

# Coding with MedDRA

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Version 18.0

# Disclaimer

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- 財團法人藥害救濟基金會接受衛生福利部食品藥物管理署委託辦理「全國藥物不良反應通報中心」及「104年創新藥品風險管理及輔導」計劃
- 本次演講內容僅代表全國藥物不良反應通報中心之觀點，凡涉及政策方向及法規解釋與適用，應依衛生主管機關之指示為準。

# Background

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- Under the auspices of International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).
  
- ICH MedDRA Management Board
  - ▣ EU, EFPIA, MHLW, JPMA, FDA, PhRMA, MHRA, Health Canada, and the WHO (as observer)

- MedDRA

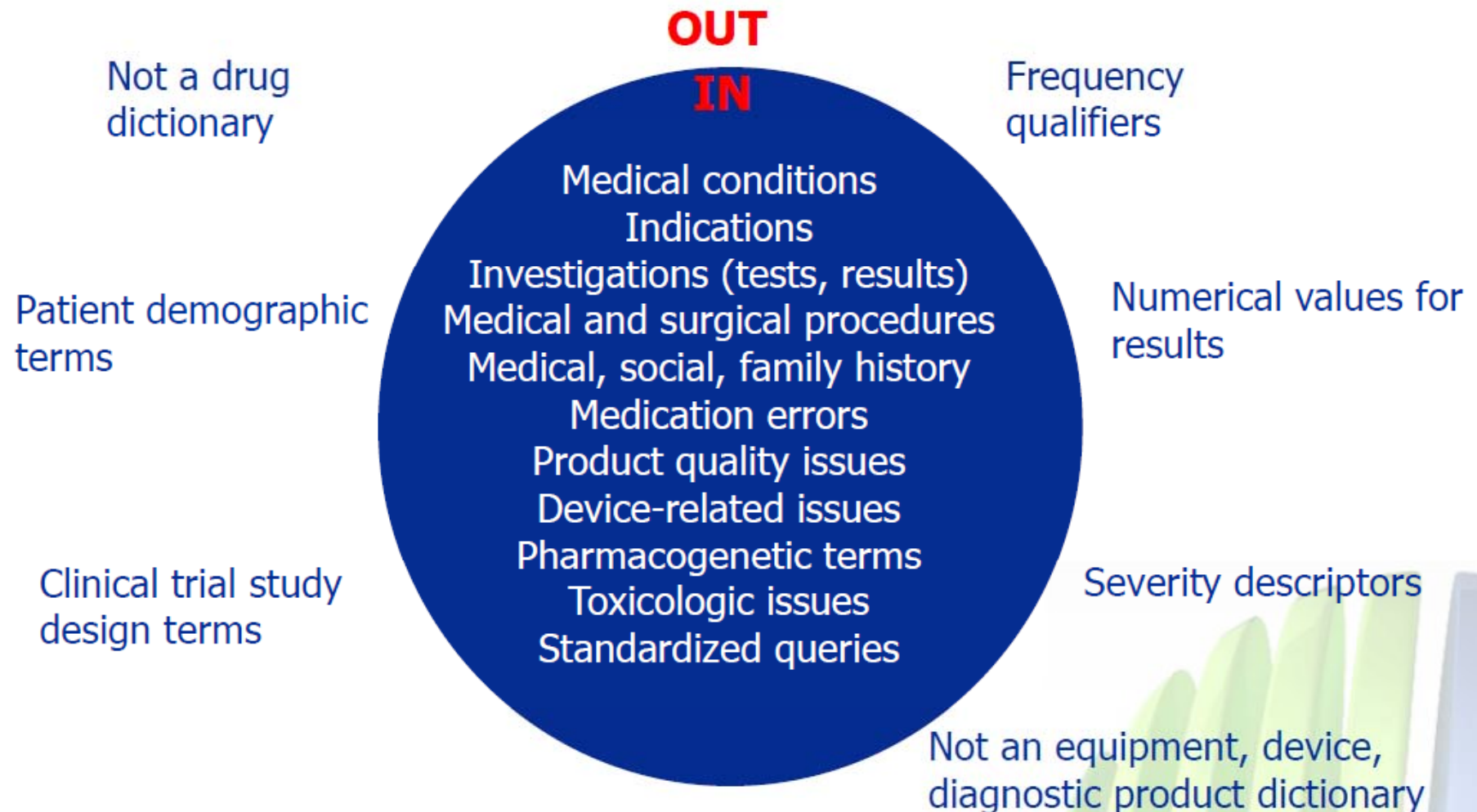
- ▣ Medical Dictionary for Regulatory Activities.

- MedDRA definition

- ▣ 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.

# Scope of MedDRA

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# Hierarchy

System Organ  
Class (SOC)

- Lack of multiple axis: Inv, SocCi, Surg

PT

LLT

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Click "Cancel Search" to stop the search

System Organ Class (SOC) (26)

High Level Group Term (HLGT) (>30)

High Level Term (HLT) (>1,700)

Preferred Term (PT) (>19,000)

Lowest Level Term (LLT) (>70,000)

+ LLT Stevens Johnson reaction

- LLT Stevens Johnson syndrome

- PT Stevens-Johnson syndrome

- HLT Bullous conditions

- HL GT Epidermal and dermal conditions

- SOC Skin and subcutaneous tissue disorders

- HLT Inflammatory disorders following infection

- HL GT Ancillary infectious topics

- SOC Infections and infestations

- HLT Allergic conditions NEC

- HL GT Allergic conditions

- SOC Immune system disorders

- HLT Poisoning and toxicity

- HL GT Exposures, chemical injuries and poisoning

- SOC Injury, poisoning and procedural complications

+ LLT Stevens Johnson type reaction

+ LLT Stevens Johnson syndrome

+ LLT Stevens-Johnson syndrome

+ LLT Syndrome Stevens-Johnson

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# General Principle

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## □ Always Select a Lowest Level Term

### □ Quantifier:

#### ■ Age

■ neonatal, newborn, childhood

#### ■ Body site

■ face, injection site, skin, extremities

#### ■ Location and microorganism of infection

■ Pneumonia, respiratory infection, chlamydial infection

### □ If no available term with designated quantifier

#### ■ Record quantifier in other field

#### ■ Event information has priority(broad term)

# General Principle

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- **Use of Medical Judgment in Term Selection**
  - ▣ Verbatim to medical terms

Reported	LLT Selected	Comment
Brittle hair	Hair breakage	There is no MedDRA term for "brittle hair". LLT <i>Hair breakage</i> more accurately reflects the reported concept than the less specific LLT <i>Hair disorder</i>



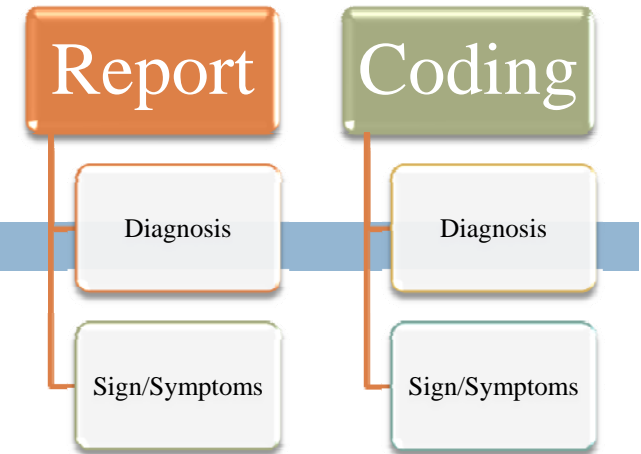
# General Principle

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- **Check the Hierarchy**
  - ▣ Check the hierarchy above the LLT (PT level and further up the hierarchy to HLT, HLGT and SOC)
- **Select Terms for All Reported Information, Do Not Add Information**
  - ▣ Regardless of causal association
  - ▣ **Do not add information by selecting a term for a diagnosis if only signs or symptoms are reported**

# General Principle

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## □ Combination Terms

■  $Dx_{\text{definitive}} + S/S \rightarrow Dx_{\text{definitive}}$

Reported	LLT Selected
Chest pain due to myocardial infarction	Myocardial infarction

■  $Dx_{\text{definitive}} + S/S + S/S_{\text{others}} \rightarrow Dx_{\text{definitive}} + S/S_{\text{others}}$

■  $Dx_{\text{provisional}} + S/S \rightarrow Dx_{\text{provisional}} + S/S$

■  $Dx_{\text{provisional}} + S/S + S/S_{\text{others}} \rightarrow Dx_{\text{provisional}} + S/S + S/S_{\text{others}}$

■  $Dx_{\text{lab}} + \text{lab} \rightarrow Dx_{\text{lab}}$

Reported	LLT Selected	Comment
Elevated potassium, K 7.0 mmol/L, and hyperkalemia	Hyperkalemia	It is not necessary to select LLT <i>Potassium increased</i>

# General Principle

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×  $Dx + Dx_{\text{specific}} \rightarrow Dx_{\text{specific}}$

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

# General Principle

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×  $DX_1 + DX_2 \rightarrow Dx_{combine}$

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

×  $DX_{1\&2} \rightarrow Dx_1 + Dx_2$

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

- Term would not need to be coded unless it is the **only information reported** or **provides significant clinical information**
  - ▣ Outcomes: Death, disability, and hospitalisation

Reported	LLT Selected	Comment
Death due to myocardial infarction	Myocardial infarction	Record death as an outcome
Constipation, ruptured bowel, peritonitis, sepsis; patient died	Constipation Perforated bowel Peritonitis Sepsis	

Reported	LLT Selected
Patient experienced a rash and had sudden cardiac death	Rash Sudden cardiac death

## □ Suicide and Self-Harm

- ▣ Do not assume that an overdose/self-injury is a suicide attempt without mention suicide or suicide attempt.

Reported	LLT Selected	Comment
Self slashing	Self inflicted laceration	LLT <i>Self inflicted laceration</i> is linked to PT <i>Intentional self-injury</i>
Cut her own wrists		
Cut wrists in a suicide attempt	Self inflicted laceration Suicide attempt	.
Took an overdose in an attempt to commit suicide	Intentional overdose Suicide attempt	If overdose is reported in the context of suicide or a suicide attempt, the more specific LLT <i>Intentional overdose</i> can be selected (see also Section 3.18)

## □ Suicide and Self-Harm

- ▣ Suicide attempt vs. Completed suicide (Fetal suicide)

Reported	LLT Selected	Comment
Suicide attempt resulted in death	Completed suicide	Record death as an outcome

## □ Conflicting/Ambiguous/Vague Information

Reported	LLT Selected	Comment
Hyperkalemia with a serum potassium of 1.6 mEq/L	Serum potassium abnormal	LLT <i>Serum potassium abnormal</i> covers both of the reported concepts (note: serum potassium of 1.6 mEq/L is a <b>low</b> result, not high)

Reported	LLT Selected	Comment
GU pain	Pain	"GU" could be either "genito-urinary" or "gastric ulcer". Since "pain" is definite,

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)



## □ Pre-existing Conditions

### □ Modified

- Choose exact term: Condition term + modifier

- Disease progression/ Disorder aggravation

Reported	LLT Selected
Exacerbation of myasthenia gravis	Myasthenia gravis aggravated

Aggravate  
Exacerbated  
Worsened  
Recurrent  
Progressive

- Database limitation

- Record the modification in a consistent, documented way
  - Second term for the modification of the condition

Examples	Reported	LLT Selected	Comment
Example 1	Jaundice aggravated	Jaundice	Record "aggravated" in a consistent, documented way
Example 2	Jaundice aggravated	Jaundice Condition aggravated	Record "aggravated" in a consistent, documented way. Select terms for the pre-existing condition and the modification.

- Event reported with pre-existing condition that has not changed
  - Code **reported event** only

Reported	LLT Selected	Comment
Shortness of breath due to pre-existing cancer	Shortness of breath	In this instance, "shortness of breath" is the event; "cancer" is the pre-existing

## □ Exposures During Pregnancy and Breast Feeding

- Events in the mother: the pregnancy with or w/o clinical consequences

Reported	LLT Selected	Comment
Pregnant patient receiving drug X experienced a pruritic rash	Maternal exposure during pregnancy Pruritic rash	LLT Pregnancy can be selected for medical history, concomitant medical condition

- Events in the child or fetus
  - Type of exposure + any adverse event

Setting/Patient	Reported	LLT Selected
Fetus with AE; exposed <i>in utero</i> ; mother took product	Pregnant woman taking drug X; fetal tachycardia noted on routine examination	Drug exposure in utero Fetal tachycardia
Baby with AE; exposed <i>in utero</i> ; father took product	Baby born with cleft palate; father had been taking drug X at time of conception	Paternal drug exposure before pregnancy Cleft palate
Newborn with AE; exposed to product via breast milk	Mother exposed to drug X; nursing newborn experienced vomiting	Drug exposure via breast milk Vomiting neonatal

## □ Congenital Terms

### ▣ Condition described as congenital

- Congenital: any condition present at birth, whether genetically inherited or occurring *in utero*
- SOC: *Congenital, familial and genetic disorders*

Reported	LLT Selected
Congenital heart disease	Heart disease congenital
Child born with heart disease	

### ▣ Condition not congenital/not present at birth

Reported	LLT Selected	Comment
Night blindness	Night blindness	LLT/PT <i>Night blindness</i> (links to primary SOC <i>Eye disorders</i> ). Do not assume the condition is congenital (LLT/PT <i>Congenital night blindness</i> )
Cholangiectasis	Cholangiectasis acquired	

## □ Neoplasms

Neoplasms Terms in MedDRA
"Cancer" and "carcinoma" are synonyms (Appendix B of Introductory Guide)
"Tumo(u)r" terms refer to neoplasia
"Lump" and "mass" terms are <u>not</u> neoplasia

## □ Medical and Surgical Procedures

### ▣ Procedure (+ diagnosis )

	Reported	LLT Selected	Preferred Option	Comment
Pat	Liver transplantation due to liver injury	Liver transplantation	✓	Selecting term for the procedure may indicate severity of the condition
Patie		Liver injury		

## □ Investigations

### ▣ Ambiguous investigation result

Reported	LLT Selected	Comment
His glucose was 40	Glucose abnormal	In this example, no units have been reported. Select LLT <i>Glucose abnormal</i> if clarification cannot be obtained

### ▣ Do not lump together separated investigation results unless reported as such

Reported	LLT Selected	Comment
Abnormalities of liver function tests	Abnormal liver function tests	
Increased alkaline phosphatase, increased SGPT, increased SGOT and elevated LDH	Alkaline phosphatase increased SGPT increased SGOT increased LDH increased	Select four individual terms for the investigation results. A single term such as LLT <i>Liver function tests abnormal</i> should <b>not</b> be selected

- Do not infer event unless specific information is provided
- EVENT+ clinical consequences

Without consequences: No adverse effect

- ▣ Medication/Administration Errors ,Accidental Exposures and Occupational Exposures
- ▣ Misuse, Abuse and Addiction
- ▣ Transmission of Infectious Agent via Medicinal Product
- ▣ Overdose, Toxicity and Poisoning
- ▣ Device-related Terms

## □ Drug interactions

### ▣ Specifically states an interaction

Reported	LLT Selected
Torsade de pointes with suspected drug interaction	Drug interaction Torsade de pointes
Patient drank cranberry juice which interacted with anticoagulant drug causing an INR increase	Food interaction INR increased

### ▣ Not specifically state an interaction

Reported	LLT Selected
Patient was started on an anti-seizure medication and a heart medication and developed syncope	Syncope
Patient was already on an anti-seizure medication and was started on a heart medication, and anti-seizure medication levels increased	Anticonvulsant drug level increased



## □ No Adverse Effect and “Normal” Terms

### ▣ LLT: No adverse effect

- Pregnancy registries, overdose and medication error reports

Examples of Terms for “Normal” States and Outcomes
Sinus rhythm
Normal baby
Normal electrocardiogram

## □ Unexpected Therapeutic Effect

- LLT: Unexpected therapeutic effect
- **Beneficial effect** of a product apart from the reason it had been given

Reported	LLT Selected
A bald patient was pleased that he grew hair while using a product	Hair growth increased Unexpected therapeutic effect

## □ Modification of Effect

- Only the “lack of effect” term even if consequences are also reported

Reported	LLT Selected	Preferred Option
Patient took drug for a headache, and her headache didn't go away	Drug ineffective	✓
	Drug ineffective Headache	
Antibiotic didn't work	Lack of drug effect	

- Do not infer lack of effect

Reported	LLT Selected	Comment
AIDS patient taking anti-HIV drug died	Death	Do not assume lack of effect in this instance. Select only a term for death (see Section 3.2)

- Increased, decreased and prolonged drug effect

## □ Social Circumstances

### □ Not AE

- only available terms for recording ARs/AEs
- may add valuable clinical information

Reported	LLT Selected
Patient's ability to drive was impaired	Impaired driving ability

## □ Medical and Social History

Reported	LLT Selected
History of gastrointestinal bleed and hysterectomy	Gastrointestinal bleed Hysterectomy
Patient is a cigarette smoker with coronary artery disease	Cigarette smoker Coronary artery disease

## □ Indication for Product Use

- If the only information reported is the type of therapy, select the most specific term.

Reported	LLT Selected
Patient received chemotherapy	Chemotherapy
Patient received antibiotics	Antibiotic therapy

## □ Off Label Use

- LLT: Off label use

Reported	LLT Selected	Preferred Option
Patient was administered a drug off label for pulmonary hypertension and suffered a stroke	Off label use Pulmonary hypertension Stroke	✓
	Pulmonary hypertension Stroke	

## □ Product Quality Issues

- ▣ With or without clinical consequences
  - Quality issue (+ clinical consequences)

Reported	LLT Selected
New bottle of drug tablets have unusual chemical smell that made me nauseous	Product odor abnormal Nauseous
I switched from one brand to another of my blood pressure medication, and I developed smelly breath	Product substitution issue brand to brand Smelly breath
Consumer noted that the toothpaste they had purchased had a mouldy odour Subsequent investigation of the product lot number revealed that the toothpaste was a counterfeit product	Product counterfeit Product odour abnormal

Reported	LLT Selected
Sterile lumbar puncture kit received in broken packaging (sterility compromised)	Product sterile packaging disrupted

## □ Product Quality Issues

### ▣ Product quality issue vs. medication error

Reported	LLT Selected	Comment
Pharmacist dispensing Drug A inadvertently attached a product label for Drug B	Wrong label placed on medication during dispensing	Medication error
The drug store clerk noted that the wrong product label was attached to some bottles in a shipment of mouthwash	Product label on wrong product	Product quality issue
The mother administered an underdose of antibiotic because the lines on the dropper were hard to read	Product dropper calibration unreadable Accidental underdose	Product quality issue and medication error. If underdose is reported in the context of a medication error, the more specific LLT <i>Accidental underdose</i> can be selected.

# The Quality assurance

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- The quality of the original reported information directly impacts the quality of data output.
- Organisations should document their term selection methods and quality assurance procedures in coding guidelines consistent.





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*Thank you for your attention.*

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