Lessons Learned From Implementing Risk Based Monitoring (RBM)

October 17th, 2019

MassBio
MASSACHUSETTS BIOTECHNOLOGY COUNCIL

Register Today!

- **Tackling New EU Requirements For Clinical Evidence For Combination Products (Including Auto-Injectors & Topicals)**
  October 24, 2019 • 8:00 AM - 10:00 AM • MassBio Offices

- **Meeting The Challenges Of Microbiome Directed Therapies**
  November 12th, 2019 • 8:00 AM - 10:00 AM • MassBio Offices

- **Closing The Real-World Evidence Gap: Pragmatic Clinical Trials & Observational Studies with Dr. Robert Califf**
  December 4th, 2019 • 8:00 AM - 10:00 AM • MassBio Offices

For full forum schedule visit the MassBio website; go to Events, Forums.
Thank you!

BSDMCT Working Group

Co-Chairs:

Kevin Anderson, MBA, Director, Global Clinical Operations, Alexion Pharmaceuticals

Michelle Harrison, Associate Director, Clinical Data Management, Vertex Pharmaceuticals

Miganush Stepanians, PhD, President & CEO, PROMETRIKA, LLC

Ilker Yalcin, PhD, VP, Biostatistics, Tesaro, Inc.

We are looking for additional Co-Chairs; if interested speak to us after the forum. Thank you!

Lessons Learned From Implementing Risk Based Monitoring (RBM)

Our Distinguished Speakers:

- **Austin Allan**, Head Research and Clinical Development Quality Operations, Alexion Pharmaceuticals
- **Shaheen Limbada**, Executive Vice President, Global Clinical Operations, Veristat LLC
- **Chelsey Ryan, PMP**, Senior Manager, Clinical Trial Management, PROMETRIKA, LLC

If you have a question, please raise your hand and wait for the microphone.
Thank you!

Key Objectives

To Understand:

- What are the most significant pros and cons?
- Are there types of studies that RBM is more or less optimal for?
- How do I ensure that I have selected the right CRO partner?
- What is the impact to cost and timelines?
- How do investigational sites feel about RBM?

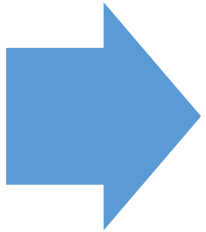
What Is RBM?

- An **adaptive approach** to clinical trial monitoring that **directs monitoring focus and activities** to the evolving areas of greatest need which have the most potential to impact **patient safety and data quality**

- FDA pushing RBQM E8 (R1)
  - FDA want us to "*stop calling it Risk-Based Monitoring and call it Risk-Based Quality Management – it's not just about monitoring, it is an end to end process*"

Setting the Stage:Risk Management Plan

ICH E6 (R2) refers to Risk Documentation and Communication

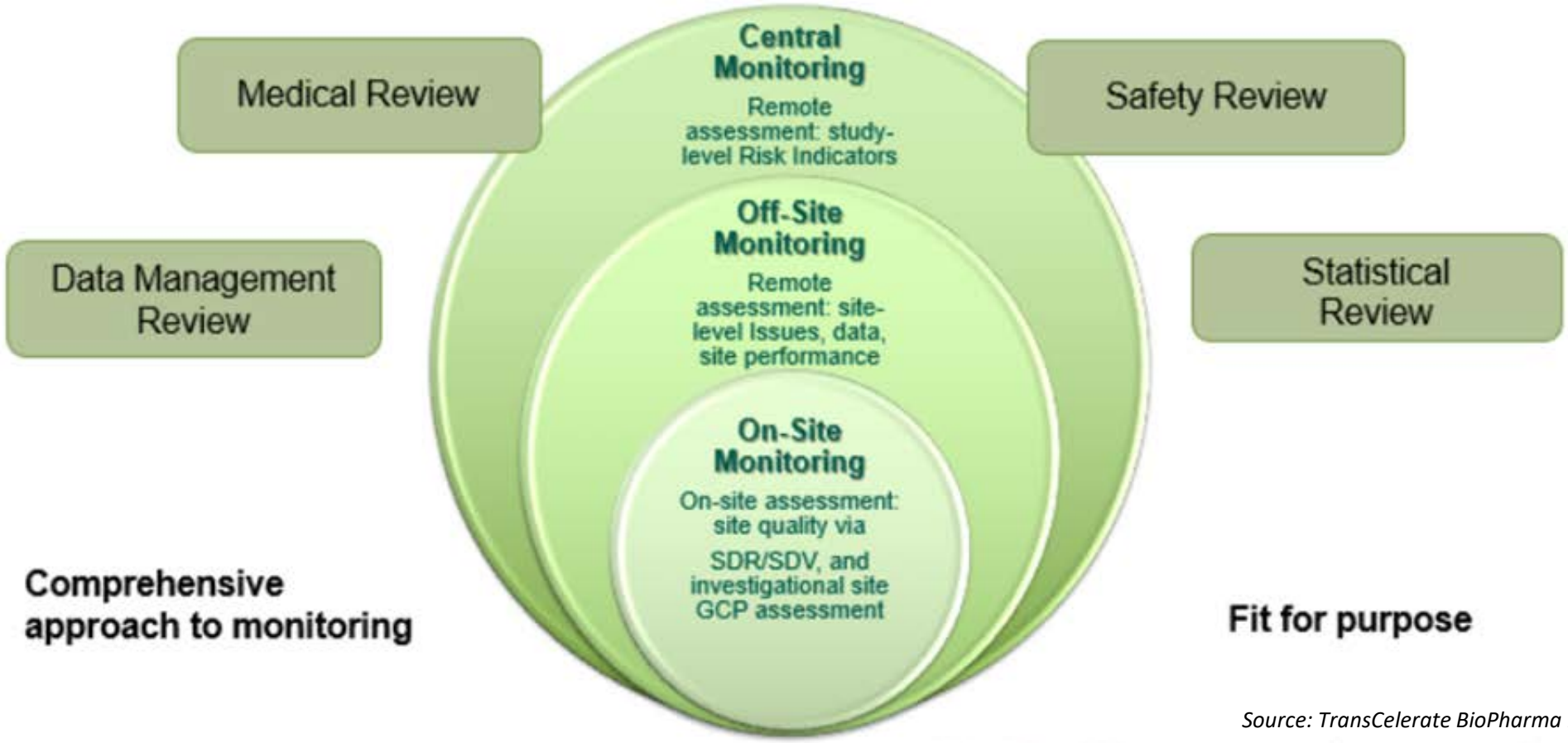


A Risk Management Plan Fulfills This Obligation

Risk Management Plan Considerations

- Must contain outputs from Risk Assessment (e.g. RACT), including the identified critical data and processes…which are linked to a monitoring strategy (which could include risk indicator review).
- Can be an “umbrella” document that typically refers to other functional plans.
- Assigns risk responsibility.
- Actions and frequency of actions taken to prevent or decrease the probability of a risk becoming an issue.

Types of Monitoring



Source: TransCelerate BioPharma Inc.

Industry Updates

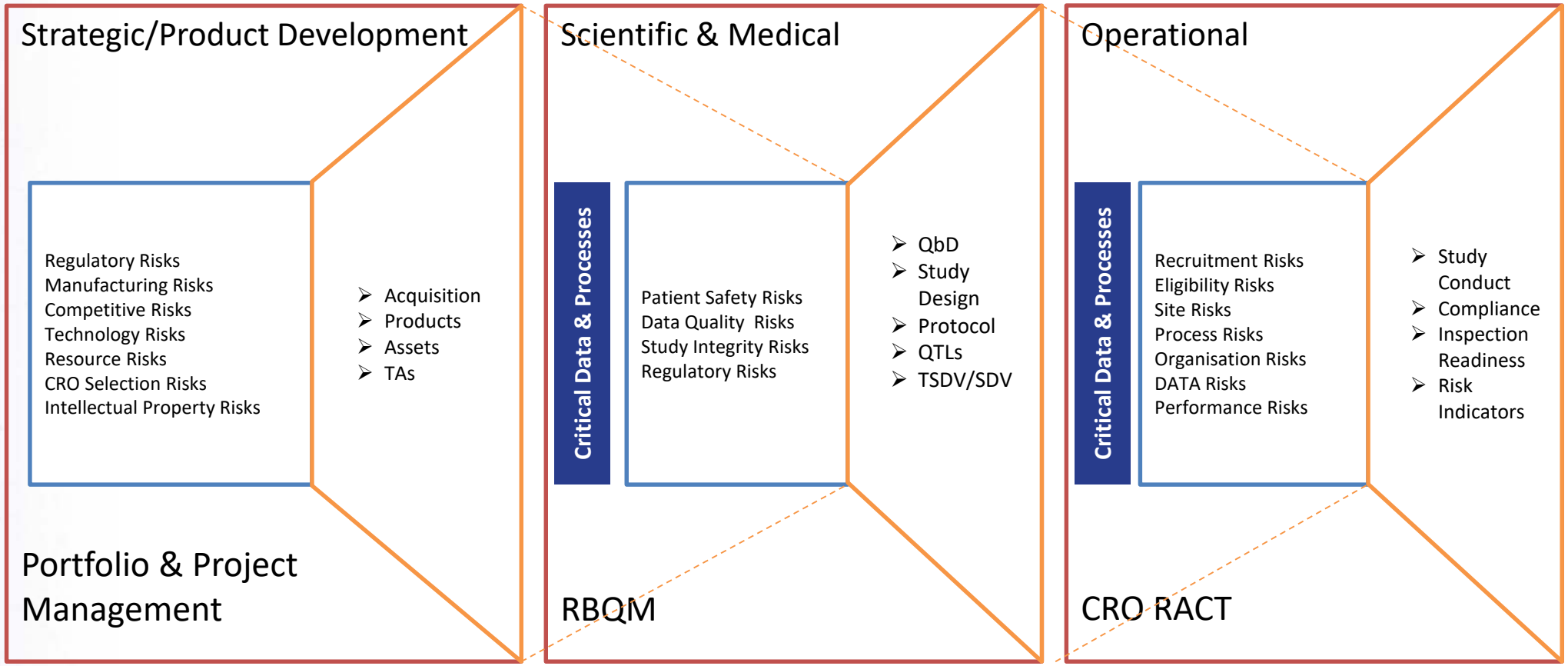
Risk based approach

- Focus on trial activities essential to ensuring subject protection and reliability of trial results
- Implement a system to manage quality
- Identification of critical data and processes
- Risk identification, risk evaluation, risk communication, risk control, risk review and risk reporting
- Risk based monitoring, including the use of centralized monitoring to compliment or reduce on-site monitoring

Where does RBQM and RBM fit?

* Acknowledgement to CluePoints

Risk breakdown Structure



Key Risk Indicators/Key Performance Indicators

- What are KRIs/KPIs and how do you develop them?
- E6R2 makes it a requirement – regulators focusing on this. How do you implement this?

KRI Selection

Top Key Risk Indicators to Consider

Site Performance

KRI

- Screen Failure Rate/Reasons
- Discontinued Rate/Reasons
- Inclusion/Exclusion Criteria
- AE/SAE Reporting
- Monitoring Issues/Observations
- Data Entry Timeliness
- Query Rate
- Query Response Time
- Protocol Deviations

Quality Question

- Is the inclusion/exclusion criteria impacting recruitment?
- Are patients completing the procedures as per the plan?
- How many protocol deviations have occurred and why?

Top Key Risk Indicators to Consider

Patient Safety

KRI

- Enrollment Rate
- Discontinuation Rate
- Subject Visit Compliance
- AE Reporting Rate
- Protocol Deviations
- SAEs Reported
- Deviation Distribution

Quality Question

- How many and what type of AEs are occurring?
- Are the subjects compliant to the visit schedule?
- How many early terminations have occurred and why?

Top Key Risk Indicators to Consider

Data Quality

KRI

- Data Entry Timeliness
- Query Rate and Response Time
- Enrollment Rate
- Discontinuation Rate
- Missing Data/Assessments
- Protocol Deviation Rate
- Lab Sample Quality
- Subject Visit Compliance

Quality Question

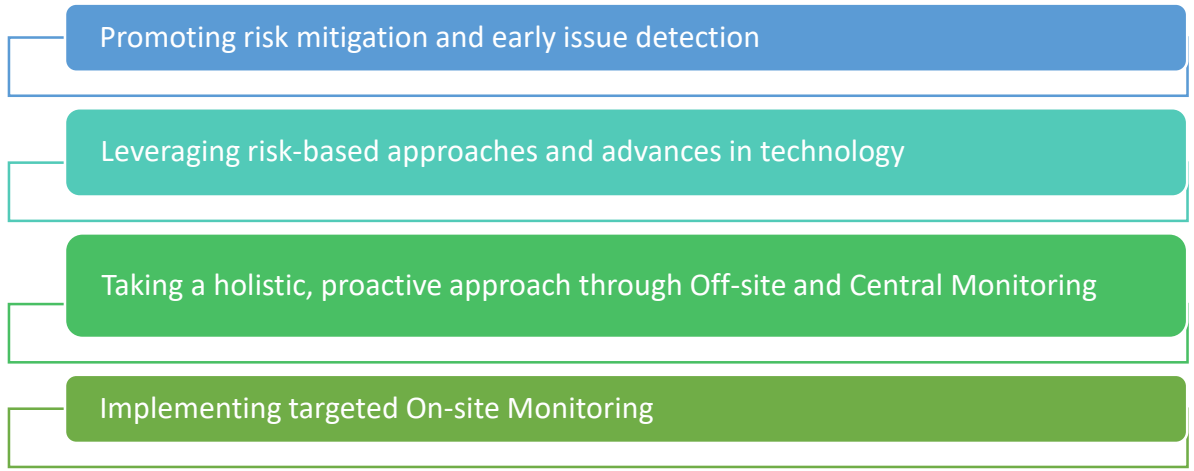
- Is data being entered on time?
- Are queries being resolved on time?
- Is the patient visit schedule being adhered to?
- How many action items and what type are outstanding?

Panel Discussion

- Risk Based Monitoring
  - What does this look like at each of our organizations?
- Tools and Resources
  - What tools and resources do the Stats/CDM/Medical/Clinical Teams use at each of our organizations to support RBM?

Wrap Up

- Plan the appropriate monitoring activities inclusive of Central, Off-Site, and/or On-site monitoring
  - Identify and resolve issues quicker
- Focus on errors that matter
  - Critical data and processes
- Adaptive monitoring
  - Adjust type, activities, frequency
  - Adjust for risks and issues



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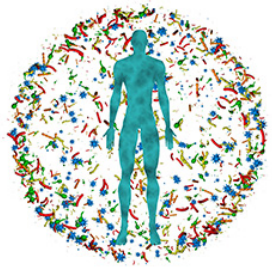

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