RISK-BASED MONITORING: SEEING THE FOREST FOR THE TREES WHEN DESIGNING AND IMPLEMENTING AN ENTERPRISE PROCESS

Ben Dudley, Executive Director
Alliance Management, Covance Inc.

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Topics Covered

Why embark on an RBM journey?

Starting with the end in mind
- Process
- Technology

Implementation examples & learnings

Value – what is the ‘return on RBM’?
Today’s Biggest RBM Risk

I Know There is a Forest In There Somewhere...

Key success factor: differentiating between enablers, elements and outputs – and solutions and objectives
WHY EMBARK ON AN RBM JOURNEY?
RBM: Coming to a Trial Near You – and Soon…

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.
Covance Definition of RBM

- 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

RBM is a logical next step to enhance efficiency and quality
Covance RBM: Transformation – and Continuity

Prediction

Secondary Prevention and Repair

Primary Prevention

Proactive Detection

Patient Safety Data Integrity

Feedback
The Journey to Develop RMB Core Expertise and Systems

- Predictive, proactive and preventative operational platform established
- Expanded informatics capability
- New site quality risk reports
- New clinical quality control process
- EMA Draft Reflections Paper and FDA Draft Guidance on RBM
- FDA Final Guidance on RBM
- TransCelerate Updated Paper on RBM

Timeline:
- 2005
  - Various academic research model studies e.g. more than 8,000 patients targeted monitoring
- 2009
  - More than 8,000 patients cardiovascular trial
- 2010
  - Reduced source data verification analytics: data action reports targeted & reduced monitoring
- 2011
  - New clinical quality control process
- 2012
  - Strategic partner portfolio ‘Fit-for-purpose’ monitoring tailored monitoring & SDV in multiple therapy areas and studies
  - More than 12,000 patients
- 2013
  - Full RMB implementation incl. tSDV web-based analytics solution
- 2014
  - Launch of Covance RBM dashboard and process
Governance: Defining the Team to Get Us There

Core Development Team

Functional Teams

- Process & Documents
- IT & Technical Requirements
- Organization Design
- Commercial

Business-Led Transformation Team
PROCESS: TYING IT ALL TOGETHER OR - STARTING WITH THE END IN MIND
Start with the End in Mind

Design & Delivery: Fit for purpose throughout the continuum

Medical
- Protocol Design

Data Management
- CRF Design

Clinical Operations
- Monitoring

Data Management
- Data Cleaning

Medical & Statistical Review
- NDA/MAA Submission

Regulatory
RBM – If You Start with Monitoring it’s Too Late

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: the protocol is the blueprint for quality
Start with the end in mind: reliable data withstanding Agency scrutiny
## Translating Risk into Action

<table>
<thead>
<tr>
<th></th>
<th>Examples</th>
<th>Management Approaches</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intrinsic Risks</strong></td>
<td>• Maturity of safety profile</td>
<td>• Average on-site visit interval</td>
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<td></td>
<td>• Phase of development</td>
<td>• Source Data Verification level</td>
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<td></td>
<td></td>
<td>• Proportion remote/on site visits</td>
</tr>
<tr>
<td><strong>Design Risks</strong></td>
<td>• Clarity of protocol</td>
<td>• Quality by design improvements</td>
</tr>
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<td></td>
<td>• Primary endpoint approach</td>
<td>• Central data surveillance</td>
</tr>
<tr>
<td></td>
<td>• Fit vs. standard of care</td>
<td>• Supplementary training (Site &amp; CRA)</td>
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<tr>
<td><strong>In-Flight Risks</strong></td>
<td>• Site experience</td>
<td>• Adjusted site-specific intervention levels</td>
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<td>• Protocol deviation rate</td>
<td>• Turnover management &amp; training plans</td>
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<td>• Investigator oversight</td>
<td>• Issue management plans</td>
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**Appropriate risk management: Not ‘one size fits all’**
# Full Portfolio of Actionable Tools

<table>
<thead>
<tr>
<th>Risk Assessment Tools</th>
<th>RBM Templates</th>
<th>Control Charts</th>
<th>Risk Libraries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site Risk Dashboards</td>
<td>Process Integrations</td>
<td>Training Materials</td>
<td>Process Manuals</td>
</tr>
<tr>
<td>Functional Process Tools</td>
<td>Web-Based Visualizations</td>
<td>Clinical Data Repository</td>
<td>RBM Teams</td>
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**Implementation-Ready, Tried and Tested**
Effective RBM is Multifaceted – Technology is Not the Be All And End All
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**
Experiences from Implementation

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

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

Example #3
- Partner portfolio
- ‘Fit-for-purpose’ monitoring
- Tailored RMV/SDV
- Multiple studies and TAs
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
VALUE:
WHAT IS THE ‘RETURN ON RBM’?
RBM Value, It’s All In The Design

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

Quality and Efficiency go Hand-in-Hand
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

Mutually Beneficial Implementation

- Fit for purpose quality
- Alignment with regulators
- Demonstrated state of control
- Timely delivery
- Improved efficiency
For more information please visit
www.covance.com/RBM