Coding with MedDRA®

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MedDRA and the MSSO

- International support and development of terminology
- Foster use of MedDRA through communications and educational offerings
- “Custodians”, not owners, of the terminology
- JMO (partner organization for Japanese-language MedDRA)
- Governed by a Management Board (industry, regulators, multi-national, other interested parties)
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.

Regulatory Status of Mandate

• US FDA
  – Used in FDA’s adverse event database (AERS)

• Japanese Ministry of Health, Labour and Welfare
  – Mandatory use for electronic reports
  – Used in Periodic Infection and Safety Reports
  – For medical devices with biological components, infections to be described with MedDRA terms
• European Union
  – Clinical trials
    • SUSARs (Suspected Unexpected Serious Adverse Reactions) – use MedDRA LLTs (current or previous version)
  – Volume 9A (all authorized medicinal products, including OTC)
    • Individual Case Safety Reports (ICSRs) – use MedDRA LLTs (current or previous version)
    • For adverse reactions in Periodic Safety Update Report
    • Standardised MedDRA Queries (SMQs) recommended for signal detection

• European Union (cont)
  – Interface between EudraVigilance and EU Risk Management Plan
    • To code indications, risks, interactions (potential and identified)
  – Summary of Product Characteristics guideline
    • Use in Undesirable Effects section
Regulatory Status of Mandate (cont)

• ICH M4E Guideline on Common Technical Document
  – Recommended in adverse event summary tables
• Canada
  – Reporting Adverse Reactions to Marketed Health Products (draft guidance)
    • Recommended as standard for adverse reaction reports
  – Product Monograph (labeling)
    • Preferred terminology for adverse drug reactions

Scope of MedDRA

- Diseases
- Diagnoses
- Signs
- Symptoms
- Therapeutic indications
- Investigation names & qualitative results
- Medical & surgical procedures
- Medical, social, family history

Terms from:
- COSTART®
- WHO-ART®
- HARTS®
- J-ART®

Frequency qualifiers
Numerical values for results
Severity descriptors
Equipment, device, diagnostic product terms

Drug product terms
Patient demographic terms
Clinical trial study design terms
MedDRA Structure

System Organ Class (SOC) (26)
High Level Group Term (HLGT) (333)
High Level Term (HLT) (1,699)
Preferred Term (PT) (18,483)
Lowest Level Term (LLT) (67,159)

MedDRA Term Level Definitions

- **SOC** - Highest level of the terminology, and distinguished by anatomical or physiological system, etiology, or purpose
- **HLGT** - Subordinate to SOC, superordinate descriptor for one or more HLTs
- **HLT** - Subordinate to HLGT, superordinate descriptor for one or more PTs
- **PT** - Represents a single medical concept
- **LLT** - Lowest level of the terminology, related to a single PT as a synonym, lexical variant, or quasi-synonym (Note: All PTs have an identical LLT)
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
- 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

Examples of LLTs

SOC = Cardiac disorders

HLGT = Cardiac arrhythmias

HLT = Rate and rhythm disorders NEC

PT = Arrhythmia

LLT Arrhythmia NOS

LLT Arrhythmia

LLT Arrhythmia

LLT (Non-current) Other specified cardiac dysrhythmias

LLT Dysrhythmias
Non-Current Terms

- Non-current terms are flagged at the LLT level within MedDRA
- Not recommended for continued use
- Retained within the terminology 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

MedDRA Codes

- Each MedDRA term assigned an 8-digit numeric code
- The code is non-expressive
- Codes can fulfill a data field in various electronic submission types (e.g., E2B)
- Initially assigned alphabetically by term starting with 10000001
  - New terms are assigned sequentially
- Supplemental terms are assigned codes
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
- Purpose of Primary SOC
  - Determines which SOC will represent a PT during cumulative data outputs
  - Is used to support consistent data presentation for reporting to regulators

A Multi-Axial Terminology (cont)

SOC = Respiratory, thoracic and mediastinal disorders

HLGT = Respiratory tract infections

HLT = Viral upper respiratory tract infections

PT = Influenza

SOC = Infections and infestations

HLGT = Viral infectious disorders

HLT = Influenza viral infections
A Multi-Axial Terminology (cont)

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*

Rules for Primary SOC Allocation

- 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
Primary SOC Priority

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

What Is “Coding”?

Code

1: a systematic statement of a body of law; especially one given statutory force
2: a system of principles or rules <moral code>
3 a: a system of signals or symbols for communication
   b: a system of symbols (as letters or numbers) used to represent assigned and often secret meanings
4: genetic code
5: a set of instructions for a computer
What Does MedDRA Offer?

- Size and specificity ("granularity")
- Hierarchy/grouping terms
- "Support" SOCs widen data collection/analysis options
- Up-to-date and medically rigorous
- User-responsive
- STANDARDIZATION

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
“MedDRA Term Selection: Points to Consider”

- An ICH-endorsed guide for MedDRA users
- Developed to promote medically accurate and consistent use of MedDRA in exchange of data (ultimately, for “medically meaningful” retrieval and analysis)
- In some cases with more than one option for selecting terms, a “preferred option” is identified but this does not limit MedDRA users to using that option

Term Selection PTC (cont)

- Developed by a working group of the ICH Steering Committee
  - Regulators and industry representatives
  - EU, Japan, USA
  - Canadian observer, MSSO, JMO
General Principles

- Quality of source data
- Level of term selection
- Use of “Current”/“Non-current” Lowest Level Terms (LLTs)
- Choice of term
- Do not subtract or add information
- Quality Assurance

Term Selection Points

- Diagnoses and provisional diagnoses with or without signs and symptoms
- Death and other patient outcomes
- Suicide and self-harm
- Conflicting/ambiguous/vague information
- Combination terms
- Age vs. Event specificity
- Body site vs. Event specificity
- Location vs. Infectious agent
- Pre-existing medical conditions
- Exposure during pregnancy and breast feeding
- Congenital terms
- Neoplasms
- Medical/surgical procedures
Term Selection Points (cont)

- Investigations
- Medication/administration errors and accidental exposures
- Transmission via medicinal product of infectious agent
- Overdose/Toxicity/Poisonings
- Device terms
- Drug interactions
- No adverse effect
- Unexpected therapeutic effect
- Modification of effect
- Social circumstances
- Medical and/or social history
- Indication for product use
- Off label use

Points to Consider About “Points to Consider”

- A “living document,” intended to grow and change as MedDRA advances from version to version
- A “companion document” to MedDRA
- Recommended to be used as the basis for individual organizations’ post-MedDRA implementation coding conventions
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