and MHRA consistently emphasize proportionality, governance, and risk-based planning as essential components of trial planning and conduct.

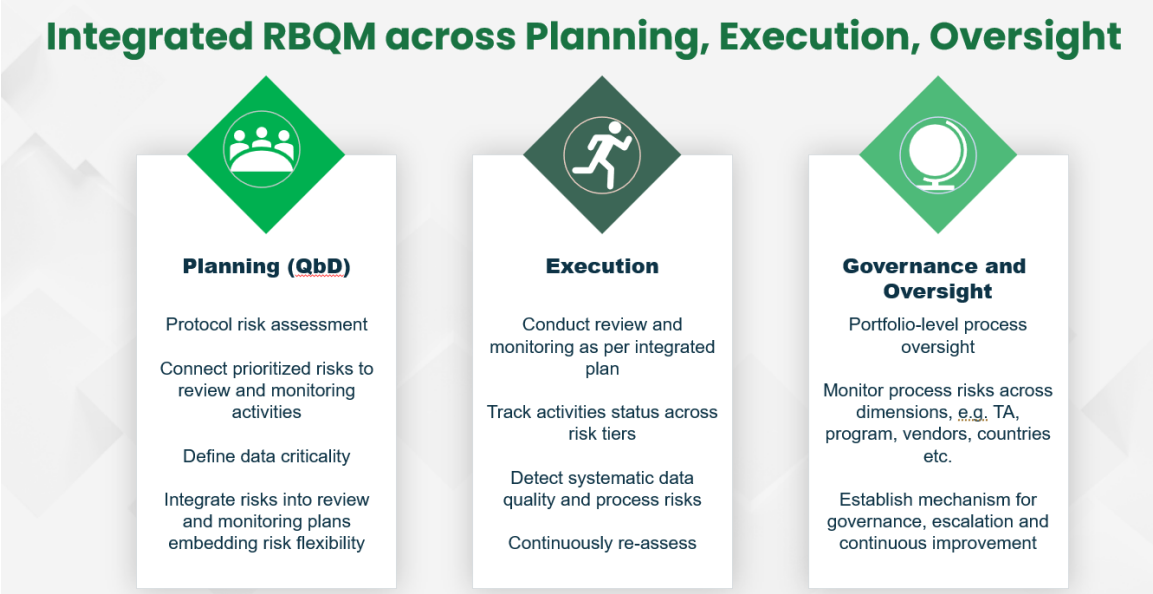
ICH E6 (R3) extends the application of risk management beyond traditional monitoring activities to encompass all functional areas: data management, medical review, safety oversight, and vendor management are now explicitly expected to align with a unified risk management strategy.

IMPACT OF ICH E6 (R3) ON RISK-BASED DATA MANAGEMENT

Process Changes

Key process changes include the identification and prioritization of risks across functions, definition of function-specific actions, cross-functional collaboration to identify critical data and processes, alignment of functional plans around risks, and continuous review and revision of the integrated quality risk management plan throughout the trial lifecycle.

An integrated RBQM operating model ensures that planning, execution, and oversight activities are driven by a shared understanding of trial risk. This approach enables organizations to focus resources on the highest-risk areas while reducing unnecessary or redundant activities.



Planning

During the planning phase, cross-functional risk assessments are used to identify critical data and processes. These risks inform the development and alignment of data management plans, monitoring strategies, medical review plans, and safety oversight activities.

Execution

During execution, activities are performed proportionate to the risk, with the ability to dynamically adjust strategies and activities based on the risks with the added granularity levels typical for the data review. This continuous feedback loop ensures that planning assumptions remain current and actionable.

Governance and Oversight

Organizational oversight provides Sponsors with the ability to surface process related deficiencies to improve the processes to enable more holistic approach. Governance and timely escalation beyond one study is one of the requirements described in the ICH E6 (R3)

TECHNOLOGY AS AN ENABLER

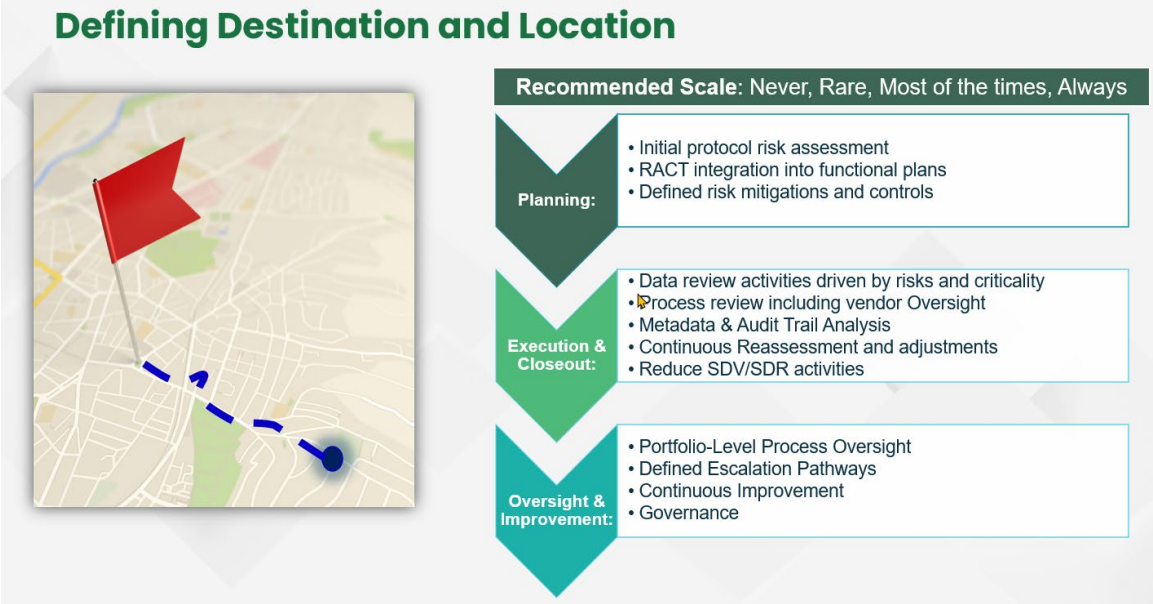
Technology plays a critical role in enabling integrated risk management. Manual and disconnected systems are insufficient to support continuous risk assessment, proportional execution, and effective oversight.

Technology Expectations

Effective technology solutions should support integrated risk assessments, automated linkage between prioritized risks and cross-functional review activities, ability to connect the activities across tiers of data criticality while providing capability to monitor the review and monitoring status during trial conduct.

IMPLEMENTATION JOURNEY: A PRACTICAL APPROACH

Successful adoption of integrated RBQM requires a structured implementation journey. Organizations should begin by defining their target state, assessing current maturity, identifying gaps, and developing a phased implementation roadmap.



Defining Destination and Assessing Maturity

Maturity assessments help organizations understand the starting point and the destination of risk based journey to define step-by-step strategy to achieve the desired state.

Starting with pilot studies allows teams to test, learn, and refine integrated RBQM approaches before scaling across the portfolio.

CONCLUSION

ICH E6 (R3) signals a clear regulatory expectation for integrated, lifecycle-based risk management in clinical trials. Risk-based data management is no longer optional or isolated but a foundational element of enterprise-wide RBQM. Organizations that align people, processes, and technology around shared risk strategies will be better positioned to meet regulatory expectations while improving trial efficiency and data quality.

CONTACT INFORMATION

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