Introduction to MedDRA

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What is Coding?
Why code??
What do you see?
How many cases of Headache??

- Head Pain
- Pounding in head
- Dull Headache
- Pain in Head
- Headache
- Hedache
- Throbbing pain in head
- Pain head
- My temples are hurting
- Cephalgia
- Headache recurrent
- Hammering pain in Head

His head started paining after he woke up from sleep.
What Happens when we code?

- A standard code is assigned to each verbatim
- 8 digit MedDRA code gets assigned to the verbatim term

<table>
<thead>
<tr>
<th>Verbatim text</th>
<th>Low Level Term (LLT)</th>
<th>LLTCode</th>
<th>Preferred Term (PT)</th>
<th>PTCode</th>
<th>System Organ Class (SOC)</th>
<th>SOC Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain in eye</td>
<td>Pain in eyes</td>
<td>10033426</td>
<td>Eye pain</td>
<td>10015958</td>
<td>Eye disorders</td>
<td>10015919</td>
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<tr>
<td>Sore eyes</td>
<td>Sore eyes</td>
<td>10041357</td>
<td>Eye pain</td>
<td>10015958</td>
<td>Eye disorders</td>
<td>10015919</td>
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<tr>
<td>Pyrexia</td>
<td>Pyrexia</td>
<td>10037660</td>
<td>Pyrexia</td>
<td>10037660</td>
<td>General disorders and administration site conditions</td>
<td>10018065</td>
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<td>Spiking temperature</td>
<td>Spiking temperature</td>
<td>10041523</td>
<td>Pyrexia</td>
<td>10037661</td>
<td>General disorders and administration site conditions</td>
<td>10018066</td>
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<tr>
<td>Suffering from Fever</td>
<td>Fever</td>
<td>10016558</td>
<td>Pyrexia</td>
<td>10037662</td>
<td>General disorders and administration site conditions</td>
<td>10018067</td>
</tr>
</tbody>
</table>
MedDRA

Importance of “Coding”

- Accuracy
- Consistency
- Transparency
- Standardisation
- Analysis
- Evaluation

Patient Safety
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.
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
Why MedDRA?

ICH initiative (M1)

• An international terminology for coding of medical information throughout the regulatory cycle (clinical trials Phase I-IV and post-marketing)

• Enables standardized communication of coded data between regulators and manufacturers/sponsors
  - Example: MedDRA used is a standard terminology in electronic transmission of Individual Case Safety Reports (ICSRs) following ICH E2B standards
  - Use of MedDRA in Vigibase [WHO global database of individual case safety reports (ICSRs)]
  - SDTM is one of the required standards for data submission to FDA (U.S.) and PMDA (Japan)
Why MedDRA?

• Enables medical accuracy and transparency in coding, since many and specific MedDRA terms
• MedDRA Hierarchy and other concept groupings (such as SMQs) allow for useful data retrieval and presentation
• Global ICH-endorsed guides for coding and data retrieval (ICH Points to Consider documents)
• Global version synchronization
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)
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
Where MedDRA is Used (Contd)

Individual Case Safety Reports (ICSRs) - ICH E2B (R3) Data Elements in MedDRA

<table>
<thead>
<tr>
<th>Element id</th>
<th>Element Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>D.7.1.r.1b</td>
<td>Medical History (disease / surgical procedure / etc.) (MedDRA code)</td>
</tr>
<tr>
<td>D.8.r.6b</td>
<td>Indication (MedDRA code)</td>
</tr>
<tr>
<td>D.8.r.7b</td>
<td>Reaction (MedDRA code)</td>
</tr>
<tr>
<td>D.9.2.r.1b</td>
<td>Reported Cause(s) of Death (MedDRA code)</td>
</tr>
<tr>
<td>D.9.4.r.1b</td>
<td>Autopsy-determined Cause(s) of Death (MedDRA code)</td>
</tr>
<tr>
<td>D.10.7.1.r.1b</td>
<td>Medical History (disease / surgical procedure / etc.) (MedDRA code)</td>
</tr>
<tr>
<td>D.10.8.r.6b</td>
<td>Indication (MedDRA code)</td>
</tr>
<tr>
<td>D.10.8.r.7b</td>
<td>Reactions (MedDRA code)</td>
</tr>
<tr>
<td>E.i.2.1b</td>
<td>Reactions / Event (MedDRA code)</td>
</tr>
<tr>
<td>F.r.2.2b</td>
<td>Test Name (MedDRA code)</td>
</tr>
<tr>
<td>G.k.7.r.2b</td>
<td>Indication (MedDRA code)</td>
</tr>
<tr>
<td>H.3.r.1b</td>
<td>Sender's Diagnosis / Syndrome and / or Reclassification of Reaction / Event (MedDRA code)</td>
</tr>
</tbody>
</table>
Where MedDRA is Used (Contd)

- 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 (Contd)

• 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
MedDRA Users Profile

- As of March 2019
  - 5,800 Subscribing organizations (MSSO+JMO)
  - 125 Countries
- Graph shows types of subscribing organizations
MedDRA Data Sharing

• Subscription grants access to MedDRA for one year
• Subscriber cannot grant any sublicense, publish or otherwise distribute MedDRA to a third party
• Data may be freely exchanged between current MedDRA subscribers
  – Sponsor-sponsor, sponsor-CRO, vendor-user, etc.
  – Use Self-Service Application to check organization’s subscription status
• Sharing MedDRA with a non-subscribing organization is a violation of the MedDRA license
# 2019 MedDRA Subscription Rate Table

<table>
<thead>
<tr>
<th>MedDRA Subscription Types</th>
<th>2019 Annual Subscription Rates</th>
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</thead>
<tbody>
<tr>
<td>Regulatory Authority</td>
<td>$0 USD</td>
</tr>
<tr>
<td>Non-Commercial / Non-Profit</td>
<td>$0 USD</td>
</tr>
<tr>
<td>Commercial (Parent Company Annual Revenue or Turnover)</td>
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</tr>
<tr>
<td>Level 0 (Annual Revenue &lt; $1 Million)</td>
<td>$154 USD</td>
</tr>
<tr>
<td>Level 1 (Annual Revenue $1-$10 Million)</td>
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<tr>
<td>Level 2 (Annual Revenue $10-$20 Million)</td>
<td>$2,496 USD</td>
</tr>
<tr>
<td>Level 3 (Annual Revenue $20-$500 Million)</td>
<td>$4,727 USD</td>
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<tr>
<td>Level 4 (Annual Revenue $500 Million-$1 Billion)</td>
<td>$9,918 USD</td>
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<tr>
<td>Level 5 (Annual Revenue $1-$5 Billion)</td>
<td>$41,150 USD</td>
</tr>
<tr>
<td>Level 6 (Annual Revenue $5-$20 Billion)</td>
<td>$54,334 USD</td>
</tr>
<tr>
<td>Level 7 (Annual Revenue &gt; $20 Billion)</td>
<td>$70,889 USD</td>
</tr>
<tr>
<td>System Developer</td>
<td>$2,556 USD</td>
</tr>
</tbody>
</table>

77% of all MedDRA users pay no fee or $654 (or less)
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**
- Not a drug dictionary
- Patient demographic terms
- Clinical trial study design terms
- Frequency qualifiers
- Numerical values for results
- Severity descriptors
- Not an equipment, device, diagnostic product dictionary
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)

MedDRA Version 22.0
**MedDRA Structure (Cont)**

- **SOC** = Cardiac disorders
- **HLGT** = Cardiac arrhythmias
- **HLT** = Rate and rhythm disorders NEC
- **PT** = Arrhythmia

- **LLT**
  - Arrhythmia
  - Arrhythmia NOS
  - Dysrhythmias
  - LLT (Non-current) Other specified cardiac dysrhythmias

Not all LLTs shown.
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 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

Hoofdpijn
Dutch

Headache
English

Céphalée
French

Bolest hlavy
Czech

Fejféjás
Hungarian

Cefalea
Italian

頭痛
Japanese

Cefalea
Spanish

Головная боль
Russian

Electronic Submission
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 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: POINTS TO CONSIDER**
ICH-Endorsed Guide for MedDRA Users

**Release 4.17**
*Based on MedDRA Version 22.0*

1 March 2019

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

• Detailed coding instructions
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
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/

• 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
How to code with MedDRA?

• 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
• If no exact match in MedDRA, use medical judgment to match to an existing term that adequately represents the concept
• Avoid company-specific “work-arounds” for MedDRA deficiencies, submit change request to MSSO
How to code with MedDRA? Example:

- Verbatim: THYROID CARCINOMA
  - Coded to LLT: Thyroid carcinoma

```
LLT  Thyroid carcinoma [10043702]
  PT   Thyroid cancer [10066474]
    HLT Thyroid neoplasms [10043747]
    HLT Thyroid neoplasms malignant [10043749]
      HT  Endocrine neoplasms malignant and unspecified [10014713]
        GT Neoplasms benign, malignant and unspecified (incl cysts and polyps) [10029104]
```
How to code with MedDRA? Example:

- Verbatim: 03/19/2012: Patient was hospitalized with severe upper abdominal burning pain radiating to the back, nausea, and vomiting that worsened with eating. Upon further investigation her serum amylase levels were found to be elevated and was diagnosed with Pancreatitis. During the hospitalization she was also found to have DVT.

  — Coded to

  1. LLT : Pancreatitis

  2. LLT : DVT
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?
How to code with MedDRA?

- Gastric Boating
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
What Terms to Select?

- Hypoglycemia (blood glucose = 200 mg/dL)

  Blood glucose abnormal
  Blood glucose increased
  Hypoglycemia
What Terms to Select?

- Clinical complication of IUD
  - IUD complication (PT Complication associated with device)
  - Intra-uterine death (PT Foetal death)
  - Unevaluable event
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
What Terms to Select?

- **MI**
  - Myocardial infarction ?
  - Mitral incompetence ?
  - Mental Illness ?
What Terms to Select?

“Husband had his uterus scrapped and frozen”
What Terms to Select?

- Patient attempted to commit suicide by walking into the sea; unfortunately, he could swim

Attempting suicide
After Coding?
How is MedDRA Used for Analysis?

- MedDRA can be used to summarise large volumes of data
  - Standard approach is to list data at PT and SOC levels for overview

- Focused searches can be made using features of MedDRA
  - Searching for specific PTs
  - Summarising at HLT or HLGT levels
  - Using multiaxial links to group diagnoses with signs and symptoms
  - Selecting a set of relevant PTs which reflect the condition of interest
  - Using Standardised MedDRA Queries (SMQs) for signal detection
  - Customized search / Modified MedDRA Queries
MedDRA Data Retrieval and Presentation: Points to Consider

• Provides data retrieval and presentation options for industry or regulatory purposes

• Recommended to be used as basis for individual organization’s own data retrieval conventions

• Most effective when used in conjunction with MedDRA Term Selection: PTC document
What is a Query?

Clinical Trial Database
Safety Database

Case
LLT1
LLT2
LLT3

"Hit"

SMQ
PT
LLT
LLT
LLT 1
PT
LLT
LLT
LLT
Standardised MedDRA Queries (SMQs)

- Tools developed to facilitate retrieval of MedDRA-coded
- Collaboration between CIOMS (Council for International Organizations of Medical Sciences) and ICH (MSSO)
- Groupings of terms from one or more MedDRA SOCs related to medical condition or area of interest
- Terms relate to signs/symptoms, diagnoses, syndromes, physical findings, laboratory and other test data, etc.
- Intended to aid in case identification
- Broad/narrow scope
- Hierarchical SMQs
- Algorithmic SMQs
SMQ in Production - Examples

- As of Version 22.0, a total of 104 level 1 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
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)
**EMA: Signal of Lactic Acidosis - PT vs. SMQ**

**Broad search** of SMQ identifies additional ICSRs with related **signs** and symptoms where no specific diagnosis is made. These would be missed if search only conducted with PT *Lactic acidosis*.

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**Acknowledgement:** Dr. Aniello Santoro, EMA
Use of SMQs at FDA – Reviewing Prescribing Information

- **Proposed Prescribing Information:**
- **Warnings & Precautions:**
  - Dizziness/Somnolence
  - Withdrawal of Antiepileptic Drugs
  - Suicidal Behavior and Ideation (class labeling)

<table>
<thead>
<tr>
<th>SMQ (Narrow Search)</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Hostility/aggression</td>
<td>4.4</td>
</tr>
<tr>
<td>(2) Vestibular disorders</td>
<td>4.258</td>
</tr>
<tr>
<td>(1) Hearing and vestibular disorders</td>
<td>4.088</td>
</tr>
<tr>
<td>(1) Hyponatraemia/SIADH</td>
<td>3.832</td>
</tr>
<tr>
<td>(2) Hearing impairment</td>
<td>3.832</td>
</tr>
<tr>
<td>(1) Dyslipidaemia *</td>
<td>2.555</td>
</tr>
<tr>
<td>(1) Biliary disorders</td>
<td>2.135</td>
</tr>
<tr>
<td>(2) Functional, inflammatory and gallstone related biliary disorders</td>
<td>2.135</td>
</tr>
</tbody>
</table>

- **Final Prescribing Information**
- **Boxed Warning:**
  - Serious Psychiatric and Behavioral Reactions
- **Warnings & Precautions:**
  - Falls
  - Dizziness & somnolence
  - Withdrawal of Antiepileptic Drugs
  - Suicidal Behavior and Ideation (class labeling)

Acknowledgement: Dr. Christopher Breder, Office of New Drugs, CDER, FDA
Required Skills?

- Coding
  - Logical approach
  - Ability to apply rules
  - Clinical knowledge
  - Research skills
  - Language abilities
  - Good memory
  - Desire to understand
  - Attention to detail
  - Ability to explain to others

- Analysis
  - Clinical knowledge
  - Desire to understand
  - Patience
  - Lateral thinking
  - Willingness to explore data
  - Ability to remain unbiased

Skill Development: A core need
Who uses MedDRA?

- **Coder** – Codes Clinical Trials and Pharmacovigilance data
- **Drug Safety Associate** – Enters cases for monitoring & reporting
- **Clinical Scientist** – Evaluates & analyses clinical trial data
- **Drug Safety Physician** – Performs periodic reporting & signal detection
- **Others**
  - Investigator site staff
  - CRA/Monitor
  - Data Manager
  - Statistician
  - Quality & documentation
  - Software designer
  - Database programmer
Know more?

- Visit: [www.meddra.org](http://www.meddra.org)
Thank You!!

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