Introduction to MedDRA

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What is Coding?
Why code??

What do you see?

How many cases of Headache??

Pounding in head

Head Pain

Dull Headache

Pain in Head

His head started paining after he woke up from sleep

Headache

Hedache

Cephalgia

Throbbing pain in head

Pain head

Headache recurrent

Hammering pain in Head

My temples are hurting

What Happens when we code?

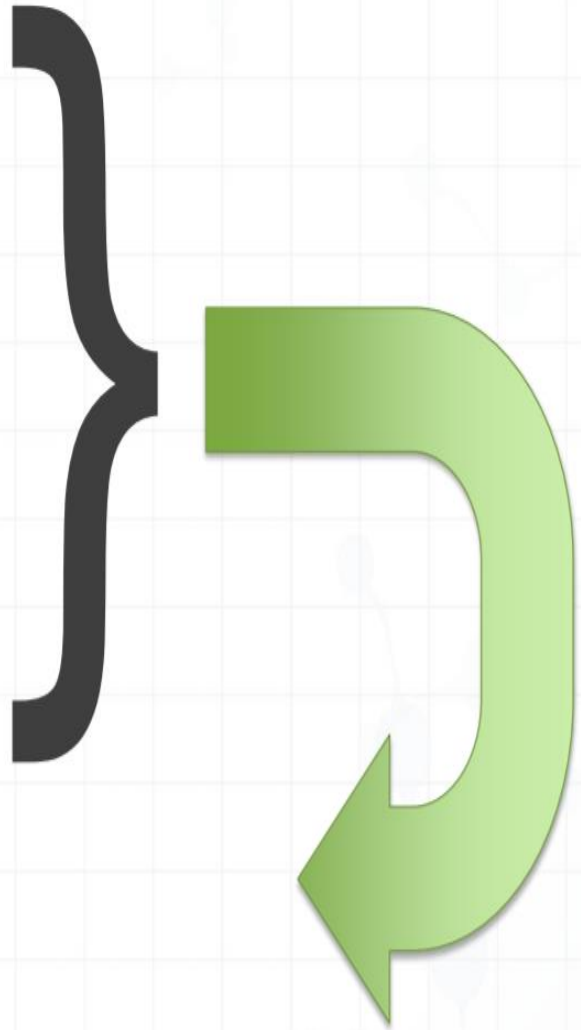
- A standard code is assigned to each verbatim
- 8 digit MedDRA code gets assigned to the verbatim term

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

Importance of "Coding"

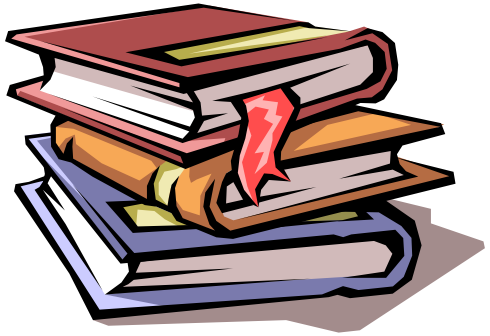
- Accuracy
- Consistency
- Transparency
- Standardisation
- Analysis
- Evaluation

- Patient Safety



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.

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)

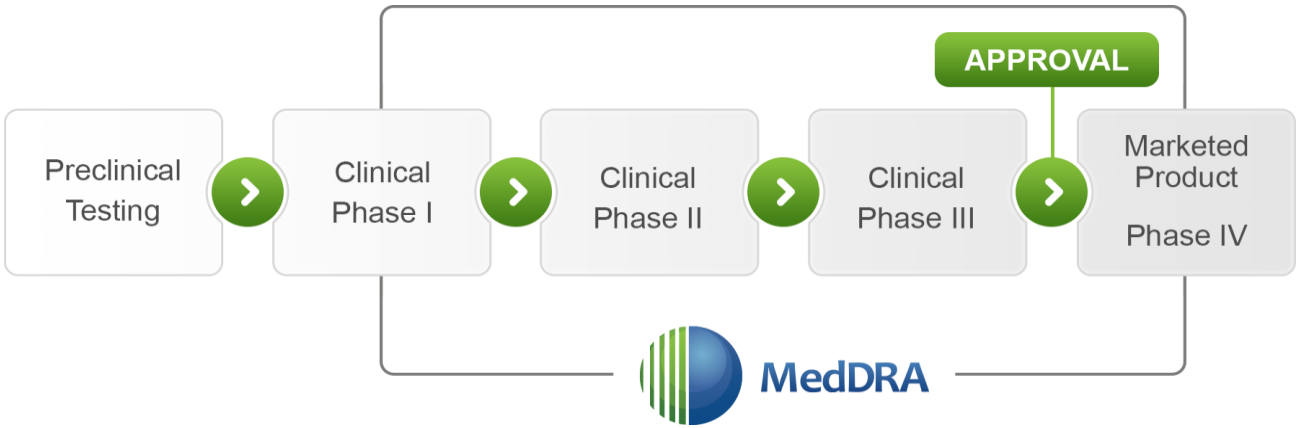
Why MedDRA?

- 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



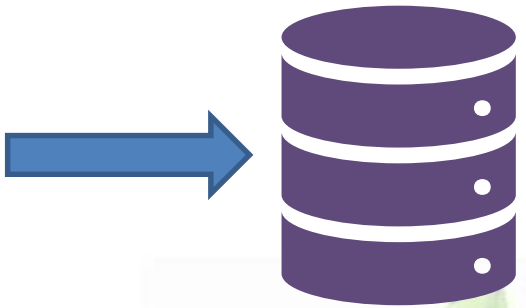
Regulatory Authority and Industry Databases
Individual Case Safety Reports and Safety Summaries
Clinical Study Reports
Investigators' Brochures
Core Company Safety Information
Marketing Applications
Publications
Prescribing Information
Advertising

Where MedDRA is Used (Contd)

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

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

Regulator Database



Where MedDRA is Used (Contd)

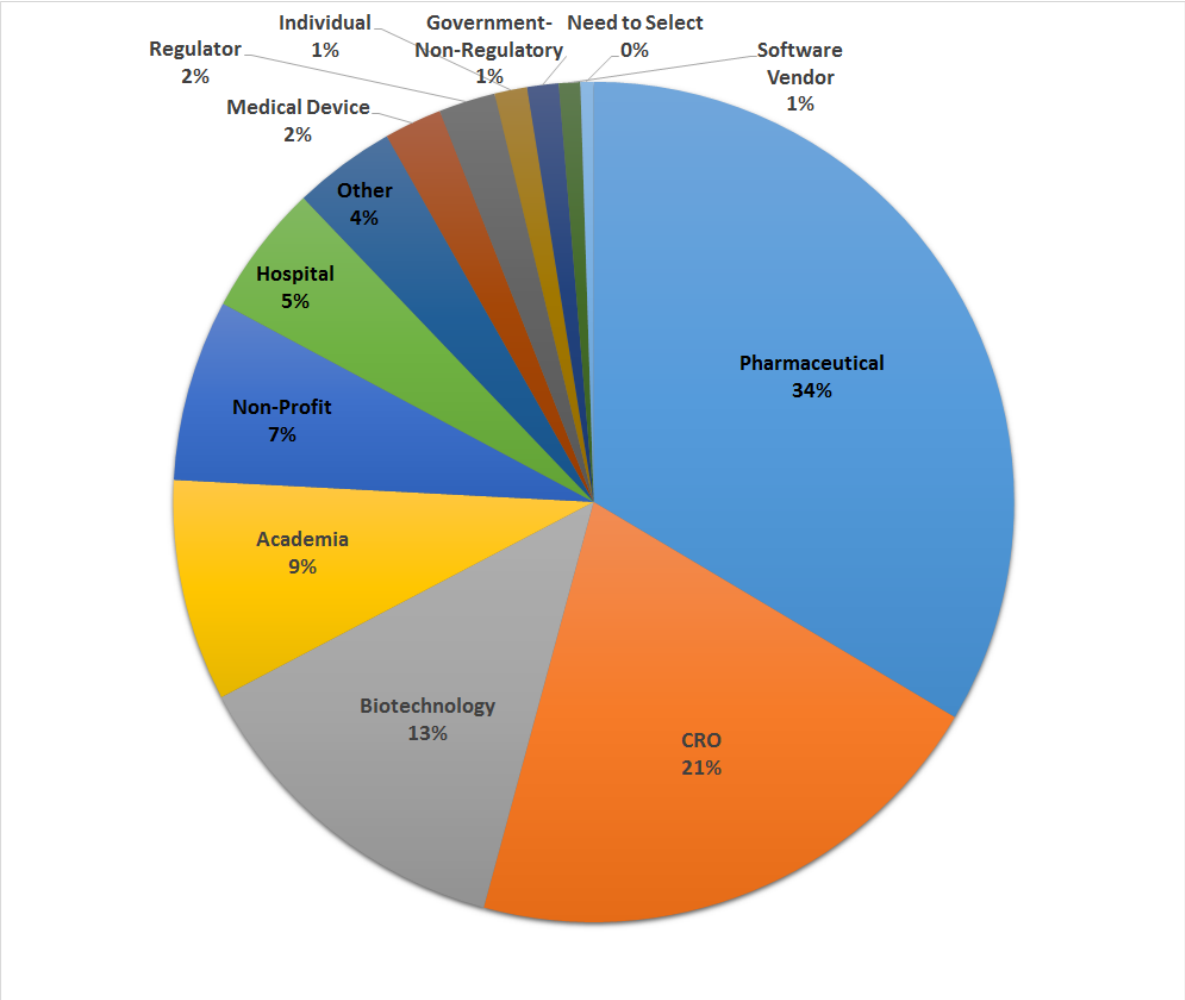
- Regulatory Safety Databases Coded in MedDRA (examples)
  - US FDA
    - FAERS: drugs and biologics
    - VAERS: vaccines
    - CAERS: foods, dietary supplements, cosmetics
  - EMA
    - EudraVigilance Database
  - Health Canada
    - Canada Vigilance Database
  - MHLW/PMDA
    - Safety database

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

MedDRA Subscription Types	2019 Annual Subscription Rates
Regulatory Authority	$0 USD
Non-Commercial / Non-Profit	$0 USD
Commercial (Parent Company Annual Revenue or Turnover)	
Level 0 (Annual Revenue < $1 Million)	$154 USD
Level 1 (Annual Revenue $1-$10 Million)	$654 USD
Level 2 (Annual Revenue $10-$20 Million)	$2,496 USD
Level 3 (Annual Revenue $20-$500 Million)	$4,727 USD
Level 4 (Annual Revenue $500 Million-$1 Billion)	$9,918 USD
Level 5 (Annual Revenue $1-$5 Billion)	$41,150 USD
Level 6 (Annual Revenue $5-$20 Billion)	$54,334 USD
Level 7 (Annual Revenue > $20 Billion)	$70,889 USD
System Developer	$2,556 USD

77% of all MedDRA users pay no fee or $654 (or less)

How to subscribe?

Online Subscription / Subscription /

Organisation

Organisation Name: *

Organisation Type: *
Select a type

Subscription Type *

Regulatory Authority
All regulatory authorities are eligible to receive MedDRA at no charge. This includes the English version of each release of MedDRA as well as all available translations.

Non-Profit / Non-Commercial
Subscription reserved for non-profit medical libraries, educational institutions, and direct patient care providers, i.e., hospitals for educational use or as a reference tool.

Commercial
Subscription for organisations that use MedDRA for commercial purposes. This includes biopharmaceutical companies and support service providers (e.g., CROs). Please provide a link to your company's financial information or attach a signed statement on your company's letterhead with your company's total revenue in PDF format.

System Developer
Subscription reserved for organisations that develop software products that utilise MedDRA. The use of MedDRA by system developers is for testing the terminology with their developed products and not for classification, analysis, or communication of data.

Contact Information

Main point of contact

First Name: *

Last Name: *

Street, No: *

City: *

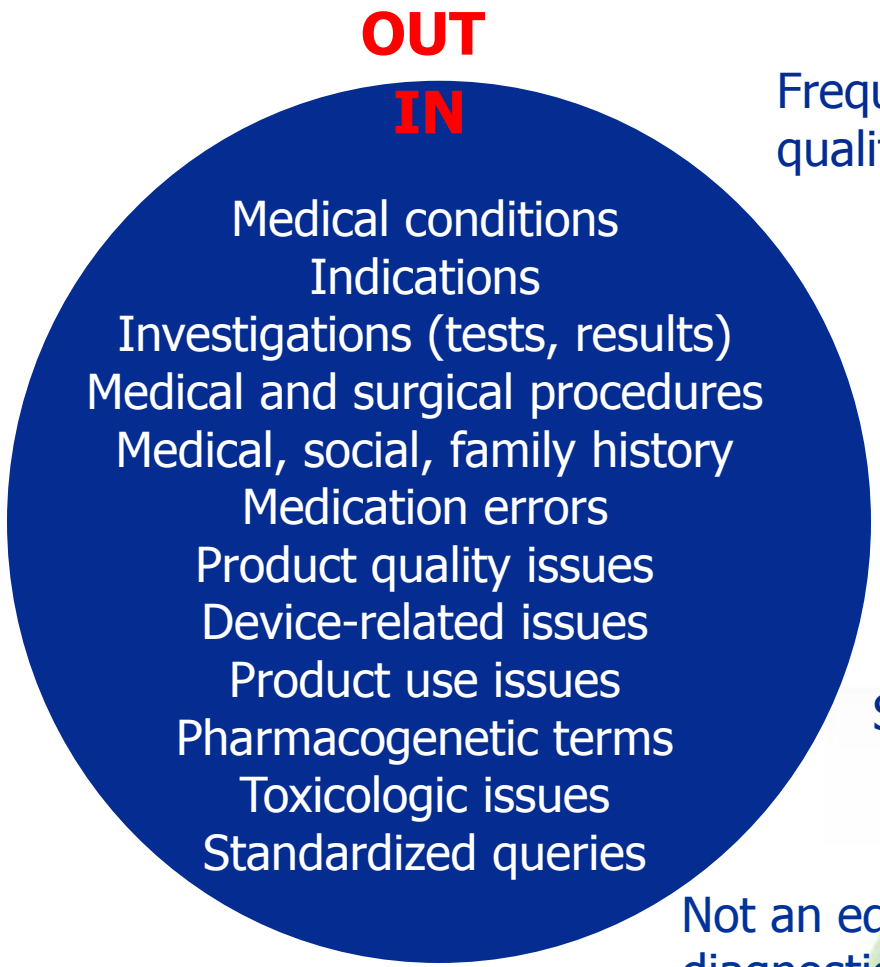
Province/State: *

Postal/Zip Code:

Country: *

Phone: *

Scope of MedDRA



Not a drug dictionary

Frequency qualifiers

Patient demographic terms

Numerical values for results

Clinical trial study design terms

Severity descriptors

Not an equipment, device, diagnostic product dictionary

MedDRA Structure

System Organ Class (SOC) (27)

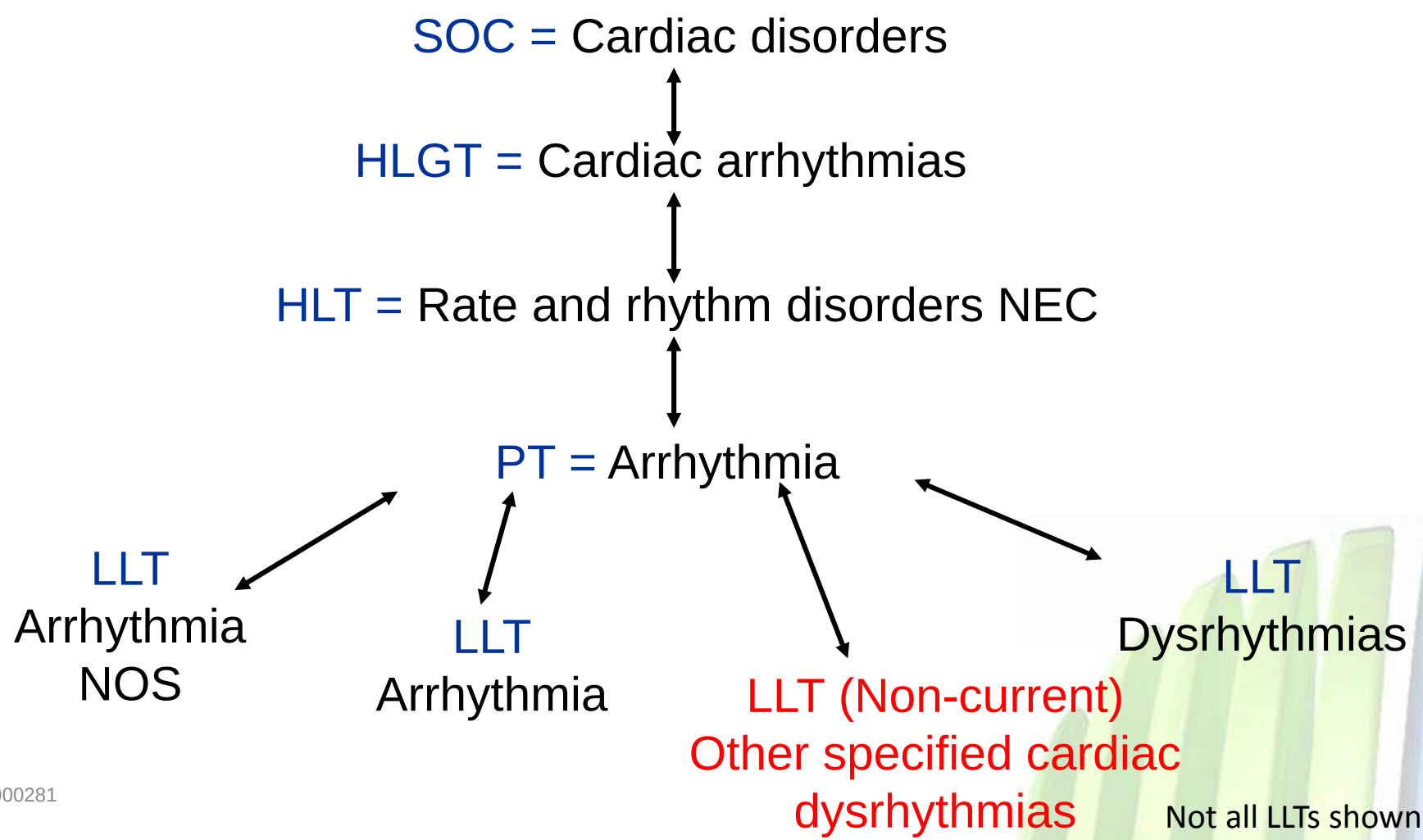
High Level Group Term (HLGT) (337)

High Level Term (HLT) (1,737)

Preferred Term (PT) (23,708)

Lowest Level Term (LLT) (80,262)

MedDRA Structure (Cont)



Not all LLTs shown

System Organ Classes

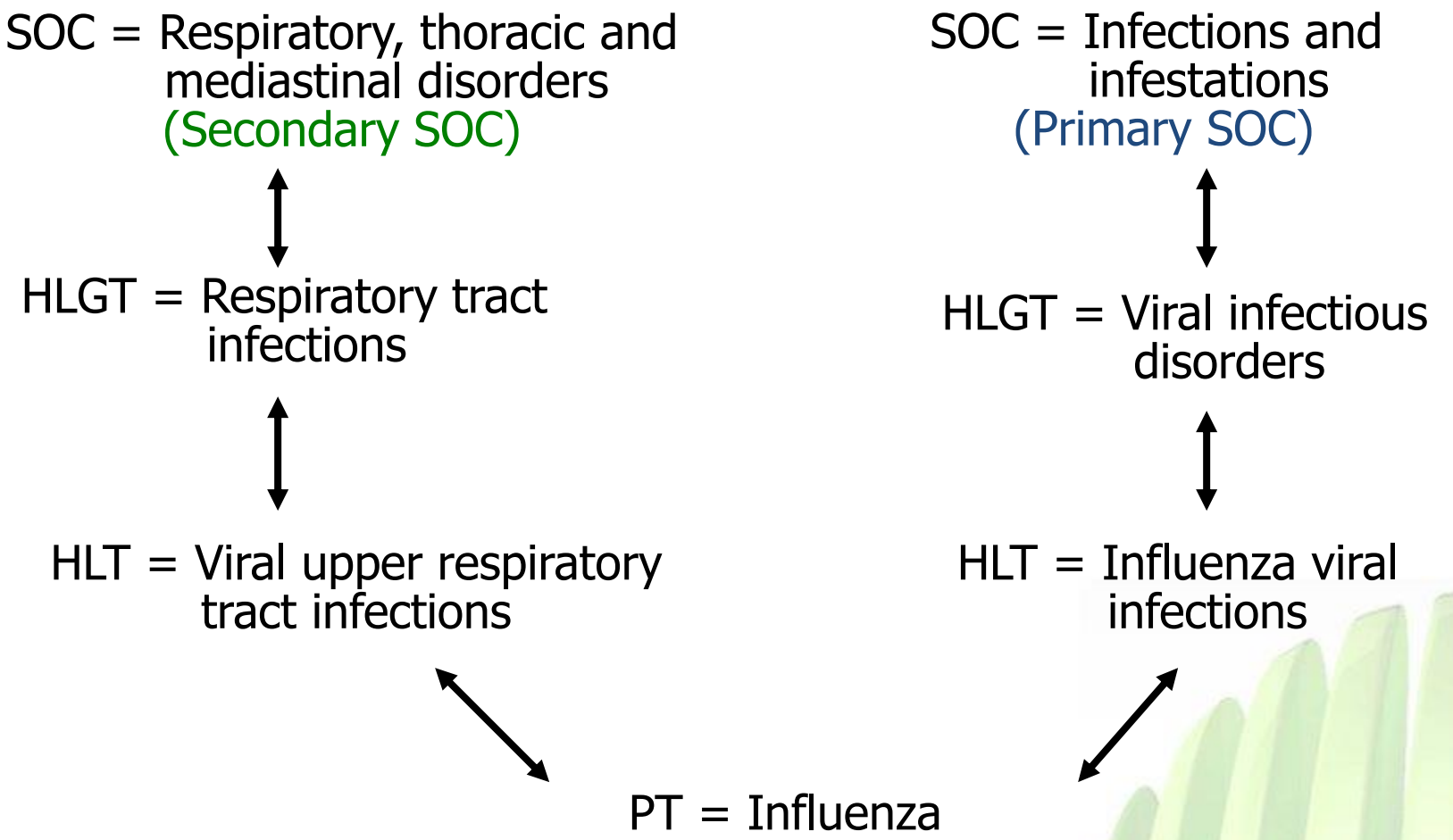
- Blood and lymphatic system disorders
- Cardiac disorders
- Congenital, familial and genetic disorders
- Ear and labyrinth disorders
- Endocrine disorders
- Eye disorders
- Gastrointestinal disorders
- General disorders and administration site conditions
- Hepatobiliary disorders
- Immune system disorders
- 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

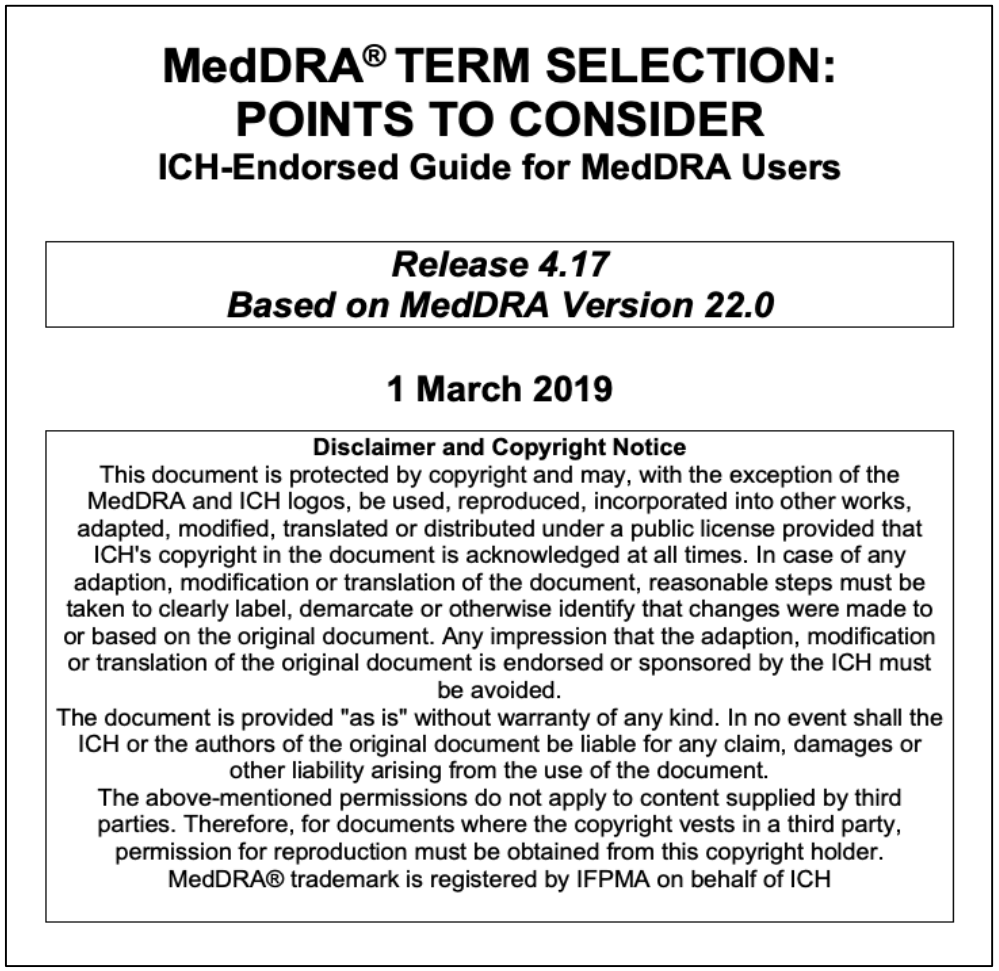
Codes and Languages

A Multi-Axial Terminology (cont)



ICH MedDRA Coding Guide

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



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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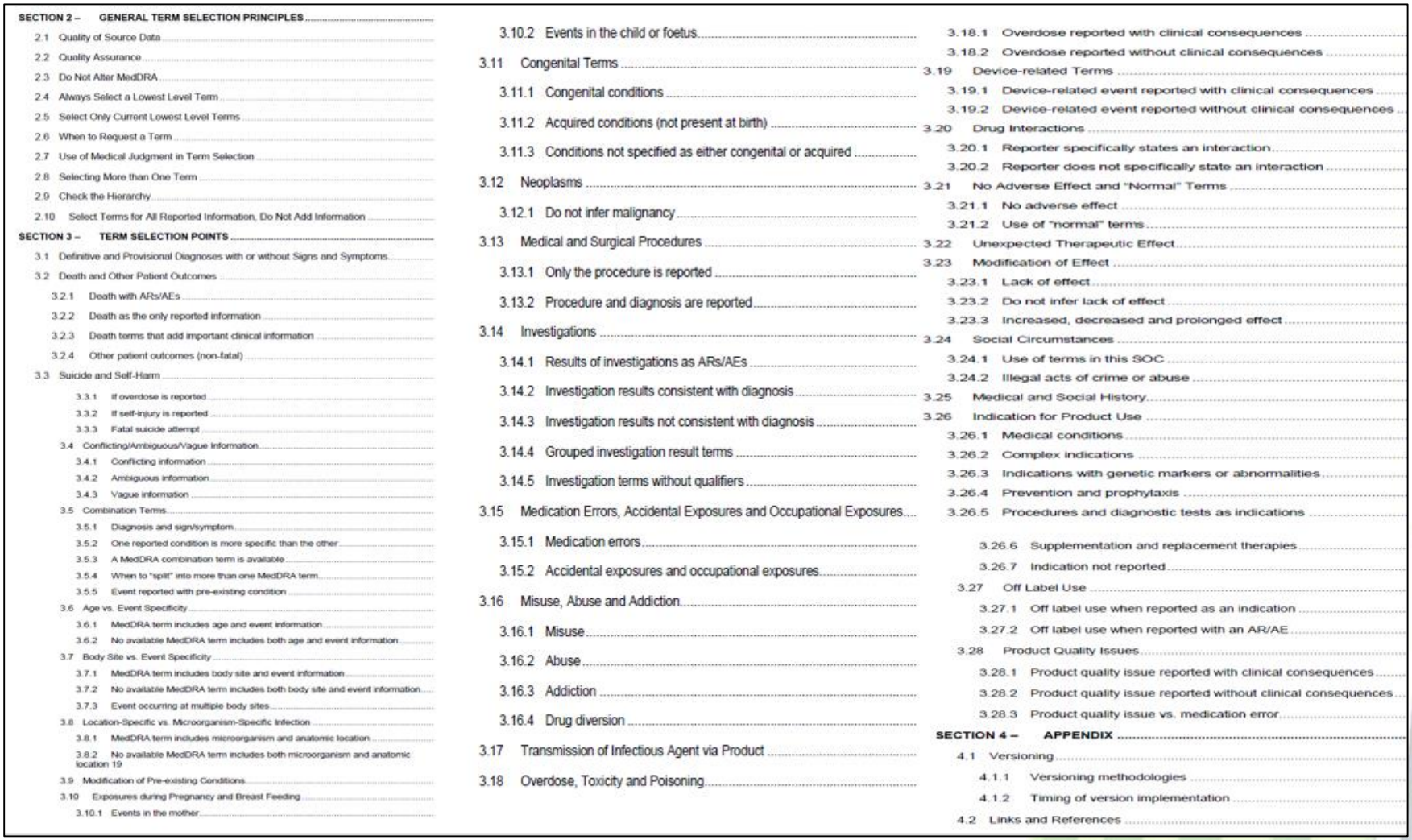
MedDRA® trademark is registered by IFPMA on behalf of ICH

- 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 (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

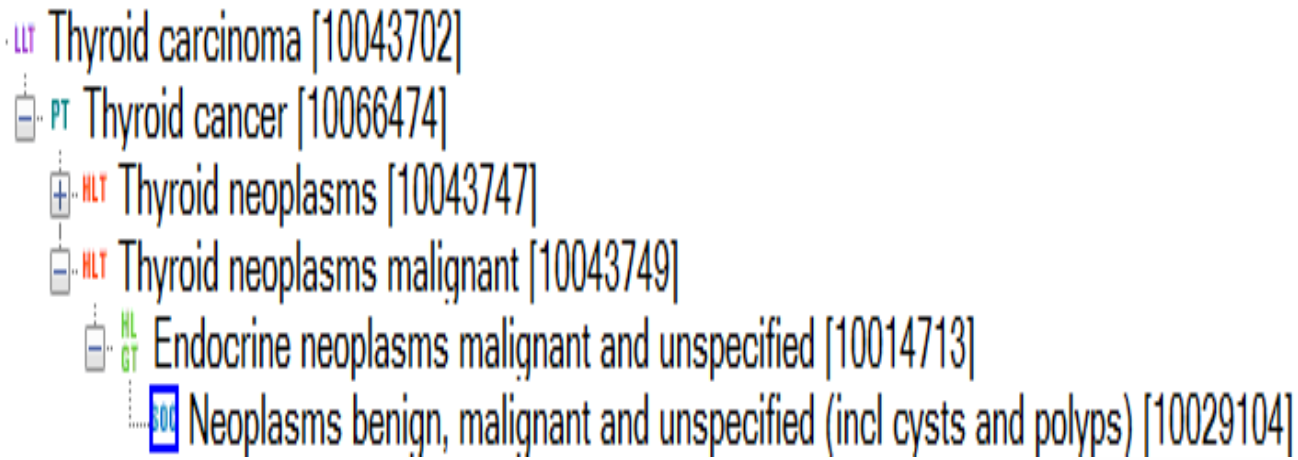
- MedDRA Desktop Browser (MDB)
  - Download MDB and release files from MedDRA website
- MedDRA Web-Based Browser (WBB)
  - https://tools.meddra.org/wbb/
- Features
  - Both require MedDRA ID and password
  - View/search MedDRA and SMQs
  - Support for all MedDRA languages
  - Language specific interface
  - 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:

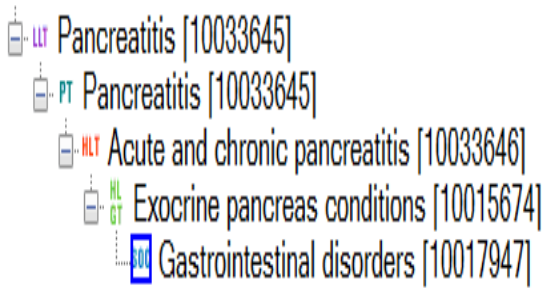
- Verbatim: THYROID CARCINOMA
  - Coded to LLT : Thyroid carcinoma



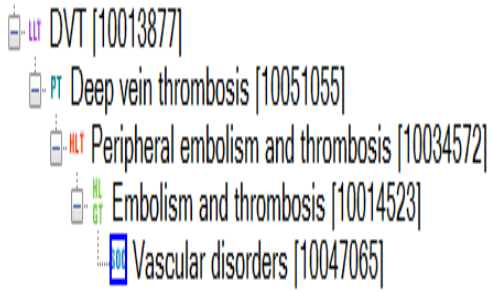
How to code with MedDRA? Example:

- 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 where found to be elevated and was diagnosed with Pancreatitis. During the hospitalization she was also found to have DVT.
  - Coded to

1. LLT : Pancreatitis



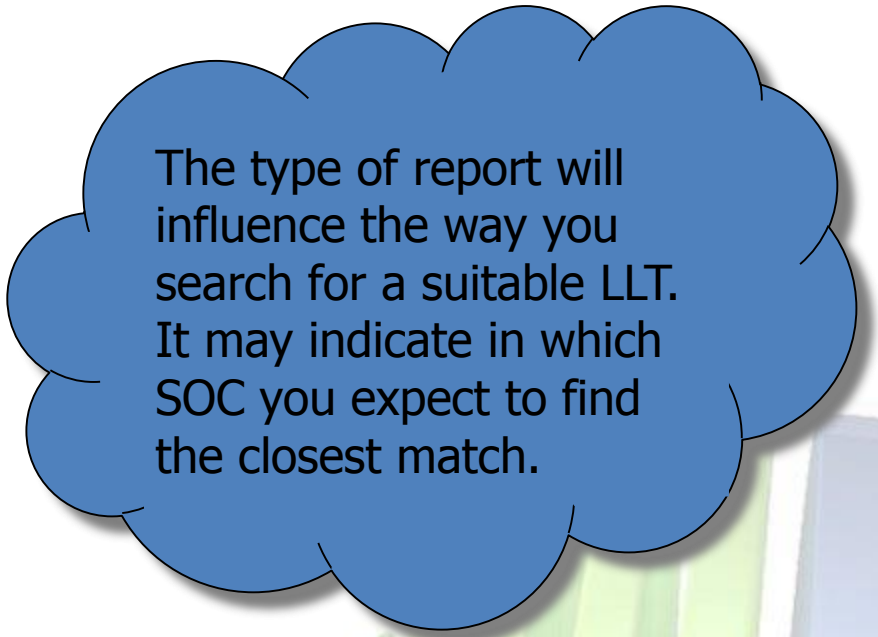
2. LLT : DVT



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

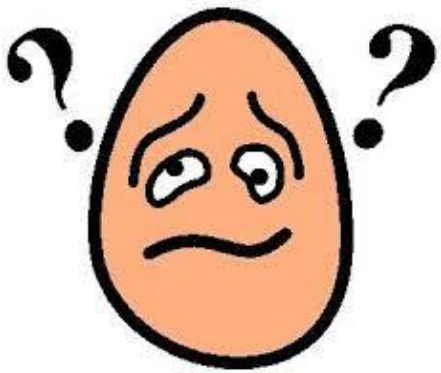
What Terms to Select?

- MI

  Myocardial infarction ?

  Mitral incompetence ?

  Mental Illness ?

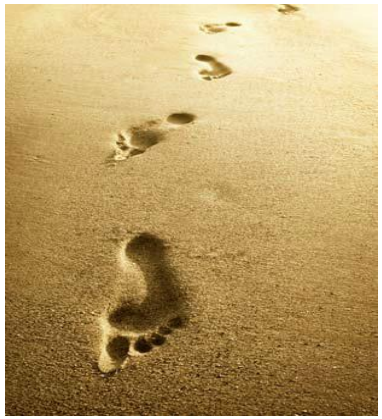


What Terms to Select?

"Husband had his uterus scrapped and frozen"

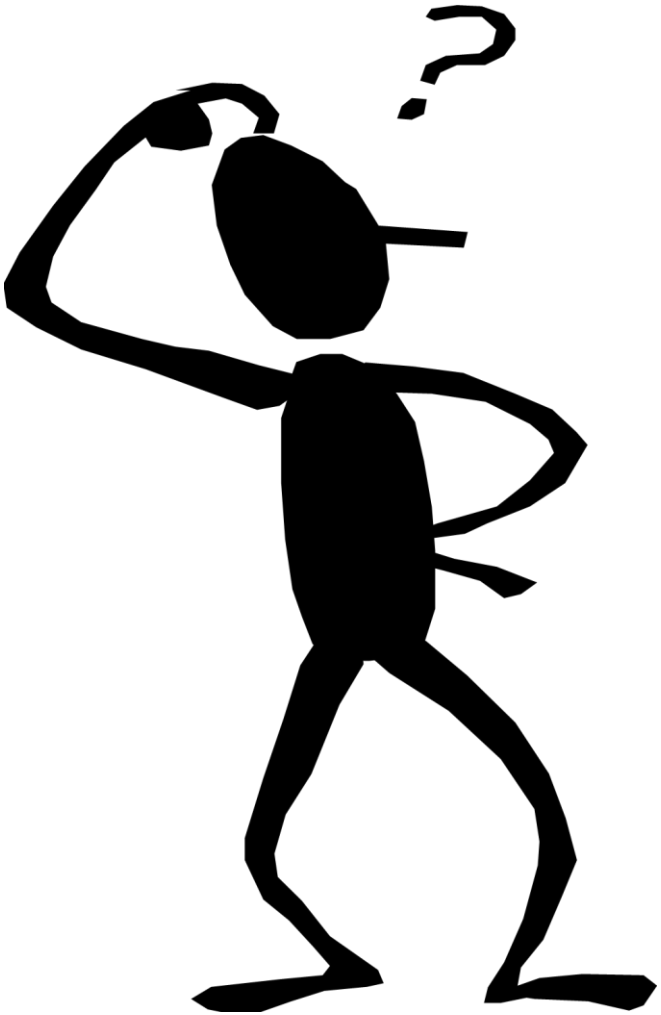
What Terms to Select?

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



Attempted suicide

After Coding?

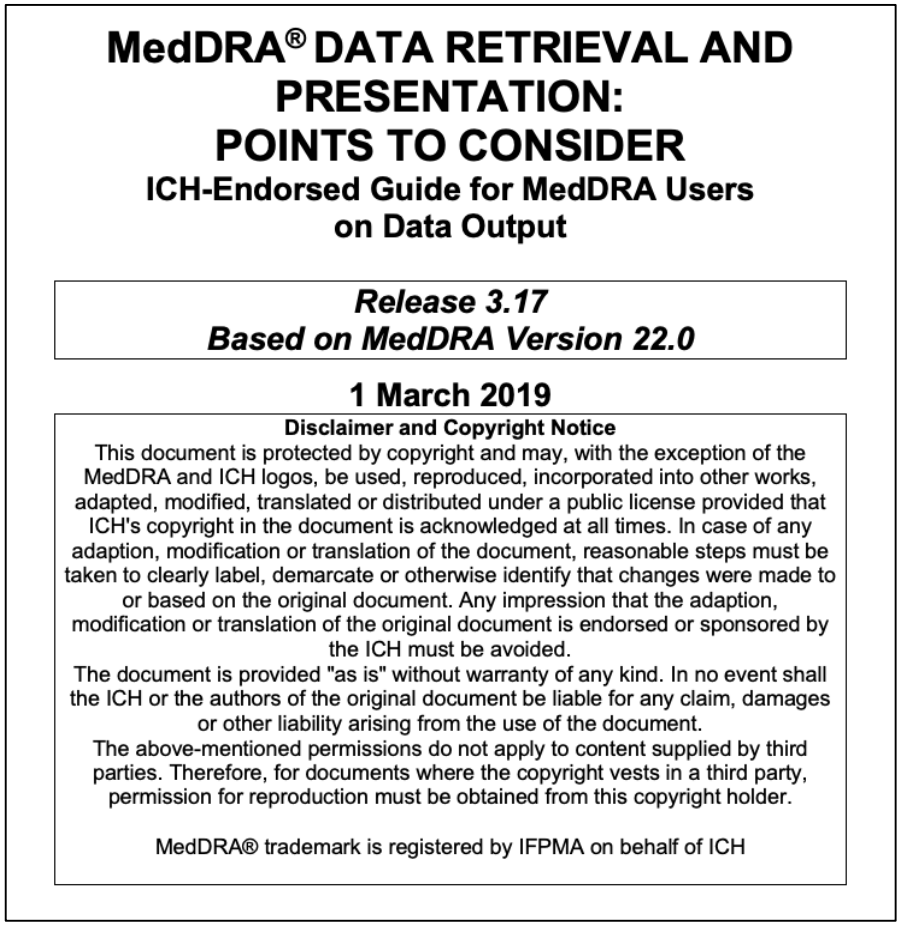


How is MedDRA Used for Analysis?

- 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

Analysis Guidelines

MedDRA Data Retrieval and Presentation: Points to Consider



MedDRA® DATA RETRIEVAL AND PRESENTATION: POINTS TO CONSIDER

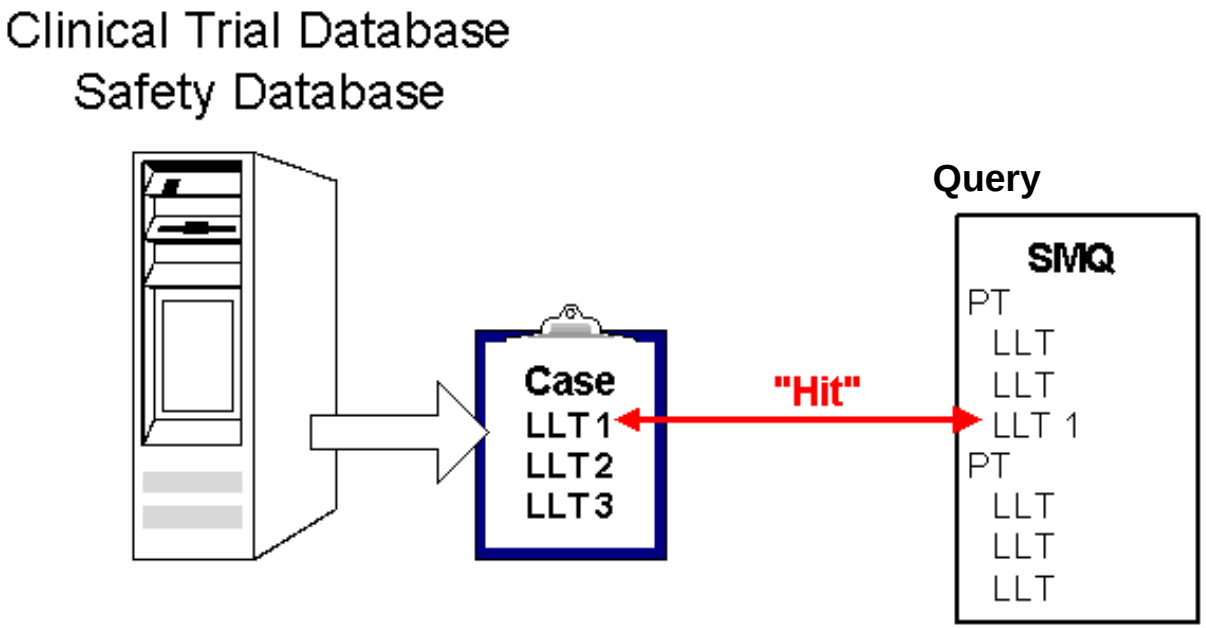
ICH-Endorsed Guide for MedDRA Users on Data Output

Release 3.17
Based on MedDRA Version 22.0

1 March 2019

- 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?



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

Active Substances	SOCs	HLGTs	HLTs	SMQ Broad	SMQ Narrow	PTs	Tot EV	PRR (-)
Drug A	Metab	Acid-Base Disorders	Metabolic Acidoses (Excl Diabetic Acidoses)	Hyperglyc/New Onset Diab_mell -- Lactic Acidosis	Lactic Acidosis	Lactic Acidosis	63	13.74

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.*

SMQ *Lactic acidosis* (Broad search)

PT	Cases
Acidosis	2
Anion gap increased	1
Blood bicarbonate abnormal	1
Blood bicarbonate decreased	6
Blood gases abnormal	1
Blood lactic acid increased	27
Hyperlactacidaemia	22
Lactic acidosis	63
Metabolic acidosis	18
PCO2 decreased	1

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)

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

- 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

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

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Thank You!!

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