MedDRA as ICH Terminology Standard for Drug Safety Information, with Coding Exercises

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MedDRA MSSO
MedDRA was developed under the auspices of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). The activities of the MedDRA Maintenance and Support Services Organization (MSSO) are overseen by an ICH MedDRA Management Committee, which is composed of the ICH parties, the Medicines and Healthcare products Regulatory Agency (MHRA) of the UK, Health Canada, and the WHO (as Observer).
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Course Overview

• Gain knowledge of MedDRA’s scope, structure, and characteristics
• Discuss important principles in the MedDRA Term Selection: Points to Consider document
• Learn about the available MedDRA browsers
• Discuss coding examples
• Present some MedDRA coding “pearls”
• Conclude with a question and answer session
MedDRA Overview
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.
Where MedDRA is Used

- Preclinical Testing
- Clinical Phase I
- Clinical Phase II
- Clinical Phase III
- Marketed Product Phase IV

Regulatory Authority and Industry Databases
Individual Case Safety Reports and Safety Summaries

- Clinical Study Reports
- Investigators’ Brochures
- Core Company Safety Information
- Marketing Applications
- Publications
- Prescribing Information
- Advertising
ICH E2B Expert Working Group

Implementation Guide for
Electronic Transmission of Individual Case Safety Reports (ICSRs)

E2B(R3) Data Elements and Message Specification

Version 5.01, 12 April 2013
MedDRA is in 125 countries
Scope of MedDRA

**IN**
- Medical conditions
- Indications
- Investigations (tests, results)
- Medical and surgical procedures
- Medical, social, family history
- Medication errors
- Product quality issues
- Device-related issues
- Product use issues
- Pharmacogenetic terms
- Toxicologic issues
- Standardized queries

**OUT**
- Frequency qualifiers
- Numerical values for results
- Severity descriptors
- Not an equipment, device, diagnostic product dictionary
- Not a drug dictionary
- Patient demographic terms
- Clinical trial study design terms
MedDRA Structure

- System Organ Class (SOC) (27)
- High Level Group Term (HLGT) (337)
  - High Level Term (HLT) (1,737)
  - Preferred Term (PT) (23,708)
  - Lowest Level Term (LLT) (80,262)
System Organ Classes

- Blood and lymphatic system disorders
- Cardiac disorders
- Congenital, familial and genetic disorders
- Ear and labyrinth disorders
- Endocrine disorders
- Eye disorders
- Gastrointestinal disorders
- General disorders and administration site conditions
- Hepatobiliary disorders
- Immune system disorders
- Infections and infestations
- Injury, poisoning and procedural complications
- Investigations
- Metabolism and nutrition disorders
- Musculoskeletal and connective tissue disorders
- Neoplasms benign, malignant and unspecified (incl cysts and polyps)
- Nervous system disorders
- Pregnancy, puerperium and perinatal conditions
- Product issues
- Psychiatric disorders
- Renal and urinary disorders
- Reproductive system and breast disorders
- Respiratory, thoracic and mediastinal disorders
- Skin and subcutaneous tissue disorders
- Social circumstances
- Surgical and medical procedures
- Vascular disorders
Synonyms, lexical variants, sub-elements

**SOC** = Cardiac disorders

**HLGT** = Cardiac arrhythmias

**HLT** = Rate and rhythm disorders NEC

**PT** = Arrhythmia

**LLT**
- Arrhythmia
- **NOS**
- **Arrhythmia**
- **(Non-current)**
  - Other specified cardiac dysrhythmias
- **Dysrhythmias**

Not all LLTs shown
Non-Current Terms

- Flagged at the LLT level in MedDRA
- Not recommended for continued use
- Retained to preserve historical data for retrieval and analysis
- Terms that are vague, ambiguous, outdated, truncated, or misspelled
- Terms derived from other terminologies that do not fit MedDRA rules
A Multi-Axial Terminology

- Multi-axial = the representation of a medical concept in multiple SOCs
  - Allows grouping by different classifications
  - Allows retrieval and presentation via different data sets
- All PTs assigned a primary SOC
  - Determines which SOC will represent a PT during cumulative data outputs
  - Prevents “double counting”
  - Supports standardized data presentation
  - Pre-defined allocations should not be changed by users
SOC = Respiratory, thoracic and mediastinal disorders (Secondary SOC)

HLGT = Respiratory tract infections

HLT = Viral upper respiratory tract infections

PT = Influenza

SOC = Infections and infestations (Primary SOC)

HLGT = Viral infectious disorders

HLT = Influenza viral infections
Rules for Primary SOC Allocation

- PTs represented in only one SOC are automatically assigned that SOC as primary
- PTs for diseases, signs and symptoms are assigned to prime manifestation site SOC
- Congenital and hereditary anomalies terms have SOC *Congenital, familial and genetic disorders* as Primary SOC
- Neoplasms terms have SOC *Neoplasms benign, malignant and unspecified (incl cysts and polyps)* as Primary SOC
  - **Exception:** Cysts and polyps have prime manifestation site SOC as Primary SOC
- Infections and infestations terms have SOC *Infections and infestations* as Primary SOC
If a PT links to more than one of the exceptions, the following priority will be used to determine primary SOC:

1st: Congenital, familial and genetic disorders
2nd: Neoplasms benign, malignant and unspecified (incl cysts and polyps)
3rd: Infections and infestations
PTs in the following SOCs *only* appear in that particular SOC and not in others, i.e., they are not multi-axial

- *Investigations*
- *Surgical and medical procedures*
- *Social circumstances*
What are Coding Conventions?

- Written guidelines for coding with MedDRA in your organization
- Support accuracy and consistency
- Common topics
  - Misspellings, abbreviations and acronyms
  - Combination terms and “due to” concepts
  - “Always query” terms, e.g., “Chest pain”
- Should be consistent with the MedDRA Term Selection: Points to Consider document
Why Do We Need 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
ICH M1 Points to Consider Working Group (PtC WG)

- Regulators and industry from EU, US, and Japan
- Health Canada, Canada
- MFDS, Republic of Korea
- ANVISA, Brazil
- NMPA, China
- MSSO
- JMO
- WHO (Observer)

November 2017, Geneva, Switzerland
<table>
<thead>
<tr>
<th>PtC Category</th>
<th>PtC Document</th>
<th>Purpose</th>
<th>Languages</th>
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</thead>
<tbody>
<tr>
<td>Term Selection</td>
<td>MedDRA Term Selection: Points to Consider</td>
<td>Promote accurate and consistent coding with MedDRA</td>
<td>English and Japanese</td>
<td>Updated with each MedDRA release</td>
</tr>
<tr>
<td></td>
<td>MedDRA Term Selection: Points to Consider Condensed Version</td>
<td>Shorter version focusing on general coding principles to promote accurate and consistent use of MedDRA worldwide</td>
<td>All MedDRA languages (except English and Japanese)</td>
<td>Update as needed</td>
</tr>
<tr>
<td>Data Retrieval and Presentation</td>
<td>MedDRA Data Retrieval and Presentation: Points to Consider</td>
<td>Demonstrate how data retrieval options impact the accuracy and consistency of data output</td>
<td>English and Japanese</td>
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<tr>
<td>General</td>
<td>MedDRA Points to Consider Companion Document</td>
<td>More detailed information, examples, and guidance on specific topics of regulatory importance. Intended as a “living” document with frequent updates based on users’ needs. First edition covers data quality and medication errors.</td>
<td>English and Japanese</td>
<td>Updated as needed</td>
</tr>
</tbody>
</table>
MedDRA® TERM SELECTION: POINTS TO CONSIDER
ICH-Endorsed Guide for MedDRA Users

Release 4.17
Based on MedDRA Version 22.0

1 March 2019

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• Provides term selection advice for industry and regulatory purposes
• Objective is to promote accurate and consistent term selection to facilitate a common understanding of shared data
• Recommended to be used as basis for individual organization’s own coding conventions
MedDRA Term Selection: PTC (cont)

- Developed by a working group of the ICH Management Committee
- Updated twice yearly with each MedDRA release
- Available on MedDRA and JMO websites
  - English and Japanese
  - Word ("clean" and "redlined"), PDF, HTML formats
  - "Redlined" document identifies changes made from previous to current release of document
In some cases with more than one option for selecting terms, a “preferred option” is identified but this does not limit MedDRA users to applying that option. Organizations should be consistent in their choice of option.

Section 4.1 – Versioning (Appendix)
  – 4.1.1 Versioning methodologies
  – 4.1.2 Timing of version implementation
General Term Selection Principles

- Quality of Source Data
- Quality Assurance
- Do Not Alter MedDRA
- Always Select a Lowest Level Term
- Select Only Current Lowest Level Terms
- When to Request a Term
- Use of Medical Judgment in Term Selection
- Selecting More than One Term
- Check the Hierarchy
- Select Terms for All Reported Information, Do Not Add Information
Quality of Source Data

Quality Assurance

• Quality of original information impacts quality of output
• Obtain clarification of data
• Can be optimized by careful design of data collection forms and proper training of staff
• Organizations’ coding guidelines should be consistent with MTS:PTC
• Review of term selection by qualified individuals
• Human oversight of automated coding results
• MedDRA is a standardized terminology with a pre-defined term hierarchy
• Users must not make *ad hoc* structural alterations, including changing the primary SOC allocation
• If terms are incorrectly placed, submit a change request to the MSSO
Always Select a Lowest Level Term
Select Only Current LLTs

- Lowest Level Term that most accurately reflects the reported verbatim information should be selected
- Degree of specificity may be challenging
  - Example: “Abscess on face” → select “Facial abscess,” not simply “Abscess”
- Select current LLTs only
  - Non-current terms for legacy conversion/historical purposes
When to Request a Term
Use of Medical Judgment

• Avoid company-specific “work-arounds” for MedDRA deficiencies. If concept not adequately represented in MedDRA, submit Change Request to MSSO.

• If no exact match in MedDRA, use medical judgment to match to an existing term that adequately represents the concept.
Introduction to the MedDRA Browsers
MSSO’s MedDRA Browsers

- MedDRA Desktop Browser (MDB)
  - Download MDB and release files from MedDRA website

- MedDRA Web-Based Browser (WBB)
  - [https://tools.meddra.org/wbb/](https://tools.meddra.org/wbb/)

- Features
  - Both require MedDRA ID and password
  - View/search MedDRA and SMQs
  - Support for all MedDRA languages
  - Language specific interface
  - Ability to export search results and Research Bin to local file system
MedDRA Desktop Browser (MDB) and Web-Based Browser (WBB) Update

• New functionality for users
  – Preview upcoming (supplemental) changes in next release*
  – View primary and secondary link information
  – Upload terms to run against SMQs
  – Advanced search options (e.g., NOT, OR)

*Supplemental view not available on MDB
Coding Exercises
Assessing the Reported Information

• Consider what is being reported. Is it a:
  – Clinical condition - Diagnosis, sign or symptom?
  – Indication?
  – Test result?
  – Injury?
  – Procedure?
  – Medication error?
  – Product use issue?
  – Product quality issue?
  – Social circumstance?
  – Device issue?
  – Procedural complication?

  – Is it a combination of these?

The type of report will influence the way you search for a suitable LLT. It may indicate in which SOC you expect to find the closest match.
Coding Exercise 1
Which LLT Would You Select?

Verbatim: “Man with decreased fertility.”

A. Infertility
B. Fertility decreased male
C. Infertility male
D. Fertility decreased
Coding Exercise 2
Which LLT Would You Select?

Verbatim: “Became color blind in adolescence”

A. Color blindness
B. Blindness color
C. Colour blindness acquired
D. Color blindness acquired
Coding Exercise 3
Which LLT Would You Select?

**Verbatim**: “Turned very greasy”

A. Ill-defined disorder
B. Unevaluable event
C. Skin greasy
D. Unevaluable reaction
Coding Exercise 4
Which LLT Would You Select?

**Verbatim:** “Deliberately took an overdose”

A. Intentional overdose
B. Overdose NOS
C. Deliberate overdose
D. Overdose
Verbatim: “The 2-year-old accidentally took his mother’s medication”

A. Accidental overdose
B. Accidental exposure to product by child
C. Accidental drug intake by child
D. Accidental ingestion
Coding Exercise 6
Which LLT Would You Select?

Verbatim: “Infection after surgery”

A. Infection
B. Postoperative wound infection
C. Surgical wound infection
D. Postoperative infection
Coding Exercise 7
Which LLT Would You Select?

Verbatim: “Had MI”

A. Myocardial infarction
B. Ill-defined disorder
C. MI
D. Unevaluable event
Coding Exercise 8
Which LLT Would You Select?

Verbatim:
“Hypernatraemia (Serum sodium = 115 mEq/L)”

A. Serum sodium abnormal
B. Hypernatraemia
C. Hyponatraemia
D. Serum sodium decreased
Coding Exercise 9
Which LLT Would You Select?

Verbatim: “Took intramuscular drug by mouth”

A. Wrong route of administration
B. Drug administered via inappropriate route
C. Medication error
D. Intramuscular formulation administered by other route
Coding Exercise 10
Which LLT Would You Select?

Verbatim: “Death from cerebral haemorrhage”

A. Sudden death
B. Death
C. Cerebral haemorrhage
D. Brain death
Coding Exercise 11

Which LLT Would You Select?

Verbatim: “The doctor mistakenly prescribed the wrong drug; the pharmacist noticed the error before dispensing the drug”

A. Wrong drug dispensed
B. Medication error
C. Intercepted drug prescribing error
D. Intercepted drug dispensing error
Coding Exercise 12
Which LLT Would You Select?

Verbatim: “Died as a result of a suicide attempt”

A. Suicide gesture
B. Attempted suicide
C. Completed suicide
D. Death
Coding Exercise 13
Which LLT Would You Select?

Verbatim: “Dose taken was below the minimum recommended dose in the product label”

A. Underdose
B. Drug administration error
C. Accidental underdose
D. Incorrect dosage administered
Coding Exercise 14
Which LLT Would You Select?

Verbatim: “Abused by her husband”

A. Physical abuse
B. Battered wife
C. Spousal abuse
D. Victim of spousal abuse
Coding Exercise 15

Which LLTs Would You Select?

Verbatim: “Because the label on the package was missing the wording on dosing information, the patient took the drug twice daily instead of once daily, resulting in the administration of an overdose.”

A. Product label issue
B. Product label missing
C. Product label missing text
D. Wrong dose administered
E. Once daily dose taken more frequently
F. Inappropriate schedule of drug administration
G. Overdose
H. Accidental overdose
Some MedDRA Coding “Pearls”
• First, try using reporter’s actual words
• Be aware of MedDRA’s specificity
• Exploit MedDRA’s hierarchy – if an LLT is close to what you need, look at its “siblings” and “parent”
• Check where the LLT lies in MedDRA (i.e., check the hierarchy above to be sure it represents the verbatim term accurately)
• Use “top-down” and “bottom-up” navigation
• Use available resources for difficult verbatim terms (web search, medical dictionaries, colleagues)
• Use advanced Boolean search terms features (i.e., “begins with”, “exact match”, “ends with”, “not contains”, “and”, “or”) when needed
• Become familiar with MedDRA Concept Descriptions
• And most important of all… get more coding training!
In this course, we:

• Reviewed the scope, structure, and characteristics of MedDRA
• Were introduced to the MedDRA Term Selection: Points to Consider document and some of its specific principles
• Were introduced to the MedDRA browsers
• Discussed coding examples with answers
• Presented some MedDRA coding “pearls”
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- Email
  - mssohelp@meddra.org
- Frequently Asked Questions
  - www.meddra.org/faq
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