The Avoca Group

A life sciences consulting firm dedicated to improving **quality** and **compliance** in the clinical trial execution process.

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Avoca Quality Consortium® (AQC)

A collaborative comprised of nearly 100 pharma, biotech, CRO, and clinical service provider companies with the shared objective of elevating clinical trial quality and execution.

Current AQC® Members

as of 09/18/2018

WEBINAR

Understanding Risk-Based Monitoring Post-ICH E6 (R2)

HOSTED BY:

September 25, 2018

Introductions

Cristin (Crissy) MacDonald, PhD
Executive Director, Client Delivery
The Avoca Group

Jeff Kingsley, DO, MBA, CPI, FACRP
CEO
IACT Health

Outline

- ICH E6 (R2) Background
- ICH E6 (R2) Impact on Sites
  - Relevant Types of Monitoring
  - Risk-Based Monitoring and Trial Quality
- Summary
- Questions and Answer Session

ICH E6 (R2) – What Has Happened and Why?

Proactive Quality Management - Incorporates QbD

- Minimize risk through planning; early signaling and mitigation of problems
- Use data and pre-established tolerance limits for decision making
- Execute routine risk reviews
- Investigate root causes of emergent problems as part of corrective action process

Risk-based Strategies

- Provide oversight commensurate with risks that matter
- Document rationale for chosen strategy; reconcile roles/responsibilities and monitoring/oversight reports with chosen strategy
- Responsive/dynamic vs static system of oversight
- RBM, Risk-based Oversight, Risk-based Inspection Preparedness, and Risk-based Quality Management must be documented as appropriate QMS

Oversight

- Sponsor and Investigator retain accountability for quality

ICH E6 (R2) – What Has Happened and Why?

Electronic Systems

- Validation and quality control through qualified users and SOPs covering system setup, installation, and use
- Implicitly advises to move away from paper-based CRFs/tracking systems

Serious Breaches

- Inform regulators, where warranted by local authorities, when non-compliance is a serious breach of protocol or GCP

Essential Records

- ALCOA+C; location of source/essential documents
- Some process documents become essential documents
  - Risk review requires traceability of decision making
- Must document how risk management oversight is exercised (Monitoring Plan/Integrated Quality Management Plan) – Quality Management Plan; outcome of any centralized/statistical monitoring with actions taken
- Monitoring activities should be traceable and documented
- End of trial report on effectiveness of risk management

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The Three Main Ways Sites Are Affected by ICH E6 (R2)

The promotion of the use of Risk-Based Monitoring	Use of Quality Tolerance Limits	Sponsor and Investigator retain responsibility for Quality

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Monitoring and Trial Quality

TransCelerate: Source Data Verification

Clinical trial sites have varying levels of experience and quality, but monitoring approaches are not designed to manage potential differences.

Research indicates that 100% SDV is not effective at **identifying material risk**. Very low amount of transcription errors that impact data evaluability. *Still, monitoring approaches remain unchanged.*

Targeted Site Monitoring and SDV could lead to improvement in data quality and patient safety for clinical trials and *reduction in effort expended on low-value activities.*

http://www.transceleratebiopharmainc.com/initiatives/risk-based-monitoring/

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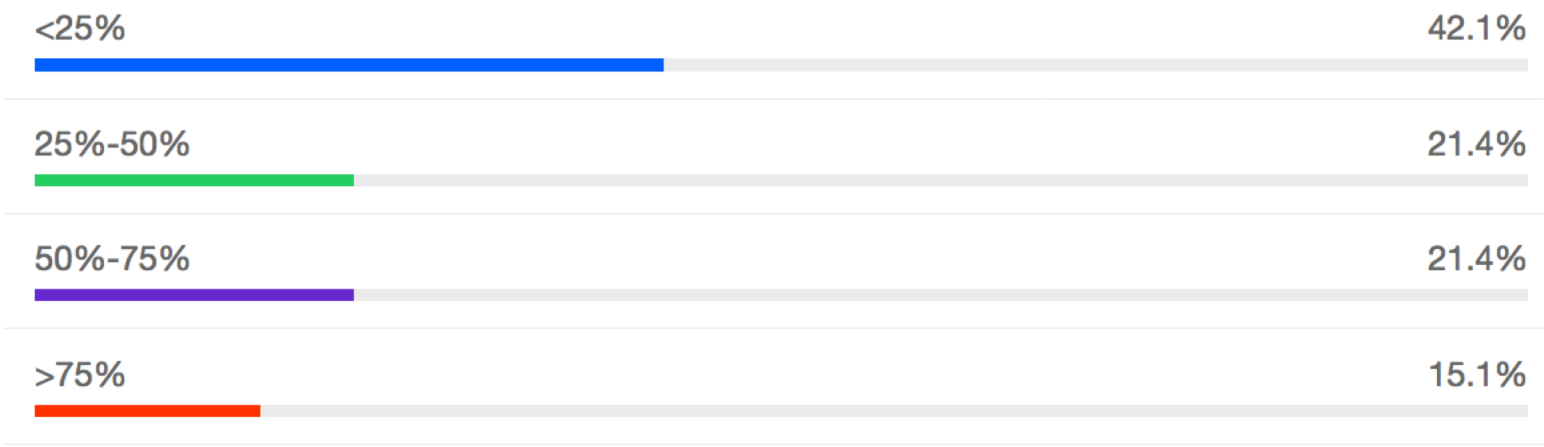
Polling Question Results

What percentage of your organization's studies utilize risk-based monitoring?



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Types of Risk-Based Monitoring

Centralized Monitoring

- **Data Analytics – Review, Statistical Reviews for** performance assessment, real-time analysis, reporting through various e-data sources
- Metrics and Tolerance Limits for acceptable 'deviation' range

Remote (Offsite) Site Management Monitoring

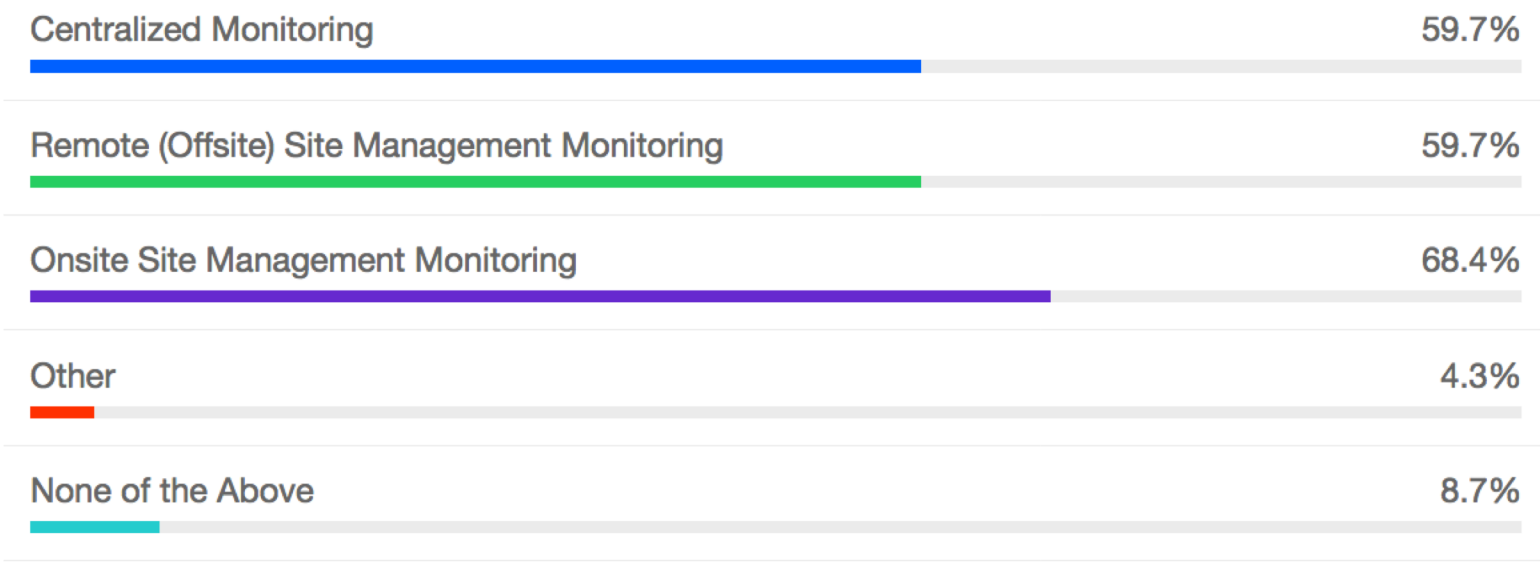
- Site Relationship and Site Management (trial progress, recruitment, ISF, etc.)
- Follow-up: anomalies or deviations identified during centralized monitoring
- Early communication, evaluation and re-training for performance issues/gaps, tracking regulatory requirements, etc.

Onsite Site Management Monitoring

- Site Management: HSP, GCP, protocol adherence
- Assess overall quality & performance – identify gaps and issues
- Monitoring critical data, processes and GCP requirements for HSP and reliability of trial results

Polling Question Results

What type of risk-based monitoring does your organization use? (check all that apply)



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QUESTIONS?

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Risk-Based Monitoring: Impact on Sites

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Summary

- Because of ICH GCP E6 (R2), risk-based approaches are **here to stay** for all Phase I-III clinical trials
- When developed and executed effectively by sponsors, sites learn **early in the study** any issues/problems to correct so that more subjects/cases are not impacted (resulting in less re-work and non-evaluable subjects)
- Impacts site resourcing, processes, procedures, and budgets
  - Site proactive time-keeping practices support their ability to negotiate contracts with evidence supporting their budget requests to sponsors

QUESTIONS?

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Upcoming Webinars & Conferences

[WEBINAR] AQC Knowledge Center Monthly Demo

October 9, 2018 | 11:00am – 12:00pm EDT

ExL's 9th Clinical Quality Oversight Forum

October 10-12, 2018 | Philadelphia, PA

Join *Steve Whittaker, Senior Consultant, The Avoca Group* for two sessions…

- Friday, October 12 | 11:15am – ***The Impact of (R2) on Sites***
- Friday, October 12 | 1:45pm – ***Panel Discussion: Inspection of Oversight Activities***

7th Annual AQC Fall Member Meeting

October 30, 2018 | Princeton, NJ

[WEBINAR] Biopharma Pre-competitive Collaboration: Delivering for Clinical Trial Excellence

November 12, 2018 | 11:00am – 12:00pm EST

Thank You!

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