MedDRA® Coding Quality: How to Avoid Common Pitfalls

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Data Quality in Clinical Development

- Highly regulated environment with strong emphasis on safety surveillance and data quality
- Applies to clinical trials and post-marketing arena
- Increasing harmonization of safety reporting regulations globally

What is Meant by Good Quality Data?

- Complete
- Accurate
- Diagnosis supported by appropriate investigations
- Causality assessment for adverse events
Coding of Clinical Trial Data

- Most data entered on Case Report Forms are “coded” in some form
- Facilitates storage, retrieval, analysis, and presentation of data
- Some coding is performed by investigators at point of data entry
  - For example, numeric codes for severity of adverse event: 1 = mild, 2 = moderate, etc.
- Other coding of text data is performed by sponsor company after data collection
- **Accuracy of initial coding determines accuracy of analysis**

Quality of Input = Quality of Output
MedDRA Definition

MedDRA is a clinically-validated international medical terminology used by regulatory authorities and the regulated biopharmaceutical industry. The terminology is used through the entire regulatory process, from pre-marketing to post-marketing, and for data entry, retrieval, evaluation, and presentation.

Key Features of MedDRA

- Structure facilitates data analysis and reporting and electronic communication
- Large terminology with >69,000 terms at lowest level – allows greater specificity
- Approx. 19,000 Preferred Terms (PTs), each representing a unique medical concept
- Used for coding adverse events, signs and symptoms, procedures, investigations, indications, medical and social histories, medication errors and product quality issues
MedDRA Structure

**SOC** = Cardiac disorders

**HLGT** = Cardiac arrhythmias

**HLT** = Rate and rhythm disorders NEC

**PT** = Arrhythmia

MedDRA Structure (cont)

- **SOC** Musculoskeletal and connective tissue disorders
  - (a) Bone disorders (excl congenital and fractures)
  - (b) Connective tissue disorders (excl congenital)
  - (c) Fractures
  - (d) Joint disorders
  - (e) Muscle disorders
    - (i) Muscle infections and inflammations
    - (ii) Muscle injuries
    - (iii) Muscle pains
      - (a) Fibromyalgia
        - (ii) Fibromyalgia
          - (iii) Fibromyalgia syndrome
          - (iv) Fibromyalgia worsened
        - (v) Fibromyositis
          - (vi) Fibrositis
          - (vii) Muscular rheumatism
        - (viii) Myalgia
        - (ix) Myalgia intercostal
        - (x) Myofascial pain syndrome
Problems With Coding Data

- Appropriate coding requires clear initial data
- What is clear to investigator at point of data entry may be unclear to sponsor at point of data coding
- Sponsor must only code reported verbatim term; not permitted to interpret or draw information from other sources
- Example: Ambiguous information
  - Congestion (nasal, liver, sinus, pulmonary?)
  - Cramp (muscle, menstrual, abdominal?)
  - Pain (pain where?)

Problems With Coding Data (cont)

- Example: Ambiguous abbreviations
  - MI (myocardial infarction or mitral incompetence?)
  - GU pain (gastric ulcer pain or genito-urinary pain?)
  - Decreased BS (breath sounds, bowel sounds or blood sugar?)
- Exercise caution with abbreviations that could be misinterpreted
- ECG, COPD, HIV are examples of standard abbreviations
Problems With Coding Data (cont)

• Example: Vague information
  – Patient felt “fuzzy”, “weird”, “experienced every adverse event”
  **Try to use accepted medical terminology**

• Example: Non-specific information
  – “Left wrist edema” (coded as LLT *Peripheral edema*)
  – More specific - “Injection site edema left wrist”
    (coded as LLT *Injection site edema*)

Problems With Coding Data (cont)

• Death, hospitalization, and disability are outcomes and are not usually considered to be adverse events
• Provide details of underlying event, if known
• Examples:
  – “Death due to myocardial infarction” (Coded as LLT *Myocardial infarction* with death captured as outcome)
  – “Hospitalization due to congestive heart failure” (Coded as *Congestive heart failure* with hospitalization captured as outcome)
Problems With Coding Data (cont)

• Example: Ambiguous laboratory data
  – “Glucose of 40”
  – (Source of specimen - blood, urine, CSF? What units?)
  – Would have to code as LLT *Glucose abnormal* if additional clarification is not obtained

• Example: Conflicting laboratory data
  – “Hyperkalemia with serum potassium of 1.6 mEq/L”
  – Would have to code as LLT *Serum potassium abnormal*

If using numeric values, provide units and reference range. Be specific about specimen source and diagnostic result/clinical diagnosis.

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Problems With Coding Data (cont)

• Example: Combination terms
  – Diarrhea, nausea and vomiting

*Try to avoid combination terms* – these will have to be split into three individual terms

Diarrhea
Nausea
Vomiting
Reporting a Specific Diagnosis

- Where possible, report most important medical event or specific diagnosis rather than individual signs and symptoms
- Can provide provisional diagnosis, e.g., “possible”, “presumed”, “rule out”
- Accuracy is important in preventing dilution of safety signals or generating false signals

<table>
<thead>
<tr>
<th>SIGNS and SYMPTOMS</th>
<th>DIAGNOSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest pain, dyspnea, diaphoresis, ECG changes</td>
<td>Myocardial infarction</td>
</tr>
</tbody>
</table>

Benefits of Quality Data

- Accuracy in diagnosis is important for detection and evaluation of safety signals
- Accurate and timely information on issues that affect conduct of clinical trial and affect patient safety
- Improved communication among sponsors, investigators, and regulatory agencies about medicinal products
  - Ensures accuracy of information about product including investigators’ brochures and prescribing information
  - Benefits medical professionals and patients
How to Achieve Quality in MedDRA Coding

• Quality assurance steps
• Coding conventions
• Synonym lists

Quality Assurance Steps

• Coding QA reports
• Human oversight of automated coding results
  – E.g., “Adrenal insufficiency secondary to chronic traditional medication intake” autoencoded as LLT Secondary adrenal insufficiency
  – Secondary adrenal insufficiency is based on lack of ACTH or CRH
  – Better term is LLT Adrenal insufficiency
Quality Assurance Steps (cont)

- Qualification of coder/review staff
- Errors in MedDRA should be addressed by submission of Change Requests to MSSO; no *ad hoc* structural alterations to MedDRA

MedDRA Coding Conventions

- Differences in medical aptitude of coders
- Consistency concerns (many more “choices” to manually code terms in MedDRA compared to older terminologies)
- Even with an autoencoder, may still need manual coding
- Should be consistent with ICH’s MedDRA Term Selection: Points to Consider document
Synonym Lists

• Can be derived from existing term lists or directly from verbatims
• For recurring, but unusual, verbatims – one-time assignment to a MedDRA term
• Enforces consistency by limiting choices once MedDRA term is assigned
• Increases likelihood of autoencoding “hit”
• Natural outgrowth of a legacy data conversion
• Maintenance required

In Summary…

• Quality of initial data and quality of coding ultimately affect quality of analysis
• Be aware of potential pitfalls in coding with MedDRA
• There are ways to address quality issues such as coding conventions, etc.
Quality Data

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Thank You