Understanding MedDRA

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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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Topics

• What is MedDRA?
• History and governance of MedDRA
• Recent worldwide trends on MedDRA use
• Purpose, scope, structure, and characteristics of MedDRA
• Where and how is MedDRA used?
• Medical Device terms in MedDRA
What is MedDRA?

Med = Medical

D = Dictionary for

R = Regulatory

A = Activities
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.
ICH Development of MedDRA

• 1990s – No standard international medical terminology
• 1993 – Working party: Industry and EU regulators amend UK Medicines Control Agency terminology
• October 1994 – ICH adopted MedDRA as basis for international terminology and established ICH M1 Expert Working Group
• March 1999 - MSSO (Maintenance & Support Services Organization) and JMO (Japanese Maintenance Organization) distribute first release of MedDRA (v2.1)
ICH Members

Members
Click here for the list

Founding Regulatory Members
- EC, Europe
- FDA, United States
- MHLW/PMDA, Japan

Founding Industry Members
- EFPIA
- JPMA
- PhRMA

Standing Regulatory Members
- Health Canada, Canada
- Swissmedic, Switzerland

Regulatory Members
- ANVISA, Brazil
- MFDS, Republic of Korea
- HSA, Singapore
- NMPA, China
- TFDA, Chinese Taipei

Industry Members
- BIO
- IGBA
- WSMI

Observers
Click here for the list

Standing Observers
- IFFPA
- WHO

Legislative or Administrative Authorities
- CDSCO, India
- CECMED, Cuba
- COFEPRIS, Mexico
- INVIMA, Colombia
- MMDA, Moldova
- National Center, Kazakhstan
- NPRA, Malaysia
- NRA, Iran
- Roszdravnadzor, Russia
- SAHPRA, South Africa
- SCDMTE, Armenia
- TGA, Australia
- TITCK, Turkey

Regional Harmonisation Initiatives (RHIs)
- APEC
- ASEAN
- EAC
- GHC
- PANDRH
- SADC

International Pharmaceutical Industry Organisation
- APIC
- International Organisation regulated or affected by ICH Guideline(s)
- Bill & Melinda Gates Foundation
- CIOMS
- EDQM
- IPEC
- PIC/S
- USP
ICH and MedDRA

• ICH Role
  – Developed MedDRA as an ICH standard
  – ICH owns MedDRA
  – ICH has oversight of the MSSO through the MedDRA Management Committee
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 Committee (industry, regulators, multi-national, other interested parties)
MedDRA’s Purpose

- Facilitate the exchange of clinical information through standardization
- Important tool for product evaluation, monitoring, communication, electronic records exchange, and oversight
- Supports coding (data entry) and retrieval and analysis of clinical information about human medical products including pharmaceuticals, biologics, vaccines, and drug-device combination products
MedDRA Subscriptions

• MedDRA is free to all regulatory authorities and non-commercial users
• Commercial users pay an annual fee based on the organization’s annual revenue
  – Commercial subscriptions start at $154 USD annually
• All users get the same access to MedDRA and MSSO services
  – MedDRA tools, training, User Groups, ability to submit changes
Where MedDRA is Used

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
Global View

MedDRA is in 125 countries
As of January 2019
- 5,700 Subscribing organizations (MSSO+JMO)
- 122 Countries
Graph shows types of subscribing organizations
MedDRA Users by Region

- **Europe**: 38%
- **Americas**: 32%
- **Japan (JMO)**: 14%
- **Asia**: 13%
- **Africa**: 1%
- **Oceania**: 2%

**Country** | **Count**
--- | ---
United States | 1571
Japan | 785
UK | 336
Germany | 325
China | 299
France | 245
Italy | 207
Spain | 150
Canada | 127
Republic of Korea | 111
Sweden | 96
Australia | 95
Netherlands | 92
India | 90
Switzerland | 84
Poland | 71
Belgium | 61
Chinese Taipei | 60
Israel | 57
Greece | 56
Portugal | 52
Denmark | 50
Austria | 43
Russian Federation | 37
Czechia | 36
Overview of MedDRA Scope, Structure, and Characteristics
Scope of MedDRA

Not a drug dictionary
Patient demographic terms
Clinical trial study design terms

Not an equipment, device, diagnostic product dictionary

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

Frequency qualifiers
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
Lowest Level Term

Synonyms, lexical variants, sub-elements

\[ \text{SOC} = \text{Cardiac disorders} \]
\[ \text{HLGT} = \text{Cardiac arrhythmias} \]
\[ \text{HLT} = \text{Rate and rhythm disorders NEC} \]
\[ \text{PT} = \text{Arrhythmia} \]

\[ \text{LLT} = \text{Arrhythmia} \]
\[ \text{LLT} = \text{Other specified cardiac dysrhythmias} \]

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
MedDRA Codes

- Each MedDRA term assigned an 8-digit numeric code starting with “1”
- The code is non-expressive
- Codes can fulfill a data field in various electronic submission types (e.g., E2B)
- New terms are assigned sequentially
Codes and Languages

- Cefaleia (Portuguese)
- Kopfschmerz (German)
- Headache (English)
- Céphalée (French)
- Bolest hlavy (Czech)
- Fejfájás (Hungarian)
- Cefalea (Italian)
- Болест голови (Ukrainian)
- 頭痛 (Japanese)
- Cefalea (Spanish)
- Головная боль (Russian)

Electronic Submission
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
A Multi-Axial Terminology (cont)

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
Medical Device Terms in MedDRA
Device Terms in MedDRA

- Device specific terms included from the inception of MedDRA
  - Currently over 700 device specific terms in MedDRA
  - Can be found in various SOCs
- The scope of MedDRA encompasses medical, health-related, and regulatory concepts pertaining to medical products for human use and these include the health effects and malfunction of devices
  - e.g., PT *Device related infection* and PT *Device failure*
- Device names/components are out of scope
Device Term Developments in MedDRA History

• March 2008 (Version 11.0), Device Patient Terms
  – A series of device patient adverse event terms were added to support the use of MedDRA for combination products
  – These terms were taken from a list of patient problem terms that were provided by the FDA

• March 2010 (Version 13.0), Device Hierarchy Change
  – Comprehensive device related term review with the help of industry volunteers
  – New device related HLGTs and HLTs were added to SOC General disorders and administration site conditions
Device Terms in MedDRA: Important Grouping Levels

- These are not all device terms though!
IMDRF and MedDRA
IMDRF and MedDRA

- International Medical Device Regulatory Forum (IMDRF)
  - Developing set of harmonized terminologies for reporting adverse events for medical devices
  - One of the terminologies being developed to describe Patient Problems
  - IMDRF posted a draft term list and structure for comment
IMDRF Patient Problem Codes

- Annex E: Health Effects – Clinical Signs, Symptoms and Conditions Terms and Codes
  - Term list includes ~700 terms (Patient Problem Codes)
  - Provides terminology to describe the observed condition of the affected persons after the medical device adverse event occurs
  - Terms are largely based on a subset of MedDRA terms

IMDRF agreed to include the mapped MedDRA terms and codes in the distributed file.

IMDRF released the mapping in March 2019.

Mapping will help manufacturers who produce drugs, combination products, and devices since many are MedDRA users.
## IMDRF Patient Problem Codes Mapping (cont)

### Annex E. Clinical signs, symptoms and conditions

Device (bold): For the purpose of this Annex, a device means a medical device including accessories and components. Wherever appropriate "patient" should be taken to include user, operator or any other person affected by the incident.

<table>
<thead>
<tr>
<th>LEVEL 1</th>
<th>LEVEL 2</th>
<th>LEVEL 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervous System</td>
<td>Balance Problems</td>
<td>A feeling of falling down which can occur whether the person is standing, sitting or lying down.</td>
</tr>
<tr>
<td></td>
<td>Brain Injury</td>
<td>Damage to the brain.</td>
</tr>
<tr>
<td></td>
<td>Cerebral Edema</td>
<td>A swelling in the brain caused by the presence of excessive fluid.</td>
</tr>
<tr>
<td></td>
<td>Cerebral Hyperperfusion Syndrome</td>
<td>Unexpected increase in cerebral blood flow after carotid endarterectomy (CEA) or carotid artery stenting (CAS).</td>
</tr>
<tr>
<td></td>
<td>Cerebral Ventriculomegaly</td>
<td>Abnormal enlargement of the cerebral ventricles.</td>
</tr>
<tr>
<td></td>
<td>Cerebrospinal Fluid Leakage</td>
<td>The loss of cerebrospinal fluid into the surrounding tissue.</td>
</tr>
<tr>
<td></td>
<td>Cognitive Changes</td>
<td>Changes in perception, thinking, or remembering.</td>
</tr>
</tbody>
</table>

http://www.imdrf.org/documents/documents.asp
Thank you, Questions?

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