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Analytical Risk-Based Monitoring (ARBM): From Targeted to Zero Source Data Verification (SDV) – Are Teams Ready for the Revolution?

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ABSTRACT

Shifting the focus from SDV on 100% of data to targeted SDV on critical data that matters most to the study objectives is currently a well-accepted approach in clinical trials. By applying it, study teams can direct monitoring and oversight on areas more likely to affect patient safety and data quality. Is the next step removing SDV altogether?

This paper presents a case which first implemented targeted SDV for a subset of subjects. To ensure data quality and integrity, several ARBM methods were implemented. After further observation on real-time data point changes, SDV was further reduced to complete shutdown.

INTRODUCTION

This paper aims to provide a thorough rationale for the potential elimination of SDV in clinical trials, highlighting the challenges encountered and insights gained from this transformative process. By adopting an ARBM approach, this paper will demonstrate how a focus on critical study factors can enhance monitoring practices while maintaining robust data quality. Ultimately, this discussion seeks to illustrate that a targeted monitoring strategy can preserve the integrity of clinical trial data while adapting to the dynamic nature of research environments.

EVOLUTION OF SDV AND SDR

"Gold Standard" in application of SDV and SDR

The evolution of SDV and SDR started with the gold standard in clinical trials of having 100% Source Data Review (SDR) and 100% Source Data Verification (SDV). While both SDR and SDV offer distinct benefits, a clear definition between the two processes is essential in order to be able to optimize their application.

SDR is a review and evaluation of the source documentation to check:

- ✓ quality of source
- ✓ compliance with ICH GCP guidelines
- ✓ site staff understanding of protocol
- ✓ site staff adherence to protocol, study-specific processes and site procedures
- ✓ site staff documenting the above in the source documentation appropriately
- ✓ where CRAs ensure comprehensive source data recording in EDC or other data collection system and check for any missed data entries.

SDV is a simple cross-check activity:

- ✓ which confirms that the data were transcribed accurately (i.e. data from source matches data in the EDC).

The comparison conclusion suggests that SDR necessitates critical thinking and a comprehensive evaluation of the entire data generation, documentation, and capture process. Unlike SDV, which primarily focuses on the accuracy of individual data points, SDR encompasses a broader assessment of the adequacy and existence of source documents. This broader perspective positions SDR as a significantly more vital process than SDV. When sites consistently meet SDR expectations, it indicates a high level of competence in data transcription with minimal errors.

Consequently, the benefit of performing SDV on every single data point is put into question, highlighting the need for a more targeted approach that prioritizes critical data review over exhaustive verification.

tSDV – a well-accepted approach

The gold standard process of SDV and SDR has evolved over the past 10 years into a more targeted SDV (tSDV) approach. Application of tSDV on study-specific critical data points is now being a risk-based monitoring approach broadly recognized and implemented by the industry.

Case Study – evolution of SDV and SDR practices

A decade after the release of the *original TransCelerate BioPharma Position Paper, 2013*, the approaches to SDV and SDR have continued to evolve to meet the dynamic needs of clinical studies. The following case study illustrates how SDV and SDR were strategically adapted in response to the changing dynamics of the study.

Stage I

The initial phase of the study implemented a well-known structure of tSDV and 100% SDR across all study data. This approach aimed to ensure comprehensive oversight, setting a high standard for data accuracy and quality.

Stage II

During the second phase, a subset of subjects was exempted from SDV for Business Continuity Planning purposes, designed to address challenges such as global pandemics or regional geopolitical disruption. Although SDV was eliminated for this subset, SDR continued at 100% whenever possible. For all other subjects, the study maintained its original SDR and SDV structure. The effectiveness of this approach was evident as data quality and subject safety remained robust, validating the flexibility of this strategic adaptation.

Stage III

In the third stage, the study implemented varying degrees of tSDV randomly assigned across subjects. One group was assigned 0% SDV and targeted SDR (tSDR), where SDR was strategically focused on critical data points. Specifically, Adverse Events (AEs), disease evaluation, and informed consent forms (ICF) were designated as critical and continued to undergo 100% SDR for all subjects. This targeted approach, with 0% SDV and tSDR for a certain group, successfully supported and maintained subject safety and data quality. Enhanced familiarity with the protocol, risk awareness by local teams, and understanding of the critical factors for the study contributed to the positive adaptation and continuity of study progression.

Stage IV

In the fourth stage, tSDV was further reduced and tSDR remained. This reduction marked another strategic refinement, driven by evidence supporting the minimal impact on data quality.

Stage V

The final stage concluded with the complete elimination of SDV and application of tSDR for all subjects. This marked the culmination of a gradual evolution, where SDV and SDR practices were successfully scaled down without compromising data quality or subject safety.

This case study underscores how the adaptation of SDR and SDV on phases can effectively respond to evolving study dynamics while maintaining high standards of data integrity and safety oversight.

REASONS TO CONSIDER SDV SHUT OFF

The consideration of eliminating SDV warrants careful examination, particularly in light of several compelling reasons that highlight its potential benefits. Firstly, the low risk to subject safety and data quality is a significant factor, given the availability of a substantial amount of data. This availability facilitates robust analyses and mitigates concerns related to the integrity of the data collected.

Moreover, the learning curve of site on the protocol and the heightened awareness of the study team regarding potential risks contribute to a reduced likelihood of erroneous data entry. As sites become more skilled at managing data, the probability of mistakes decreases, further strengthening the argument for SDV reduction.

Additionally, the implementation of oversight tools plays a crucial role in supporting data quality. These tools provide the necessary framework for ensuring that data integrity is maintained, even in the absence of reduced or eliminated SDV practices. By relying on these mechanisms, study teams can assure themselves that the quality of the data remains high.

Lastly, a strategic shift in focus from SD Verification to SD Review represents a revolutionary change that prioritizes efficiency and effectiveness in clinical trials monitoring. This approach reduces the time spent on SDV which enables CRAs to concentrate on more critical tasks and to oversee systemic errors resulting in improving data quality. By redirecting efforts away from mere data transcription errors, CRAs can engage more meaningfully with the most pressing aspects of monitoring the clinical trial.

In summary, the rationale for considering the elimination of SDV is substantiated by the potential for enhanced data integrity, improved operational efficiencies, and an increased focus on quality oversight and subject safety.

DATA QUALITY VERIFICATION AFTER SDV SHUT OFF?

How to verify that the data quality is maintained after the SDV shut off?

A pressing question is how to ensure that data quality remains uncompromised following the implementation of SDV shut off. Addressing this concern necessitates a multifaceted approach that leverages various resources and strategies to maintain the data quality throughout the clinical trial, as visualized on the graph below:

One of the elements is the enhanced support provided to CRAs. By allowing CRAs to adopt a more flexible role, they can prioritize and concentrate on critical issues for a study. This flexibility is essential, as it empowers CRAs to allocate their time and expertise to areas that demand immediate attention, in that way adopting a proactive approach to data quality oversight.

In addition to CRA support, the creation of a robust central team is crucial. This team uses various systems and includes roles that oversee critical data elements, ensuring that both data quality and subject safety are maintained. The collaborative efforts of this central team create a safety net that mitigates risks associated with the absence of SDV, supporting the overall integrity of the trial's data.

Moreover, the implementation of enhanced data analytics plays a significant role in maintaining oversight over data quality. Advanced analytical tools provide valuable insights and oversight of errors and systemic issues that may emerge during the trial, enabling the central team and the CRAs to identify trends and address potential pitfalls proactively. These tools also support CRAs in their remote activities and monitoring visit preparations, thereby streamlining processes and enhancing overall operational efficiency.

Supporting this oversight are internal review processes that correspond with the data outlined in the *TransCelerate BioPharma Paper*, *2013* and demonstrate remarkably low incidence of data changes resulting from CRA queries. Such low numbers indicate a high level of data quality and suggest that the systems in place for monitoring are effective.

Finally, ongoing training for CRAs is imperative to ensure a sustained focus on continuous data review throughout the SDR process still in place. This training equips CRAs with the necessary skills and knowledge to navigate the data quality oversight in a free-SDV environment.

In conclusion, by integrating flexible CRA support, centralized oversight, advanced data analytics, and comprehensive training, it is possible to uphold data quality in clinical trials even after the switch off of SDV. This multifaceted strategy not only addresses immediate concerns related to data quality but also positions clinical trials to operate more efficiently and effectively adapting the approach to the changing study dynamics.

CHALLENGES AND LESSONS LEARNED FOR TEAMS MONITORING "NO SDV" TRIALS

Challenges in "No SDV" Trials: Sponsor, Site, and Data Quality Perspectives

Effective monitoring of "No SDV" trials may face multiple challenges that can be broadly categorized into sponsor-related, site-specific, and data quality challenges.

Sponsor-Level Challenges

At the sponsor level, key challenges include the need for robust change management processes and additional support from central teams to aid CRAs in their tasks. As trials evolve, managing adjustments efficiently ensures that CRAs are well-supported and aligned with the updated monitoring practices, helping them understand how to navigate this new environment, focusing on holistic SDR rather than the simple action of SDV.

On-Site Challenges

Challenges at the site level include ensuring regular communication with sites. This regular interaction helps clarify study requirements, particularly in specifying items that need review during monitoring visits, that any discrepancies that were found were corrected, and that the review was expanded when issues were found. Clear guidance and consistent information flow enhance compliance and streamline monitoring tasks.

Data Quality Challenges

Maintaining data quality presents a distinct set of challenges. CRAs are required to apply critical thinking when conducting SDR, emphasizing its role as an ongoing quality check. Clearly defining that SDR process is still a quality check which can be expanded as per the discretion of the CRA in case of identifying data issues is crucial for the oversight of data quality preservation.

Lessons Learned from monitoring "No SDV" trials

Based on the challenges encountered throughout the monitoring process, teams are encouraged to prioritize SDR during site visits, focusing on critical data points and site processes, and any source areas where risk indicators are identified. As part of SDR review expectations, CRAs should systemically access EDC or any other electronic data capture system to ensure comprehensive data recording and to check for any missed data entries even after the SDV switch off, safeguarding data completeness and accuracy. Additionally, continuous regular communication with study sites between monitoring visits is essential to ensure they receive timely study updates and EDC metric reports.

Recommendations for monitoring teams

To address any challenges, the following recommendations are proposed:

1. **Training for CRAs**: train the CRAs on changes to SDV/SDR approach, including the need to check EDC even after the SDV switch off and that this action is part of SDR review expectations.
2. **Guidance in On-Site Monitoring Guidelines**: On-site monitoring guidelines for CRAs should include explicit instructions on SDR tasks, outlining the specific forms and data points that require SDR review.

3. **Central Monitoring Oversight**: A comprehensive central monitoring process is recommended, incorporating a multi-faceted, cross-functional approach. This centralized system will enable a holistic monitoring of trial data, enhancing the data quality and maintaining subject safety.

These approaches aim to strengthen monitoring practices, improve data quality, and ensure that clinical trials operate efficiently and in compliance with regulatory standards.

CONCLUSION

The findings presented in this paper highlight the feasibility and benefits of transitioning from tSDV towards its strategic reduction and eventual elimination of SDV altogether. Through the application of ARBM approaches, clinical trials can maintain robust data quality and ensure subject safety without the need for exhaustive SDV practices.

This case study demonstrates that, by focusing monitoring efforts on critical data points and employing targeted oversight mechanisms, clinical research teams can effectively manage risks associated with data quality. The evidence collected throughout the study phases emphasizes SDR's central role as a quality checkpoint, underscoring that critical thinking in data review—rather than exhaustive SDV—is key to maintaining data integrity.

Furthermore, the implementation of advanced data analytics, centralized oversight, and ongoing CRA training plays a crucial role in upholding data quality in a zero-SDV environment. These tools and practices mitigate the risks associated with SDV elimination and enhance monitoring efficiencies. The evidence from each phase of this study indicates that a structured approach, focusing on critical data points and empowering CRAs with robust training and support, allows clinical monitoring teams to address risks proactively and flexibly.

In conclusion, the evolution of monitoring strategies in clinical trials not only supports the notion of reducing or eliminating SDV but also reinforces the idea that effective oversight can be achieved through targeted review processes. Through ARBM strategies, clinical teams can achieve high standards of data quality and safety, positioning clinical trials for operational efficiency while adapting seamlessly to evolving study dynamics.

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