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%

More than regulatory questions holding back RBM

Source: Covance commissioned RBM study, 2013
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’

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

Appropriate risk management requires a broad range of tools.

<table>
<thead>
<tr>
<th>Intrinsic risks</th>
<th>Examples</th>
<th>Management Approaches</th>
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<tbody>
<tr>
<td></td>
<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>Design risks</td>
<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>In-Flight Risks</td>
<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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<td>Adverse event reporting levels</td>
<td>Issue management plans</td>
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Sponsor and CRO Perspectives

SPONSOR
- Compound level focus, integrates with TPP
- Drivers for change vary
- Executive urgency for improved efficiency
- Functional conservatism and variable silos to overcome
- Opportunities to leverage CRO partners

CRO
- Study/Program level focus
- Robust RBM solution a differentiator (+ or –)
  - Impetus to develop
  - Readiness to invest
- Operational excellence and process innovation in our DNA
- Critical need for flexibility and adaptability – Sponsor agnostic
Fit for Purpose Throughout the Continuum

Start with the end in mind
## Overcoming Functional Barriers

<table>
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<tr>
<th>Functional View</th>
<th>Holistic View</th>
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<tbody>
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<td>• “RBM is all about clinical cost reduction”</td>
<td>• Quality of critical data &amp; processes enhanced through preferential focus</td>
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<td>• “Quality will suffer on variables not monitored” – risk prevention not considered</td>
<td>• Cost saving is a consequence of monitoring what matters</td>
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<tr>
<td>• “There is nothing wrong with how we’ve done things before”</td>
<td>• Focus on Quality by Design and Risk, not SDV reduction</td>
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<tr>
<td>• ‘Burning platform’ challenge is only for Clinical Operations</td>
<td>• Areas reduced are not critical from an outcome perspective</td>
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**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

## SPONSOR PRIORITIES
- Fit for purpose quality
- Alignment with regulators
- Demonstrated state of control
- Timely delivery
- Improved efficiency

## CRO PRIORITIES
- Fit for purpose quality
- Alignment with regulators
- Demonstrated state of control
- Timely delivery
- Improved efficiency

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