What is MedDRA?

Med = Medical

D = Dictionary for

R = Regulatory

A = Activities
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
Regulatory Status

- **US FDA**
  - Used in several databases including FAERS (drugs and biologics), VAERS (vaccines), and CAERS (foods, dietary supplements, cosmetics)

- **Japanese Ministry of Health, Labour and Welfare**
  - Mandatory use in electronic reporting

- **European Union (EudraVigilance database)**
  - Post-authorization Individual Case Safety Reports (ICSRs)
  - Clinical trial SUSARs (Suspected Unexpected Serious Adverse Reactions)
MedDRA Structure

MeDRA Version 17.0

System Organ Class (SOC) (26)

High Level Group Term (HLGT) (334)

High Level Term (HLT) (1,720)

Preferred Term (PT) (20,559)

Lowest Level Term (LLT) (72,637)
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
Subordinate only to SOCs and superordinate grouping for one or more HLTs

- SOC: Cardiac disorders
  - HLGT: Coronary artery disorders
  - HLGT: Cardiac arrhythmias
  - HLGT: Cardiac valve disorders
Subordinate to HLGTs and superordinate grouping for the PTs linked to it

- **SOC**
  - Cardiac disorders
  - **HLGT**
    - Cardiac arrhythmias
  - **HLT**
    - Cardiac conduction disorders
    - **HLT**
      - Rate and rhythm disorders NEC
    - **HLT**
      - Supraventricular arrhythmias
Preferred Terms

Represents a single medical concept

- **SOC** Cardiac disorders
  - **HLGT** Cardiac arrhythmias
  - **HLT** Rate and rhythm disorders NEC
    - **PT** Arrhythmia
    - **PT** Bradycardia
    - **PT** Tachyarrhythmia
Synonyms, lexical variants, sub-elements

SOC = Cardiac disorders

HLGT = Cardiac arrhythmias

HLT = Rate and rhythm disorders NEC

PT = Arrhythmia

LLT = Other specified cardiac dysrhythmias

LLT (Non-current)
Codes and Languages

- Hoofdpijn (Dutch)
- Headache (English)
- Céphalée (French)
- Bolest hlavy (Czech)
- Cefaleia (Portuguese)
- Kopfschmerz (German)
- Fejfájás (Hungarian)
- Cefalea (Italian)
- 头痛 (Chinese)
- Cefalea (Spanish)

Electronic Submission
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
<table>
<thead>
<tr>
<th>PT</th>
<th>HLT</th>
<th>HLGT</th>
<th>SOC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital HIV infection</td>
<td>Viral infections congenital</td>
<td>Infections and infestations congenital</td>
<td>Congenital, familial and genetic disorders (P)</td>
</tr>
<tr>
<td>Congenital neonatal infections</td>
<td>Neonatal and perinatal conditions</td>
<td></td>
<td>Pregnancy, puerperium and perinatal conditions</td>
</tr>
<tr>
<td>Retroviral infections</td>
<td>Viral infectious disorders</td>
<td></td>
<td>Infections and infestations</td>
</tr>
<tr>
<td>Acquired immunodeficiency syndromes</td>
<td>Immunodeficiency syndromes</td>
<td></td>
<td>Immune system disorders</td>
</tr>
</tbody>
</table>
### Conditions vs. Investigations

<table>
<thead>
<tr>
<th>PT</th>
<th>HLT</th>
<th>HLGT</th>
<th>SOC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy test positive</td>
<td>Reproductive hormone analyses</td>
<td>Endocrine investigations (incl sex hormones)</td>
<td>Investigations</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Normal pregnancy, labour and delivery</td>
<td>Pregnancy, labour, delivery and postpartum conditions</td>
<td>Pregnancy, puerperium and perinatal conditions</td>
</tr>
</tbody>
</table>

Be careful to distinguish between a condition and an investigation or a result of an investigation.
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 Term Selection: Points to Consider (MTS:PTC)

MedDRA® TERM SELECTION: POINTS TO CONSIDER

ICH-Endorsed Guide for MedDRA Users

Release 4.7
Based on MedDRA Version 17.0

1 March 2014

• 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
Analysis with MedDRA
<table>
<thead>
<tr>
<th>SOC</th>
<th>HLGT</th>
<th>HLT</th>
<th>PT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatobiliary disorders</td>
<td>Hepatic and hepatobiliary disorders</td>
<td>Hepatocellular damage and hepatitis NEC</td>
<td>Autoimmune hepatitis</td>
</tr>
<tr>
<td>Blood and lymphatic system disorders</td>
<td>Haemolyses and related conditions</td>
<td>Anaemias haemolytic immune</td>
<td>Coombs positive haemolytic anaemia</td>
</tr>
<tr>
<td>Renal and urinary disorders</td>
<td>Nephropathies</td>
<td>Glomerulonephritis and nephrotic syndrome</td>
<td>Nephritis allergic</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Epidermal and dermal conditions</td>
<td>Bullous conditions</td>
<td>Stevens-Johnson syndrome</td>
</tr>
<tr>
<td>SOC</td>
<td>HLGT</td>
<td>HLT</td>
<td>PT</td>
</tr>
<tr>
<td>----------------------------</td>
<td>----------------------------</td>
<td>--------------------------</td>
<td>----------------------------</td>
</tr>
<tr>
<td>Immune system disorders</td>
<td>Autoimmune disorders</td>
<td>Hepatic autoimmune disorders</td>
<td>Autoimmune hepatitis</td>
</tr>
<tr>
<td></td>
<td>Blood autoimmune disorders</td>
<td></td>
<td>Coombs positive haemolytic anaemia</td>
</tr>
<tr>
<td>Allergic conditions</td>
<td>Allergic conditions NEC</td>
<td></td>
<td>Nephritis allergic</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Stevens-Johnson syndrome</td>
</tr>
</tbody>
</table>
Standardised MedDRA Queries (SMQs)
• Obvious starting point – HLGT *Cardiac arrhythmias* (“Top-down” search)
• Also use “Arrhythmia” terms as starting point of “Bottom-up” search
• What about non-multi-axial SOCs?
Example – Cardiac Arrhythmias (cont)

- SOC Investigations
  - PTs subordinate to HLT ECG investigations and HLT Heart rate and pulse investigations should be reviewed
  • Example: PT Heart rate irregular
• **SOC *Surgical and medical procedures**
  Important to review:
  – PTs subordinate to HLT *Cardiac device therapeutic procedures*  
    • Example: PT *Implantable defibrillator insertion*
  – PTs subordinate to HLT *Cardiac therapeutic procedures NEC*  
    • Example: PT *Cardioversion*

*Note: Pacemaker and other cardiac therapeutic procedure terms were not included in SMQ *Cardiac arrhythmias*
• Because arrhythmias may produce various signs and symptoms, you may wish to review PTs subordinate to the following HLTs:

  – HLT Disturbances in consciousness NEC
  – HLT Neurological signs and symptoms NEC
  – HLT Cardiac disorders NEC
  – HLT Cardiac signs and symptoms NEC
  – HLT Dyspnoeas
Lastly…

- PTs subordinate to HLT *Death and sudden death* (under SOC *General disorders and administration site conditions*) should be reviewed
  - Example: PT *Cardiac death*
Connect the DOTSS!

- **Diagnosis/disease terms**
- **Operations** (Surgical and medical procedures)
- **Tests** (Investigations)
- **Signs & symptoms**
- **Social circumstances**
Cases of viral hepatitis in a hospital

Selection of patients with transaminases > twice the normal value (very sensitive but not specific, too many cases, false positive present)

Selection of patients with transaminases > 1000 UI (very specific, but not sensitive, cases lost, false negative present)
SMQs in Production - Examples

Groupings of terms from more than one SOC related to defined medical condition or area of interest

94 SMQ topics available in MedDRA v17.0

- Agranulocytosis
- Anaphylactic reaction
- Cerebrovascular disorders
- Convulsions
- Depression and suicide/self-injury
- Hepatic disorders
- Hypersensitivity
- Ischaemic heart disease
- Lack of efficacy/effect

- Osteonecrosis
- Peripheral neuropathy
- Pregnancy and neonatal topics
- Pseudomembranous colitis
- Rhabdomyolysis/myopathy
- Severe cutaneous adverse reactions
- Systemic lupus erythematosus
• “Narrow” scope – specificity (cases highly likely to be condition of interest)
• “Broad” scope – sensitivity (all possible cases)
• “Broad search” = All broad + all narrow terms
Narrow vs. Broad Example

SMQ *Lactic acidosis*

**Definition**
Lactic acidosis is a form of high anion gap metabolic acidosis - Intrinsic cardiac contractility may be depressed, but inotropic function can be normal because of catecholamine release - Peripheral arterial vasodilatation and central vasoconstriction can be present - Central nervous system function is depressed, with headache, lethargy, stupor, and, in some cases, even coma - Glucose intolerance may occur - Characterized by an increase in plasma L-lactate - Acidosis is seldom significant unless blood lactate exceeds 5 mmol/l - Clinical presentation in type B lactic acidosis - Symptoms: hyperventilation or dyspnea, stupor or coma, vomiting, drowsiness, and abdominal pain - Onset of symptoms and signs is usually rapid accompanied by deterioration in the level of consciousness.

**Source**

**Note**
Testing in two regulatory databases confirmed that the term list is adequate; in one regulatory database, the term "acidosis" identified cases, but this may be a phenomenon of the database characteristics (coding of verbatims to terms of an older terminology or other coding conventions).

**Narrow Terms**
- Blood lactic acid increased
- Hyperlactacidemia
- Lactic acidosis

**Broad Terms**
- Acid base balance abnormal
- Acidosis
- Anion gap abnormal
- Anion gap increased
- Blood bicarbonate abnormal
- Blood bicarbonate decreased
- Blood gases abnormal
- Blood lactic acid abnormal
- Blood pH abnormal
- Blood pH decreased
- Coma acidotic
- Kussmaul respiration
- Metabolic acidosis
- PCO2 abnormal
- PCO2 decreased
- Urine lactic acid increased
Hierarchical SMQ Example

Haematopoietic cytopenias

Haematopoietic cytopenias affecting more than one type of blood cell

Haematopoietic erythropenia

Haematopoietic leukopenia

Haematopoietic thrombocytopenia
SMQ Applications

• Clinical trials
  - Where safety profile is not fully established, use multiple SMQs on routine basis as screening tool
  - Selected SMQs to evaluate previously identified issue (pre-clinical data or class effect)

• Post-marketing
  - Selected SMQs to retrieve cases for suspected or known safety issue
  - Signal detection (multiple SMQs employed)
  - Single case alerts
  - Periodic reporting (aggregate cases for safety and other issues, e.g., lack of efficacy)
¡Muchas gracias!
dúvidas e questões?
muito obrigado!
¿Preguntas!?
A Multi-Axial Terminology (cont)

SOC = Cardiac disorders

HLGT = Congenital cardiac disorders

HLT = Congenital cardiac valve disorders

HLT = Mental retardations

PT = Rubinstein-Taybi syndrome

SOC = Psychiatric disorders

HLGT = Cognitive and attention disorders and disturbances

HLGT = Mental impairment disorders

SOC = Nervous system disorders

HLGT = Musculoskeletal and connective tissue disorders congenital

Primary SOC

SOC = Congenital, familial and genetic disorders

SOC = Musculoskeletal and connective tissue disorders

HLGT = Musculoskeletal and connective tissue disorders of face, neck and jaw congenital

SOC = Congenital, familial and genetic disorders

SOC = Musculoskeletal and connective tissue disorders
A Multi-Axial Terminology (cont)