IMPLEMENTING RISK-BASED MONITORING: A CRO PERSPECTIVE

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Topics Covered

- The RBM Landscape, Drivers and Barriers
- RBM Process Implementation
- Implementation Learnings
- Accessing RBM Benefits
Significant Conversion to RBM Expected

Current use of RBM solutions

Expected use of RBM solution in the next 5 years*

Expected use of RBM solution in the next 10 years*

Increased quality expectations
Development cost increases
RBM process maturation
Regulatory mandate

RBM will become the new normal

Source: Industry interviews commissioned by Covance. * Note: Not a quantitative forecast
RBM: What Is It?

- Holistically identifies risk of failure
- Designs monitoring approaches to prevent or mitigate risk
- Differentiates critical vs. non-critical
- Delivers fit for purpose quality – flexible to study and regulatory need
- End to end trial conduct transformation
- An extension to smart study design

Holistic; proactive; preventive; dynamic; iterative

RBM is a logical next step to enhance efficiency and quality
What Might Be Slowing Adoption of RBM?

What are the biggest challenges with implementing RBM? (Select top 3)

- Maintaining sufficient quality: 46%
- Inability of CRO to rapidly adapt to changing needs: 38%
- Greater cost: 34%
- Identification of risk associated with clinical trial: 34%
- Lack of internal knowledge/expertise to implement RBM: 34%
- Increased risk: 32%
- Convincing senior management of benefits of RBM: 28%
- Risk/reward for RBM not sufficient: 10%
- Other*: 6%

Source: Covance commissioned RBM study, 2013

More than regulatory questions holding back RBM
RBM Process Implementation

1. Protocol Design
2. Risk Assessment
3. Monitoring Plan
4. Performance Analytics
5. Monitoring Interventions
6. Issue Resolution

Feedback throughout study

- Starts with designing out risk: protocol is the blueprint for quality
- **Start with the end in mind** – reliable data withstanding Agency scrutiny
RBM Process Implementation, cont.

Study Planning
- Protocol Quality by Design
- Proactive Risk Identification & Mitigation
- Identify Critical Data / Processes
- Risk-based Site Selection

Study Delivery
- Risk Factor Analytics
- Centralized Data Surveillance
- Intervention & Adaptation
- Demonstrated ‘State of Control’

RBM Plan

Patient safety, data integrity & regulatory compliance
Translating Risk into Action

<table>
<thead>
<tr>
<th>Examples</th>
<th>Management Approaches</th>
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<tbody>
<tr>
<td><strong>Intrinsic risks</strong></td>
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<tr>
<td>Maturity of safety profile</td>
<td>Adjusted average site visit interval</td>
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<td>Phase of development</td>
<td>Adjusted average SDV level</td>
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<td>Proportion remote/on site</td>
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<td><strong>Design risks</strong></td>
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<tr>
<td>Clarity of protocol</td>
<td>Quality by design improvements</td>
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<td>Primary endpoint approach</td>
<td>Central data surveillance</td>
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<td>Fit vs. standard of care</td>
<td>Supplementary training (site/CRA)</td>
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<td><strong>In-Flight Risks</strong></td>
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<td>Site experience</td>
<td>Adjusted site-specific intervention levels</td>
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<td>Staff turnover</td>
<td>Turnover management and training plans</td>
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<tr>
<td>Adverse event reporting levels</td>
<td>Issue management plans</td>
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Appropriate risk management requires a broad range of tools
## Sponsor and CRO Perspectives

<table>
<thead>
<tr>
<th>SPONSOR</th>
<th>CRO</th>
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<tr>
<td>• Compound level focus, integrates with TPP</td>
<td>• Study/Program level focus</td>
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<td>• Drivers for change vary</td>
<td>• Robust RBM solution a differentiator (+ or −)</td>
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<td>• Executive urgency for improved efficiency</td>
<td>• Impetus to develop</td>
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<td>• Functional conservatism and variable silos to overcome</td>
<td>• Readiness to invest</td>
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<td>• Opportunities to leverage CRO partners</td>
<td>• Operational excellence and process innovation in our DNA</td>
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<td>• Critical need for flexibility and adaptability – Sponsor agnostic</td>
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Fit for Purpose Throughout the Continuum

Start with the end in mind
Overcoming Functional Barriers

**Functional View**
- “RBM is all about clinical cost reduction”
- “Quality will suffer on variables not monitored” – risk prevention not considered
- “There is nothing wrong with how we’ve done things before”
- ‘Burning platform’ challenge is only for Clinical Operations

**Holistic View**
- Quality of critical data & processes enhanced through preferential focus
- Cost saving is a consequence of monitoring what matters
- Focus on Quality by Design and Risk, not SDV reduction
- Areas reduced are not critical from an outcome perspective

Focused change management
Implementation Learnings

**Sponsor**
- Variable needs and priorities
- Tailored solution needed, consistent but flexible

**Site**
- Managing monitor support expectations
- Expectation-setting and alternative methodologies

**Monitors**
- Resource management
- Change management
- Access to information
Experiences from Implementation

**Example #1**
- Cardiovascular outcomes study
- Full RBM Design
- tSDV implemented
- Ongoing, enrolling

**Example #2**
- Ph III Pivotal Study
- Reduced SDV
- Targeted RMV strategy
- NDA/MAA approved

**Example #3**
- Partner portfolio
- ‘Fit-for-purpose’ monitoring
- Tailored RMV/SDV
- Multiple TA studies
RBM Value Hierarchy

- Protocol simplification
- Quality-by-design
- Risk-based site selection
- Systematic mitigation
- Centralized data surveillance
- Risk-targeted on-site review

Ultimate aim – de-risking development
Impact of Efficiencies in Clinical Monitoring

*Relates to clinical monitoring activities, not full study costs. Covance internal data
### Mutually Beneficial Implementation

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<th>SPONSOR PRIORITIES</th>
<th>CRO PRIORITIES</th>
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<tr>
<td>• Fit for purpose quality</td>
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<tr>
<td>• Alignment with regulators</td>
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<tr>
<td>• Demonstrated state of control</td>
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<tr>
<td>• Timely delivery</td>
<td>• Timely delivery</td>
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<tr>
<td>• Improved efficiency</td>
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**RBM can transform risks into returns**

- Effective, adaptive resources allocated targeting maximum impact and value
- Proactive planning and focus on primary quality and state of control
- Efficiency gains a consequence of fitness-for-purpose
For more information, visit
www.covance.com/RBM