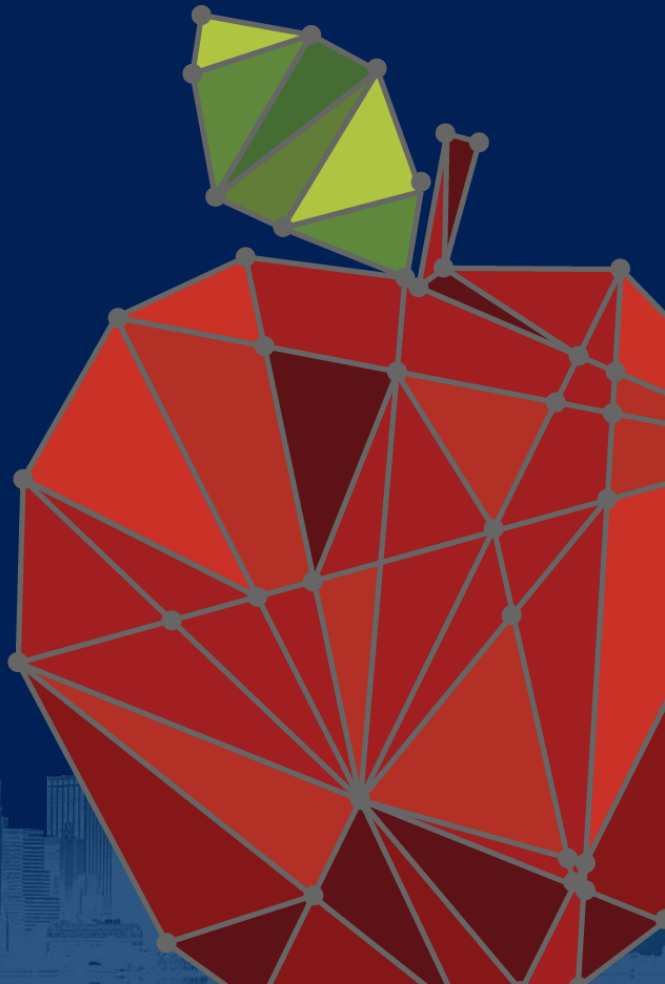
medidata

NEXT

WHERE SCIENCE
MEETS TECHNOLOGY
MEETS THE FUTURE



Innovative Clinical Development Solutions

The Era of Flexible Monitoring Models:

Centralized Real-Time Data Review and Utilization of Targeted Source Document Verification

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Heather Paden, Head of Clinical Operations

- Local regulatory knowledge, strong relationships with investigational sites and medical experts, and highly experienced cross-functional teams, worldwide.
- World-class data science powered by cutting-edge technologies, expert biostatistical analyses, and experienced regulatory medical writing.

What's required?

Overview

- A change in mindset
- Rationale for different approaches to monitoring data
- Pre-requisites and tools
- Case Study: Value proposition in rare disease studies
- Considerations

A Change in Mindset

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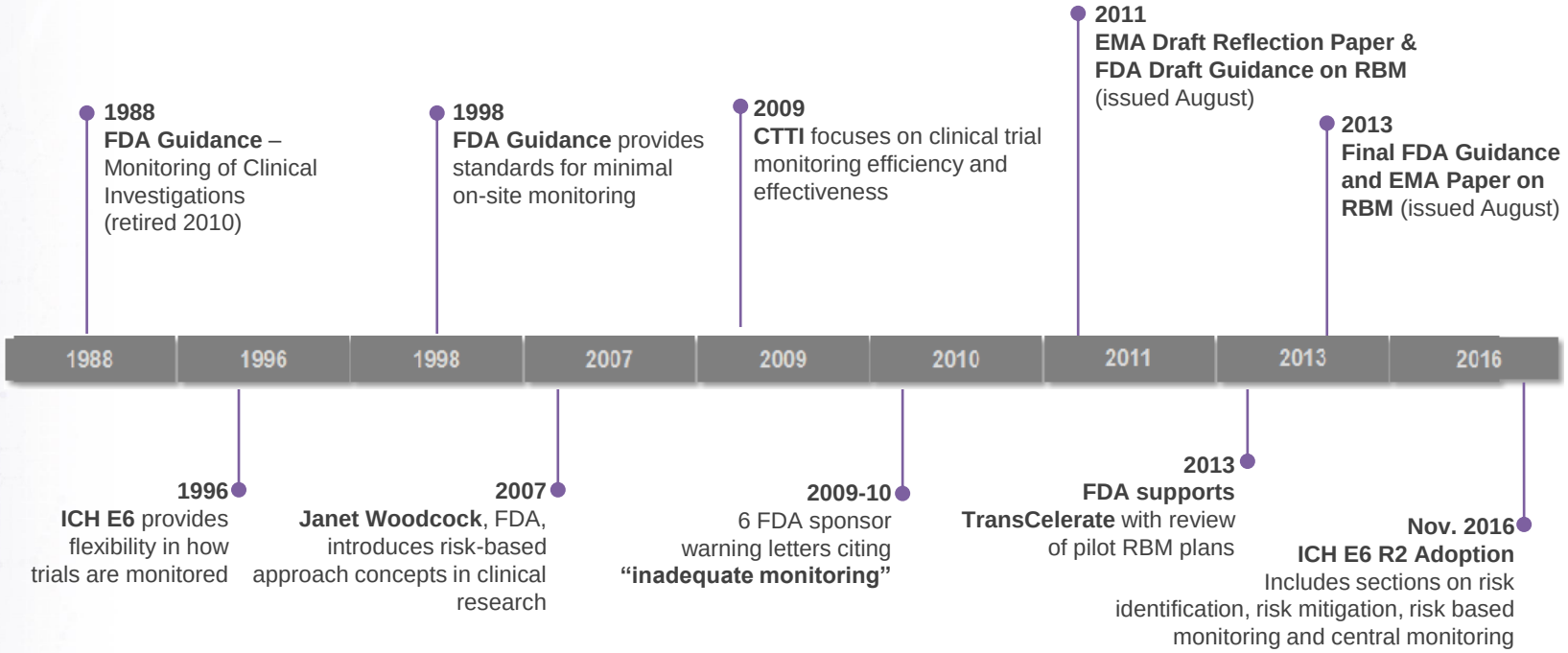
Regulatory Agencies Acknowledge Flexibility



Source: TransCelerate

The Evolution of Risk Based Monitoring

CTTI	FDA Guidance	EMA Reflections Paper	TransCelerate Paper
Quality by Design • Tailor monitoring approach • Protocol quality impacts monitoring quality	Quality Clinical Trial Data • Assess Risk • Combination of monitoring activities • Tailor Monitoring Plan	Risk Based Quality Management • Plan • Adapt • Build on experience and advances	RBM Methodology • Holistic, proactive approach; risk assessment, mixture of remote & on-site monitoring

Source: TransCelerate

ICH E6 Good Clinical Practices (R2)

- Since original allowed flexibility in monitoring approaches
- Increased focus on Critical Data and Processes (trial activities essential to ensuring subject protection and reliability of trial results)
- Implement a system to manage quality
- Risk identification, risk evaluation, risk communication, risk control, risk review and risk reporting
- Monitoring based on Risk including the use of centralized monitoring to compliment or reduce on-site monitoring

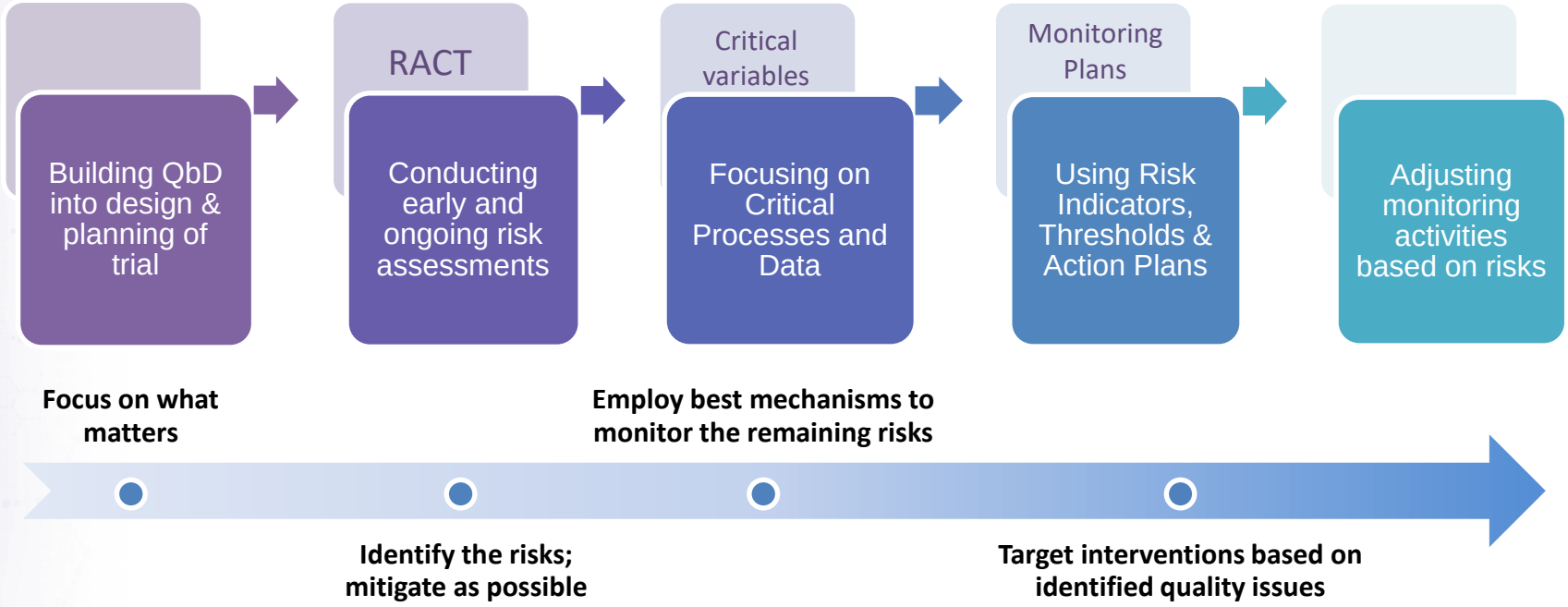
Source: TransCelerate

Risk-Based Monitoring Methodology

- Risk Based Monitoring is more that just onsite monitoring, it is an end to end approach based upon Risk Assessments and Quality by Design
- TransCelerate has created an approach that has been adopted (and adapted) by big Pharma, CROs, etc.
- It has also given the software providers such as Medidata a roadmap to develop new tools to support the methodology

Source: TransCelerate

Risk-Based Monitoring Methodology



Source: TransCelerate

Rationale for Different Approaches to Monitoring Data

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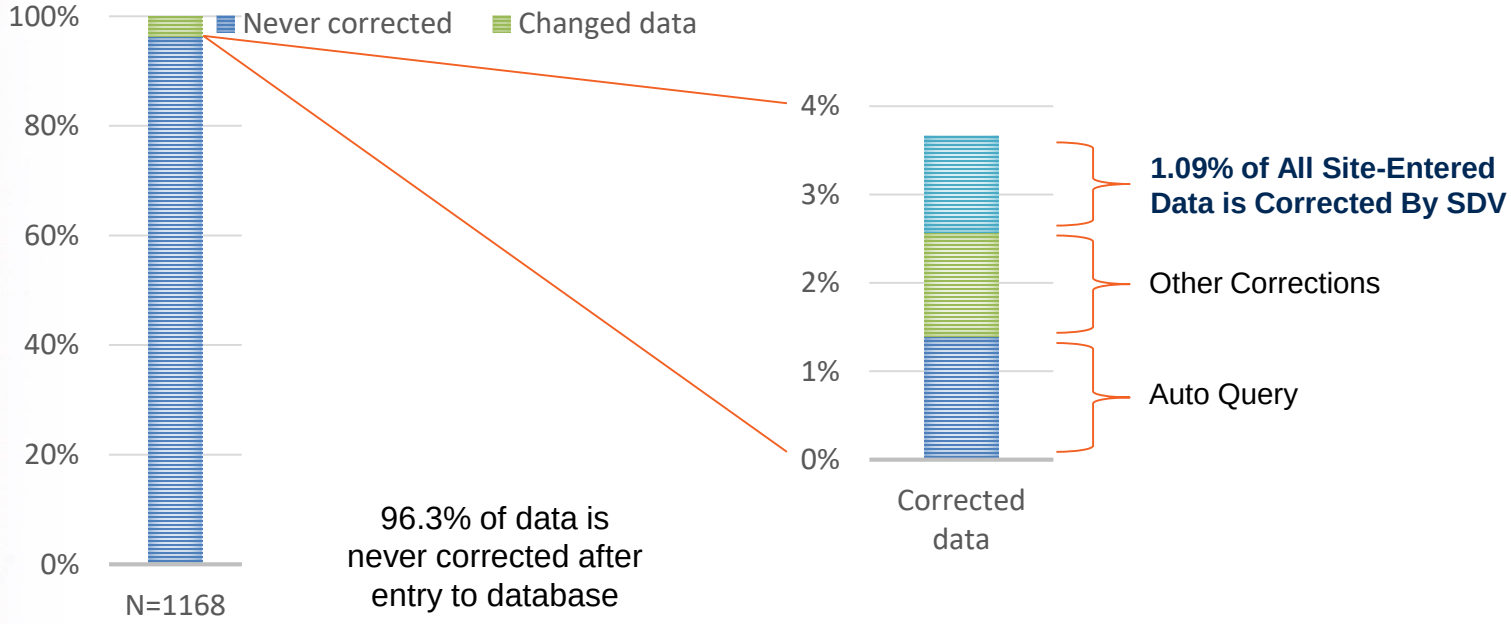
One Size Does Not Fit All

- Not all studies are the same, similarly not all sites are the same….
  ….so why monitor them in the same way?
- The traditional 100% Source Data Review (SDV) approach has been shown in studies to have little impact on overall data quality but is time consuming for CRAs
- Programmatic assisted monitoring centrally is faster, cheaper and more effective at monitoring data
- Free up CRA time on-site to perform higher value tasks that cannot be assessed directly from the data

Source: TransCelerate

Retrospective SDV Analysis*: Additional Insight into Metric #2
Impact of SDV on Site-Entered Data



* Evaluating Source Data Verification as a Quality Control Measure in Clinical Trials: Therapeutic Innovation & Regulatory Science 2014, Vol. 48(6) 671-680

Source: TransCelerate

Pre-Requisites & Tools

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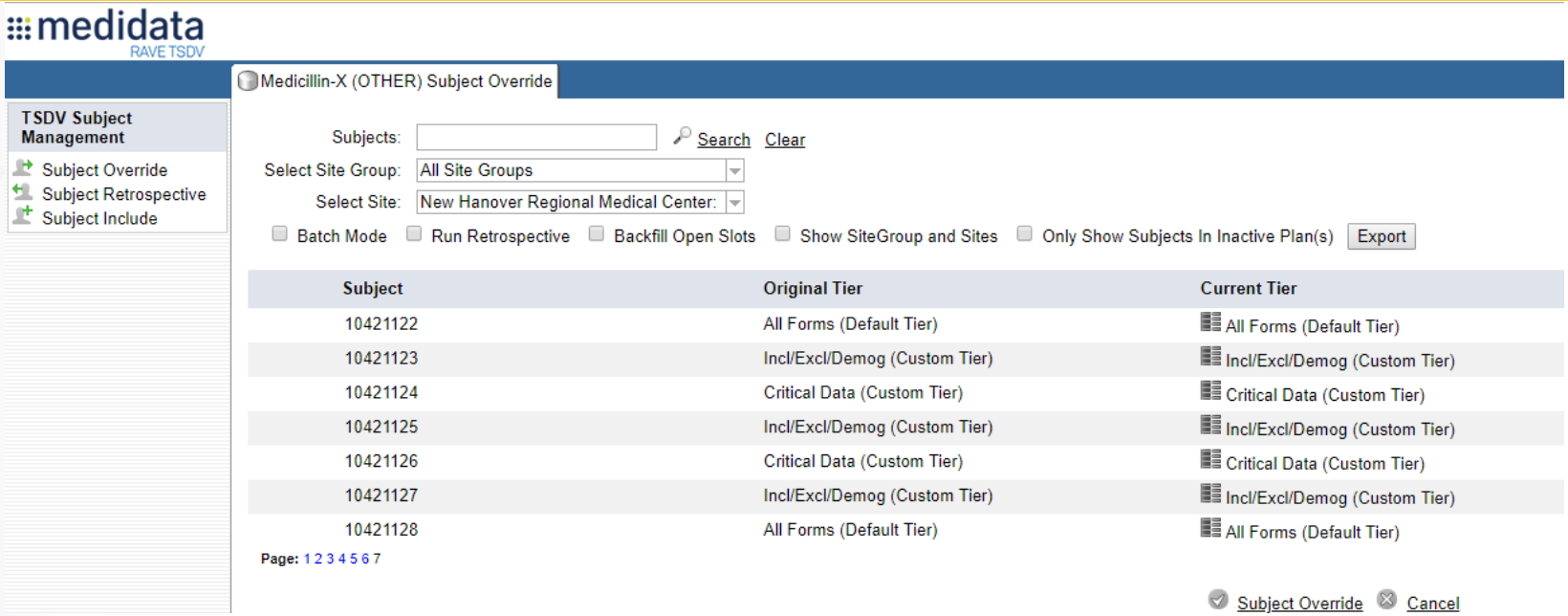
Pre-Requisites

- An organization willing to change!
- Successful TSDV relies on proper risk identification
- A solid foundation based upon risk and understanding what data/processes are important
- Agreement on which monitoring strategies are best suited to ensure quality and data integrity
- Centralized monitoring is reliant upon timely access to data
- Tools to support
  - The assignment and tracking of onsite monitoring
  - Centralized monitoring (from programmed edit checks, monitoring listings and tables…to advance statistical machine learning tools)

Targeted SDV (TSDV)

- TSDV is a tool that allows for a advanced method to assign and track SDV
- Through the use of Blocks and Tiers advanced assignments can be made
  - e.g. the first subject at each site could be 75% SDV, followed by 25% for each subsequent subject
- Changes at study, region, individual sites or individual subjects can be made

Case Study



Subject TSDV Tier assignment.
Subjects 10421127 and 10421128 assigned to different tiers.

Case Study: Value Proposition in Rare Disease Studies

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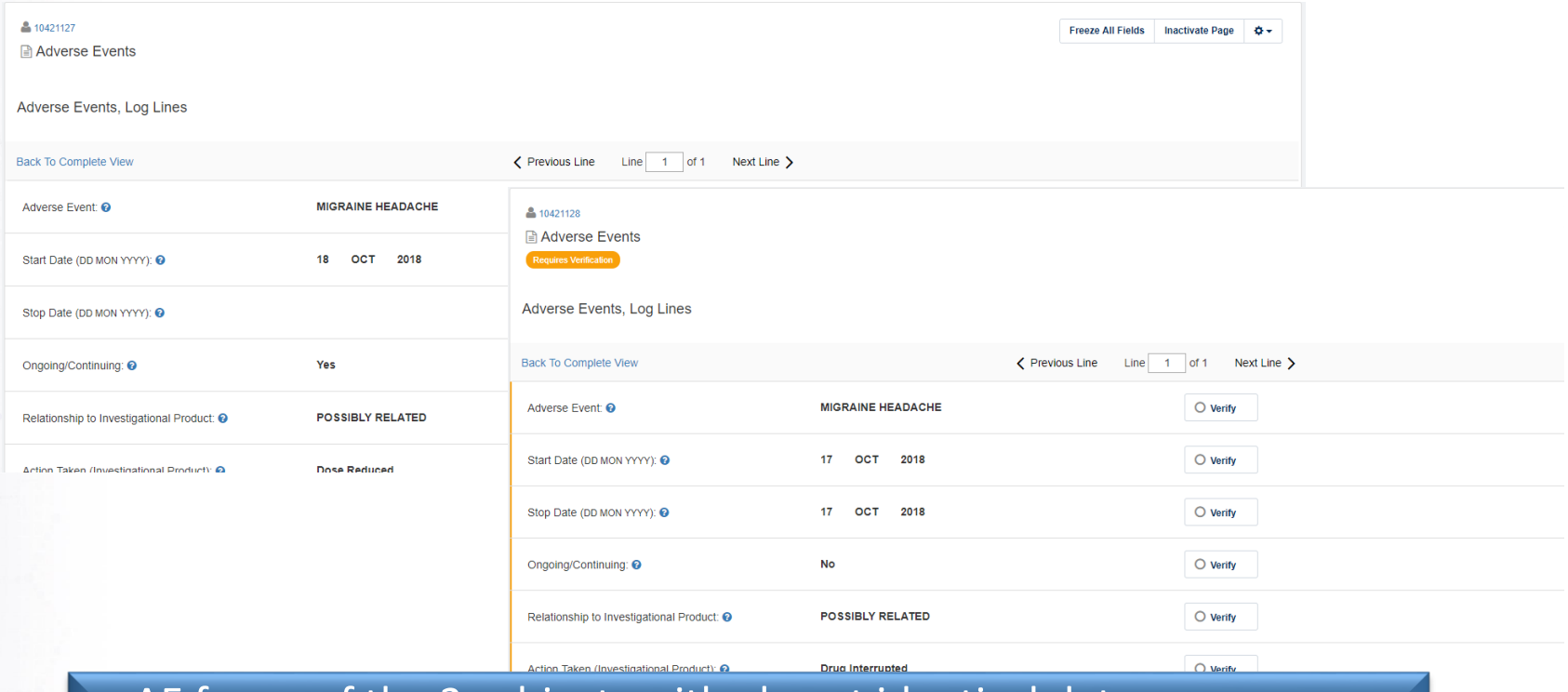
Case Study

Study Design:

- Phase 2, Open-Label
- Three times a week dosing of ABC-123456 in subjects with a transfusion dependent rare blood disorder
- Local and central labs
- MRI derived key secondary endpoint
- Duration: 12 months

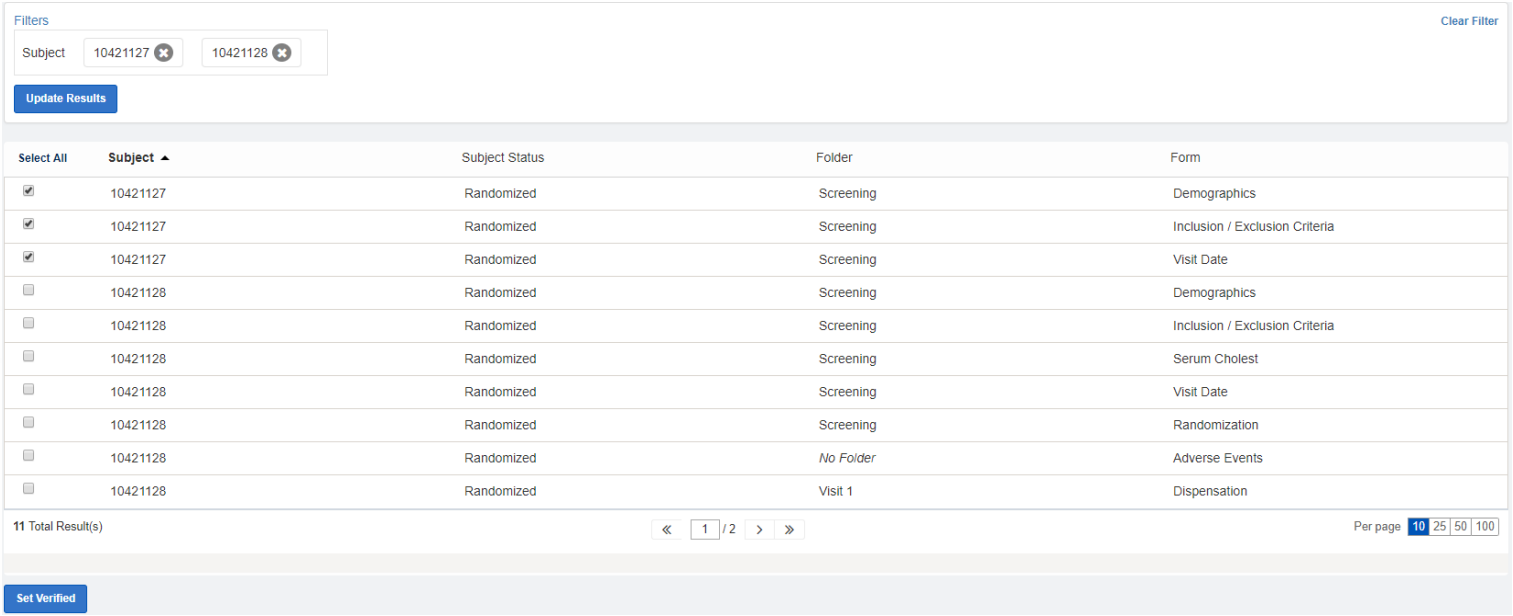
Which terms above that reflect potential Critical Data and/or Critical Processes?

Case Study



AE forms of the 2 subjects with almost identical data.
10421128 requires all fields be verified while the other does not.

Case Study



As you can see, only 3 forms requiring verification for 10421127 and multiple others for 10421128 even though they have virtually identical data entry.

Considerations

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Considerations

- CRA visits – saving an hour on SDV, what does it actually mean?
- Centralized monitoring relies upon near real-time access to data to be most effective
- All monitoring needs to be documented, including centralized monitoring

ANY QUESTIONS?

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