Discrepancy Management & Data Closure



Module 8 Topic 4

Discrepancy

- What is Discrepancy?
- In simple terms it is an ERROR!
- Discrepancies are "Inconsistencies" found in clinical trial data which need to be corrected as per study protocol



Discrepancy

Why do we need this?

- Medical data is complex
- The data that is generated has regulatory implications
- In order to clean data to such a high level, questions will need to be asked
- These questions is known as Queries
- For Discrepancy we raise Query...therefore sometimes the activity that we do is known as Query management.



Types of Discrepancies

- System generated:
 - Univariate
 - Multivariate
- Manually raised:
 - Clinical Research Associate
 - Data entry
 - Data Manager raised query
 - Coders
 - Medical/ Clinical team



System Generated Discrepancy

Univariate:

 It is called as Univariate as it looks for a single field (E.g.: If data in the field is missing or incomplete)

Multivariate:

 It looks/compare with two or more different fields in single page, multiple page or multiple visits (E.g.: Conmed and Adverse event page)



Manually Generated Discrepancy

Clinical Research Associate:

After Source Data verification (SDV) or performing in-house review.

Data Entry Operator:

Operator comments



Manually Generated Discrepancy (contd)

Data Manger:

Reference to manual review, external checks, reports and listings, or some outliers detected by Statistical review

Coders:

Inconsistency in Medical terms in Medical History, Concomitant medications, Adverse event, Serious AE, etc...



Medical/ Clinical team

Types of Discrepancy

- Missing pages
- Inconsistent header information
- Incomplete data
- Incorrect data
- Missing data
- Illogical data
- Illegible data
- Inconsistent data
- To check if visits are compliant with the protocol
- To check whether the subjects meet the inclusion/exclusion criteria.



Creating Queries

- In paper studies CDM staff send out "Data Clarification Forms" or DCFs in process of query management
- Other names given to this form: Query forms,
 Correction forms, Discrepancy forms
- In eDC, Queries are generated within the system which can be viewed by the other parties involved like Monitors and Investigator sites.
- Discrepancies covered on a single form will all belong to one site but may refer to:
 - One or more patient for that investigator
 - A single patient but multiple CRF pages
 - A single patient & a single CRF page only



Tips for Generating Query

How to write a query:

- Be accurate, specific and sufficient
- Use simple language.
- Be neutral and non threatening
- And do NOT write queries that suggest a specific answer.
- Be polite, use 'Please clarify', 'Please provide' or 'Please amend' and rarely use 'Please confirm'



Tracking Queries

- What discrepancies were sent?
 - Data management tracks flow of queries to & fro between self & investigator
- Have queries been returned & processed?
 - Data management ensures that query responses are received & integrated within specified timeliness
- Which queries went & when?
 - Tracking spreadsheets to be maintained



Resolving Queries

- Data management integrates query response into database
- Common types of resolutions:
 - Value in question maybe correct as is
 - Actual measurement may replace a missing value
 - Corrected value may replace an incorrect value
 - Value maybe wrong but no corrected value is available



Re-queries

- Needed when investigator provides
 - No response
 - Incorrect response
 - Inconsistent response
 - Incomplete response (including signature)
 - Same response
- Possible approaches to handle incomplete resolutions:
 - Re-issue discrepancy on a new query form
 - Leave that one discrepancy as unresolved & await a re-send of query form
 - Leave it as unresolved & await correct CRF



Discrepancy Statuses

- Identified or registered
- Reviewed & still open
- Sent to investigator
- Passively linked
- Data updated
- Closed

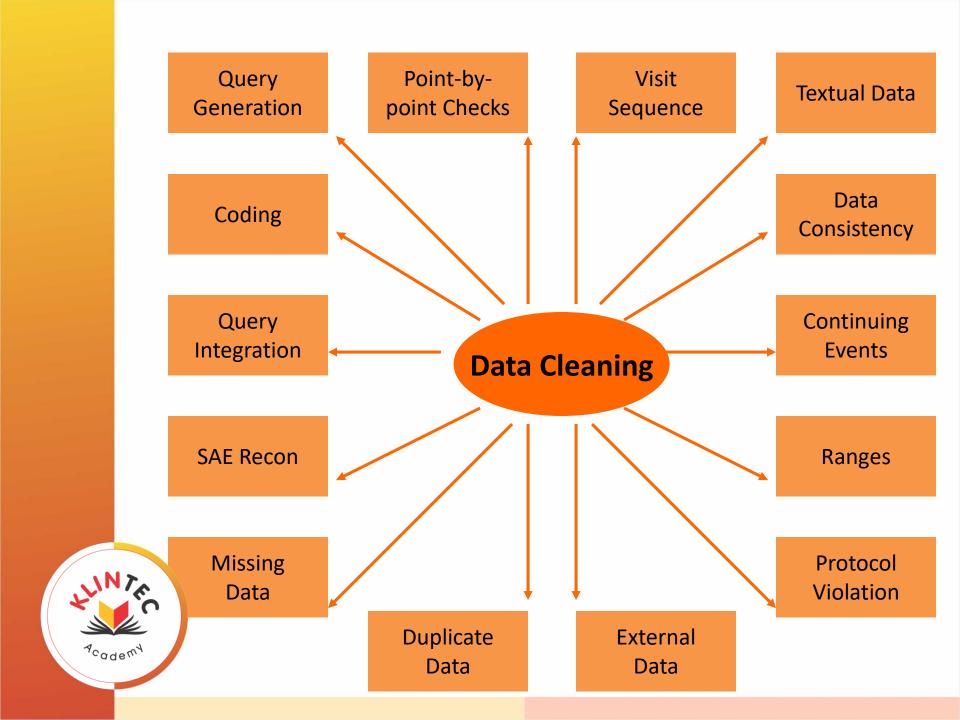


Clean Data Checklist

- Refers to a list of checks to be performed by data management while cleaning database
- Checklist is developed & customized as per client specifications
- Provides list of checks to be performed both on
 - Ongoing/periodic basis
 - Towards end of study
- Strict adherence to checklist prevents missing out on any of critical activities







Database Closure and Freezing



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

- 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.
- Statistical analysis on an open data is risky and tedious hence done on locked database
- To maintain data integrity, unblinding is only after database lock.
- 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.



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

