

# Risk-Based Monitoring Update – Volume II

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## 1. Introduction

TransCelerate's Risk-Based Monitoring (RBM) project has been productive in the first half of 2014. The purpose of RBM Update Volume II is to share new and relevant information on the accomplishments of the RBM workstream including the following:

- RACT version 2.0 released on April 29, 2014
- Central Monitoring Capability
- Technology Considerations to Enable RBM
- External Engagement
- Upcoming Deliverables in 2014

## 2. Risk-Assessment Categorization Tool (RACT) Version 2.0

The previous RBM update released information on important lessons learned while performing risk assessments on TransCelerate pilot studies. An RBM focus group assessed the recommendations and worked through the detailed feedback. The [new version](#) incorporated those lessons and was released to the TransCelerate website on April 29, 2014. Some of the new features of the tool include:

- Guidance on completion of the RACT
  - Addition of instructions for use including a process overview that highlights the importance of a cross-functional review and decision making
- Ranking and rationale of risks
  - Ability to enter a score for Impact, Probability and Detectability of risks
  - Rationale for the score within a category
  - Recommendations for numerical ranges at the overall and category levels
  - Examples for each level of risk revised based on member feedback
- Alignment of the RACT with risk mitigations
  - Functional plans documented where management of the risk is documented, as well as a prompt to document examples of mitigations that may be used
- Addition of a place to document critical processes and critical data within the tool
- Place to document who was involved in the RACT discussions / decisions

## 3. Central Monitoring Capability

Central monitoring is part of an integrated monitoring strategy that includes both On-site and Off-site monitoring activities. TransCelerate has completed Part I of an expected two-part series on Central Monitoring Capabilities. The article, which has been accepted for publication in a Special Section of the September 2014 issue of DIA's *Therapeutic Innovation and Regulatory Science* entitled "TransCelerate BioPharma: Central Monitoring Model and Technology Specification Proposals to Enable Risk-Based Monitoring Adoption," describes the people, process and technology needs to enable effective central monitoring. By using examples of various models TransCelerate member companies are piloting, the article provides workflows that differentiate how different companies have set up their pilots. A follow-up article is planned for release in early 2015 to highlight the lessons learned from these pilots.

## 4. Technical Considerations to Enable RBM

TransCelerate's RBM Position Paper initially described high level technology needs to support RBM. In order to better articulate the needs of Risk-Based Monitoring as experience has grown, TransCelerate member companies brought together a group of data, technology and RBM process experts. The resulting work is a paper intended to support people who make decisions on technology needs both from a development perspective and from a procurement perspective. In detail, the paper describes the collection, aggregation, analytical and documentation needs to support a quality management framework.

This Technology paper was accepted for publication in a Special Section of the September 2014 issue of DIA's *Therapeutic Innovation and Regulatory Science* entitled "TransCelerate BioPharma: Central Monitoring Model and Technology Specification Proposals to Enable Risk-Based Monitoring Adoption." Efforts will be underway to support the communication of this paper beyond the written publication beginning in the fall of 2014.

## 5. Upcoming RBM Deliverables in the 2<sup>nd</sup> Half of 2014

### 5.1 Challenging the Value of SDV

Challenging the Value of SDV as a quality control measure concluded its analysis at the end of June 2014. The overall goal of this activity was to assess the value of SDV as a quality measure and to understand the optimal use of SDV in maintaining data integrity and subject safety. Information supporting the hypothesis that SDV queries constitute a very small percentage of corrections to critical data was published in the Position Paper. This information was collected on 9 studies. The analysis that is being performed now extends to more than 1000 studies and includes a broader analysis to determine the percentage of data corrected by SDV, the percentage of queries issued by site monitors that resulted in a data change and the percentage of missing adverse events detected by SDV or SDR. This analysis also includes a comprehensive review of the literature regarding SDV, as well as a review of audit findings with root cause analysis across multiple sponsor companies. Discussion on SDR and its purpose during monitoring is expected to be included in this paper which will be published later this fall.

### 5.2 Data Integrity and GCP Misconduct

Data Integrity and GCP Misconduct is an area TransCelerate is currently studying as part of the RBM workstream. The output from this working sub-team, expected in late 2014, will be a framework or series of best practices for the detection of serious data integrity issues.

## 6. External Engagement

### 6.1 Pilots and Metrics Lessons Learned

Pilots continue within companies across multiple disease areas and in different phases of development. As of April 2014, eight of the more than 40 studies being piloted by TransCelerate member companies had been submitted to the FDA for feedback on the incorporation of RBM methodology. Initial feedback from the FDA on the first of those pilots has been shared in the RBM Update Volume I.

The lessons learned including initial metrics will be shared publically once discussed with the regulatory authorities that have provided feedback on the methodology.

## 6.2 Site Advocacy Groups (SAGs)

To facilitate conversations with sites on a number of TransCelerate workstreams including RBM, TransCelerate has partnered with a site organization (SCRS) to form a number of SAGs. Over the course of the next year, discussions with the SAG focused on RBM will help define the relationships between sites and TransCelerate companies with an overarching mutual benefit of enabling the high quality execution of clinical studies.

## 6.3 External Meeting Highlights

The RBM workstream continues to engage the external community through participation in conferences to discuss and address questions related to the methodology. The following is a list of conferences that the RBM team plans to attend through the remainder of 2014.

Venue	Date	Location	Topic
<b>19th Annual Meeting of the German Society of Good Research Practice</b>	18/19 September, 2014	Madgeburg, Germany	Risk-Based Monitoring from a Compliance Perspective
<b>The World Congress Summit on Collaboration and Open Innovation</b>	22/23 September 2014	Philadelphia, PA	Risk-Based Monitoring Panel on Implementation Experiences
<b>12th Annual Partnerships in Clinical Trials Congress</b>	5/6 November 2014	Barcelona, Spain	<ul style="list-style-type: none"> <li>• TransCelerate Panel: Risk-Based monitoring</li> <li>• TransCelerate Panel: Working with Investigators</li> </ul>
<b>CBI: Risk-Based Monitoring in Clinical Studies</b>	6/7 November 2014	Philadelphia, PA	TransCelerate Panel on Risk-Based Monitoring Implementation Experiences
<b>MAGI Clinical Research Conference</b>	9-12 November 2014	San Francisco, CA	Risk-Based Monitoring Orientation Session for Clinical Research Professionals