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

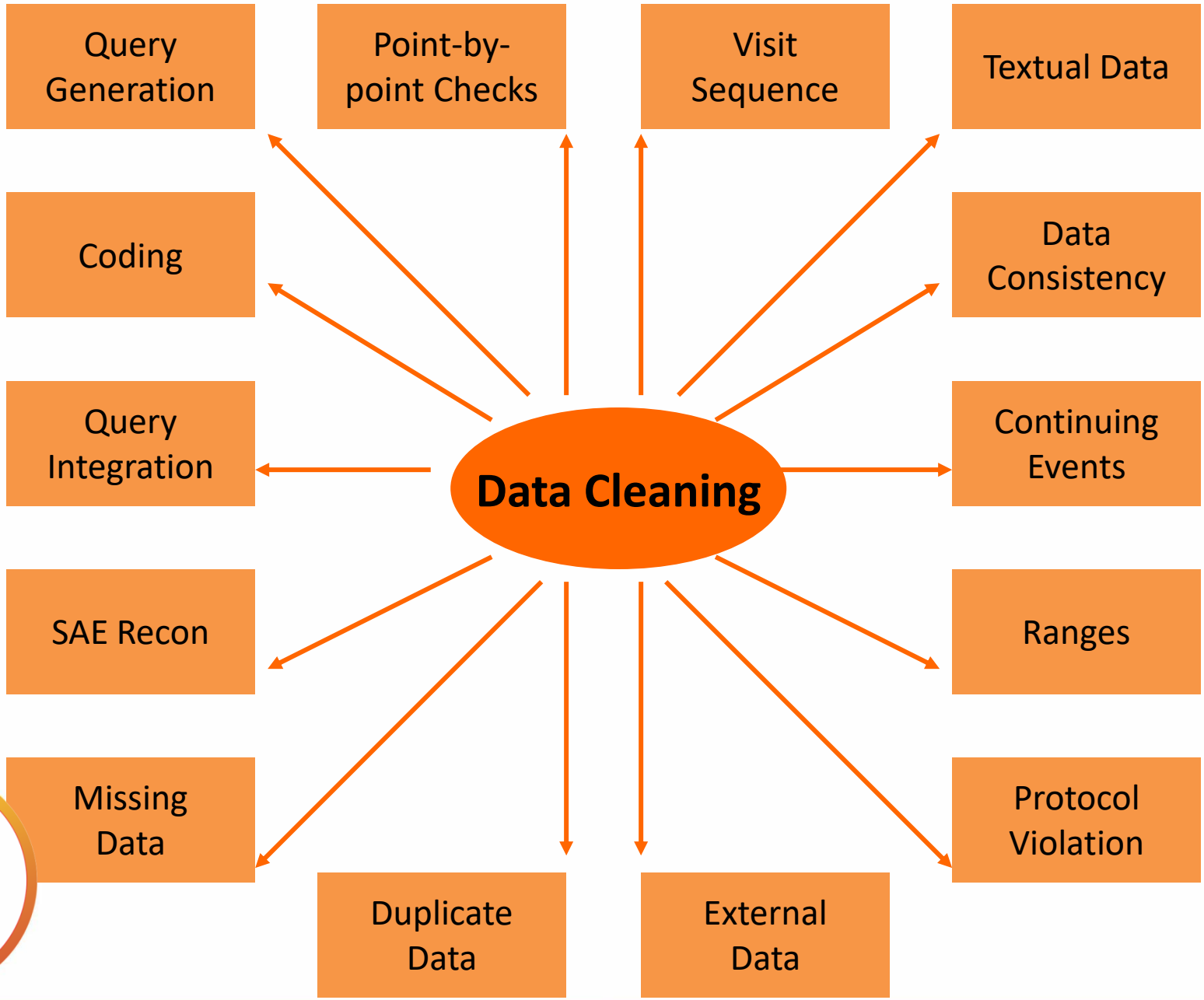
- Possible approaches to handle incomplete resolutions:
  - Re-issue discrepancy on a new query form
  - Leave that one discrepancy as unresolved & await a re-send of query form
  - Leave it as unresolved & await correct CRF

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


Data Cleaning
Query Generation
Point-by-point Checks
Visit Sequence
Textual Data
Coding
Data Consistency
Query Integration
Continuing Events
SAE Recon
Ranges
Missing Data
Protocol Violation
Duplicate Data
External Data

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