Module 4: Medical (MedDRA) Coding

Agenda

- Overview of MedDRA
- MedDRA Structure
- AE Term Selection: Points to consider
- Practice Cases

Overview of MedDRA

- Introduction
- History
- Scope
- Purpose

What is MedDRA?

- Medical Dictionary for Regulatory Activities
- A Dictionary for coding all medical information obtained during all phases of development and marketing:
  - Symptoms & Signs
    Diseases
  - Diagnosis
  - Indications
  - Investigations/Procedures
  - Medical/Social/Family History

Development, ownership and maintenance

- MedDRA was developed by the **International Conference on Harmonisation (ICH)**

- It is owned by the **International Federation of Pharmaceutical Manufacturers and Associations (IFPMA)** acting as trustee for the ICH steering committee

- Maintained by **Maintenance and Support Service Organization (MSSO)** that is responsible for updating and maintaining MedDRA and distributing the terminology, on license, to users in the industry and regulatory agencies.

Development, ownership and maintenance

Before MedDRA:

- **Available Tools -** FDA's COSTART, WHO-ART, J-ART, H-ARTS, ICD-9 and ICD-9CM
- **Challenges - I**nfrequent updates leading to individual users creating their own version and standardization was lost.
- **Need -** Standard Medical Terminology to provided the scope and level of granularity that was needed by regulatory authorities and industry

Rationale for MedDRA

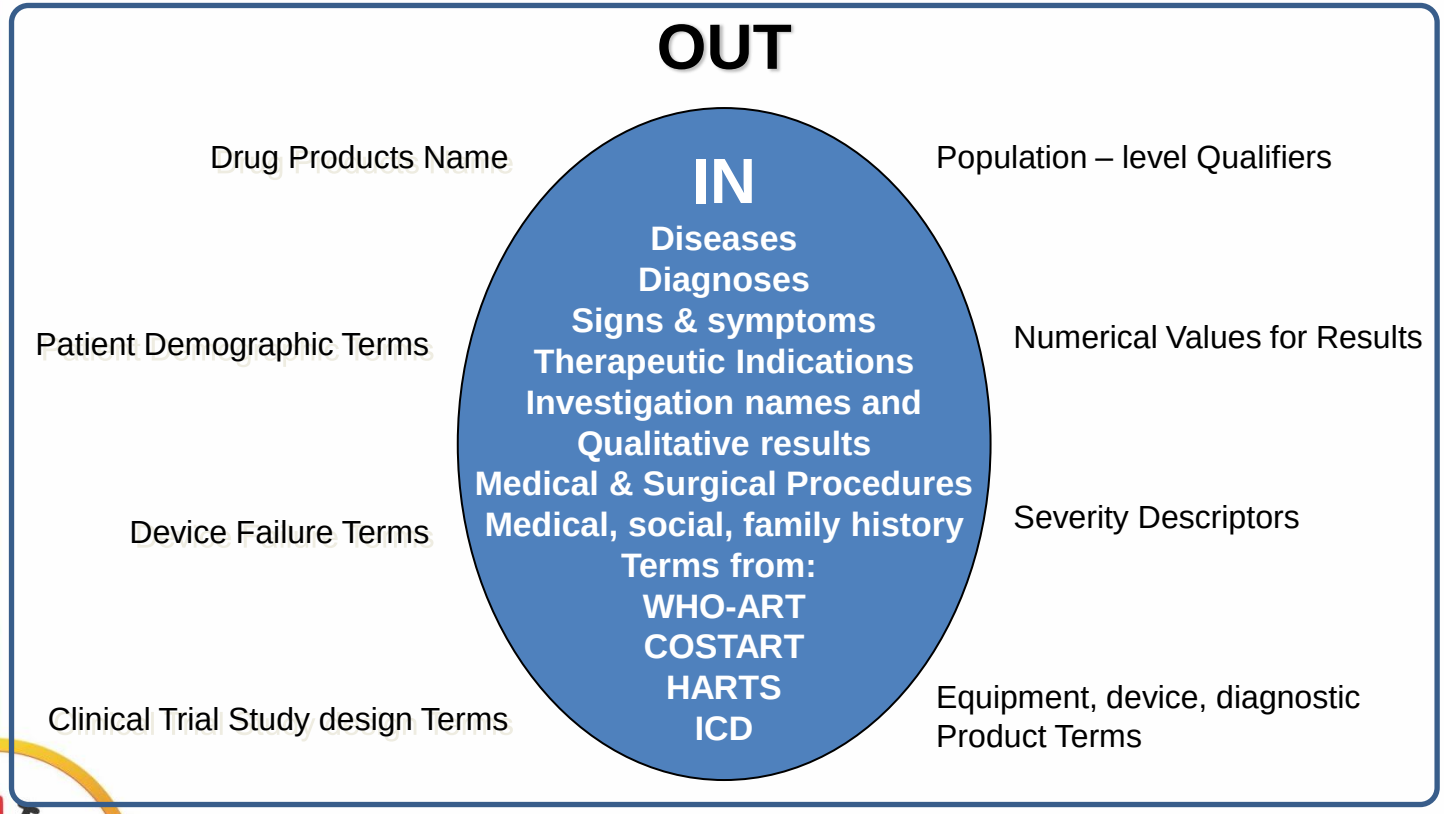
Challenges with Established terminologies (WHO-ART, COSTART, etc.)

- Lack specificity
- Have limited data retrieval options
- Unable to handle complex combinations of signs and symptoms (syndromes)

Need for global standardization

- Across regulatory agencies
- Across multinational pharmaceutical companies
- Necessary through-out product lifecycle
- Necessary for electronic data transfer
- Avoids translation distortions/errors across countries

Scope of MedDRA



Purpose of using MedDRA

- To aggregate reported terms in medically meaningful groupings for the purpose of reviewing and /or analyzing safety data.
- To facilitate consistent retrieval of specific cases or medical conditions from a database .
- To improve consistency in comparing and understanding “safety signals” and aggregated clinical data.
- To facilitate electronic data interchange of clinical safety information.

Purpose of using MedDRA contd

- To report adverse reaction/adverse event (ADR/AE) terms via individual case safety reports.
- To include ADR/AE's in tables, analyses, and line listings for report .
- To identify frequency of medically similar ADR/AEs.
- To capture and present product indications, investigations, medical history and social history data.

Objectives of Medical Coding

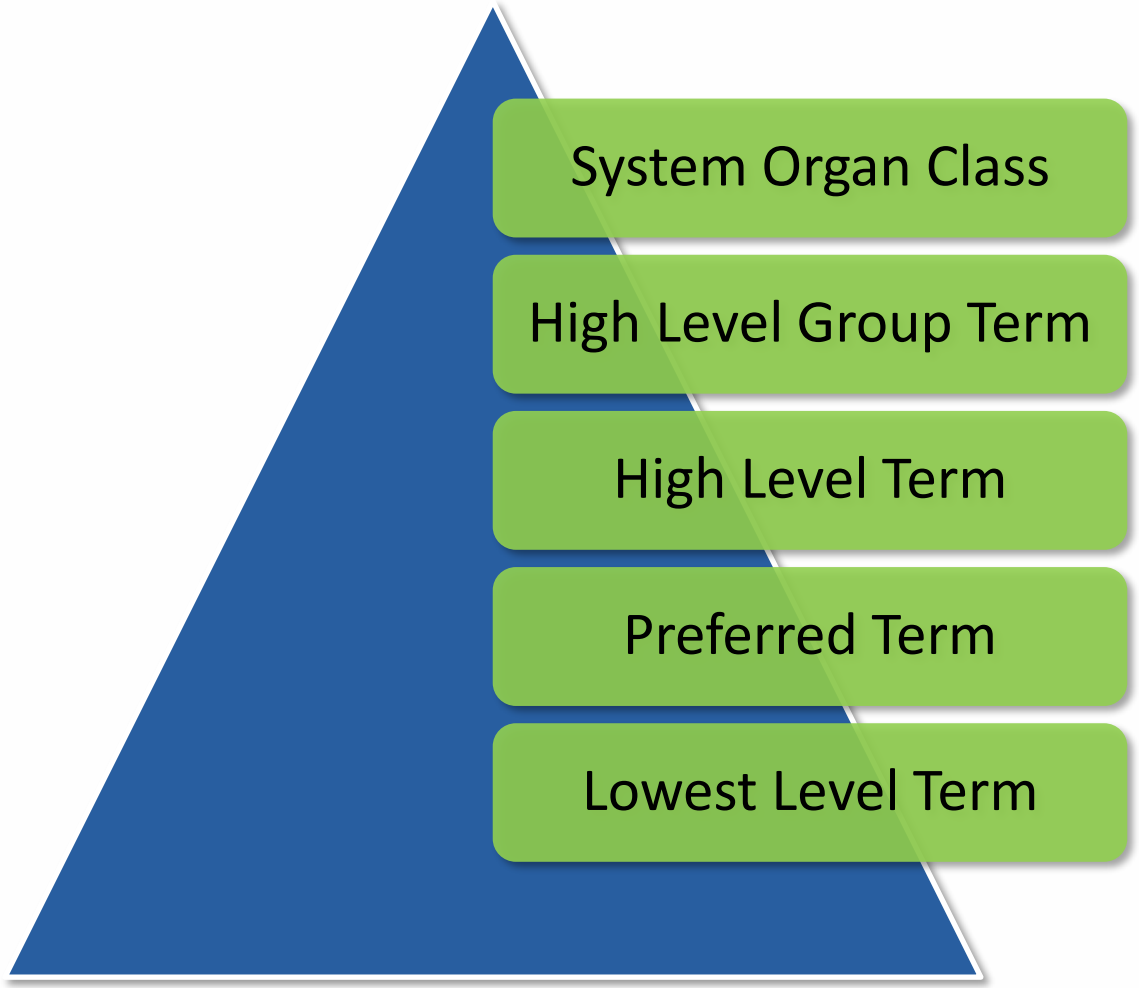
- Record data accurately
- Preserve specificity and meaning
- In uniform and consistent manner

WHY?

- Data Retrievability
- Presentation
- Organization
- Manipulation
- Statistical analysis

MedDRA Structure

MedDRA Structure



Structural elements in MedDRA terms

- **SOC (System Organ Class)** - Highest level of the terminology, and distinguished by anatomical or physiological system, etiology, or purpose
- **HLGT (High-Level Group Terms)** – Subordinate to SOC, superordinate descriptor for one or more HLTs
- **HLT (High-Level Terms)** – Subordinate to HLGT, superordinate descriptor for one or more PTs (links PTs related to it by anatomy, pathology, physiology, etiology or function)
- **PT (Preferred Term)** – Represents a single medical concept. PT can be connected to a single SOC (Single Axiality) or to SOC through multiple branches (Multiaxiality)
- **LLT (Lower-Level term)** – Lowest level of the terminology. The LLT is the term that most accurately reflects the reporter's words. There is 1:1 correspondence between LLT and VT terms

System Organ Class (SOC)

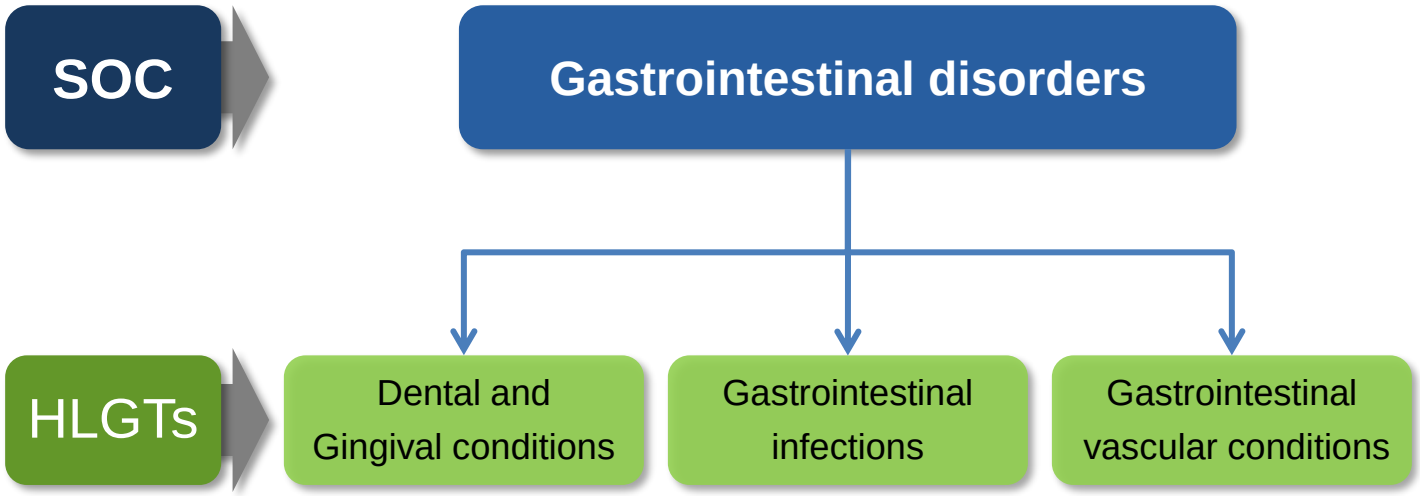
- **Highest level of the hierarchy** that provides the broadest concepts for data retrieval.
- **SOC –** investigations, Surgical and medical procedures and social Circumstances are independent
- **Other SOCs** (e.g. cardiac system, Nervous system, Vascular system) can be connected to each other through multiaxiality

System Organ Class (SOC)

- 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
- Infections and infestations
- Immune system disorders
- Injury, poisoning and procedural complications
- Investigations
- Metabolism and nutrition disorders
- Musculoskeletal and connective tissue disorders
- Neoplasms benign, malignant and unspecified (including 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

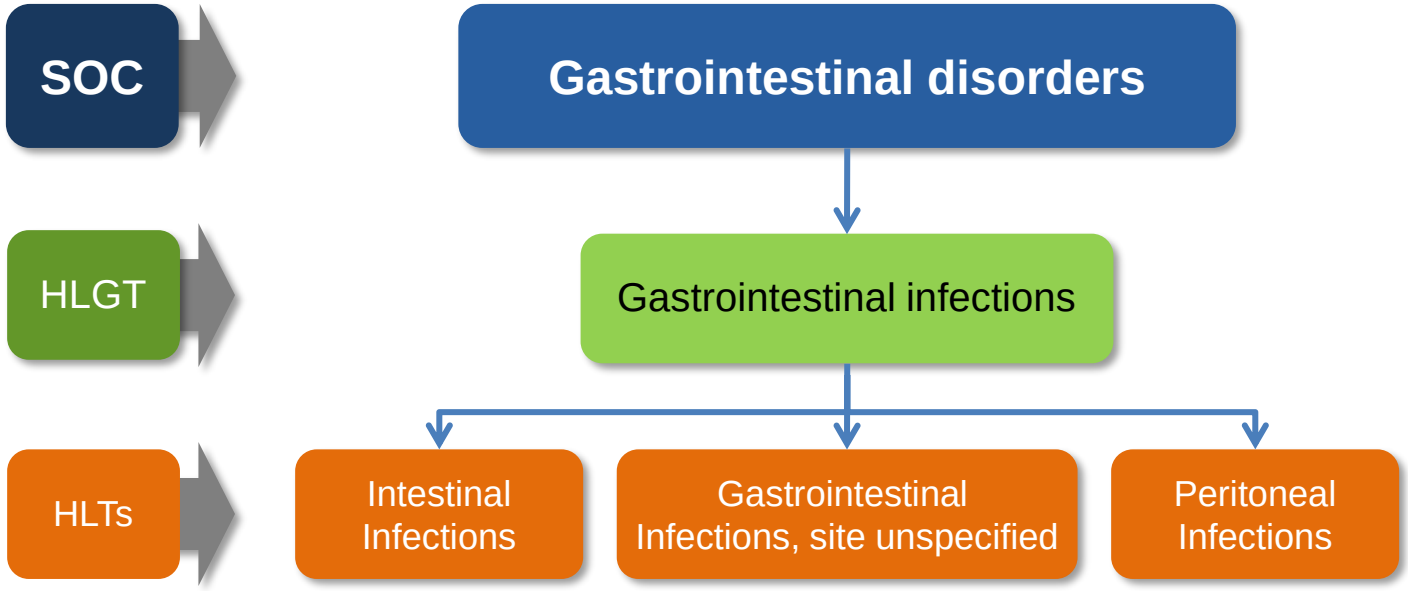
High Level Group Term (HLGT)

Subordinate only to System Organ Classes and superordinate descriptor for one or more HLTs



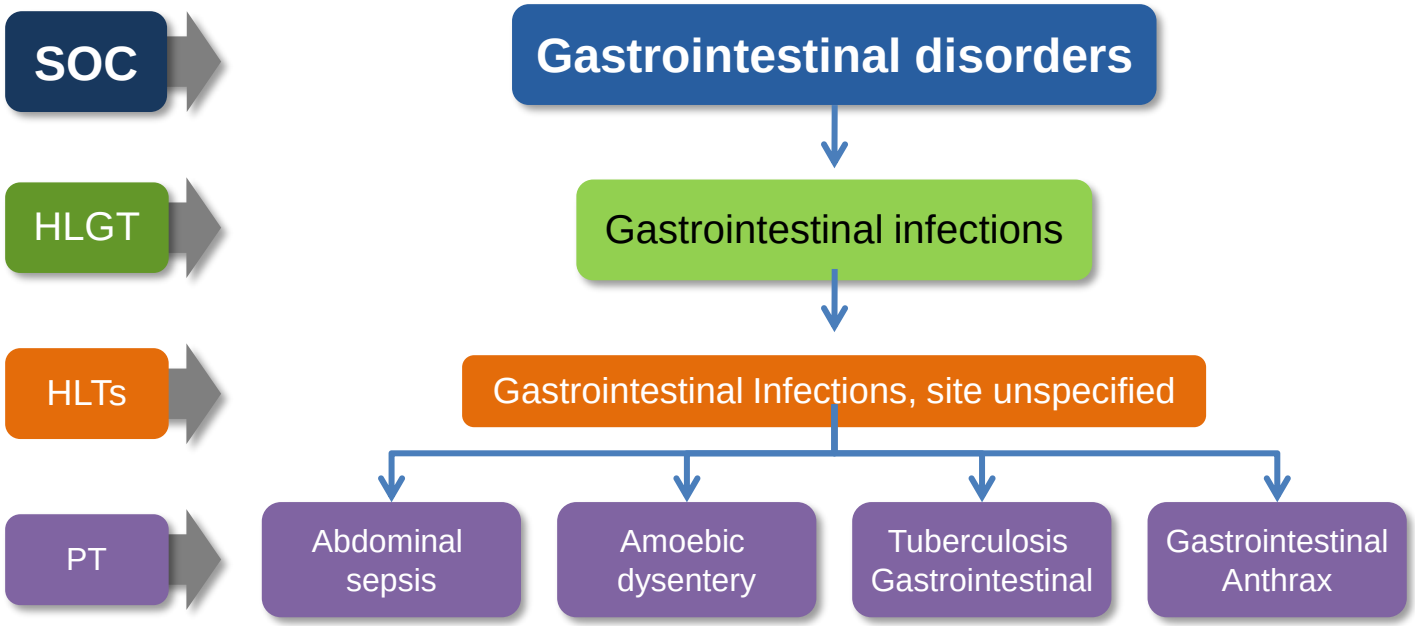
High Level Term (HLT)

Subordinate only to HLGTs and superordinate descriptor for the PTs linked to it



Preferred Term (PT)

Each Preferred Term represents a single medical concept:



Preferred Term Characteristics

- No limit to the amount of LLTs that can be associated with a single PT
- An identical LLT is created for every PT
- Each path to a SOC from a PT should have exactly one HLT and HLGT (one route)

  PT → HLT → HLGT → SOC

- PTs can be represented in multiple SOCs (multiaxality)

Preferred Term (PT)

PT

Dizziness

Associated LLTs

- Dizziness
- Dizziness (exc vertigo)
- N/C Dizziness and giddiness
- Dizzy
- Dizzy spells
- Felt faint
- Light headedness
- Light-headed
- Light-headed feeling
- Lightheadedness
- Pre-syncope
- Presyncope

Structure MedDRA

Single Axiality

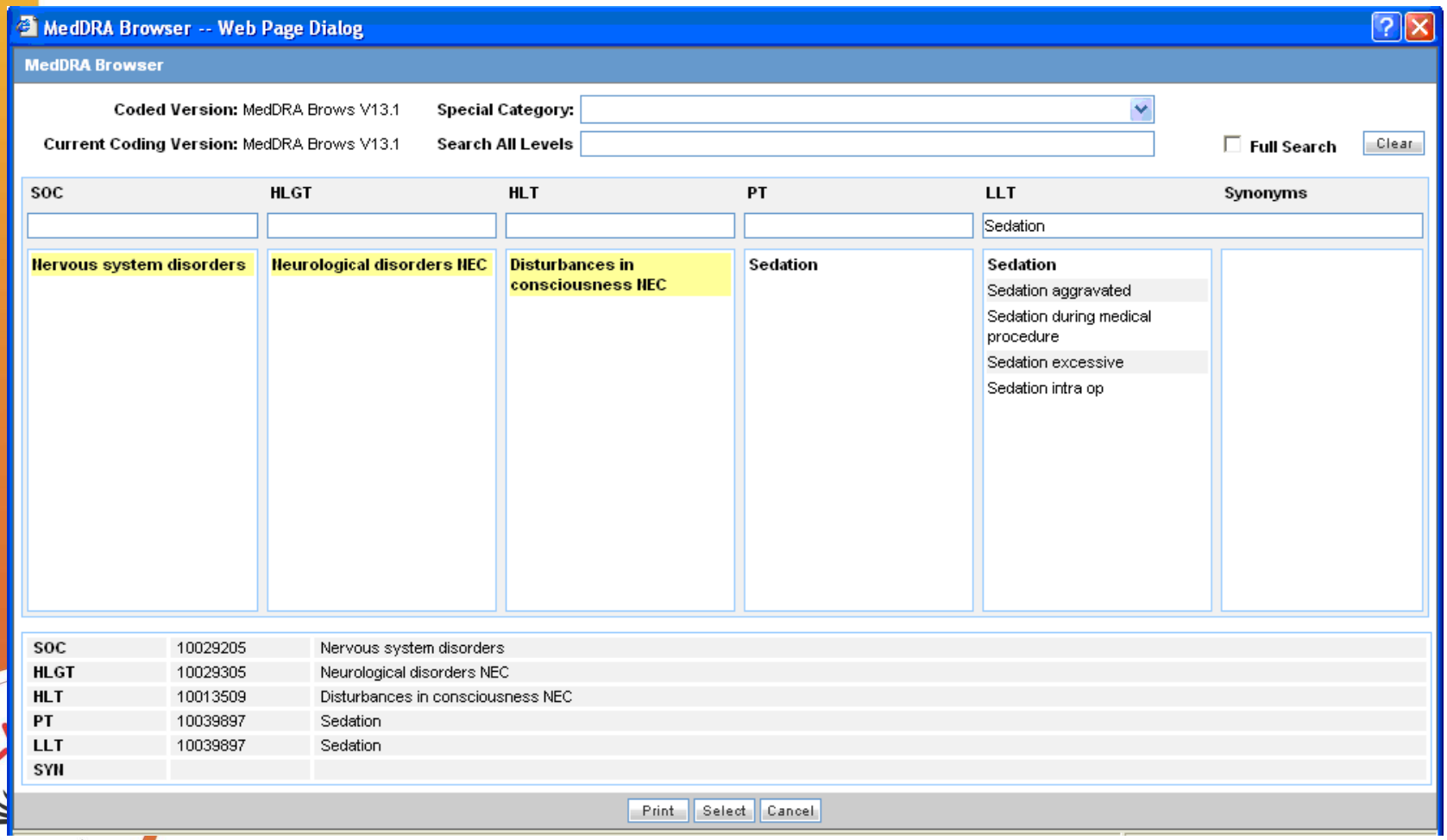
- The term is connected to a single SOC

  E.g. Sedation → follows a single path to the SOC Nervous system disorders

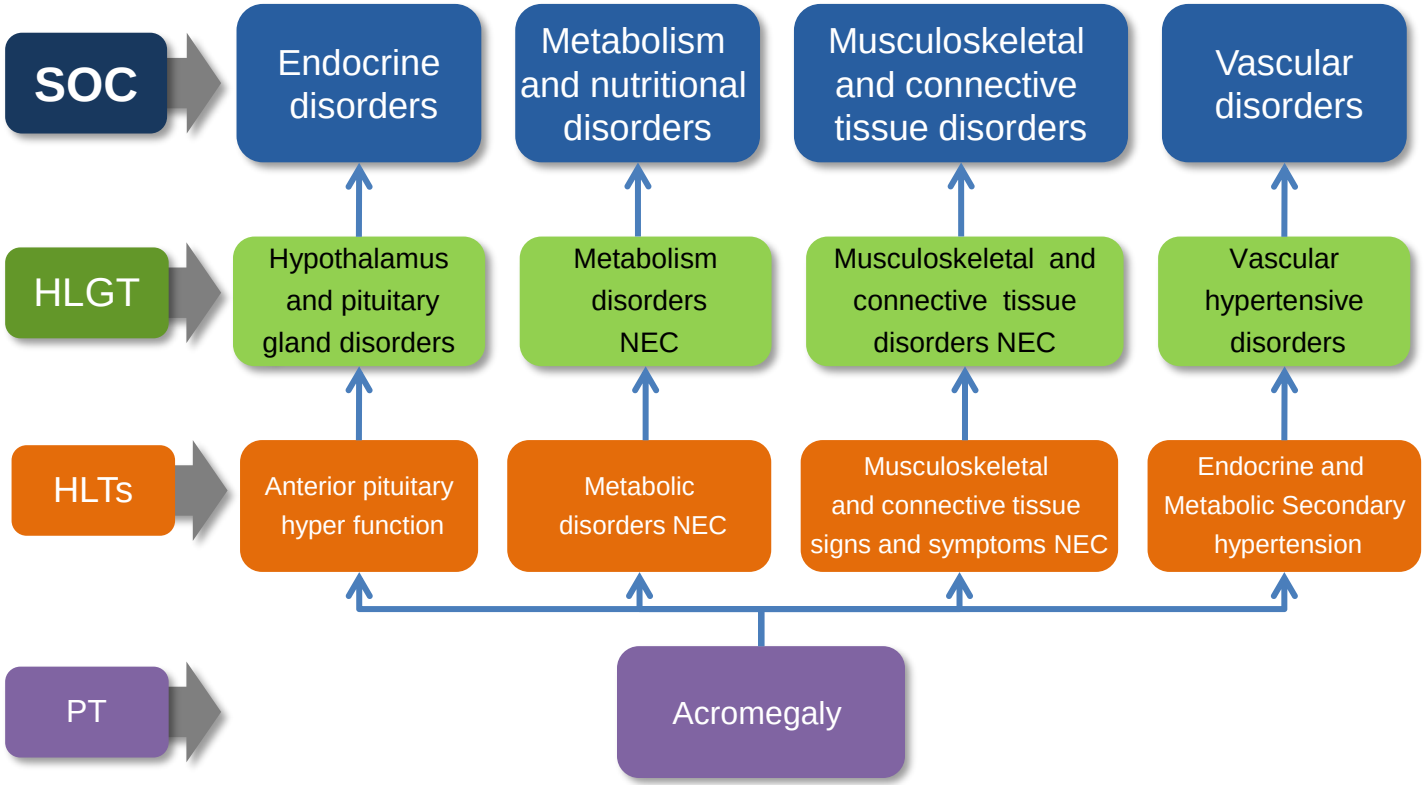
Multi-Axiality

- No branching at LLT level. Branching begins at PT level.

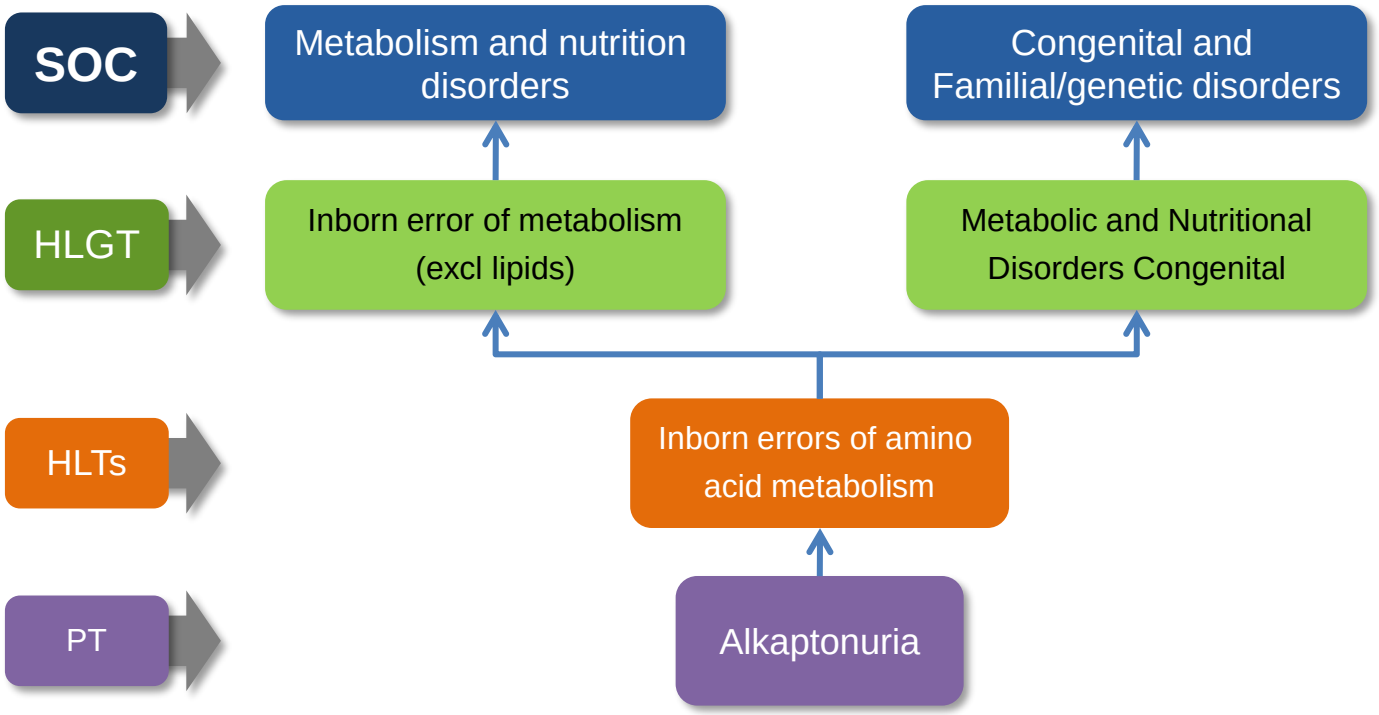
Single Axiality



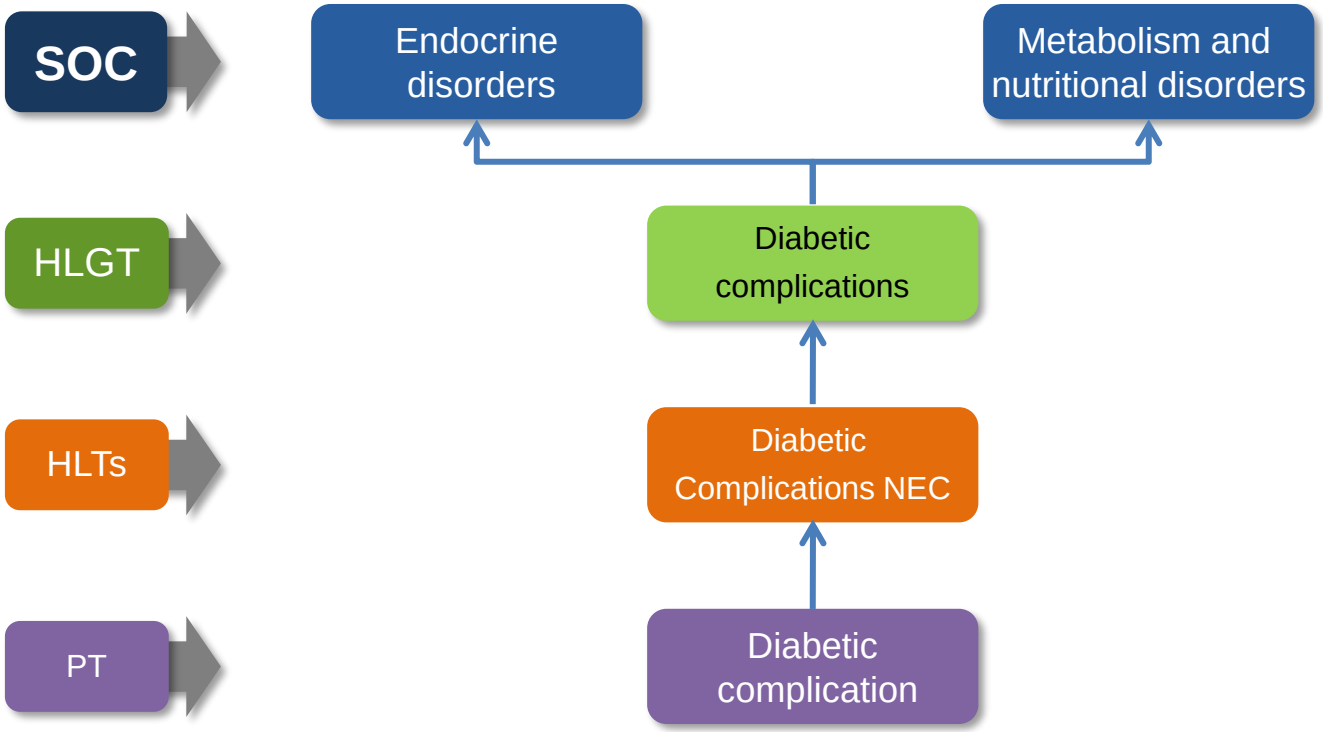
Multiple Axiality - PT



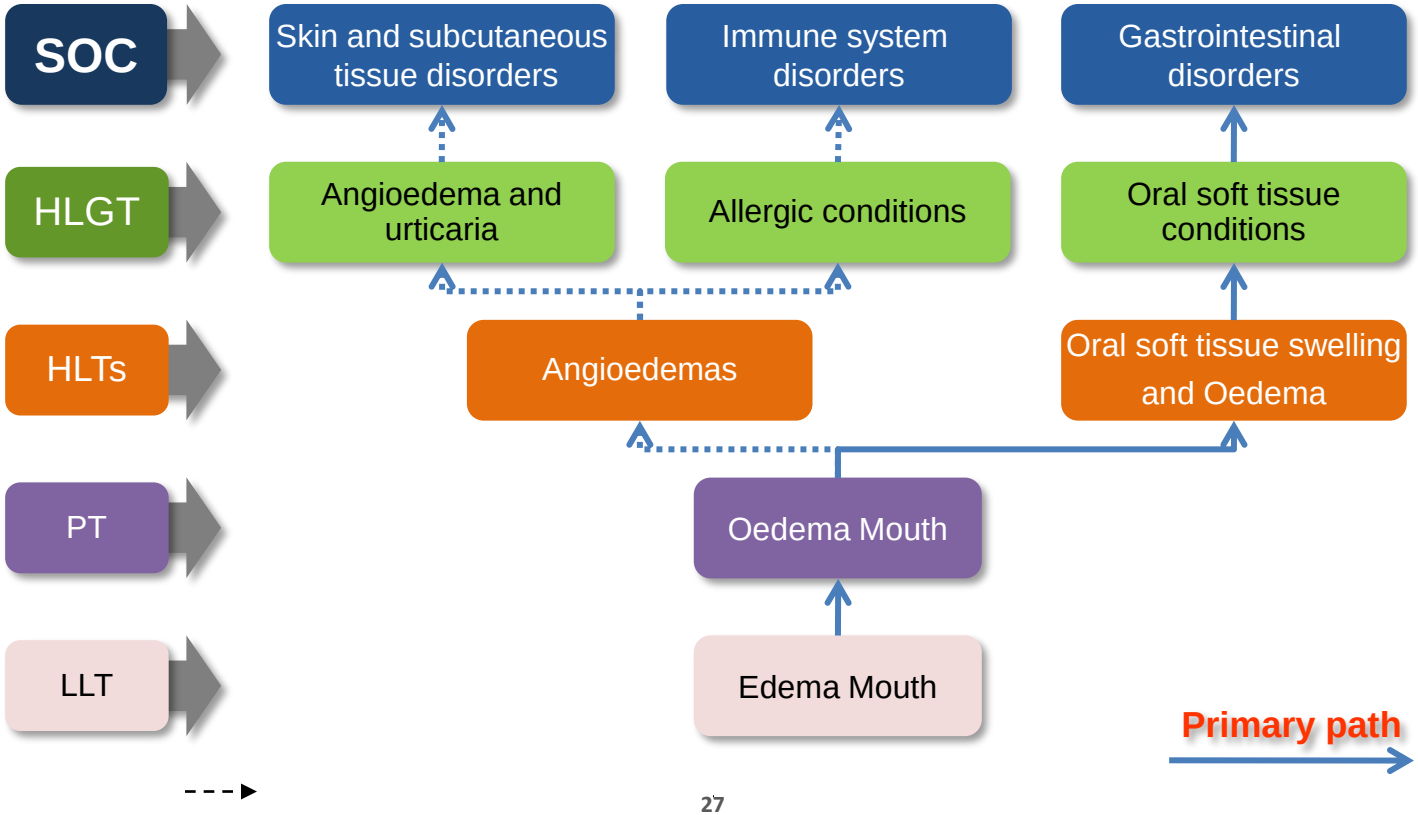
Multiple Axiality - HLT



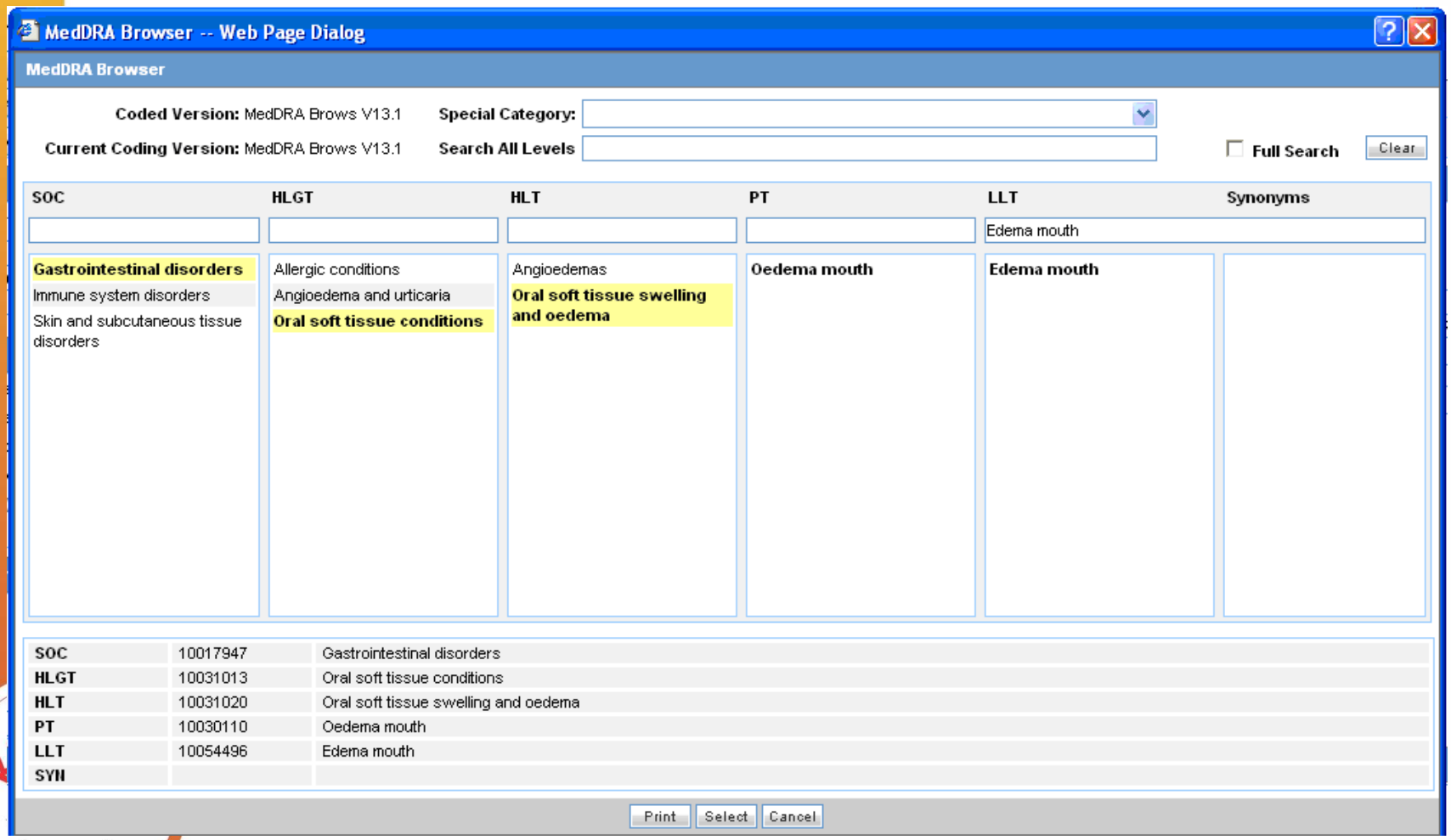
Multiple Axiality (HLGT)



Multiple Axiality -> Primary Path



Multiple Axiality-> Primary Path



SSC/SMQs

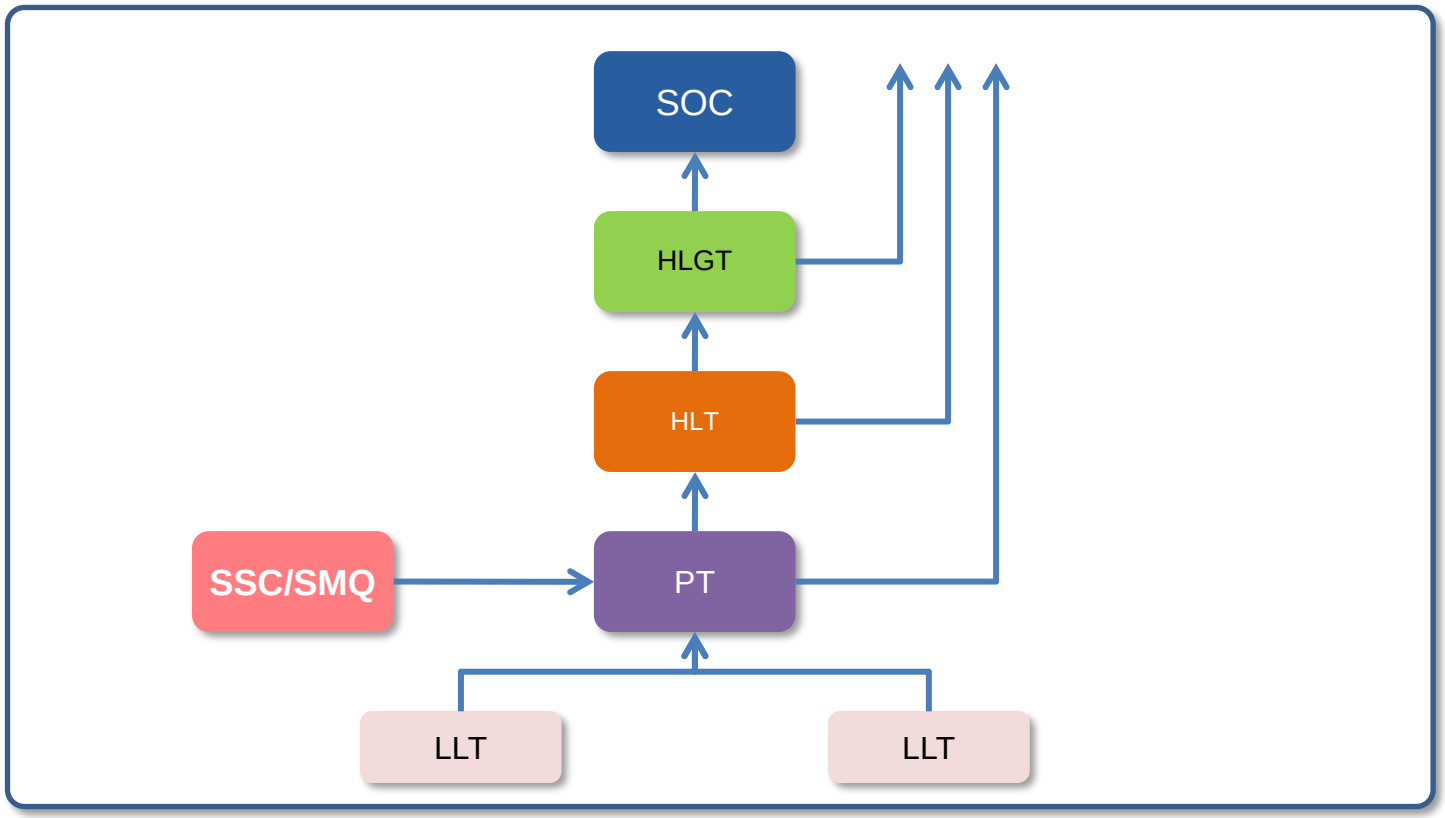
Associative - grouping of PTs indicative of a specified medical concept

Special Search Category (**SSC**) /Standardized MedDRA Queries (**SMQ**)

Illustrated for **Anaphylaxis**

- PT Acute circulatory failure
- PT Anaphylactic reaction
- PT Anaphylactic shock
- PT Angioneurotic oedema
- PT Blood pressure decreased
- PT Bronchospasm
- PT Chest tightness
- PT Collapse
- PT Dyspnoea
- PT Eyelid oedema
- PT Face oedema
- PT Histamine-like rash
- PT Hypotension
- PT Laryngeal oedema
- PT Larygospasm
- PT Larygotracheal oedema
- PT Oedema mouth
- PT Periorbital oedema
- PT Pruritus
- PT Pulse absent

Structure Summary



Structure Summary: Category wise

Number of Terms MedDRA Version 16.1	
System Organ Classes (SOC)	26
High Level Group Terms (HLGT)	334
High Level Terms (HLT)	1717
Preferred Terms (PT)	20307
Lowest Level Terms (LLT)	72072

AE Term Selection: Points to consider

AE Term Selection

Information should neither be added nor subtracted

- Reported information should not be omitted. Terms should be selected for every adverse event reported, regardless of perceived relationship to the drug product. No reported medical concept should be excluded from the term selection process.
- No new medical concepts should be added. Neither a diagnosis nor a mechanism of action should be derived or inferred from reported signs and symptoms.

Example: *If "abdominal pain, increased serum amylase and increased serum lipase" are reported, it is inappropriate to assign a diagnosis such as "pancreatitis"*

AE Term Selection

Diagnosis reported with signs and symptoms

- If the reporter provides both a diagnosis and its characteristic signs and symptoms, select a term for the diagnosis and not for the signs and symptoms.
- However, terms should also be selected for signs and symptoms that are not generally recognized as part of that diagnosis.

Example: If "anaphylactic reaction" is reported with rash, dyspnea, hypotension and laryngospasm select "Anaphylactic reaction"

AE Term Selection

Diagnosis and provisional diagnosis with signs and symptoms

- If only a single provisional diagnosis (e.g. “suspicion of”, “probable”, “presumed”, “likely”, “questionable”) is provided, in the absence of additional clinical information, it must be managed as if a confirmed diagnosis.

Example: If “possible myocardial infarction” is the only information reported, “Myocardial infarction” must be selected.

AE Term Selection

Diagnosis and provisional diagnosis with signs and symptoms

- If there are multiple diagnoses or provisional diagnoses without signs and symptoms, terms for each diagnosis or provisional diagnosis must be selected.

  Example: If a differential diagnosis that includes "pulmonary embolism, myocardial infarction, and congestive heart failure" is reported, "Pulmonary embolism", "Myocardial infarction", "Congestive heart failure" must be selected

AE Term Selection

Diagnosis and provisional diagnosis with signs and symptoms

- If multiple diagnoses are reported together with signs and symptoms, one must select terms for both

Example: *If a differential diagnosis that includes "pulmonary embolism, myocardial infarction, and congestive heart failure" is reported along with "chest pain, cyanosis, shortness of breath, and blood pressure decreased", then, "Pulmonary embolism", "Myocardial infarction", "Congestive heart failure" along with "Chest pain", "Cyanosis", "Shortness of breath", and "Blood pressure decreased" must be selected.*

AE Term Selection

Death and Other Patient Outcomes

- Although death is an outcome yet will be considered to be an ADR/AE. The Pharmacovigilance (PV) Associates will follow-up on each case of death (subject to the convention of the specific process).

  Example: *If "death due to myocardial infarction" is reported, " Death" and "Myocardial infarction" must be selected and outcome will be kept as fatal.*

- If multiple ADR/AEs are reported in association with a fatal outcome, MedDRA terms for each reported event must be selected.

  Example: *If "constipation, ruptured bowel, peritonitis, sepsis, and patient died" are reported, "Constipation", "Perforated bowel", "Peritonitis", and "Sepsis" can be selected, and death must be captured as primary event and the outcome for all will be fatal.*

AE Term Selection

Death and Other Patient Outcomes

- If the only information reported is death, then the most specific death term available should be selected.

  Example: *If a reporter states only that "a patient was found dead", "Found dead" must be selected.*

- If circumstances of the death are provided (e.g., natural, accidental, suicide, homicide), and the term exists, it should be selected.

  Example: *If the autopsy report states, "the cause of death was natural," "Death from natural causes" must be selected.*

AE Term Selection

Death and Other Patient Outcomes

- If the only information reported is the death, then the most specific death term available should be selected.

Example: *If a reporter states only "death" then "Death Unexplained" must be selected.*

Example: *If a reporter states only that "a patient was hospitalized", "Hospitalization" must be selected.*

AE Term Selection

Death and Other Patient Outcomes

- If the particular death term adds important clinical information to the case, it can be selected.

  Example: If “patient experienced a rash and had sudden cardiac death” is reported, “Rash” and “Sudden cardiac death” can be selected.

- Other patient outcomes such as hospitalization and disability are not generally considered to be ADR/AEs.

  Example: If “hospitalization due to congestive heart failure” is reported, “Congestive heart failure” must be selected and hospitalization should be captured as the consequence of the event.

AE Term Selection

Conflicting/ambiguous/vague information

- When conflicting, ambiguous, or vague information is provided, attempts must be made to obtain more specific information. If attempts have failed, proceed on the following lines:

- Conflicting information:

  Example: *If only "hyperkalemia with serum potassium of 1.6 mEq/L", "hyperkalemia" is selected over "serum potassium abnormal" because the term of serum potassium abnormal is a vague term.*

AE Term Selection

Ambiguous/vague information

- Ambiguous information:

  Example: If "GU pain" is reported, "GU" could refer to either "genito-urinary" or "gastric ulcer". However, since pain was reported, "Pain" must be selected. However, an advice must be sought from Physician for approval.

- Vague information:

  Example: If the only information reported is "patient experienced every listed adverse event", and attempts to obtain more specific information are unsuccessful, "unevaluable event" must be selected.

AE Term Selection

Conflicting/ambiguous/vague information

- *If one term is more specific than the other, then the most specific term should be selected.*

  Example: *If "arrhythmia due to atrial fibrillation" is reported, "Atrial fibrillation" can be selected.*

- *If splitting provides more clinical information, it is considered appropriate to select more than one term.*

  Example: *If "diarrhea and vomiting" is reported, "Diarrhea" and "Vomiting" can be selected.*

AE Term Selection

Age vs. Event Specificity

- Some MedDRA terms describe the age group and the event. If available, the term with the specific age group and event must be selected.
  Example: If "jaundice in a newborn" is reported, "Neonatal jaundice" must be selected.

- If a term is not available to capture both concepts, the preferred option is to select the term for the event and capture the age group in a demographic field.
  Example: If "oral candidiasis in a neonate" is reported, then "Oral candidiasis" must be selected and the neonatal status must be captured in a demographic field.

AE Term Selection

Body Site Vs Event Specificity

- MedDRA term with both the specific body site and the event
  Example: If "skin rash on face" is reported, "Rash on face" must be selected.

- Not all MedDRA terms describe body sites; in such cases the relevant medical event must have priority.
  Example: If "skin rash on chest" is reported, "Skin rash" can be selected.
  Example: If "cyanosis at injection site" is reported, "Injection site reaction" can be selected instead of "Cyanosis" as cyanosis implies a generalized disorder.

- If a term contains multiple body sites, and all link to the same PT, each term will be coded to the relevant LLT.
  Example: If "skin rash on face and neck" is reported, "Rash face "and "Neck rash" must be selected even though the PT is the same (Rash).

AE Term Selection

Pre-existing medical conditions

- Pre-existing medical conditions that have not changed must generally be classified as medical and/or social history. Pre-existing medical conditions that have changed must be classified as ADR/AEs.

  Example: If "exacerbation of myasthenia gravis" is reported, "Myasthenia gravis aggravated" can be selected.
- *In the absence of such a term, the condition and the modification must be captured.*

  Example: If "progression of Addison's disease" is reported, "Addison's disease" and "Disease progression" must be selected. Example: If "aggravation of jaundice" is reported, "Jaundice" and "Condition aggravated" can be selected.
- If the reported term is a combination of an event and a pre-existing condition that has not changed and the combination term does not exist in MedDRA, the associate must select a term for the event.

  Example: If "shortness of breath due to cancer" is reported in a patient with cancer, "Shortness of breath" must be selected.

AE Term Selection

Exposures during pregnancy and breast feeding

- For events in the Mother i.e. the patient became pregnant whilst receiving medication, the occurrence of pregnancy will be documented in the database.

  Example: *If there is no pregnancy outcome and no adverse event has occurred (and reported so), then "Drug exposure during pregnancy" and "No adverse effect" must be selected.*

  Example: *If there is no pregnancy outcome and it is unknown yet as to whether any ADR/AE occurred, then "Drug exposure during pregnancy" only must be selected.*

  Example: *If the pregnant patient experienced ADR/AEs while receiving medication, "Drug exposure during pregnancy" must be selected in addition to the reported ADR/AE. Pregnancy information will also be documented in the patient demographic details.*

AE Term Selection

Exposures during pregnancy and breast feeding

- For ADR/AEs in the child/foetus, it must firstly be identified whether the ADR/AE occurred through exposure or potential exposure to the medicinal product via the mother or father.

  Example: If the child or foetus experienced ADR/AEs and was exposed to the drug in utero; mother received the product, then “Maternal drugs affecting foetus” must be selected in addition to the reported ADR/AE.

  Example: If the Child or foetus experienced adverse event(s) and was exposed to the drug in utero; father received the product, then “Paternal drugs affecting foetus” must be selected in addition to the reported ADR/AE.

  Example: If a child experienced an AE and was exposed to the drug from breast milk, then “Drug exposure via breast milk” must be selected in addition to the reported AE.

AE Term Selection

Congenital terms

- Terms from the SOC ‘Congenital, familial and genetic disorders’ correspond to conditions described as congenital by the reporter, or when medical judgment establishes that the condition was present in the child at the time of birth.

Example: *If either “congenital heart disease” or “child born with heart disease” is reported, “Heart disease congenital” can be selected*

AE Term Selection

Investigations

- SOC Investigations includes test names without qualifiers and test names with qualifiers (e.g., increased, decreased, abnormal, normal).
- Corresponding medical conditions, such as “hyper” and “hypo” terms, are represented in other “disorder” SOCs.
- By design, the terms in SOC Investigations are not multi-axial.
- Therefore, for data retrieval, SOC Investigations should always be considered, in addition to the specific “disorder” SOC(s).

Practice Cases

Case 1

Narrative:

After IUD insertion a female patient started to complain of acne-like rash followed by visual flashing. Investigation revealed a fluid collection in the labyrinth.

Case 1 *(Contd.)*

EVENT	MedDRA CODING
"Acne-like rash"	PT Dermatitis acneiform LLT Rash acneiform
"Visual flashing"	PT Photopsia LLT Visual flashes
"Fluid collection in the labyrinth"	PT Endolymphatic hydrops LLT Labyrinthine hydrops

Case 2

Narrative:

- On 11- Aug pt (with medical history of asthma) had Drug X (inhaler) filled by local pharmacy. On August 15, while mountain climbing, patient experienced an asthma attack and attempted to use her inhaler. Family reported “inhaler failed” and she had to be life-lined out of the park. Pt told physician she was experiencing more frequent asthma attacks. The lot number of the suspect inhaler did not match that of the recalled lot.

Case 2 *(Contd.)*

EVENT	MedDRA CODING
“Inhaler failed”	LLT – Device failure
“More frequent Asthma attacks”	LLT Asthma aggravated

Case 3

Narrative:

Jul/20/98 pt took his morning dose of Drug X, an antihypertensive. Later that day he reported that he actually had an erection for the first time in many years. Pt repeated this routine the next day with the same positive results. 2002: Pt's attorney filed legal summons claiming heart injury.

Case 3 *(Contd.)*

EVENT	MedDRA CODING
“Erection – positive effect”	LLT Spontaneous penile Erection Or LLT Unexpected therapeutic effect
“Heart injury”	LLT Heart injury

Case 4

Narrative:

Report from center for poison control states patient was admitted to ER after having taken Drug X. She was admitted for overnight observation. Diagnosed with tubular nephropathy as a result of toxicity. On review of her medication history, it was discovered that pharmacist had dispensed the wrong drug

Case 4 *(Contd.)*

EVENT	MedDRA CODING
Tubular nephropathy due to toxicity	LLT Nephropathy tubular
Toxicity	LLT Drug Toxicity
Wrong drug	PT Medication error LLT Wrong drug Administered

Case 5

Narrative:

After ingesting over 20 tablets of Drug X of his mother's prescription, a 4 year old male developed stuffy nose, dark urine, and arrhythmia.

Case 5 *(Contd.)*

EVENT	MedDRA CODING
"Mother's prescription"	PT Accidental exposure • LLT Accidental ingestion
"Stuffy nose"	PT Nasal congestion • LLT Nasal stuffiness
"Dark urine"	PT Chromaturia • LLT Urine discoloration
"Arrhythmia"	PT-LLT Arrhythmia NOS