MedDRA - International standard for coding safety information

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MedDRA MSSO

The Golden Triangle

Efficacy

Safety (MedDRA)

Product

Quality (MedDRA)
Drug Safety Story

- Thalidomide
- 1950s and 1960s
- Global impact

Manage Safety Reports

- Overwhelming?
- eReports - eliminate paper
- Code safety reports with MedDRA - organize and sort reports
**Topics**

- Where MedDRA is used
- Introduction of MedDRA and MSSO
- Implementation of MedDRA
- MedDRA Fundamentals
- MedDRA Tools
- Coding with MedDRA
- Analyzing and Retrieving Safety Data with MedDRA

**Where MedDRA Is Used**
Where MedDRA is Used

- MedDRA is used to encode the information, e.g., adverse events, of a patient who took/used the product

Where MedDRA is Used (cont)

- Individual Case Safety Reports (ICSRs) for clinical trials and post-marketing – ICH E2B

<table>
<thead>
<tr>
<th>Element ID</th>
<th>E2B/CRF Element Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>B.1.7.1.a.2</td>
<td>Structured Medical History Information (disease / surgical procedure / etc.)</td>
</tr>
<tr>
<td>B.1.8.1.2</td>
<td>Indication</td>
</tr>
<tr>
<td>B.1.8.f.2</td>
<td>Reaction</td>
</tr>
<tr>
<td>B.1.8.4.b1</td>
<td>Reported cause(s) of death</td>
</tr>
<tr>
<td>B.1.9.4.c.b1</td>
<td>Autopsy-determined cause(s) of death</td>
</tr>
<tr>
<td>B.1.10.7.1.a.2</td>
<td>Structured information (disease / surgical procedure / etc.) - parent/child report (parent)</td>
</tr>
<tr>
<td>B.1.10.8.f.2</td>
<td>Indication - parent/child report (parent)</td>
</tr>
<tr>
<td>B.1.10.8.f.g.2</td>
<td>Reactions (if any and known) - parent/child report (parent)</td>
</tr>
<tr>
<td>B.2.1.1.b</td>
<td>Reaction/event in MedDRA terminology</td>
</tr>
<tr>
<td>B.3.c.2</td>
<td>Text Name (MedDRA code)</td>
</tr>
<tr>
<td>B.4.k.7.e.2a</td>
<td>Indicator in MedDRA terminology</td>
</tr>
<tr>
<td>B.5.3.1.2</td>
<td>MedDRA’s diagnosis/syndrome and/or reclassification of reaction/event</td>
</tr>
</tbody>
</table>

Regulatory Database
Where MedDRA is Used (cont)

- Regulatory Safety Databases Coded in MedDRA (examples)
  - US FDA
    - FAERS: drugs and biologics
    - VAERS: vaccines
    - CAERS: foods, dietary supplements, cosmetics
  - EMA
    - EudraVigilance Database
  - Health Canada
    - Canada Vigilance Database
  - MHLW/PMDA
    - Safety database

Where MedDRA is Used (cont)

- e-Marketing Applications – ICH eCTD, for example
  - US FDA
    - NDAs: New Drug Applications, including Integrated Summary of Safety (ISS) - adverse event dataset
    - ANDAs: Abbreviated New Drug Applications
    - INDs: Investigational New Drugs
    - BLAs: Biologics License Applications
  - EMA
    - MAAs: Marketing Authorisation Applications
  - Health Canada
    - New Drug Submissions (NDSs)
  - MHLW/PMDA
    - NDAs: New Drug Applications
Where MedDRA is Used (cont)

- Clinical study reports
- Investigator’s Brochures
- Core Company Safety Information
- Prescribing information
- Advertising

Introduction of MedDRA and MSSO
What is MedDRA?

**Med** = Medical

**D** = Dictionary for

**R** = Regulatory

**A** = Activities

An ICH Standard Medical Terminology

MedDRA Governance

- MedDRA Management Committee
MedDRA Governance (cont)

- MedDRA community

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
MSSO

• MedDRA Maintenance and Support Services Organization (MSSO)
  – Distribute MedDRA: deliver MedDRA to subscribers worldwide
  – Maintain MedDRA: process users’ change requests
  – Develop MedDRA: further develop MedDRA to keep up with the changes in medicine and meet the regulatory needs
  – Provide user support:
    • Help desk
    • Training
    • User group meetings
• Headquartered in Washington, DC, USA
  – Staff also in France, Germany, Spain, UK

MedDRA Maintenance

• MedDRA is a user-responsive terminology
• Users may submit change requests (CRs) to the MSSO for consideration
  – Electronic change request submission tool
• MSSO review and implement approved changes
• Twice yearly official updates
  – 1 March X.0 release
  – 1 September X.1 release
Implementation of MedDRA

• Establish an implantation team
  – Set goals and objectives

• Have an implementation plan to consider
  – Define roles and responsibilities
    • Who is responsible for getting a MedDRA subscription?
    • Who is responsible for IT?
    • Who is in charge of communication?
    • Who is responsible for data conversion (if applicable)?
  – Identify impacts to your organization’s standard operating procedures
  – Plan for staff training: who, when, and what
  – Include IT considerations: database, system, and tools
  – Set implementation timeline
Obtaining MedDRA Subscription

• A valid MedDRA subscription is required for any person/organization to obtain and use MedDRA

• Step by step instruction on how to apply for MedDRA subscription and pay for MedDRA invoice (commercial organizations) are available at: https://www.meddra.org/subscription/process

MedDRA Subscription Rates

• Enterprise wide subscription
• Free subscription
  – Nonprofit organizations
  – Regulatory authorities
• Paid subscription
  – Software developers
  – Commercial organizations, such as pharma companies, CROs
    • Sliding scale subscription fee based on annual revenue
    • Example, A company with annual revenue less than $1 million pays $162 per year.
Users access MedDRA through subscription
Regulators, Non-Profits, Academics, Healthcare providers have free subscription
Commercial users pay a subscription fee
  – Funds MSSO
  – Rates reviewed and approved by ICH MedDRA Management Board
  – Sliding scale fee based on organization’s annual revenue, starting at $162
  – MedDRA rates flat or decreased for 12 years
All subscribers receive the same quality services from the MSSO

Commercial 0-2 subscription rates reduced in 2018
Reduction is a reflection of the continued success of MedDRA as a global standard in public health
Costs of maintaining and developing MedDRA are distributed over a wider base
  – While still providing the same high standard of tools and services to MedDRA users
  – In fact, expanding services to include more translation and more software tools
2018 MedDRA Subscription Fee Table

<table>
<thead>
<tr>
<th>MedDRA Subscription Types</th>
<th>2018 Annual Transaction Rates</th>
<th>Additional Rates for Japanese Transaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regulatory Authority</td>
<td>$0 USD</td>
<td>$0 USD</td>
</tr>
<tr>
<td>Non-Commercial / Non-HIP</td>
<td>$0 USD</td>
<td>$0 USD</td>
</tr>
<tr>
<td>Commercial</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Parent Company Annual Revenue &lt; $1 Billion)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level 1 (Annual Revenue $1-$4.99 Billion)</td>
<td>$192 USD</td>
<td>$302 USD</td>
</tr>
<tr>
<td>Level 2 (Annual Revenue $5-$19.99 Billion)</td>
<td>$3,537 USD</td>
<td>$6,563 USD</td>
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<tr>
<td>Level 3 (Annual Revenue $20-$99.99 Billion)</td>
<td>$6,070 USD</td>
<td>$6,070 USD</td>
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<tr>
<td>Level 4 (Annual Revenue $100 Million-$1 Billion)</td>
<td>$15,440 USD</td>
<td>$15,440 USD</td>
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<tr>
<td>Level 5 (Annual Revenue $1-$5 Billion)</td>
<td>$43,711 USD</td>
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<tr>
<td>Level 6 (Annual Revenue $5.01-$10 Billion)</td>
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<td>$60,734 USD</td>
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<tr>
<td>Level 7 (Annual Revenue &gt; $10 Billion)</td>
<td>$714,202 USD</td>
<td>$714,202 USD</td>
</tr>
<tr>
<td>System Developer</td>
<td>$2,501 USD</td>
<td>$2,501 USD</td>
</tr>
</tbody>
</table>

76% of all MedDRA users pay no fee or $688 (or less)

MedDRA Data Sharing

- MSSO Statement on MedDRA Data Sharing is posted at [https://www.meddra.org/subscription/process](https://www.meddra.org/subscription/process)
- According to MedDRA Subscription Agreement
### Downloading and Installing MedDRA

- Step-by-step instructions in Appendix slides
  - Downloading the latest release of MedDRA
  - Installing the MedDRA Desktop Browser
  - Loading MedDRA into the Desktop Browser

### IT Considerations

- Many software tools available to support the use of MedDRA
  - Several provided free with the MedDRA subscription
    - Two browsers (Desktop and Web-Based)
    - MedDRA Version Analysis Tool (MVAT)
  - Need for software tools should be driven by the volume of data to be supported
    - With small amounts of data users can use simple software tools (e.g., free MSSO browsers, spreadsheets)
    - Larger implementations should consider commercial data management software products
    - List of third-party software tools on MedDRA website
IT Considerations (cont)

• At MedDRA.org

• Build robust MedDRA safety database based on the knowledge of
  – Structure and relations of MedDRA tables
  – Versioning impact
  – Data retrieval needs

• Reference document – (MedDRA Distribution File Format Document)
  – Describe the relationships among MedDRA tables.

MedDRA Fundamentals
Scope of MedDRA

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

OUT

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

Frequency qualifiers
Numerical values for results
Severity descriptors
Not an equipment, device, diagnostic product dictionary

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
MedDRA Structure

System Organ Class (SOC) (27)

High Level Group Term (HLGT) (337)

High Level Term (HLT) (1,737)

Preferred Term (PT) (23,088)

Lowest Level Term (LLT) (78,808)

MedDRA Structure

SOC = Cardiac disorders

HLGT = Cardiac arrhythmias

HLT = Rate and rhythm disorders NEC

PT = Arrhythmia

LLT = Arrhythmia NOS

LLT = Arrhythmia

LLT (Non-current) Other specified cardiac dysrhythmias

LLT 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

- Dutch
- Portuguese
- German
- Hungarian
- Italian
- Japanese
- Spanish

Upcoming Russian Translation

- Translated by the MSSO
- Being reviewed by Roszdravnadzor
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

Rules for Primary SOC Allocation

Primary SOC allocation assignment priority:

1st: Congenital, familial and genetic disorders
2nd: Neoplasms benign, malignant and unspecified (incl cysts and polyps)
3rd: Infections and infestations
4th: Primary site of manifestation
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

MedDRA Tools
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 Version Analysis Tool (MVAT)

- Web-based ([https://tools.meddra.org/mvat](https://tools.meddra.org/mvat))
- Free to all users
- Features
  - Version Report Generator (produces exportable report comparing any two versions)
  - Data Impact Report (identifies changes to a specific set of MedDRA terms or codes uploaded to MVAT)
  - Search Term Change (identifies changes to a single MedDRA term or code)
- User interface and report output available in all MedDRA languages
MedDRA Version Analysis Tool

Coding with MedDRA
MedDRA Term Selection: Points to Consider (MTS:PTC)

- 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

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

Always Select a Best Match LLT
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
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-Specific vs. Microorganism-Specific Information
- Modification of Pre-existing Conditions
- Exposures During Pregnancy and Breast Feeding
- Congenital Terms
- Neoplasms
- Medical and Surgical Procedures
- Investigations

Term Selection Points (cont)

- Medication Errors, Accidental Exposures and Occupational Exposures
- Misuse, Abuse and Addiction
- Transmission of Infectious Agent via Product
- Overdose, Toxicity and Poisoning
- Device-related Terms
- Drug Interactions
- No Adverse Effect and “Normal” Terms
- Unexpected Therapeutic Effect
- Modification of Effect
- Social Circumstances
- Medical and Social History
- Indication for Product Use
- Off Label Use
- Product Quality Issues
### Diagnoses and Provisional Diagnoses

#### SINGLE DIAGNOSIS

<table>
<thead>
<tr>
<th>DEFINITIVE DIAGNOSIS</th>
<th>PROVISIONAL DIAGNOSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single diagnosis without signs and symptoms</td>
<td>Single provisional diagnosis without signs and symptoms</td>
</tr>
<tr>
<td>• Diagnosis (only possible option)</td>
<td>• Provisional diagnosis (only possible option)</td>
</tr>
</tbody>
</table>

**Example:** "Myocardial infarction" → select "Myocardial infarction"  
**Example:** "Possible myocardial infarction" → select "Myocardial infarction" (select term as if definitive diagnosis)

---

#### Diagnoses and Provisional Diagnoses (cont)

<table>
<thead>
<tr>
<th>DEFINITIVE DIAGNOSIS</th>
<th>PROVISIONAL DIAGNOSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single diagnosis with signs/symptoms</td>
<td>Single provisional diagnosis with signs/symptoms</td>
</tr>
<tr>
<td>• Preferred: Diagnosis only</td>
<td>• Preferred: Provisional diagnosis and signs/symptoms</td>
</tr>
</tbody>
</table>

**Example:** "Anaphylactic reaction with rash, dyspnoea, hypotension, and laryngospasm" → select "Anaphylactic reaction"  
**Example:** "Possible myocardial infarction with chest pain, dyspnoea, diaphoresis" → select "Myocardial infarction" "Chest pain", "Dyspnoea", and "Diaphoresis"

---

Similar principles apply for multiple diagnoses.
## Diagnoses and Provisional Diagnoses (cont)

### SINGLE DIAGNOSIS

<table>
<thead>
<tr>
<th>DEFINITIVE DIAGNOSIS</th>
<th>PROVISIONAL DIAGNOSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single diagnosis with signs/symptoms</td>
<td>Single provisional diagnosis with signs/symptoms</td>
</tr>
<tr>
<td>• Alternate: Diagnosis and signs/symptoms</td>
<td>• Alternate: Signs/symptoms only (as provisional diagnosis may change)</td>
</tr>
<tr>
<td>Example: “Anaphylactic reaction with rash, dyspnoea, hypotension, and laryngospasm”</td>
<td>Example: “Possible myocardial infarction with chest pain, dyspnoea, diaphoresis” select “Chest pain”, “Dyspnoea”, and “Diaphoresis”</td>
</tr>
</tbody>
</table>

Similar principles apply for multiple diagnoses

## What Terms to Select?

Influenza with body aches, fever, cough

- LLT *Influenza*
- LLT *General body pain*
- LLT *Fever*
- LLT *Cough*
- All of the above
What Terms to Select?

72 year old man with aphasia and right hemiplegia. Rule out stroke in middle cerebral artery territory.

- LLT *Aphasia*
- LLT *Right hemiplegia*
- LLT *Middle cerebral artery stroke*
- All of the above

What Terms to Select?

After taking the first dose of Drug X, the patient complained of facial and tongue swelling. The physician reports that the patient suffered from a hypersensitivity reaction to the drug.

- LLT *Facial swelling*
- LLT *Swelling of tongue*
- LLT *Drug hypersensitivity*
- All of the above
What Terms to Select?

Sepsis leading to shock from possible spontaneous bacterial peritonitis or bowel perforation

- LLT Sepsis
- LLT Shock
- LLT Septic shock
- LLT Spontaneous bacterial peritonitis
- LLT Bowel perforation

Combination Terms

- One condition is more specific than the other

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrhythmia due to atrial fibrillation</td>
<td>Atrial fibrillation</td>
</tr>
<tr>
<td>Hepatic function disorder (acute hepatitis)</td>
<td>Hepatitis acute</td>
</tr>
</tbody>
</table>

- A MedDRA combination term is available

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retinopathy due to diabetes</td>
<td>Diabetic retinopathy</td>
</tr>
<tr>
<td>Rash with itching</td>
<td>Itchy rash</td>
</tr>
</tbody>
</table>
Combination Terms (cont)

- If splitting provides more clinical information, select more than one term
- In all cases of combination terms, apply medical judgment

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhoea and vomiting</td>
<td>Diarrhoea Vomiting</td>
</tr>
<tr>
<td>Wrist fracture due to fall</td>
<td>Wrist fracture Fall</td>
</tr>
</tbody>
</table>

What Terms to Select?

Retinal disease from HIV with near total blindness (R and L)
- LLT Retinal damage
- LLT Retinal disorder
- LLT HIV disease
- LLT Blindness
- LLT HIV retinopathy
- LLT Blindness, both eyes
### Conflicting/Ambiguous Information

- First, try to obtain more specific information

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperkalaemia with a serum potassium of 1.6 mEq/L</td>
<td>Serum potassium abnormal</td>
<td>LLT Serum potassium abnormal covers both of the reported concepts (note: serum potassium of 1.6 mEq/L is a low result, not high)</td>
</tr>
<tr>
<td>GU pain</td>
<td>Pain</td>
<td>“GU” could be either &quot;genito-urinary&quot; or &quot;gastric ulcer&quot;. If additional information is not available, then select a term to reflect the information that is known, i.e., LLT Pain</td>
</tr>
</tbody>
</table>

### Vague Information

- First, try to obtain more specific information

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turned green</td>
<td>Unevaluable event</td>
<td>“Turned green” reported alone is vague; this could refer to a patient condition or even to a product (e.g., pills)</td>
</tr>
<tr>
<td>Patient had a medical problem of unclear type</td>
<td>Ill-defined disorder</td>
<td>Since it is known that there is some form of a medical disorder, LLT Ill-defined disorder can be selected</td>
</tr>
</tbody>
</table>
What Terms to Select?

Hypoglycemia (blood glucose = 200 mg/dL)
- LLT Blood glucose abnormal
- LLT Blood glucose increased
- LLT Hypoglycemia

Analyzing and Retrieving Safety Data with MedDRA
MedDRA Data Retrieval and Presentation: Points to Consider

- Provides data retrieval and presentation options for industry or regulatory purposes
- Most effective when used in conjunction with MedDRA Term Selection: PTC document
- Recommended to be used as basis for individual organization’s own data retrieval conventions

Visualization of Safety Data Using MedDRA
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

Safety Profile
Signal Detection and MedDRA

MedDRA Structure & Size

- System Organ Class (SOC) (27)
  - High Level Group Term (HLGT) (337)
    - High Level Term (HLT) (1,737)
      - Preferred Term (PT) (23,088)
      - Lowest Level Term (LLT) (78,808)

SMQs (103)

Granularity Increases

Signal Strength Increases
MedDRA Hierarchy Example

SOC = Cardiac disorders

HLGT = Cardiac arrhythmias

HLT = Cardiac conduction disorders

HLT = Rate and rhythm disorders NEC

HLT = Supraventricular arrhythmias

HLT = Ventricular arrhythmias and cardiac arrest

PT = Tachycardia

PT = Arrhythmia

PT = Bradycardia

LLT = Tachycardia

LLT = Reflex tachycardia

LLT = Arrhythmia

LLT = Dysrhythmias

Not all LLTs shown

Use of MedDRA at FDA

Acknowledgement: Dr. Chuck Cooper, Office of Translational Sciences, CDER, FDA
Standardised MedDRA Queries (SMQs)

- Groupings of terms from one or more MedDRA System Organ Classes related to defined medical condition or area of interest
- Included terms may relate to signs, symptoms, diagnoses, syndromes, physical findings, laboratory and other physiologic test data, etc., related to medical condition or area of interest
- Intended to aid in case identification and signal detection

SMQs in Production - Examples

- As of Version 21.0, a total of 103 SMQs in production
  - Agranulocytosis
  - Anaphylactic reaction
  - Cerebrovascular disorders
  - Convulsions
  - Depression and suicide/self-injury
  - Hepatic disorders
  - Hypersensitivity
  - Ischaemic heart disease
  - Lack of efficacy/effect
  - Medication errors
  - Osteonecrosis
  - Peripheral neuropathy
  - Pregnancy and neonatal topics
  - Pseudomembranous colitis
  - Rhabdomyolysis/myopathy
  - Severe cutaneous adverse reactions
  - Systemic lupus erythematosus
Signal Detection at EMA

- MedDRA supports signal detection and management in EU
  - Early detection of possible safety signals associated with medicinal products
  - Continuous monitoring and evaluation of potential safety issues in relation to reported adverse reactions
  - Decision making process based on a broader knowledge of the adverse reaction profile of medicinal products especially in the frame of the continuous benefit risk assessment of medicines
Signal Detection in EudraVigilance (cont)

- 43 signals were validated, prioritised and analysed in 2013
- 21 of the 43 signals led to a recommendation for changes to the product information
  - Directly (n=7)
  - Cumulative review (n=14)
  - DHPCs to increase awareness about the new safety information (n=4)
- One signal led to a formal evaluation of the benefit-risk balance via an Article 31 referral

Questions?
Appendix: Downloading and Installing MedDRA

First Steps

• You just received your subscription letter from the MSSO, what’s next?
  – Download the latest release
• Identify the components and distribute accordingly
  – Install the MedDRA Desktop Browser
  – Load MedDRA into the Desktop Browser
Download the Latest Release

Click on Downloads

Download the Latest Release (cont)

- Enter Subscriber ID and password
Download the Latest Release (cont)

- Select the version and language(s)
  - Password protected zip file
- Save the zip file to your computer

Extract the Release Files

- Zip file structure and contents
  - Select a file to extract
  - Enter Unzip password from Welcome letter
What’s in the Zip File?

- Full Release of MedDRA Data and relationships files
- Changes in this release
- Description of contents of zip file
- Narrative discussion of changes in this release
- SMQ Spreadsheet
- SMQ Introductory Guide
- SMQ Spreadsheet with lists of new and modified terms
- Details of implemented changes
- File Format Descriptions

What to do with the Contents of the Zip File?

<table>
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<tr>
<th>Item</th>
<th>Who should receive it?</th>
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<tr>
<td>MedASCII Directory</td>
<td>IT staff to load MedDRA</td>
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<tr>
<td>SEQASCII Directory</td>
<td>IT staff to review changes</td>
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<tr>
<td>Readme</td>
<td>All users</td>
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<tr>
<td>SMQ Spreadsheet</td>
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<td>Distribution File Format</td>
<td>IT staff to load MedDRA</td>
</tr>
<tr>
<td>MedDRA Introductory Guide</td>
<td>All users</td>
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</tbody>
</table>
Contents of MedASCII Directory

- MedDRA term and relationship files
- ASCII File format

Download and Install MedDRA Desktop Browser

1) Click on Downloads page from Home page
2) Log in (if not already)
3) Click on Desktop Browsers
Download and Install MedDRA Desktop Browser (cont)

Load MedDRA into Desktop Browser

- Install MedDRA Desktop Browser
  - Create a directory on your computer
  - Unzip the contents of the zip file downloaded to this directory
  - Double click the file MedDRABrowserWIN.exe to start the browser
    - For future use, right click the MedDRABrowserWIN.exe file and choose “Send to” and then “Desktop” and an icon will be placed on your desktop
Load MedDRA into Desktop Browser (cont)

• Use the browse button to identify the directory where the MedDRA ASCII files are stored

• Click Import

Load MedDRA into Desktop Browser (cont)

• The load process will display a progress bar and then the load process will complete
• At the top of MedDRA Desktop Browser screen, select the version of MedDRA to display
Load MedDRA into Desktop Browser (cont)

- MedDRA Desktop Browser is loaded and ready for use