Coding with MedDRA

MedDRA was developed under the auspices of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). The activities of the MedDRA Maintenance and Support Services Organization (MSSO) are overseen by an ICH MedDRA Management Committee, which is composed of the six ICH parties (EU, EFPIA, MHLW, JPMA, FDA, PhRMA), the Medicines and Healthcare products Regulatory Agency (MHRA) of the UK, Health Canada, and the WHO (as Observer).

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Course Overview

- MedDRA background
- MedDRA's structure, scope, and characteristics
- MedDRA maintenance
- Coding conventions
- Synonym lists
- Quality assurance (QA) of coding
- MedDRA Term Selection: Points to Consider document
- Hands-on coding exercises

MedDRA

MedDRA Background

MedDRA

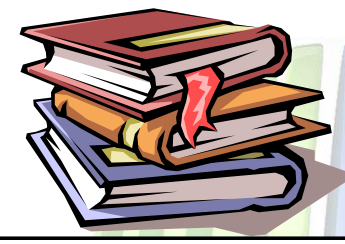
What is MedDRA?

Med = Medical

D = Dictionary for

R = Regulatory

A = Activities



MedDRA Definition

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.

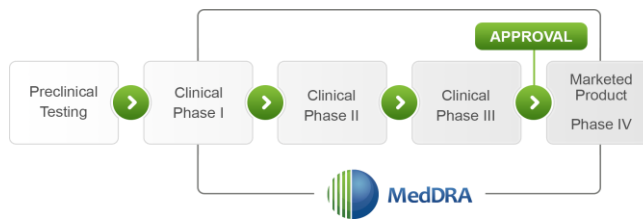
MedDRA's Purpose

- 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

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

Regulatory Status

- FDA, US
  - Used in several databases including FAERS (drugs and biologics), VAERS (vaccines), and CAERS (foods, dietary supplements, cosmetics)
  - Electronic submission required for study data and postmarketing reports (uses ICH standards)
- MHLW/PMDA, Japan
  - Mandatory use in electronic reporting

Regulatory Status (cont)

- EC, Europe
  - EudraVigilance database
    - Clinical trial SUSARs (Suspected Unexpected Serious Adverse Reactions)
    - Post-authorization Individual Case Safety Reports (ICSRs)
    - Requires current version of MedDRA or the one previous to it
  - Good pharmacovigilance practices (GVP) specifically mention MedDRA

Regulatory Status (cont)

- EC, Europe (cont)
  - Used throughout Summary of Product Characteristics (labeling)
  - Pharmacovigilance legislation covers suspected adverse reactions from:
    - Use inside **and outside** terms of marketing authorization
    - Overdose, misuse, abuse, and medication errors
    - Occupational exposures

Regulatory Status (cont)

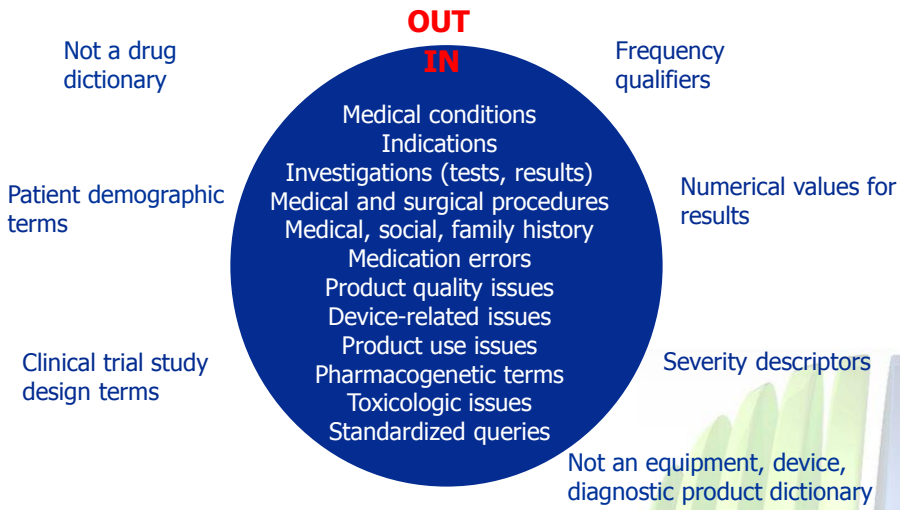
- ICH M4E Guideline on Common Technical Document
  - Recommended in adverse event summary tables
- Health Canada, Canada
  - Used in Canada Vigilance database
  - Recommended terminology for adverse reaction reporting and Product Monograph (labeling)
  - Electronic reporting requires current version of MedDRA

Regulatory Status (cont)

- CFDA, China
  - Implementing ICH standards
    - M4 Common Technical Document (February 2018)
    - Clinical trial SUSARs use electronic reporting [E2B(R3)] and MedDRA (May 2018)
    - Postmarketing ICSRs may use E2B(R3) and MedDRA (July 2019)

MedDRA Overview

Scope of MedDRA



MedDRA Structure

System Organ Class (SOC) (27)

High Level Group Term (HLGT) (337)

High Level Term (HLT) (1,737)

Preferred Term (PT) (23,088)

Lowest Level Term (LLT) (78,808)

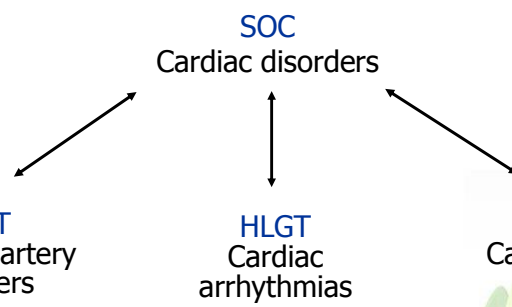
MedDRA Version 21.0

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

High Level Group Terms

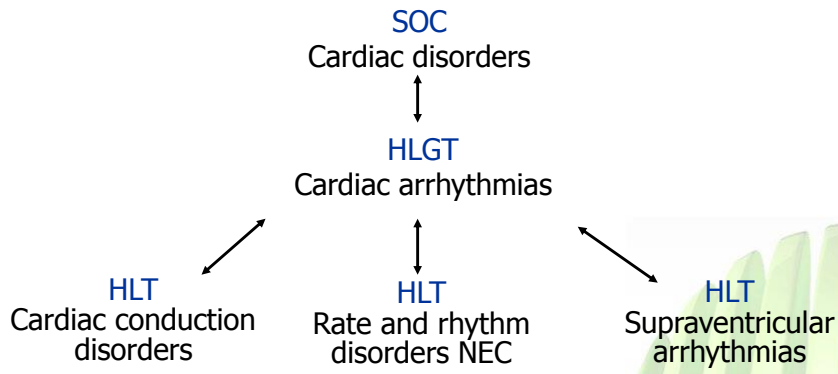
Subordinate only to SOCs and superordinate grouping for one or more HLTs



Not all HLGTs shown

High Level Terms

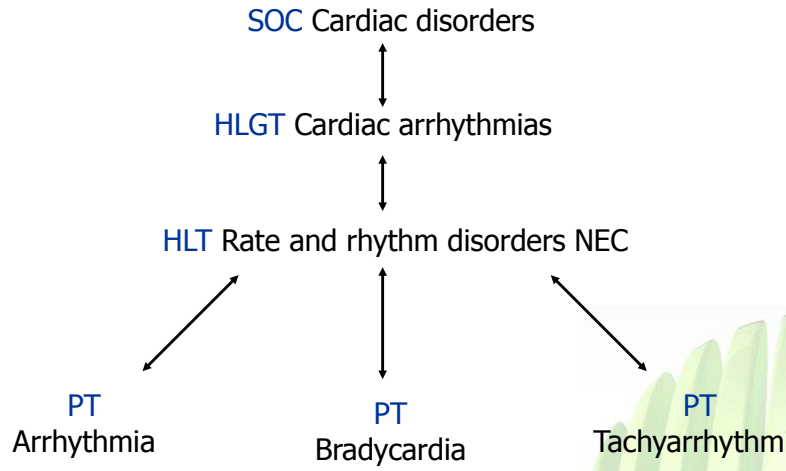
Subordinate to HLGTs and superordinate grouping for the PTs linked to it



Not all HLTs shown

Preferred Terms

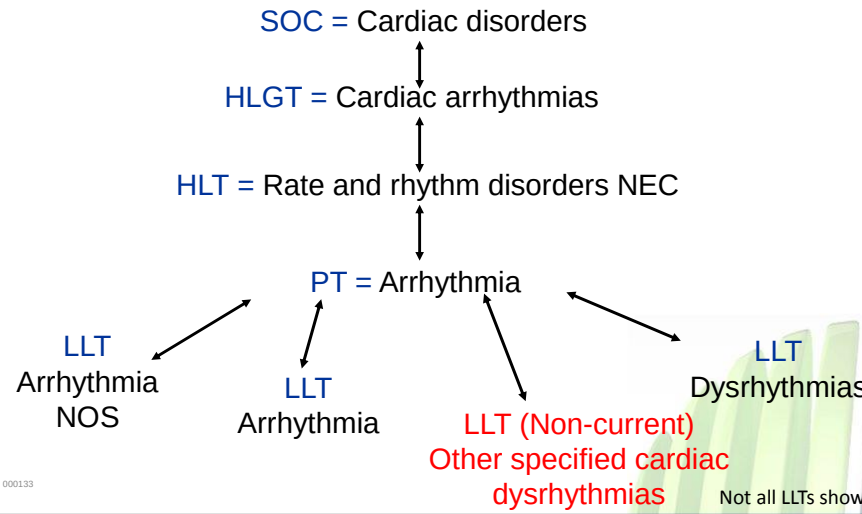
Represents a single medical concept



Not all PTs shown

Lowest Level Term

Synonyms, lexical variants, sub-elements



Not all LLTs shown

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, out-dated, truncated, or misspelled
- Terms derived from other terminologies that do not fit MedDRA rules

MedDRA Codes

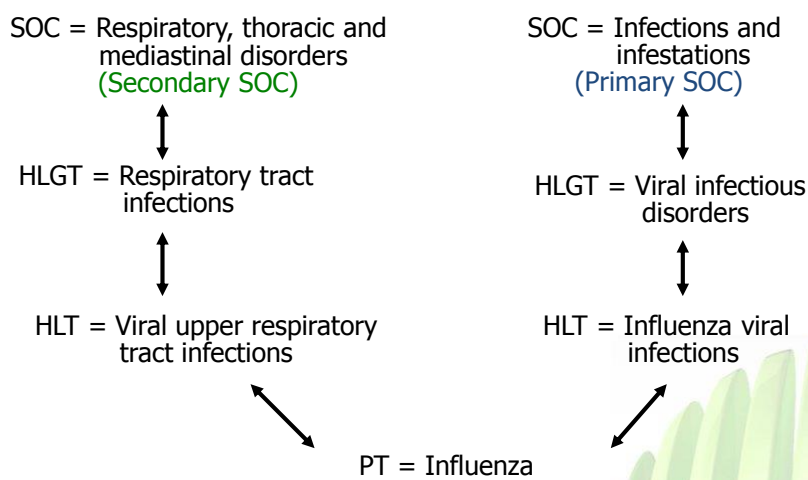
- Each MedDRA term assigned an 8-digit numeric code starting with "1"
- The code is non-expressive
- Codes can fulfill a data field in various electronic submission types (e.g., E2B)
- New terms are assigned sequentially

Codes and Languages

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

A Multi-Axial Terminology (cont)



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

Primary SOC Priority

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*

A Multi-Axial Terminology (cont)

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?

PT	HLT	HLGT	SOC
Congenital HIV infection	Viral infections congenital	Infections and infestations congenital	Congenital, familial and genetic disorders
	Congenital neonatal infections	Neonatal and perinatal conditions	Pregnancy, puerperium and perinatal conditions
	Retroviral infections	Viral infectious disorders	Infections and infestations
	Acquired immunodeficiency syndromes	Immunodeficiency syndromes	Immune system disorders

MedDRA Maintenance

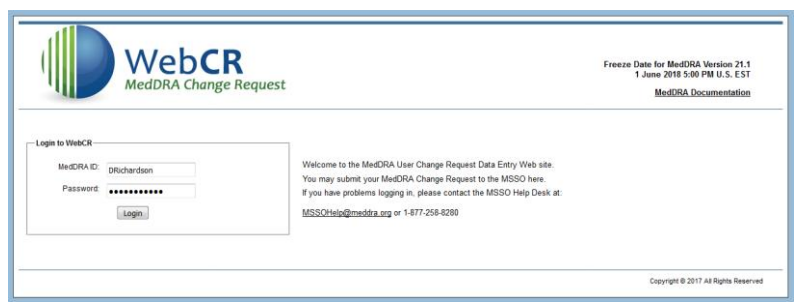
MedDRA Maintenance

- Users can send change requests (CRs) to MSSO for consideration
  - Organizations allowed 100 CRs/month
  - For simple changes (PT and LLT levels), response within 7-10 working days
  - Complex changes (above PT level) posted for comments mid-year
- Two MedDRA updates/year
  - 1 March X.0 (Complex release)
  - 1 September X.1 (Simple release)

WebCR

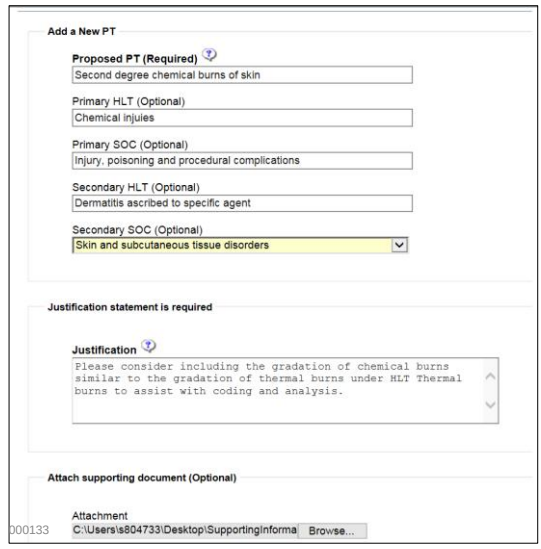
- Web-based tool for Change Requests (CR)
  - –URL: https://mssotools.com/webcr/
  - –Via the Change Request Information page
- Ability to submit CRs online
- Immediate confirmation
- Review unsubmitted CRs online
- Ability to query CR history back to v5.1

Submitting Changes



- Online change request submission tool
- Guides the user to enter all needed information

Submitting Changes (cont)



- Sample entry for a new PT in WebCR
- Justification and supporting documentation is important to help MSSO understand the need

Proactive MedDRA Maintenance

- What is the proactive approach?
  - Corrections/improvements made internally by the MSSO
  - General changes suggested by users
- Submitting ideas
  - Send to MSSO Help Desk. Justification is helpful.
  - Example: Review placement of bruise and contusion terms to facilitate coding and analysis
- Evaluation of proposals
  - Final disposition is not time limited; MSSO may take time to review
  - Proactive approach does not replace usual CR process

MedDRA Version Analysis Tool (MVAT)

- Web-based (https://tools.meddra.org/mvat)
- Free to all users
- Features
  - Version Report Generator (produces exportable report comparing any two versions)
  - Data Impact Report (identifies changes to a specific set of MedDRA terms or codes uploaded to MVAT)
  - Search Term Change (identifies changes to a single MedDRA term or code)
- User interface and report output available in all MedDRA languages

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

MedDRA

MedDRA Browser Demonstration and Instruction

MedDRA

Coding Exercises

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.

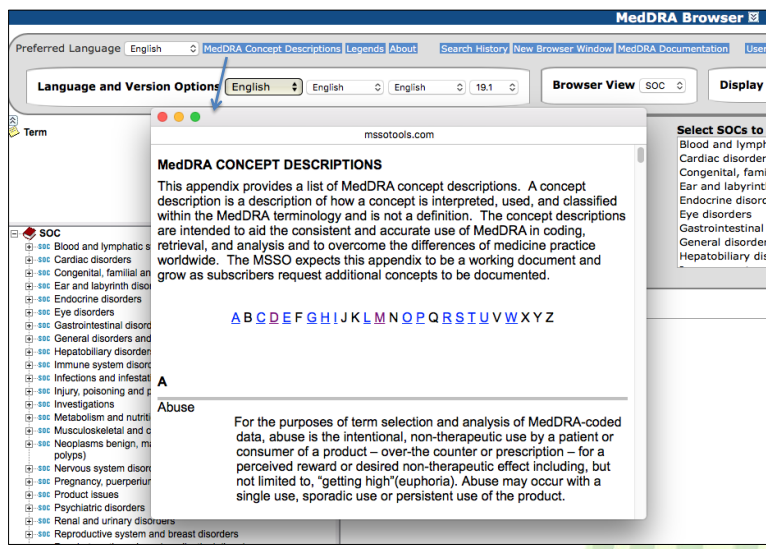
MedDRA Browsing Tips

- First, try using actual words from reporter
- Use "top-down" and "bottom-up" approaches
- Look at the "neighbors" and check the hierarchy
- Consider synonyms, e.g., "Liver" and "Hepatic"
- Use word stems, e.g., "Pancrea"
- Use available resources for difficult verbatim terms (web search, medical dictionaries, colleagues)
- Become familiar with MedDRA Concept Descriptions

Concept Descriptions

- Descriptions of how a concept is interpreted, used, and classified in MedDRA
- Not a definition
- Intended to aid accurate and consistent use of MedDRA in coding and retrieval
- Overcome differences in medical practice worldwide
  - Descriptions aim to be broadly consistent with definitions across different regulatory regions
- See Appendix B of MedDRA Introductory Guide
- Accessible in MSSO's Browsers

Concept Descriptions (cont)



Exercise 1

The patient states she has been experiencing <u>headaches, dizziness and vertigo</u>.

_____ LLT → _____ PT
_____ LLT → _____ PT
_____ LLT → _____ PT

Exercise 2

Lab results indicate an <u>increase in erythrocytes</u>.

_____ LLT → _____ PT

Exercise 3

Drug was contaminated with Staphylococcus.

_____ LLT → _____ PT

Exercise 4

A six year old boy was admitted for toxicity after accidentally ingesting the remaining antihypertensive tablets in the bottle.

_____ LLT → _____ PT
_____ LLT → _____ PT

Exercise 5

The patient's urinary catheter was blocked.

_____ LLT → _____ PT

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Coding with MedDRA

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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

Why Do We Need Coding Conventions?

- Differences in medical aptitude of coders
- Consistency concerns (many more "choices" to manually code terms in MedDRA compared to older terminologies)
- Even with an autoencoder, may still need manual coding

Can I Make Coding Conventions Specific to My Company/Product?

- MedDRA may reduce the need to do this because:
  - Increased size/granularity results in more accurate representation of data
  - Secondary SOC allocations allow for different "views" of the data
- This type of approach should be done cautiously

Quality of Serious Adverse Event (SAE) Reporting in Clinical Trials

- Study finds frequent errors in SAE reports to academic trial sponsors
  - Event verbatim inconsistent with report: 15%
  - Patient outcome not reported: 12.1%
  - Investigational product not identified: 11.2%
  - No causality assessment reported: 9.3%
  - Event seriousness unknown: 3.6%
- Study authors: Knowledge of MedDRA basics and coding practices key to data accuracy and completeness

Crepin S, Villeneuve C, Merle L. Quality of serious adverse events reporting to academic sponsors of clinical trials: far from optimal. Poster at 18th Annual Meeting of French Society of Pharmacology and Therapeutics; 2014 April 22-24, Poitiers, France.

Synonym Lists

- Recurring verbatims – one-time assignment to an LLT
- Promotes consistency
- Increases likelihood of autoencoding "hit"
- Maintenance required

Verbatim	LLT	Comment
Throbbing above temple Aching all over head Pulsing pain in head	Headache	
Muscular pain in legs	Myalgia of lower extremities	LLT *Myalgia of lower extremities* is a better choice than LLT *Muscular pain* since it captures both the event and body site

Quality Assurance (QA) Reports

- Allows reviewers to check for consistency (both auto-encoded and human-coded terms)
- Check for adherence to/deviation from coding conventions
- Check for emerging drifts/biases
- Multiple data views (verbatims to coded terms; coded term to verbatims; by SOC, etc.)

MedDRA

QA Sample Report

SOC	HLT	PT	Verbatim	Count
Respiratory, thoracic and mediastinal disorders				
	Bronchospasm and obstruction			
		Wheezing		
			WHEEZING	16
			Wheeze	5
			INCREASED WHEEZING	1
			Breathing suppressed wheezing	1
			HYPERREACTIVITY AND WHEEZING	1
			wheeze in chest	1
	Laryngeal and adjacent sites disorders NEC (excl infections and neopla			
		Vocal cord disorder		
			SPASMODIC DYSTONIA OF THE VOCAL CORDS	1
	Newborn respiratory disorders NEC			
		Transient tachypnoea of the newborn		
			Transient hazy vision	1
			Transient tachypnea, neonatal	1
			Tachypnea of the newborn, transient	1

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MedDRA

Unqualified Test Name Term List

- MSSO developed and maintains list of unqualified test name terms
  - These terms (e.g., PT *Blood glucose*) should never be reported as AEs
  - Intended for use in E2B test name field only
- List can be used to check data quality
  - Identifies inappropriate terms in data fields other than test name data element
  - Intended as recommendation only

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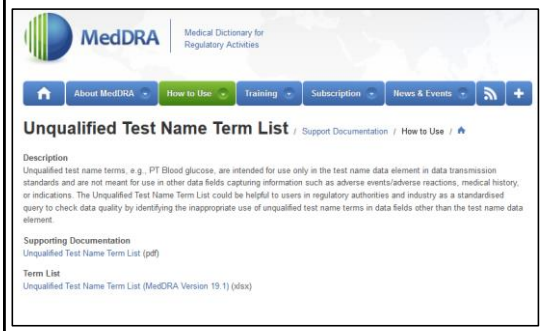
List Available for Download

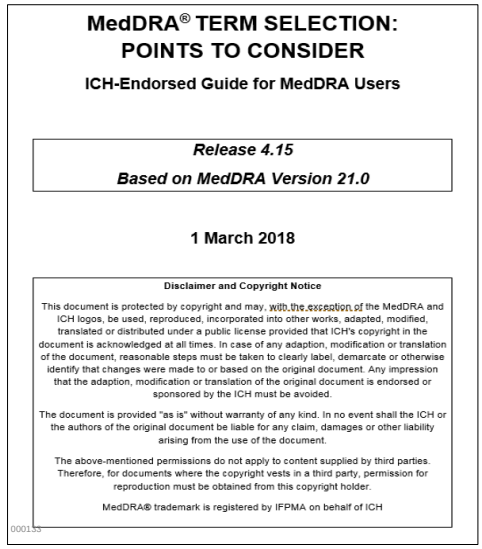


- Link on Support Documentation page on MedDRA website
- Spreadsheet of LLT/PT names and codes from SOC *Investigations*
  - >3,700 terms in v21.0
- Explanatory document
  - Purpose, uses, development of list
- Also available in Japanese on JMO website

List v21.0

	A	B	C
1	Term	Code	Level
2	17 ketosteroids urine	10000005	PT
3	17-hydroxycorticosteroid activity	10051618	LLT
4	2',5'-oligoadenylate synthetase test	10058945	PT
5	24 hour electrocardiogram	10073349	LLT
6	5-HIAA urine	10060014	LLT
7	5-hydroxyindolacetic acid	10050342	PT
8	5-hydroxyindolacetic acid in urine	10059972	PT
9	5'nucleotidase	10059898	PT
10	A/G ratio	10000037	LLT
11	Abdomen CT	10077423	LLT
12	Abdomen scan	10061936	PT
13	Abdominal CAT	10057791	LLT
14	Abdominal scan NOS	10000091	LLT
15	Abdominal wall biopsy	10000102	LLT
16	Abdominal X-ray	10061612	PT
17	Abdominal X-ray NOS	10050402	LLT
18	Absolute lymphocyte count	10073552	LLT
19	Absolute neutrophil count	10052033	LLT

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



MedDRA® TERM SELECTION: POINTS TO CONSIDER

ICH-Endorsed Guide for MedDRA Users

Release 4.15

Based on MedDRA Version 21.0

1 March 2018

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- 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

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MedDRA Term Selection: PTC (cont)

- Developed by a working group of the ICH Management Committee
- 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

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ICH M1 Points to Consider Working Group (PtC WG)

•Regulators and industry from EU, US, and Japan
• Health Canada
• MSSO
• JMO
• WHO (Observer)

New members 2017/2018
• MFDS, Republic of Korea
• ANVISA, Brazil
• CFDA, China

Meeting 13-15 November 2017, Geneva, Switzerland

MTS:PTC Points of Note

- In some cases with more than one option for selecting terms, a "preferred option" is identified but this does not limit MedDRA users to applying that option. Organizations should be consistent in their choice of option.
- Section 4.1 – Versioning (Appendix)
  - 4.1.1 Versioning methodologies
  - 4.1.2 Timing of version implementation

General Term Selection Principles

- Quality of Source Data
- Quality Assurance
- Do Not Alter MedDRA
- Always Select a Lowest Level Term
- Select Only Current Lowest Level Terms
- When to Request a Term
- Use of Medical Judgment in Term Selection
- Selecting More than One Term
- Check the Hierarchy
- Select Terms for All Reported Information, Do Not Add Information

Quality of Source Data Quality Assurance

- Quality of original information impacts quality of output
- Obtain clarification of data
- Can be optimized by careful design of data collection forms and proper training of staff
- Organizations' coding guidelines should be consistent with MTS:PTC
- Review of term selection by qualified individuals
- Human oversight of automated coding results

Do Not Alter MedDRA

- MedDRA is a standardized terminology with a pre-defined term hierarchy
- Users must not make *ad hoc* structural alterations, including changing the primary SOC allocation
- If terms are incorrectly placed, submit a change request to the MSSO

Always Select a Lowest Level Term
Select Only Current LLTs

- 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

When to Request a Term Use of Medical Judgment

- Avoid company-specific "work-arounds" for MedDRA deficiencies. If concept not adequately represented in MedDRA, submit Change Request to MSSO.
- If no exact match in MedDRA, use medical judgment to match to an existing term that adequately represents the concept

Selecting More than One Term Check the Hierarchy

- Can select more than one LLT to represent reported information. Document procedures.
  - Selecting one term may lead to loss of specificity
  - Selecting more than one term may lead to redundant counts
- Check the hierarchy above a selected LLT (PT, HLT, HLGT, SOC) to ensure placement accurately reflects meaning of reported term

Select Terms for All Reported Information

- Select terms for every AR/AE reported, regardless of causal association
- Select terms for device-related events, product quality issues, medication errors, medical and social history, investigations and indications as appropriate

Do Not Add Information

- Do not make diagnosis if only signs/symptoms reported

Reported	LLT Selected	Comment
Abdominal pain, increased serum amylase, and increased serum lipase	Abdominal pain	It is inappropriate to assign an LLT for diagnosis of "pancreatitis"
	Serum amylase increased	
	Lipase increased	

Autoencoder Pitfalls

- Inappropriate terms may be selected by autoencoder
- Review all autoencoding carefully
  - "Allergic to CAT scan" autoencoded as:
    LLT *Allergic to cats*
  - "Myocardial infarction in the fall of 2000" autoencoded as:
    LLT *Myocardial infarction*
    LLT *Fall*

Important Coding Errors

- 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

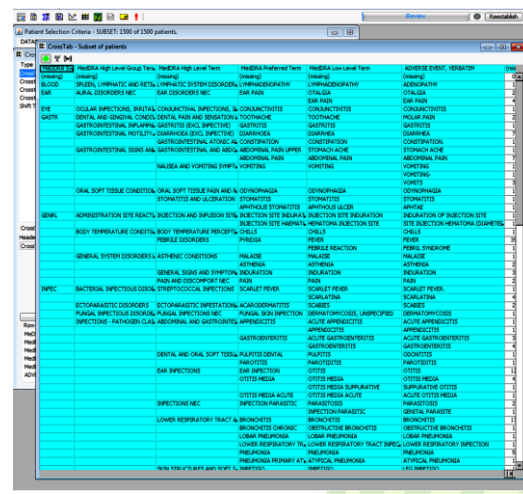
Important Coding Errors (cont)

- "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

Review of Coding Quality - FDA's Approach

- Detailed review:
  - Adverse event verbatim
  - LLT selected
  - MedDRA hierarchy



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

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

SINGLE DIAGNOSIS	
DEFINITIVE DIAGNOSIS	**PROVISIONAL DIAGNOSIS**
Single diagnosis without signs and symptoms •Diagnosis (only possible option)	Single provisional diagnosis without signs and symptoms •Provisional diagnosis (only possible option)
Example: *"Myocardial infarction"* → select *"Myocardial infarction"*	Example: *"Possible myocardial infarction"* → select *"Myocardial infarction"* (select term as if definitive diagnosis)

Similar principles apply for multiple diagnoses

Diagnoses and Provisional Diagnoses (cont)

SINGLE DIAGNOSIS	
DEFINITIVE DIAGNOSIS	**PROVISIONAL DIAGNOSIS**
Single diagnosis with signs/ symptoms •Preferred: Diagnosis only	Single provisional diagnosis with signs/symptoms •Preferred: Provisional diagnosis and signs/symptoms
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	
DEFINITIVE DIAGNOSIS	**PROVISIONAL DIAGNOSIS**
Single diagnosis with signs/ symptoms •Alternate: Diagnosis and signs/symptoms	Single provisional diagnosis with signs/symptoms •Alternate: Signs/symptoms only (as provisional diagnosis may change
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*"

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Similar principles apply for multiple diagnoses

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Diagnoses and Provisional Diagnoses (cont)

- Always include signs/symptoms not associated with diagnosis

Reported	LLT Selected
Myocardial infarction, chest pain, dyspnoea, diaphoresis, ECG changes and jaundice	Myocardial infarction Jaundice (note that jaundice is not typically associated with myocardial infarction)

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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

Reported	LLT Selected	Comment
Hyperkalaemia with a serum potassium of 1.6 mEq/L	Serum potassium abnormal	LLT *Serum potassium abnormal* covers both of the reported concepts (note: serum potassium of 1.6 mEq/L is a low result, not high)
GU pain	Pain	"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*

Vague Information

- First, try to obtain more specific information

Reported	LLT Selected	Comment
Turned green	Unevaluable event	"Turned green" reported alone is vague; this could refer to a patient condition or even to a product (e.g., pills)
Patient had a medical problem of unclear type	Ill-defined disorder	Since it is known that there is some form of a medical disorder, LLT *Ill-defined disorder* can be selected

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

Reported	LLT Selected
Arrhythmia due to atrial fibrillation	Atrial fibrillation
Hepatic function disorder (acute hepatitis)	Hepatitis acute

- A MedDRA combination term is available

Reported	LLT Selected
Retinopathy due to diabetes	Diabetic retinopathy
Rash with itching	Itchy rash

Combination Terms (cont)

- If splitting provides more clinical information, select more than one term
- In all cases of combination terms, apply medical judgment

Reported	LLT Selected
Diarrhoea and vomiting	Diarrhoea Vomiting
Wrist fracture due to fall	Wrist fracture Fall

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

Reported	LLT Selected	Comment
Hypoglycaemia	Hypoglycaemia	LLT *Hypoglycaemia* links to SOC *Metabolism and nutrition disorders*
Decreased glucose	Glucose decreased	LLT *Glucose decreased* links to SOC *Investigations*

Investigations (cont)

- Unambiguous investigation result

Reported	LLT Selected	Comment
Glucose 40 mg/dL	Glucose low	Glucose is clearly below the reference range

- Ambiguous investigation result

Reported	LLT Selected	Comment
His glucose was 40	Glucose abnormal	No units have been reported. Select LLT *Glucose abnormal* if clarification cannot be obtained.

Investigations (cont)

- Investigation results consistent with diagnosis

Reported	LLT Selected	Comment
Elevated potassium, K 7.0 mmol/L, and hyperkalaemia	Hyperkalaemia	It is not necessary to select LLT *Potassium increased*

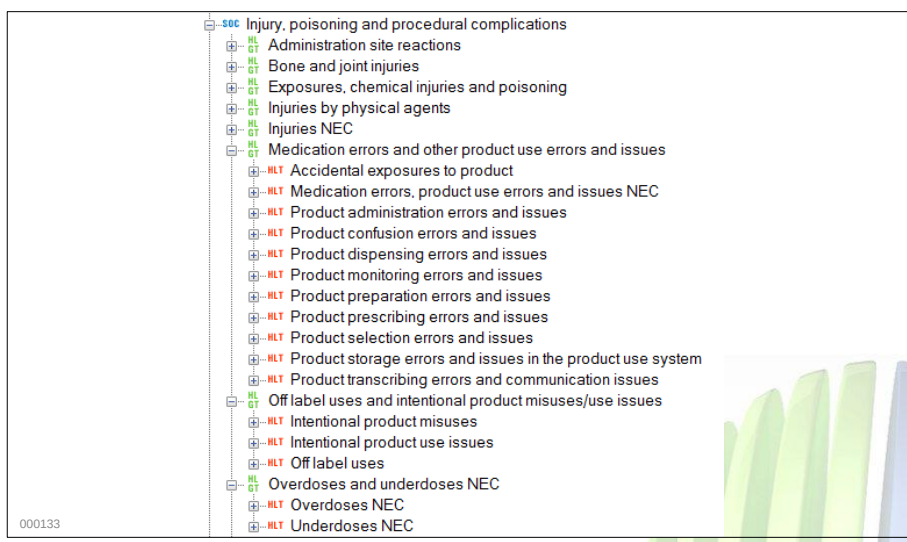
- Grouped investigation result terms

Reported	LLT Selected	Comment
Increased alkaline phosphatase, increased SGPT, increased SGOT and elevated LDH	Alkaline phosphatase increased SGPT increased SGOT increased LDH increased	Select four individual terms. A single term such as LLT *Liver function tests abnormal* should not be selected.

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
- Patient had features of aldosterone excess
  Aldosterone increased
  Aldosteronism
  Blood aldosterone abnormal

Medication Errors/Product Use Issues Hierarchy



Advantages of Hierarchy

- Avoids force-classification of medication errors vs. product use issues
- Classification by stage in the medication/product use process
  - Prescribing
  - Dispensing
  - Preparation for administration
  - Administration
  - Storage in product use system
- Intercepted medication errors under relevant stage HLTs
- Intentional concepts separated from errors/unspecified issues
- "Product" at HLT level covers medication and other product concepts such as device use/error terms

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 <u>with</u> clinical consequences

Reported	LLT Selected	Comment
Patient was administered wrong drug and experienced hypotension	Wrong drug administered Hypotension	
Insulin was given using the wrong syringe resulting in the administration of an overdose. The patient developed hypoglycaemia.	Drug administered in wrong device Accidental overdose Hypoglycaemia	If an overdose is reported in the context of a medication error, the more specific term *LLT Accidental overdose* can be selected

Medication Errors (cont)

- Medication error <u>without</u> clinical consequences

Reported	LLT Selected	Preferred Option
Medication was given intravenously instead of intramuscularly without any adverse effect	Intramuscular formulation administered by other route	✓
	Intramuscular formulation administered by other route No adverse effect	

Medication Errors (cont)

- Important to record potential occurrence of medication error
- Unlikely to be reported as an adverse event but may need to be recorded in periodic safety reports

Reported	LLT Selected	Comment
Pharmacist notices that the names of two drugs are similar and is concerned that this may result in a medication error	Drug name confusion Circumstance or information capable of leading to medication error	Note: this example is a potential medication error and LLT *Drug name confusion* provides additional information about the nature of the potential medication error

Overdose, Toxicity and Poisoning

If overdose, poisoning or toxicity is explicitly reported, select the appropriate term

- Overdose <u>with</u> clinical consequences

Reported	LLT Selected
Stomach upset from study drug overdose	Stomach upset Overdose

- Overdose <u>without</u> clinical consequences

Reported	LLT Selected	Preferred Option
Patient received an overdose of medicine without any adverse consequences	Overdose	✓
	Overdose No adverse effect	

What Term to Select?

- The patient's renal function was measured every six months instead of on the monthly schedule recommended in the label for the drug
  Medication monitoring error
  Renal function test abnormal
  Drug monitoring procedure incorrectly performed

- Unintentionally took more than maximum recommended dose due to dispensing error
  Accidental overdose
  Incorrect dose administered
  Drug dispensing error

Misuse, Abuse and Addiction

Concept	Intentional?	By Whom?	Therapeutic Use?	Additional Sections in this Document
Misuse	Yes	Patient/consumer	Yes*	3.16.1
Abuse	Yes	Patient/consumer	No	3.16.2
Addiction	Yes	Patient/consumer	No	3.16.3
Medication error	No	Patient/consumer **or** healthcare provider	Yes	3.15
Off label use	Yes	Healthcare provider	Yes	3.27

* Definitions of misuse may not always include the concept of therapeutic use; misuse may be similar to the concept of abuse in some regions.

Coding Exercises

- Narratives and short verbatims
- Assess the reported terms
  - Identify what concepts are reported (diagnosis, death, investigations, etc.)
- Refer to the appropriate sections of the MTS:PTC for guidance on term selection
  - For example, Section 3.2 for death terms
- Use MTS:PTC preferred options (forget your organization's conventions)
- Use browser to search for and select LLTs (also record PT and primary SOC)

Specific Tips for Narrative Exercises

- Overall, coding principles are the same as for short verbatim exercises
- Code all of the following:
  - Events (including procedures and investigations as needed)
  - Indications
  - Medical history
  - Social history

Sample Narrative

A 75-year-old male receiving Drug X for rheumatoid arthritis developed an area of darkened skin on his chest. The patient's medical history is significant for peripheral vascular disease and cigarette smoking. The skin lesion was excised; it was revealed to be a seborrhoeic wart.

Course Summary

- In this course, we covered:
  - A review of MedDRA's scope and structure, including primary SOC allocation rules
  - Coding conventions, synonym lists, and coding QA
  - Introduction to the MedDRA Term Selection: Points to Consider document
  - Coding exercises

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