The Past, Present, and Future of Risk Based Monitoring

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Introduction
Disclosure

The presenter(s) for today’s session: J. Dema Poppa, PMP

☐ I/We have no relevant financial relationship in relation to this educational activity.

☑ I/We have relevant financial relationship(s) with respect to this educational activity with the following organizations (list here):

   CEO of Invio, Inc.
Learning Objectives

Upon completion of this presentation, participants should be able to:

• Explain how three key organizations shaped Risk Based Monitoring
• Examine how risk assessments drive monitoring plan development
• Describe five emerging technologies that could impact the future of monitoring
Agenda

• The Past: how RBM came to be
• The Present: the current state of RBM
• The Future: technologies that might shift RBM
The PPF of RBM

The Past
Monitoring Classic™

- Frequent site visits – every 4-8 weeks
- Review regulatory binders, etc.
- 100% Source Data Verification
What’s wrong with that?

- Multicenter is now standard
- Expensive vs. quality Impact
- Driven by (mis?)perception of FDA requirements
Key Players

- Food and Drug Administration (FDA)
- Clinical Trials Transformation Initiative (CTTI)
- TransCelerate Biopharma, Inc. (TransCelerate)
2007 – CTTI Formed

- Public-private partnership
- Quality by Design (QbD) and Risk Management (QRM)
2011 – Draft RBM Guidance

- Previous 1988 guidance withdrawn
- CTTI Goal: “Identify best practices and provide sensible criteria to help sponsors select the most appropriate monitoring methods for a clinical trial, thereby ensuring reliable and informative trial results and human subjects’ protection”
- Communicated to Biomedical Monitoring (BIMO), etc.
2012 – TransCelerate Formed

- Industry Group
- Cooperation with CTTI
2013 – Procedural RBM Guidance

- Out of “draft purgatory”
- Officially the Agency’s “Best Thinking” on monitoring
- Only minor differences from draft guidance
2013 – TransCelerate Position Paper

• Detailed operational recommendations
• Too complex for practical purposes?
• NOT guidance
Electronic Data Capture

- IBRD Mainframe – mid 70’s
- Remote data entry (RDE) – mid 80’s
- Electronic Data Capture – mid 90’s
  - Thick vs. thin clients
The PPF of RBM

The Present
Current Adoption of RBM

- Guidance establishes it as the norm
- Compare to 2012
- Still in a “wait and see” mode
- No best practices: scary to sponsors
Unpacking Risk Based Monitoring

- Monitoring Plan
- Centralized & Remote Monitoring
- Targeted Monitoring
  - De-emphasizes 100% SDV
A Thought Experiment

- Protocol says patients must be over 18
- eCRF says Nov. 20, 1972
- Source says Nov. 02, 1972
...what do you do?
Implementing RBM

- What does your infrastructure look like?
- Protocol risk assessment
- Document everything!
Risk Management Matrix

- Measures: probability, severity, detectability
- Directed monitoring efforts
- Aided protocol revision
TransCelerate: SDV vs. SDR

• Transcription checking vs. overall quality
• Reduced SDV according to plan
• EDC tools might not distinguish!
Centralized & Remote Monitoring

- Site visits still important!!
- New workflows possible
- What about source documents?
Establishing Best Practices

- Is FDA guidance and TransCelerate enough?
- Indicators, triggers, and sampling, oh my!
- Need the right tools
Back to First Principles of RBM

- Success measured vs. CTTI goal
- Do analytics-based approaches reduce cost/burden?
- Where do opportunities exist?
Improved Access to Site Records?

- 2013 eSource guidance and definitions:
  - Source documents
  - Certified copy
- Part 11
- HIPAA
Cloud Subject and Regulatory Binders

- HIPAA & Part 11 compliant content management
- Management reporting
- No assembly required
Cloud Subject Binder - Example
EHR Integration

- Direct data extraction from health records
  - CDISC ODM
  - HL7
  - FHIR
- Challenging w/ multicenter
- Is enough in the EHR?
Computer Vision

- Optical Character Recognition (OCR)
- Facilitated transcription/verification
  - “Have your cake and eat it too”
- All study records searchable?
Document Mapping

- Perfect for consistently represented data
- Coordinates facilitate Source Data Review
- Helps shortcomings of OCR
Natural Language Processing

- Interpret language, e.g., in clinic notes
- Convert from free text to CDISC ODM
- Hard for computers, easy for us
Risk Based Robots

- Perfect for repetitive tasks
  - Data transcription/verification
  - AE/ConMed monitoring
  - Centralized statistical monitoring
- Frees YOU up to do the important things
Are Robots Coming for My Job?

No.
References

https://www.ctti-clinicaltrials.org/files/ctti_general.pptx

TransCelerate Position Paper. TransCelerate (2013)  


BIMO CPGM. FDA (2011)  

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Thanks! Questions?

J. Dema Poppa, PMP
CEO of Invio, Inc.

@demapoppa
dema@invioinc.com
(206) 915-3563