Database Closure and Freezing

Module 10 Topic 10

Definition

- Data lock is a process which applies a condition to the Clinical Database where NO further updates/changes can be made.
- The Clinical Database is prevented from any accidental or unauthorized updates.
- This is generally done by revoking edit permissions to the Database to the study team members.

Why

- In CDM, the data that is collected is sent for statistical analysis. If the data is constantly being entered or changed in the database then each time the statistician has to refresh his datasets with the new data. Also the data will be inconsistent across different tables, thus statistical analysis in open data is risky and a very tedious process to do. Thus statistical analysis is done in Locked database.

Why (contd)

- Also in blinded randomized study, breaking of blind for analysis is always undertaken only after data lock. If the blind is broken prior to the lock then integrity of the clinical data can be questioned. If unblinding for any cause before data lock is done, it needs to be clearly documented in the report with reasons.

When

- Interim Analysis
- Safety reporting for Regulatory submission
- Independent Drug Monitoring Committee (IDMC)
- Final Analysis and reporting.

Interim Analysis

- Done per protocol specifications
- Regular intervals.
- Done on specified modules / on all modules
- Decides the proceedings of the trial
- Critical in planning any amendments for the protocol for successful completion of trial
- Helps in deciding progress of the trial and in deciding decisions related to regulatory submissions

Final Analysis

- Done after the LPLV is completed
- Collates the data of all the Interim analysis as well as the data after the last interim
- Collective results of all the modules
- Collective conclusion about the safety, efficacy and satisfaction of subjects about the study
- Final conclusion about the trial submission to the Regulatory authorities

Standards and Minimum Requirements

- Standard Operating Procedure
- Documentation of completed tasks and criteria.
- Notification to all team members about the database closure.
- Removal of the edit access to the study database
- Have written procedures with clear criterion for unlocking a database after closure
- Personnel who are authorized to order unlocking of the Database

Activities before Database Lock

- Make sure that all data have been received and processed
- All queries have been resolved
- Final review of all checks has taken place
- Manual checks has been completed
- Coding list has been reviewed for completeness and consistency
- Confirm that all hand written queries have been received

Activities before Database Lock (contd)

- External data (e.g. electronic laboratory data) are reconciled with the study database and are complete.
- If a separate, serious adverse event database exists, it is reconciled with the main study database
- Check that all electronic laboratory data is in-house
- Check that all PK/ PD data is in-house
- Identification and confirmation of protocol violators
- Confirm that all project database updates have been made

Database Closure Steps

- Perform a quality audit of database
- Estimate database error rate
- Check acceptability of error rate
- Document all these activities
- Notify team members of Database Closure

Database Closure Steps (contd)

- Perform comparison and issue report for all applicable studies
- Confirmation of Safety Database-to-Project Database Reconciliation
- Perform project database updates based on reconciliation
- Confirm that reconciliation is complete
- If no SAEs are reported, confirm that no adverse events are marked as serious
- Database Release Notification
- Restrict write access to the database

Database Closure Steps (contd)

- Once all steps are complete, a documented approval process should take place, which includes sign-off by relevant study personnel:
  - Clinical Data Manager
  - Biostatistician
  - Monitoring representative
  - Clinical/scientific representative
- Once approvals have been obtained, edit access to the database should be removed and the date documented

Errors after Database Lock

- After so much of validation, cleaning and review, some errors may still be detected after the database closure. To handle such situation, procedures and criteria for unlocking database should be prepared in advance.
- Careful consideration should be given as to how to handle and document the errors found after the Database lock.
- Assess the impact of errors on the database as a whole.
- Although some companies choose to change all errors found, others may only change those that have a major impact on the safety/efficacy analysis.

Errors after Database Lock (contd)

- Errors may also be documented in the statistical or clinical report.
- If the database is unlocked after initial lock, the process must be well controlled and once again, documented.
- Procedures should include notification to the project team, a clear definition of the change/s being made and the date of the change.
- Re-locking the database should follow the same process as the initial lock for notification/approval.

Lock and Freeze

- Database Lock:
  - Changes can be made by users with Privileged access only
  - New subjects can be added
  - Can run batch validation
  - Can be unlocked

- Database freeze:
  - No changes to existing data
  - No new data for existing subjects
  - Can add new subjects
  - Can run batch validation
  - Cannot Unfreeze

Best Practice

- Enter data as soon as possible after it is received.
- Run cleaning procedures throughout the study as data is collected so that the queries go out early. Towards the end of the study, the outstanding query should be only those pertaining to recently received data.
- Identify missing CRF pages and lab data by knowing what is expected. Use tracking systems.
- Audit data against the CRF early in the study to detect systematic problems.
- Maintain study documentation at the start of the study and make an effort to keep it updated as the study progresses.

Best Practice (contd)

- Database closure checklist
- Documentation / Audit trial
- Proper communication and efficiency
- A well defined and organized procedure must be followed to ensure that all data have been processed, the quality level assessed and relevant study personnel are notified or approve the database lock