RISK BASED SDV UNDER ISO14155 settings

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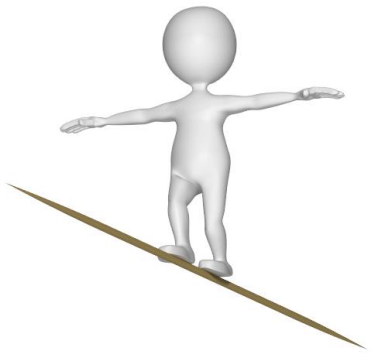
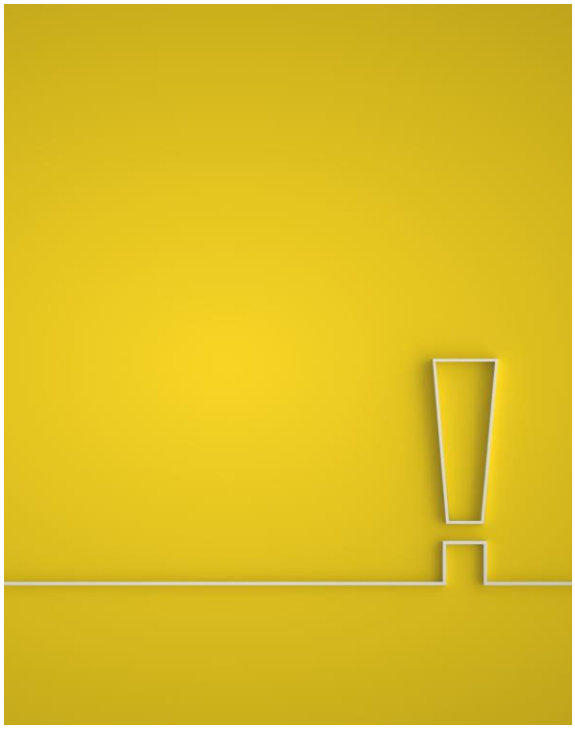
Risk Based SDV

A risk-based approach focuses on verifying the:

- **most critical data elements that contribute to primary endpoints, safety data, and data integrity**





Why the need for Risk Based SDV?

- Significant resource dedicated to SDV of data has no or minimal impact on study conclusions (*e.g. phys exams, med history, con com meds especially when they are not analysis variables)*
- Human review process is only 85% accurate!
- Not effective/efficient in dealing with other factors (transcription errors in SD, subject not reported or misreported data –etc)
- Significant cost implications

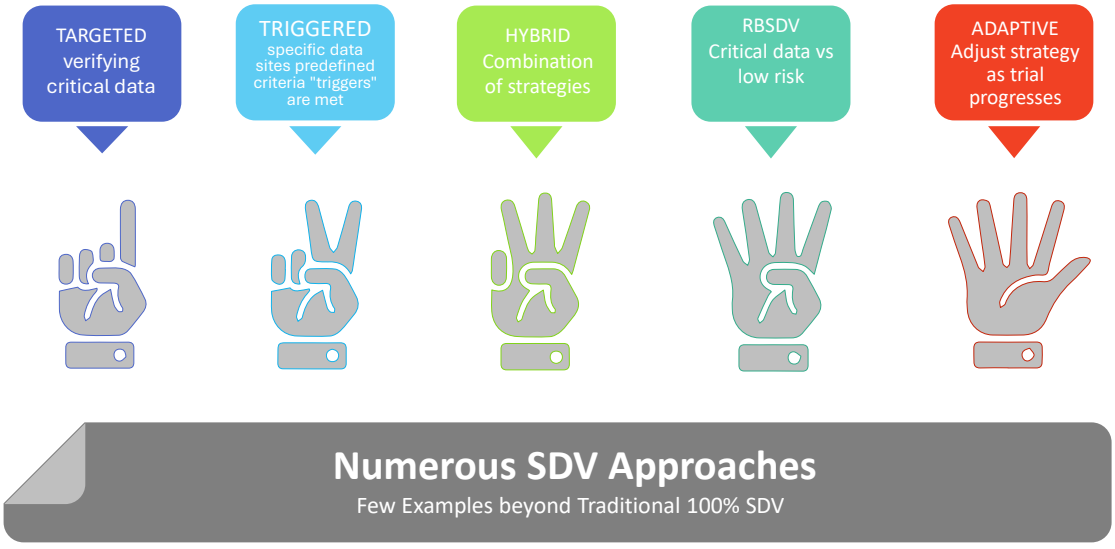
What will Risk Based SDV do?

Increase in data quality as focus will be on critical data elements that are vital for analysis and interpretation of study data

What does ISO14155 say…..

6.7
'The sponsor shall determine the extent and nature of monitoring appropriate for the clinical investigation based on the risk assessment.

The extent and nature of the monitoring, including the **strategy for source data verification versus centralized data review (evaluation without visiting the investigation site)**, subject protection and timely reporting, shall be based on the objective, design, complexity, size, critical data points and endpoints of the clinical investigation and the degree of deviation from normal clinical practice – risk-based monitoring.'



RBSDV Approaches - Tiered

	TIER 1 High Priority	Tier 2: Moderate Priority	Tier 3 Low Priority
DATA TYPE	Includes critical data points linked to primary endpoints, safety outcomes, or other key aspects of the study.	Consists of important but less critical data which might influence secondary endpoints or provide supportive information to primary data.	Includes data that have minimal impact on study outcomes and are unlikely to affect patient safety or the overall integrity of the trial.
SDV FREQUENCY	These data undergo frequent or even 100% SDV due to their significant impact on study results and patient safety.	These data are subjected to less frequent SDV, potentially on a randomized or sample basis, depending on the risk assessment.	These data might receive very limited SDV or might only be verified under certain conditions, such as when anomalies are detected in higher-priority data.

RBSDV - Tiered

Aligned

a risk-based management strategy, focus on managing the risks associated with data integrity and compliance.

Efficient

use of monitoring resources, focusing on what matters for the trial's outcomes.

Flexible

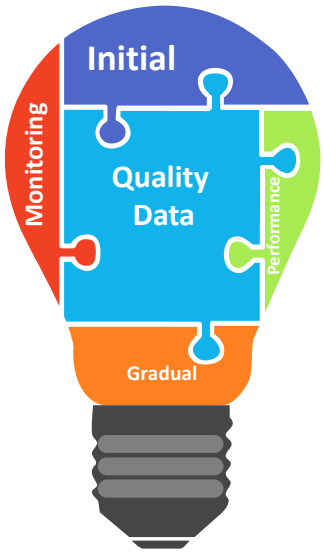
This approach can adapt over the course of the study.

Declining SDV

The intensity and frequency of SDV decrease over time based on the accruing evidence of data quality and reliability from the trial sites.

Approach designed to optimize the use of monitoring resources while maintaining adequate oversight of data accuracy and integrity throughout the trial.

Declining SDV



Initial Intensive SDV

Start of the clinical trial, a higher percentage of SDV is conducted establish a baseline of data accuracy and to assess the performance of the trial sites.

Performance Evaluation

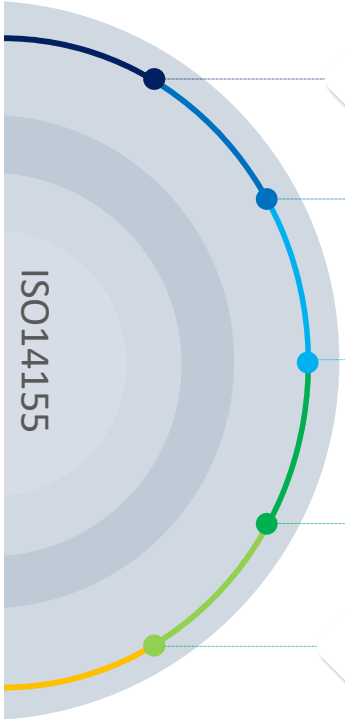
Sites that demonstrate high levels of compliance and few errors in the initial phase may qualify for reduced SDV.

Gradual Reduction

For sites that meet these criteria, the frequency and scope of SDV are gradually reduced. This means that less data will be verified on-site, assuming that past performance predicts future performance.

Continuous Monitoring

Despite the reduction in SDV, ongoing monitoring and occasional quality checks continue to ensure that standards remain high and that any emerging issues are quickly addressed.



RISK ASSESSMENT & CATERGORISATION

Identify critical data and processes
Assess and categorize risks based on their potential impact and likelihood.
Section 6.2

DEVELOP RISK BASED MONITORING PLAN

Develop a monitoring plan that prioritizes monitoring activities, including SDV, based on the identified risks.
Section 9.2.3, 6.7, A.6.5

RBSDV

Implement targeted SDV focusing on high-risk data points identified during the risk assessment.
Section 6.7

CONTINUOUS REVIEW & ADAPTATION

Continuously review the effectiveness of the monitoring activities and adapt the monitoring plan as necessary based on ongoing risk assessments and findings from monitoring activities
Section 6.7

DOCUMENT AND REPORT

Document all risk assessments, monitoring activities, and any adjustments made to the monitoring plan.
Section 6.7

EXAMPLE

- A global medical device company was conducting a Phase III clinical trial to evaluate the safety and efficacy of a new cardiac stent.
- The trial involved multiple sites across various countries, each with differing levels of experience and performance history in clinical trials.

EXAMPLE

Initial Setup and Risk Assessment

- Company conducted a thorough risk assessment for each trial site.
- Analysed historical performance data, regulatory inspection results, and staff qualifications.
- The cardiac stent being tested was considered a high-risk device due to its direct involvement in patient critical pathways (e.g., blood flow management). Therefore, ensuring data integrity was paramount.

Critical Data Identification

- The company identified critical data points such as:
  - stent placement accuracy
  - patient survival data
  - serious adverse events (SAEs).
- These data points were deemed essential for regulatory submissions and decision-making regarding the device's safety and effectiveness.

	TIER 1 High Risk Sites	Tier 2: Medium Risk Sites	Tier 3 Low Risk Sites
DATA TYPE	Includes critical data points linked to primary endpoints, safety outcomes	Includes critical data points linked to primary endpoints, safety outcomes	Includes critical data points linked to primary endpoints, safety outcomes
SDV FREQUENCY	Received more frequent on-site visits and a higher percentage of data points underwent SDV, particularly focusing on critical data.	Subject to less frequent SDV checks but maintained a focus on critical data.	Had the least frequent SDV focusing primarily on random and triggered checks.

RBSDV Approaches - Tiered

Risk-Based SDV: Tiered Strategy

- Adaptive Monitoring:
  - The monitoring plan was designed to be adaptive, allowing for modifications based on interim data reviews. For example, if a site improved its data quality over time, it could be moved to a lower-risk category with less intensive SDV requirements.

- Use of Technology:
- To support the RBSDV approach, the company employed a sophisticated Electronic Data Capture (EDC) system with built-in checks for anomaly detection, which could trigger additional SDV or site visits if needed.

Summary

Risk-based SDV

Efficiency: strategically allocates monitoring resources to ensure data integrity and patient safety in clinical trials hence more effective use of monitoring resources.

Cost-Effectiveness: Reduces overall monitoring costs.

Quality Improvement: enhancing efficiency and compliance while focusing on critical data points where the potential impact on study outcomes is greatest.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