Optimizing Clinical Database Lock: Strategies for Success

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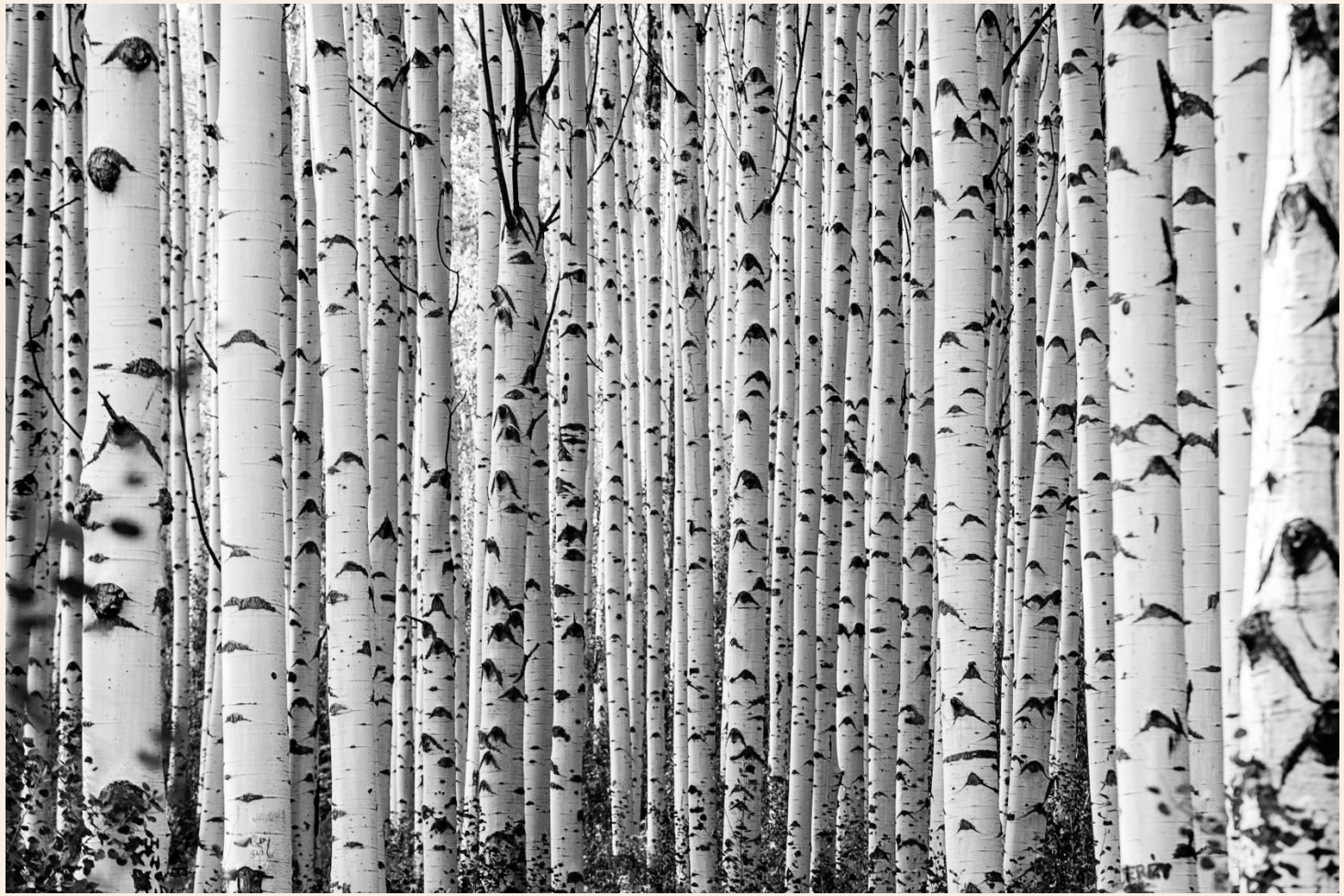
Agenda

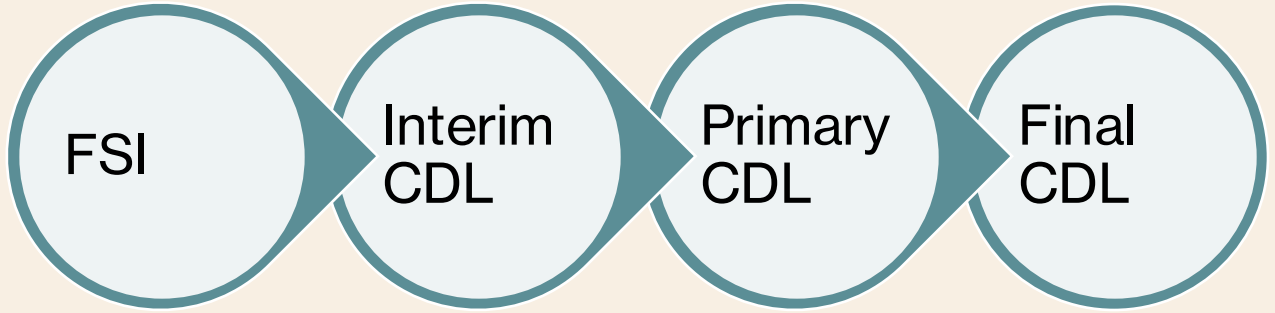
- Introduction
- Background and Context
- Objectives
- Flow of Activities
- Common challenges
- Strategies for success
- Conclusions
- Close-out, Q&A



Introduction

The clinical trial process is a multistage journey with the database lock being one of the crucial phases.

A database lock is a critical milestone. It marks the point at which the data collected during the trial is considered complete for analysis. After the database is locked, no further changes can be made to the data, ensuring its integrity and reliability for subsequent statistical analysis.



The aim of this presentation is to explore effective strategies for optimizing the clinical database lock (CDL) process. By focusing on practices and techniques, we aim to enhance the efficiency and accuracy of clinical data handling, ultimately supporting faster and more reliable decision-making in clinical research and trial management.

Background and Context

- Planning the delivery of a CDL is a multifaceted challenge that requires intensive communication and agreement with key stakeholders. It involves the careful coordination of several interdependent activities; all aimed at achieving a common goal.
- There is no universal standard or one-size-fits-all approach for delivering a CDL, as each study may have unique requirements. However, numerous standard methodologies can be employed to achieve a successful CDL.

Objectives

- The objective of this presentation is to explore the various factors contributing to accelerated timelines and discuss strategies for optimizing the delivery of a clinical database lock.
- This presentation provides insights from the Global Study Management Team, highlighting our comprehensive strategies and collaborative efforts to optimize CDL.

Flow of Activities in a Study

Planning

-objectives(study endpoints), statistical assumptions
-number of data locks (interim, primary and final CDL), need for additional interim analysis post primary CDL
-review committees (DMC, URC etc)
-Critical to Quality(CtQ) factors(DQRM, IQRMP)
- selection and onboarding of relevant vendors

Execution

- exhaustive planning few months before DCO/CDL
-dates are fixed and shared with every stakeholder
-scope of CDL
-documents outlining data review activities approved
-timetable defined considering all supporting activities (data cleaning ,reconciliation and SDV/SDR rounds)
-regular review of data metrics, ongoing reconciliations
-intensive communication and follow-up with sites and country site management team
-potential risks/mitigations

Completion

-clean file
-declaration of CDL
-analysis & reporting
-interpretation meetings and decision about study next steps (GNG)
-CSR preparation and submission
-health authority interactions
-future research directions (in case of successful outcome patients' treatment protocols)
-controlled unlock(unfavorable)

Common challenges

- **Timelines**: Delays in confirming timelines and frequent revisions can disrupt the flow and delivery of CDL and planned analysis. Timelines alignment among vendors (reconciliation- central lab data, PRO etc.)
- **Communication**: Inefficient communication can pose substantial risks to project success.
- **Resources**: There may be a limited number of CRAs, and site staff compared to the number of recruited participants, impacting study capacity. Challenges are also posed by team handovers.
- **Scope Changes**: Significant alterations in the scope can lead to extended timelines for planned activities.
- **Experience and Training**: Some team members may lack experience with database locking activities. Similarly, investigational sites, particularly naïve ones, may also face these challenges.
- **Compliance:** possible issues jeopardizing data integrity.
- **Team Collaboration**: Disagreements and lack of effective collaboration within the team can result in failure.
- **High Pressure**: Excessive pressure and stress even if it is justified by tight deadlines.

Common challenges

- **Redundant activities:**
  - inclusion of out-of-scope data points
  - no targeted SDV(no CtQ approach)
  - data reports that are difficult to interpret and follow-up with truly pending items
  - unjustified need to collect additional data points
  - monitoring low risk and high-risk sites with the same approach (no Site Quality Risk Assessment)
- **eCRF amendment :** Due to eCRF migration number of queries may increase significantly and affect the workload of the sites and CRAs.
- **Technical Discrepancies**: There can be differences in technical requirements between vendor and sponsor systems, which need alignment. System incompatibility, different configurations and so on.
- **Site Commitment**: Investigator engagement is crucial. They may not fully understand data collection requirements, which can pose challenges in data entry and query resolution. Their availability might also be limited for CRA visits and addressing numerous queries. They can also underestimate the value of data base lock.
- **Availability of Key Members During Critical Stage:** one of the best examples is unexpected PI leave-

the PI is currently on vacation, with no sub-investigator trained or delegated to handle the eCRF sign-off responsibilities

or

the PI has a problem with accessing eCRF, and the global support team is unavailable to resolve this issue promptly

These circumstances have given rise to a series of unexpected and sometimes humorous stories as the study approaches the final day of database sign-off.

Strategies for success (1)

Challenges	Mitigations
Timelines	• Establish timelines early in the process with minimal chances for alteration to ensure a structured project flow. • Conduct a feasibility assessment with the involvement of all key stakeholders to ensure realistic planning and resource allocation. • Implement mini milestones for data cleaning (incremental approach) and source verification prior to the Data Cut-Off (DCO). This approach helps prevent data backlogs during intensive cleaning cycles. Consider batch processing, such as cleaning visits' or subjects' batches, to streamline the process.
Communication	• Clearly communicate expectations to all stakeholders to ensure alignment and understanding. • Hold consistent meetings with delivery team members- DM teams, local study teams, and vendors, to facilitate coordination and progress updates. • Ensure CRAs receive reliable reports, including metrics on pending items and SDV/SDR, on a regular basis. • Distribute newsletters/use appropriate channels to keep all team members informed about project developments, expectations, and important updates. • Communication with Biostatistician can help to avoid data quality and integrity issues.
Resources	• Leadership should ensure proper resourcing, coverage and continuity. • Allocate resources according to the anticipated workload. For instance, the FTE for CRAs should align with the expected volume of source verification activities and site support. • DM team regional coverage could be crucial for urgent support.
Experience	• Ensure that the right individuals are assigned to the project to leverage their expertise effectively. Seek additional support from experienced specialists when necessary. Support can be temporary.
Compliance	• Make sure CDL panning accounts for all procedural requirements. • Current SOPs/WI should be checked in advance. • In case of Sponsor/Vendor partnership, clearly determine and specify which processes should be followed to avoid confusion.
Team Collaboration	• With strong collaboration and a unified commitment to common goals, achieving success becomes possible. • Foster an environment of collaboration to ensure team members work effectively towards common goals. • Counterpart meetings should be encouraged

Strategies for success(2)

Challenges	Mitigations
eCRF revision	• To prevent the need for updates during the study, design the electronic eCRF and data entry instructions meticulously. This approach ensures site staff enter data correctly from the outset, eliminating the necessity for adding extra variables or modifying existing fields. • Create edit checks meticulously to avoid generating misleading automatic queries. Ensure that query text is clear and understandable. Regularly monitor the number of queries to identify those that are unclear or incorrectly generated.
Technical discrepancies	• Proactively identify and escalate technical discrepancies to the appropriate team for swift resolution. • Conduct troubleshooting and access verification well in advance to prevent potential delays or issues. • Risk assessment.
Scope Changes	• The global study team should engage in thorough planning and define the project scope clearly. Present this plan to senior leaders for endorsement to minimize potential changes. • Variables supporting endpoint assessment should be clearly defined and shared in the plan.
High Pressure	• It is important to justify the reasons for high pressure and communicate them transparently. Both best and worst-case scenarios should be analyzed, considering the effort required for each. A thorough discussion should weigh different scenarios, and the best course of action should be collectively decided.

Strategies for success(3)

Challenges	Mitigations
Minimize or eliminate redundant activities	• Recent changes in data verification activities emphasize a focus on critical tasks that enhance study endpoints and address safety and data integrity issues effectively. • Carefully choose data points that require SDV. The Critical-to-Quality (CtQ) SDV tier should include only the variables that genuinely need verification, acknowledging that not all critical variables necessitate SDV. • Consider increasing the frequency of Remote Data Checks to promptly identify and address issues that can be detected remotely, avoiding unnecessary delays. • Monitoring intensity should be adjusted per site quality risk assessment level which assumes lower monitoring intensity for lower risk level sites.
Site commitment	• Maintain strong relationships with site staff and ensure clear, consistent communication. • Distribute regular newsletters or investigator letters outlining expectations and instructions for a successful database lock. • Provide robust support from the global medical monitoring team for effective query resolution. • Ensure all clinical trial agreements with Principal Investigators (PIs) are fulfilled promptly, including payments and the timely provision of study supplies.

Conclusions

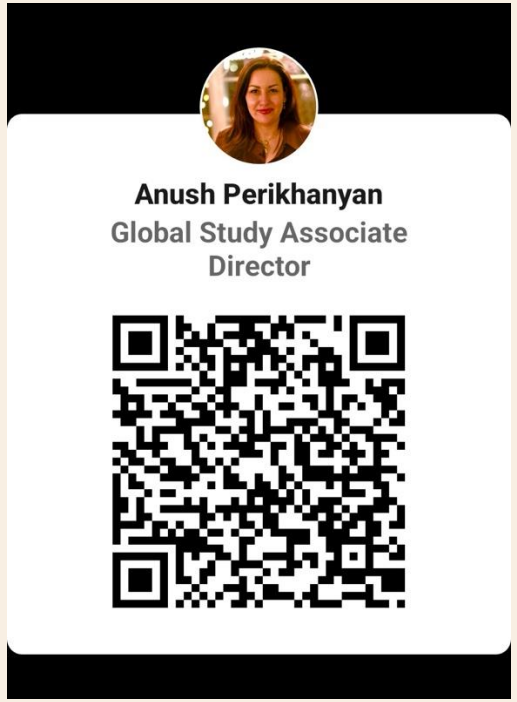
✳While modern, cost-effective approaches to data cleaning and oversight have proven their value, they are not yet universally embraced by all organizations.

✳Successful database lock can be achieved through thorough planning and by collaboratively addressing several key factors with the team and important stakeholders.

✳The database milestone is planned as a critical timepoint for data analysis and is crucial for the Sponsor to deliver on time. To achieve this, it's essential to foster a common understanding among all functions and vendors. Instead of pushing back against challenges, they should collaborate to suggest solutions that aid in achieving the planned database lock.

Closing Note and Q&A

An orchestra is a great example of a high-performing team. Any musical performance comes alive when everyone is playing in harmony, yet it only takes one person to be off-key and out of tune for the performance to be marred.
*How well are your team members playing together? **



*https://www.cio.com/article/230524/high-performing-teams-lessons-from-the-symphony-orchestra.html