Essentials on MedDRA
Overview

• MedDRA’s structure, scope, and characteristics
• MedDRA maintenance
• Coding conventions: MedDRA Term Selection Points to Consider document
• Hands-on coding exercises
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 EDI Coordination

M1 Medical Terminology

M2 (ESTRI)
- the transport vehicle and format definitions

E2b Clinical Safety Data Management: Content of Report

Pharmaceutical Company

Regulatory Authority
I2B(M)

- Information about the safety report itself
  - A.1 Report identification
  - A.2 Primary source of information
  - A.3.1 Who sends the information
  - A.3.2 Who receives it

- Case information
  - B.1 Patient characteristics
  - B.2 Adverse reaction/event
  - B.3 Investigation test and procedures
  - B.4 Information about drugs (both suspect and concomitant)
  - B.5 Narrative case summary and further information
Where MedDRA is Used

- Individual Case Safety Reports and Safety Summaries
- Clinical Study Reports
- Investigators’ Brochures
- Core Company Safety Information
- Marketing Applications
- Publications
- Prescribing Information
- Advertising

Regulatory Authority and Industry Databases

Preclinical Testing ➔ Clinical Phase I ➔ Clinical Phase II ➔ Clinical Phase III ➔ Marketed Product Phase IV
**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) (1,738)
      - Preferred Term (PT) (22,499)
    - Lowest Level Term (LLT) (77,248)
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

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System Organ Classes

- Blood and lymphatic system disorders
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- Psychiatric disorders
- Reproductive system and breast disorders
- Respiratory, thoracic and mediastinal disorders
- Skin and subcutaneous tissue disorders
- Social circumstances
- Surgical and medical procedures
- Vascular disorders
High Level Group Terms

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

Not all HLGTs shown
High Level Terms

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

Not all HLTs shown
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

Not all PTs shown
Synonyms, lexical variants, sub-elements

**SOC** = Cardiac disorders

**HLGT** = Cardiac arrhythmias

**HLT** = Rate and rhythm disorders NEC

**PT** = Arrhythmia

**LLT**
- Arrhythmia NOS
- Arrhythmia
- LLT (Non-current) Other specified cardiac dysrhythmias
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
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*
Can You Select the Primary SOC for This PT?

<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</td>
</tr>
<tr>
<td></td>
<td>Viral infections congenital</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neonatal and perinatal conditions</td>
<td></td>
<td>Pregnancy, puerperium and perinatal conditions</td>
</tr>
<tr>
<td></td>
<td>Viral infectious disorders</td>
<td>Infections and infestations</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Immunodeficiency syndromes</td>
<td>Immune system disorders</td>
<td></td>
</tr>
</tbody>
</table>

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A Multi-Axial Terminology (cont)
MedDRA Maintenance
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 Maintenance

- MedDRA is a user-responsive terminology
- Users may submit change requests (CRs) to the MSSO for consideration
  - Each organization: up to 100 CRs per month
  - For simple changes (PT and LLT levels), notification of final disposition within 7-10 working days
  - Complex changes above PT level received all year round. Posted for users’ comments mid-year.
- Twice yearly official updates
  - 1 March X.0 release (Complex and simple changes)
  - 1 September X.1 release (Simple changes only)
WebCR

- Web-based tool for Change Requests (CR)
  - URL: https://mssotools.com/webcr/
  - Via the Change Request Information page
- Ability to submit CRs online
- Immediate confirmation
- Review unsubmitted CRs online
- Ability to query CR history back to v5.1
Submitting Changes

- Online change request submission tool
- Guides the user to enter all needed information
• Sample entry for a new PT in WebCR
• Justification and supporting documentation is important to help MSSO understand the need
Implemented Changes in MedDRA
Coding with MedDRA
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.
<table>
<thead>
<tr>
<th>Verbatim term</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Disconnected feeling</td>
<td>Unspecified neurological condition</td>
</tr>
<tr>
<td>Echoing in ears</td>
<td>After the patient's drug was substituted with a generic drug, his response to therapy was different</td>
</tr>
<tr>
<td>Severe bronchospasm on induction of anesthesia</td>
<td>Elderly woman complained her arm was tender where she had received her seasonal flu vaccine</td>
</tr>
<tr>
<td>PANDAS</td>
<td>Influenza with body aches, fever, cough</td>
</tr>
<tr>
<td>72 year old man with aphasia and right hemiplegia. Stroke in middle cerebral artery territory is suspected.</td>
<td>Patient said she received flu vaccine 3 months before she became pregnant</td>
</tr>
</tbody>
</table>
Disconnected feeling

**Gastrointestinal disorders**
- Gastrointestinal distress syndrome (NOS)
- Gastrointestinal endoscopy
- Gastrointestinal perforation
- Gastrointestinal hemorrhage
- Gastrointestinal obstruction

**General disorders and administration site conditions**
- Administration site reactions
- Body temperature conditions
- Complications associated with device
- Fatal outcomes
- General system disorders NEC
  - Acquired gene mutations and other alterations
  - Adverse effect absent
  - Asthenic conditions
  - Feelings and sensations NEC
    - Alcoholic hangover
    - Burning sensation
    - Chills
    - Decreased appetite
    - Early satiety
    - Feeling abnormal
      - Cotton wool in head
      - Feeling abnormal
      - Feeling bad
      - Feeling dazed
      - Feeling floating
      - Feeling lifeless
      - Feeling miserable
      - Feeling stoned
      - Feeling strange
      - Feeling weightless
      - Feels awful
      - Feels bad
      - Feels poorly
      - Felt like a zombie
      - Floating feeling
      - Feeling detached
      - Feeling remote

**Psychiatric disorders**
- Adjustment disorders (incl subtypes)
- Anxiety disorders and symptoms
- Changes in physical activity
- Cognitive and attention disorders and disturbances
- Communication disorders and disturbances
- Deliria (incl confusion)
- Dementia and amnestic conditions
- Depressed mood disorders and disturbances
- Developmental disorders NEC
- Dissociative disorders
  - Dissociative amnesia
  - Dissociative disorder
  - Dissociative identity disorder
  - Disturbances in thinking and perception
  - Eating disorders and disturbances
  - Impulse control disorders NEC
Unspecified neurological condition

Nervous system disorders
- Central nervous system infections and inflammations
- Central nervous system vascular disorders
- Congenital and peripartum neurological conditions
- Cranial nerve disorders (excl neoplasms)
- Demyelinating disorders
- Encephalopathies
- Headaches
- Increased intracranial pressure and hydrocephalus
- Mental impairment disorders
- Movement disorders (incl parkinsonism)
- Nervous system neoplasms benign
- Nervous system neoplasms malignant and unspecified NEC

Neurological disorders NEC
- Abnormal reflexes
- Coma states
- Coordination and balance disturbances
- Cortical dysfunction NEC
- Disturbances in consciousness NEC
- Nervous system disorders NEC
  - Anaesthetic complication neurological
  - Atypical haemolytic uraemic syndrome
  - Bing-Neel syndrome
  - Bloch-Sulzberger syndrome
  - Brain satellitosis
  - Brain stem syndrome
  - Central bradycardia
  - Central nervous system injury
  - Central nervous system lesion
  - Central nervous system leukaemia
  - Central nervous system lupus

Nerve degeneration
Nerve injury
Nervous system disorder
- Central nervous system disorder
- Central nervous system disorder NOS
- Cerebellar disorder NOS
- Cerebellar hemisphere disorder
- Cerebral dysfunction
- CNS disorder (NOS)
- Disorder central nervous system
- Disorder nervous system
- Nervous system disorder
- Nervous system disorder NOS
- Nervous system disorder, central
- Neurologic complication
- Neurologic disorder NOS
- Neurological complication
- Neurological disorder NOS
- Neurological impairment
- Other and unspecified cerebral irritability in newborn
- Other and unspecified disorders of the nervous system
- Other conditions of brain
- Other specified conditions of brain
- Other specified disorder of nervous system
- Other specified disorders of nervous system
- Unspecified condition of brain
- Unspecified disorders of nervous system

Nervous system injury
Neuroacanthocytosis
Neurodegenerative disorder
Neurogenic shock
Echoing in ears
... response to therapy was different

After the patient's drug was substituted with a generic drug, his response to therapy was different
Severe bronchospasm on induction of anesthesia
Severe bronchospasm on induction of anesthesia (cont)
Severe bronchospasm on induction of anesthesia (cont)
Elderly woman complained her arm was tender where she had received her seasonal flu vaccine.
A Multi-Axial Terminology (cont)
Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) is a hypothesis that there exists a subset of children with rapid onset of obsessive-compulsive disorder (OCD) or tic disorders and these symptoms are caused by group A beta-hemolytic streptococcal (GABHS) infections.
Influenza with body aches, fever, cough
72 year old man with aphasia and right hemiplegia. Stroke in middle cerebral artery territory is suspected.
Patient said she received flu vaccine 3 months before she became pregnant.
A Multi-Axial Terminology (cont)
A Multi-Axial Terminology (cont)

- SOC = Cardiac disorders
  - HLGT = Congenital cardiac disorders
  - HLT = Congenital cardiac valve disorders
- SOC = Psychiatric disorders
  - HLGT = Cognitive and attention disorders and disturbances
- SOC = Nervous system disorders
  - HLGT = Mental retardations
- SOC = Congenital, familial and genetic disorders
- SOC = Musculoskeletal and connective tissue disorders
- PT = Rubinstein-Taybi syndrome

Primary SOC

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

SOC = Congenital, familial and genetic disorders
SOC = Musculoskeletal and connective tissue disorders
<table>
<thead>
<tr>
<th>Verbatim term</th>
<th>LLT</th>
<th>PT</th>
<th>Primary SOC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disconnected feeling</td>
<td>Feeling detached</td>
<td>Dissociation</td>
<td>Psychiatric disorders</td>
</tr>
<tr>
<td>Unspecified neurological condition</td>
<td>Neurological disorder NOS</td>
<td>Nervous system disorder</td>
<td>Nervous system disorders</td>
</tr>
<tr>
<td>Echoing in ears</td>
<td>Echoacousia</td>
<td>Dysacusic</td>
<td>Ear and labyrinth disorders</td>
</tr>
<tr>
<td>After the patient's drug was substituted with a generic drug, his response to therapy was different</td>
<td>Generic substitution altered therapeutic response</td>
<td>Therapeutic response changed</td>
<td>General disorders and administration site conditions</td>
</tr>
<tr>
<td>Severe bronchospasm on induction of anesthesia</td>
<td>Bronchospasm on induction</td>
<td>Airway complication of anaesthesia</td>
<td>Injury, poisoning and procedural complications</td>
</tr>
<tr>
<td>Elderly woman complained her arm was tender where she had received her seasonal flu vaccine</td>
<td>Vaccination site tenderness</td>
<td>Vaccination site pain</td>
<td>General disorders and administration site conditions</td>
</tr>
<tr>
<td>PANDAS</td>
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<td>Paediatric autoimmune neuropsychiatric disorders associated with streptococcal infection</td>
<td>Psychiatric disorders</td>
</tr>
<tr>
<td>Influenza with body aches, fever, cough</td>
<td>Influenza</td>
<td>Influenza</td>
<td>Infections and infestations</td>
</tr>
<tr>
<td>72 year old man with aphasia and right hemiplegia. Stroke in middle cerebral artery territory is suspected.</td>
<td>Aphasia</td>
<td>Aphasia</td>
<td>Nervous system disorders</td>
</tr>
<tr>
<td></td>
<td>Right hemiplegia</td>
<td>Hemiplegia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Middle cerebral artery stroke</td>
<td>Cerebrovascular accident</td>
<td></td>
</tr>
</tbody>
</table>
NARRATIVE #1

• A 75-year-old male developed anginal pain on 21 Feb 2017 resulting in hospitalization while enrolled in a randomized, open-label study. The patient’s medical history is significant for triple bypass graft surgery 2014, postural hypotension and stage D prostate carcinoma. On 26 Feb 2017, the patient underwent percutaneous transluminal coronary angioplasty with stent placement in the right coronary and proximal left anterior descending arteries.
NARRATIVE #1

- A 75-year-old male developed anginal pain on 21 Feb 2017 resulting in hospitalization while enrolled in a randomized, open-label study. The patient’s medical history is significant for triple bypass graft surgery 2014, postural hypotension and stage D prostate carcinoma. On 26 Feb 2017, the patient underwent percutaneous transluminal coronary angioplasty with stent placement in the right coronary and proximal left anterior descending arteries.
NARRATIVE #1

• A 75-year-old male developed **anginal pain** on 21 February 2017 resulting in **hospitalization** while enrolled in a randomized, open-label study.
  - The patient’s medical history is significant for **triple bypass graft surgery** 2014, **postural hypotension** and **stage D prostate carcinoma**.

• On 26 February 2017, the patient underwent **percutaneous transluminal coronary angioplasty** with **stent placement** in the right **coronary** and proximal left anterior descending arteries.
MedDRA “Points to Consider” document
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
MedDRA Term Selection: PTC (cont)

- Developed by a working group of the ICH Steering Committee
  - Regulators and industry representatives from EU, Japan, and USA
  - Canadian and Korean regulatory authorities
  - WHO
  - MSSO and JMO
- 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
Do not make diagnosis if only signs/symptoms reported

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain, increased serum amylase, and increased serum lipase</td>
<td>Abdominal pain</td>
<td>It is inappropriate to assign an LLT for diagnosis of “pancreatitis”</td>
</tr>
<tr>
<td></td>
<td>Serum amylase increased</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lipase increased</td>
<td></td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Single Diagnosis</th>
<th>DEFINITIVE DIAGNOSIS</th>
<th>PROVISIONAL DIAGNOSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single diagnosis without signs and symptoms</td>
<td>• Diagnosis (only possible option)</td>
<td>• Provisional diagnosis (only possible option)</td>
</tr>
<tr>
<td>Example: “Myocardial infarction” → select “Myocardial infarction”</td>
<td></td>
<td>Example: “Possible myocardial infarction” → select “Myocardial infarction” (select term as if definitive diagnosis)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>SINGLE DIAGNOSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DEFINITIVE DIAGNOSIS</strong></td>
</tr>
<tr>
<td>Single diagnosis <em>with signs/symptoms</em></td>
</tr>
<tr>
<td>•Preferred: Diagnosis only</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>
</tbody>
</table>

**Example:** “Anaphylactic reaction with rash, dyspnoea, hypotension, and laryngospasm” → select “Anaphylactic reaction”, “Rash”, “Dyspnoea”, “Hypotension”, and “Laryngospasm”

**Example:** “Possible myocardial infarction with chest pain, dyspnoea, diaphoresis” → select “Chest pain”, “Dyspnoea”, and “Diaphoresis”

Similar principles apply for multiple diagnoses.
Always include signs/symptoms not associated with diagnosis

<table>
<thead>
<tr>
<th>Reported</th>
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</tr>
</thead>
</table>
| Myocardial infarction, chest pain, dyspnoea, diaphoresis, ECG changes and jaundice | Myocardial infarction  
Jaundice (note that jaundice is not typically associated with myocardial infarction) |
What Terms to Select?

- Sepsis leading to shock from possible spontaneous bacterial peritonitis or bowel perforation
  - Sepsis
  - Shock
  - Septic shock
  - Spontaneous bacterial peritonitis
  - Bowel perforation
### Conflicting/Ambiguous Information

First, try to obtain more specific information

<table>
<thead>
<tr>
<th>Reported</th>
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<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 “genito-urinary” or “gastric ulcer”. 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>
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<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 <em>Ill-defined disorder</em> can be selected</td>
</tr>
</tbody>
</table>
What Terms to Select?

• **Clinical complication of IUD**
  IUD complication (PT Complication associated with device)
  Intra-uterine death (PT Foetal death)
  Unevaluable event

• **Hypoglycemia (blood glucose = 200 mg/dL)**
  Blood glucose abnormal
  Blood glucose increased
  Hypoglycemia
Combination Terms

- One condition is more specific than the other

<table>
<thead>
<tr>
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</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)
  - Retinal damage
  - Retinal disorder
  - HIV disease
  - Blindness
  - HIV retinopathy
  - Blindness, both eyes
## Investigations

- Medical condition vs. investigation result

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoglycaemia</td>
<td>Hypoglycaemia</td>
<td>LLT <em>Hypoglycaemia</em> links to SOC <em>Metabolism and nutrition disorders</em></td>
</tr>
<tr>
<td>Decreased glucose</td>
<td>Glucose decreased</td>
<td>LLT <em>Glucose decreased</em> links to SOC <em>Investigations</em></td>
</tr>
</tbody>
</table>
### Unambiguous investigation result

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose 40 mg/dL</td>
<td>Glucose low</td>
<td>Glucose is clearly below the reference range</td>
</tr>
</tbody>
</table>

### Ambiguous investigation result

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>His glucose was 40</td>
<td>Glucose abnormal</td>
<td>No units have been reported. Select LLT Glucose abnormal if clarification cannot be obtained.</td>
</tr>
</tbody>
</table>
• Investigation results consistent with diagnosis

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated potassium, K 7.0 mmol/L, and hyperkalaemia</td>
<td>Hyperkalaemia</td>
<td>It is not necessary to select LLT <em>Potassium increased</em></td>
</tr>
</tbody>
</table>

• Grouped investigation result terms

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased alkaline phosphatase, increased SGPT, increased SGOT and elevated LDH</td>
<td>Alkaline phosphatase increased SGPT increased SGOT increased LDH increased</td>
<td>Select four individual terms. A single term such as LLT <em>Liver function tests abnormal</em> should not be selected.</td>
</tr>
</tbody>
</table>
What Terms to Select?

- Testing showed increased serum creatinine and BUN, with increased BUN/creatinine ratio
  - Increased serum creatinine
  - BUN increased
  - Blood urea nitrogen/creatinine ratio increased
  - Renal function tests NOS abnormal
What Terms to Select?

• Due to a prescribing error, the child was given drug X, which is labeled for use in adults only

Adult product administered to child
Accidental overdose
Drug prescribing error
Medication error
Medication Errors (cont)

See Appendix B of MedDRA Introductory Guide or MedDRA Browser (both WBB and MDB) for Concept Descriptions

“Top-down” navigation in HLGT *Medication errors and other product use errors and issues* is best approach for term selection

- **Medication error with clinical consequences**

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient was administered wrong drug and experienced hypotension</td>
<td>Wrong drug administered Hypotension</td>
<td></td>
</tr>
<tr>
<td>Insulin was given using the wrong syringe resulting in the administration of an overdose. The patient developed hypoglycaemia.</td>
<td>Drug administered in wrong device Accidental overdose Hypoglycaemia</td>
<td>If an overdose is reported in the context of a medication error, the more specific term LLT Accidental overdose can be selected</td>
</tr>
</tbody>
</table>
Medication Errors (cont)

- Medication error **without** clinical consequences

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
<th>Preferred Option</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication was given intravenously instead of intramuscularly without any adverse effect</td>
<td>Intramuscular formulation administered by other route</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Intramuscular formulation administered by other route</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No adverse effect</td>
<td></td>
</tr>
</tbody>
</table>
New Medication Errors/Product Use Issues Hierarchy
Definitions of misuse may not always include the concept of therapeutic use; misuse may be similar to the concept of abuse in some regions.
<table>
<thead>
<tr>
<th>Verbatim term</th>
<th>LLT</th>
<th>MTS:PTC Section</th>
<th>Section #</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disconnected feeling</td>
<td>Feeling detached</td>
<td>Always Select a Lowest Level Term</td>
<td>2,4</td>
</tr>
<tr>
<td>Unspecified neurological condition</td>
<td>Neurological disorder NOS</td>
<td>Always Select a Lowest Level Term</td>
<td>2,4</td>
</tr>
<tr>
<td>Echoing in ears</td>
<td>Echoacousia</td>
<td>Always Select a Lowest Level Term</td>
<td>2,4</td>
</tr>
<tr>
<td>After the patient’s drug was substituted with a generic drug, his response to therapy was different</td>
<td>Generic substitution altered therapeutic response</td>
<td>Modification of Effect</td>
<td>3,23</td>
</tr>
<tr>
<td>Severe bronchospasm on induction of anesthesia</td>
<td>Bronchospasm on induction</td>
<td>Always Select a Lowest Level Term</td>
<td>2,4</td>
</tr>
<tr>
<td>Elderly woman complained her arm was tender where she had received her seasonal flu vaccine</td>
<td>Vaccination site tenderness</td>
<td>Always Select a Lowest Level Term</td>
<td>2,4</td>
</tr>
<tr>
<td>PANDAS</td>
<td>PANDAS</td>
<td>Always Select a Lowest Level Term</td>
<td>2,4</td>
</tr>
<tr>
<td>Influenza with body aches, fever, cough</td>
<td>Influenza</td>
<td>Definitive and Provisional Diagnoses with or without Signs and Symptoms</td>
<td>3,1</td>
</tr>
<tr>
<td>72 year old man with aphasia and right hemiplegia. Stroke in middle cerebral artery territory is suspected.</td>
<td>Aphasia, Right hemiplegia, Middle cerebral artery stroke</td>
<td>Definitive and Provisional Diagnoses with or without Signs and Symptoms</td>
<td>3.1</td>
</tr>
<tr>
<td>Patient said she received flu vaccine 3 months before she became pregnant</td>
<td>Vaccine exposure before pregnancy</td>
<td>Exposures during Pregnancy and Breast Feeding</td>
<td>3,10</td>
</tr>
</tbody>
</table>
• Missed Concepts
  – All medical concepts described after the product is taken should be coded
  – Example: “The patient took drug X and developed alopecia, increased LFTs and pancreatitis”. Manufacturer only codes alopecia and increased LFTs (missed concept of pancreatitis)
  – Example: “The patient took drug X and developed interstitial nephritis which later deteriorated into renal failure”. Manufacturer only codes interstitial nephritis (missed renal failure concept)

Acknowledgement: Dr. Toni Piazza-Hepp, Office of Surveillance and Epidemiology, CDER, FDA
Important Coding Errors (cont)

• “Soft Coding”
  – Selecting a term which is both less specific and less severe than another MedDRA term is “soft coding”
  – Example: “Liver failure” coded as hepatotoxicity or increased LFTs
  – Example: “Aplastic anemia” coded as unspecified anemia
  – Example: “Rash subsequently diagnosed as Stevens Johnson syndrome” coded as rash

Acknowledgement: Dr. Toni Piazza-Hepp, Office of Surveillance and Epidemiology, CDER, FDA
MedDRA subscription
# 2018 MedDRA Subscription Rate Table

<table>
<thead>
<tr>
<th>MedDRA Subscription Types</th>
<th>2018 Annual Subscription Rates</th>
<th>Additional Rates for Japanese Translation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regulatory Authority</td>
<td>$0 USD</td>
<td>$0 USD</td>
</tr>
<tr>
<td>Non-Commercial / Non-Profit</td>
<td>$0 USD</td>
<td>$850 USD</td>
</tr>
<tr>
<td>Commercial (Parent Company Annual Revenue or Turnover)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level 0 (Annual Revenue &lt; $1 Million)</td>
<td>$162 USD</td>
<td>$850 USD</td>
</tr>
<tr>
<td>Level 1 (Annual Revenue $1-$10 Million)</td>
<td>$688 USD</td>
<td>$850 USD</td>
</tr>
<tr>
<td>Level 2 (Annual Revenue $10-$20 Million)</td>
<td>$2,627 USD</td>
<td>$850 USD</td>
</tr>
<tr>
<td>Level 3 (Annual Revenue $20-$500 Million)</td>
<td>$4,976 USD</td>
<td>$850 USD</td>
</tr>
<tr>
<td>Level 4 (Annual Revenue $500 Million-$1 Billion)</td>
<td>$10,440 USD</td>
<td>$850 USD</td>
</tr>
<tr>
<td>Level 5 (Annual Revenue $1-$5 Billion)</td>
<td>$43,316 USD</td>
<td>$850 USD</td>
</tr>
<tr>
<td>Level 6 (Annual Revenue $5-$20 Billion)</td>
<td>$57,194 USD</td>
<td>$850 USD</td>
</tr>
<tr>
<td>Level 7 (Annual Revenue &gt; $20 Billion)</td>
<td>$74,620 USD</td>
<td>$850 USD</td>
</tr>
<tr>
<td>System Developer</td>
<td>$2,691 USD</td>
<td>$850 USD</td>
</tr>
</tbody>
</table>

Note: 76% of all MedDRA users pay no fee or $724 (or less)
As of August 2017
- ~5,000 Subscribing organizations (MSSO+J MO)
  - 109 Countries

Graph shows type of organizations (self identified)
MedDRA Users by Region and Top 20 Countries

- Europe: 49%
- North America: 35%
- Asia: 11%
- Oceania: 2%
- Central and South America, Caribbean: 2%

Top 20 Countries:

<table>
<thead>
<tr>
<th>Country</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>1386</td>
</tr>
<tr>
<td>Germany</td>
<td>324</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>310</td>
</tr>
<tr>
<td>France</td>
<td>242</td>
</tr>
<tr>
<td>Italy</td>
<td>218</td>
</tr>
<tr>
<td>Spain</td>
<td>139</td>
</tr>
<tr>
<td>China</td>
<td>129</td>
</tr>
<tr>
<td>Canada</td>
<td>115</td>
</tr>
<tr>
<td>Poland</td>
<td>78</td>
</tr>
<tr>
<td>Australia</td>
<td>77</td>
</tr>
<tr>
<td>South Korea</td>
<td>76</td>
</tr>
<tr>
<td>Netherlands</td>
<td>75</td>
</tr>
<tr>
<td>India</td>
<td>74</td>
</tr>
<tr>
<td>Switzerland</td>
<td>72</td>
</tr>
<tr>
<td>Sweden</td>
<td>70</td>
</tr>
<tr>
<td>Belgium</td>
<td>68</td>
</tr>
<tr>
<td>Greece</td>
<td>51</td>
</tr>
<tr>
<td>Denmark</td>
<td>47</td>
</tr>
<tr>
<td>Austria</td>
<td>46</td>
</tr>
<tr>
<td>Israel</td>
<td>46</td>
</tr>
</tbody>
</table>
MSSO Contacts

- Website
  - www.meddra.org
- Email
  - mssohelp@meddra.org
- Frequently Asked Questions
  - www.meddra.org/faq
- My email
  - tomas.moraleda@meddra.org