MedDRA® TERM SELECTION: POINTS TO CONSIDER

ICH-Endorsed Guide for MedDRA Users

Release 4.7
Based on MedDRA Version 17.0

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Section 1 – INTRODUCTION

The **Med**ical **D**ictionary for **R**egulatory **A**ctivities terminology (MedDRA) was designed for sharing regulatory information for human medical products. However, unless users achieve consistency in how they assign terms to verbatim reports of symptoms, signs, diseases, etc., use of MedDRA cannot have the desired harmonising effect in the exchange of coded data.

This *MedDRA Term Selection: Points to Consider* (MTS:PTC) document is an ICH-endorsed guide for MedDRA users. It is updated in step with new MedDRA versions and is a companion document to MedDRA. It was developed and is maintained by a working group charged by the ICH Steering Committee. The working group consists of regulatory and industry representatives of the European Union, Japan and the United States, as well as representatives from the Canadian regulatory authority, the MedDRA Maintenance and Support Services Organization (MSSO) and the Japanese Maintenance Organization (JMO). (See Appendix, Section 4.3 for list of members).

1.1 – Objectives of this Document

The objective of the MTS:PTC document is to promote **accurate** and **consistent** term selection.

Organisations are encouraged to document their term selection methods and quality assurance procedures in organisation-specific coding guidelines which should be consistent with the MTS:PTC.

Consistent term selection promotes medical accuracy for sharing MedDRA-coded data and facilitates a common understanding of shared data among academic, commercial and regulatory entities. The MTS:PTC could also be used by healthcare professionals, researchers, and other parties outside of the regulated biopharmaceutical industry.

The document provides term selection advice for business purposes and regulatory requirements. There may be examples that do not reflect practices and requirements in all regions. This document does not specify regulatory reporting requirements, nor does it address database issues. As experience with MedDRA increases, and as MedDRA changes, there will be revisions to this document.

1.2 – Uses of MedDRA

Term selection for adverse reactions/adverse events (ARs/AEs), device-related events, product quality issues, medication errors, exposures, medical history, social history, investigations, misuse and abuse, off label use, and indications is addressed in this MTS:PTC document.

MedDRA's structure allows for aggregation of those reported terms in medically meaningful groupings to facilitate analysis of safety data. MedDRA can also be

used to list AR/AE data in reports (tables, line listings, etc), compute frequencies of similar ARs/AEs, and capture and analyse related data such as product indications, investigations, and medical and social history.

1.3 – How to Use this Document

The MTS:PTC document does not address every potential term selection situation. Medical judgment and common sense should also be applied.

This document is not a substitute for MedDRA training. It is essential for users to have knowledge of MedDRA's structure and content. For optimal MedDRA term selection, one should also refer to the MedDRA Introductory Guide (See Appendix, Section 4.2).

1.4 – Preferred Option

In some cases, where there is more than one option for selecting terms, a "preferred option" is identified in this document. **Designation of a "preferred option" does not limit MedDRA users to applying that option.** An organisation should be consistent in the option that they choose to use.

1.5 – MedDRA Browsing Tools

The MSSO and JMO provide two browsers (a desktop browser and a Web-based browser) that allow for searching and viewing the terminology (See Appendix, Section 4.2). Users may find these browsers useful aids in term selection.

Section 2 – GENERAL TERM SELECTION PRINCIPLES

2.1 – Quality of Source Data

The quality of the original reported information directly impacts the quality of data output. Clarification should be obtained for data that are ambiguous, confusing, or unintelligible. If clarification cannot be obtained, refer to Section 3.4.

2.2 – Quality Assurance

To promote consistency, organisations should document their term selection methods and quality assurance procedures in coding guidelines consistent with this MTS:PTC document.

Clear initial data can be promoted through careful design of data collection forms, and training of individuals in data collection and follow-up (e.g., investigators, drug sales representatives).

Term selection should be reviewed by a qualified individual, i.e., a person with medical background or training who has also received MedDRA training.

Human oversight of term selection performed by IT tools (such as an autoencoder) is needed to assure that the end result fully reflects the reported information and makes medical sense.

2.3 – Do Not Alter MedDRA

MedDRA is a **standardised** terminology with a pre-defined term hierarchy that should not be altered. Users must not make *ad hoc* structural alterations to MedDRA, including changing the primary SOC allocation; doing so would compromise the integrity of this standard. If terms are found to be incorrectly placed in the MedDRA hierarchy, a change request should be submitted to the MSSO.

Example

Change Request to Re-Assign Primary SOC
In a previous version of MedDRA, PT *Factor VIII deficiency* was incorrectly assigned to primary SOC *Blood and lymphatic system disorders*. By means of a Change Request, the PT was re-assigned to primary SOC *Congenital, familial and genetic disorders* (making SOC *Blood and lymphatic system disorders* its secondary SOC assignment)

2.4 – Always Select a Lowest Level Term

MedDRA Lowest Level Term(s) (LLT) that **most accurately reflects the reported verbatim information** should be selected.

The degree of specificity of some MedDRA LLTs may be challenging for term selection. Here are some tips for specific instances:

- *A single letter difference in a reported verbatim text can impact the meaning of the word and consequently the term selection*

Example

Reported	LLT Selected
Lip sore	Lip sore (PT Lip pain)
Lip sore**s**	Sores lip (PT Cheilitis)
Sore gums	Sore gums (PT Gingival pain)
Sore**s** gum	Sores gum (PT Gingival inflammation)

- *Gender-specific terms*

MedDRA generally excludes terms with demographic descriptors (age, gender, etc.), but some terms with gender qualifiers are included if the gender renders the concept unique.

Example

Distinct Gender-Specific Terms
In MedDRA, there are separate LLTs/PTs for *Infertility*, *Infertility female* and *Infertility male*

Organisation-specific coding guidelines should address instances when it is important to capture gender-specific concepts.

MedDRA users should also consider the impact of gender-specific terms when comparing current data to data coded with a legacy terminology in which such gender specificity may not have been available.

Example

Gender Specificity – Legacy Terms vs. MedDRA
Consider the impact of selecting gender-specific MedDRA terms for breast cancer (e.g., LLT *Breast cancer female*) when comparing data coded in a legacy terminology with only a single "Breast cancer" term.

- *Postoperative and post procedural terms*

MedDRA contains some "postoperative" and "post procedural" terms. Select the most specific term available.

Example

Reported	LLT Selected
Bleeding after surgery	Bleeding postoperative
Sepsis occurred after the procedure	Post procedural sepsis

- *Newly added terms*

More specific LLTs may be available in a new version of MedDRA. See Appendix, Section 4.2.

2.5 – Select Only Current Lowest Level Terms

Non-current LLTs should not be used for term selection.

2.6 – When to Request a Term

Do not address deficiencies in MedDRA with organisation-specific solutions. If there is no MedDRA term available to adequately reflect the reported information, submit a change request to MSSO.

Example

Change Request for a New Term
LLT *HBV coinfection* was added to MedDRA following a user's request.

2.7 – Use of Medical Judgment in Term Selection

If an exact match cannot be found, **medical judgment** should be used to adequately represent the medical concept with an existing MedDRA term.

 Example

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

2.8 – Selecting More than One Term
When a specific medical concept is not represented by a **single** MedDRA term, consider requesting a new term through the change request process (See Section 2.6). Whilst waiting for the new term, select one or more existing terms using a consistent approach with careful consideration of the impact on data retrieval, analysis, and reporting.

In some cases, it may be appropriate to select more than one MedDRA LLT to represent the reported information. If only one term is selected, specificity may be lost; on the other hand, selecting more than one term may lead to redundant counts. Established procedures should be documented.

Example

More Than One LLT Selected
There is no single MedDRA term for "metastatic gingival cancer". Therefore, the options are: 1. Select LLT *Gingival cancer* OR LLT *Metastatic carcinoma* 2. Select LLT *Gingival cancer* AND LLT *Metastatic carcinoma*

2.9 – Check the Hierarchy

When considering selecting an LLT, check the hierarchy above the LLT (PT level and further up the hierarchy to HLT, HLGT and SOC) to ensure the placement accurately reflects the meaning of the reported term.

2.10 – Select Terms for All Reported Information, Do Not Add Information

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

If a diagnosis is reported with characteristic signs and symptoms, the **preferred option** is to select a term for the diagnosis only (see Section 3.1 for details and examples).

When selecting terms, no reported information should be excluded from the term selection process; similarly, do not add information by selecting a term for a diagnosis if only signs or symptoms are reported.

Example

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	

Section 3 – TERM SELECTION POINTS

3.1 – Definitive and Provisional Diagnoses with or without Signs and Symptoms

The table below provides term selection options for definitive and provisional diagnoses with or without signs/symptoms reported. Examples are listed below the table.

A provisional diagnosis may be described as "suspicion of", "probable", "presumed", likely", "rule out", "questionable", "differential", etc.

The **preferred option** for a single or multiple provisional diagnosis(es) is to select a term(s) for the diagnosis(es) *and* terms for reported signs and symptoms. This is because a provisional diagnosis may change while signs/symptoms do not.

SUMMARY OF PREFERRED AND ALTERNATE OPTIONS	
SINGLE DIAGNOSIS	
DEFINITIVE DIAGNOSIS	**PROVISIONAL DIAGNOSIS**
Single definitive diagnosis without signs/symptoms • Diagnosis (only possible option)	**Single provisional diagnosis without signs/symptoms** • Provisional diagnosis (only possible option)
Single definitive diagnosis with signs/symptoms • **Preferred:** Diagnosis only • Alternate: Diagnosis and signs/symptoms *Note: Always include signs/symptoms not associated with diagnosis* **SEE EXAMPLE 1**	**Single provisional diagnosis with signs/symptoms** • **Preferred:** Provisional diagnosis and signs/symptoms • Alternate: Signs/symptoms only *Note: Always include signs/symptoms not associated with diagnosis* **SEE EXAMPLE 2**
MULTIPLE DIAGNOSES	
DEFINITIVE DIAGNOSES	**PROVISIONAL DIAGNOSES**
Multiple definitive diagnoses without signs/symptoms • Multiple diagnoses (only possible option)	**Multiple provisional diagnoses without signs/symptoms** • Multiple provisional diagnoses (only possible option)
Multiple definitive diagnoses with signs/symptoms • **Preferred:** Multiple diagnoses only • Alternate: Diagnoses and signs/symptoms *Note: Always include signs/symptoms not associated with diagnosis* **SEE EXAMPLE 3**	**Multiple provisional diagnoses with signs/symptoms** • **Preferred:** Multiple provisional diagnoses and signs/symptoms • Alternate: Signs/symptoms only *Note: Always include signs/symptoms not associated with diagnosis* **SEE EXAMPLE 4**

EXAMPLES			
Example	**Reported**	**LLT Selected**	**Preferred Option**
1	Anaphylactic reaction, rash dyspnoea, hypotension, and laryngospasm	Anaphylactic reaction	✔
		Anaphylactic reaction Rash Dyspnoea Hypotension Laryngospasm	
2	Possible myocardial infarction with chest pain, dyspnoea, diaphoresis	Myocardial infarction Chest pain Dyspnoea Diaphoresis	✔
		Chest pain Dyspnoea Diaphoresis	
3	Pulmonary embolism, myocardial infarction, and congestive heart failure with chest pain, cyanosis, shortness of breath, and blood pressure decreased	Pulmonary embolism Myocardial infarction Congestive heart failure	✔
		Pulmonary embolism Myocardial infarction Congestive heart failure Chest pain Cyanosis Shortness of breath Blood pressure decreased	
4	Chest pain, cyanosis, shortness of breath, and blood pressure decreased. Differential diagnosis includes pulmonary embolism, myocardial infarction, and congestive heart failure	Pulmonary embolism Myocardial infarction Congestive heart failure Chest pain Cyanosis Shortness of breath Blood pressure decreased	✔
		Chest pain Cyanosis Shortness of breath Blood pressure decreased	
Always include signs/ symptoms not associated with diagnosis	Myocardial infarction, chest pain, dyspnoea, diaphoresis, ECG changes and jaundice	Myocardial infarction Jaundice (note that jaundice is not typically associated with myocardial infarction)	

3.2 – Death and Other Patient Outcomes

Death, disability, and hospitalisation are considered **outcomes** in the context of safety reporting and not usually considered ARs/AEs. Outcomes are typically recorded in a separate manner (data field) from AR/AE information. A term for

the outcome should be selected if it is the only information reported or provides significant clinical information.

(For reports of suicide and self-harm, see Section 3.3).

3.2.1 Death with ARs/AEs

Death is an outcome and not usually considered an AR/AE.If ARs/AEs are reported along with death, select terms for the ARs/AEs. Record the fatal outcome in an appropriate data field.

Example

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

3.2.2 Death as the only reported information

If the only information reported is death, select the most specific death term available. Circumstances of death should not be inferred but recorded only if stated by the reporter.

Death terms in MedDRA are linked to HLGT *Fatal outcomes*.

Example

Reported	LLT Selected
Patient was found dead	Found dead
Patient died in childbirth	Maternal death during childbirth
The autopsy report stated that the cause of death was natural	Death from natural causes

3.2.3 Death terms that add important clinical information

Death terms that add important clinical information should be selected along with any reported ARs/AEs.

Example

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

3.2.4 Other patient outcomes (non-fatal)

Hospitalisation, disability, and other patient outcomes are not generally considered ARs/AEs.

Example

Reported	LLT Selected	Comment
Hospitalisation due to congestive heart failure	Congestive heart failure	Record hospitalisation as an outcome

If the only information reported is the patient outcome, select the most specific term available.

Example

Reported	LLT Selected
Patient was hospitalised	Hospitalisation

3.3 – Suicide and Self-Harm

Accurate and consistent term selection for reports of suicide attempts, completed suicides, and self-harm is necessary for data retrieval and analysis. If the motive for reported injury is not clear, seek clarification from the source.

3.3.1 If overdose is reported

Do not assume that an overdose – including an intentional overdose – is a suicide attempt. Select only the appropriate overdose term (See Section 3.18).

3.3.2 If self-injury is reported

For reports of self-injury that do not mention suicide or suicide attempt, select only the appropriate self-injury term.

Example

Reported	LLT Selected	Comment
Self slashing	Self inflicted laceration	LLT *Self inflicted laceration* is linked to PT *Intentional self-injury*
Cut her own wrists		
Cut wrists in a suicide attempt	Suicide attempt	In addition, LLT *Self inflicted laceration* can be selected

3.3.3 Fatal suicide attempt

If a suicide attempt is fatal, select the term that reflects the outcome instead of the attempt only.

Example

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

3.4 – Conflicting/Ambiguous/Vague Information

When conflicting, ambiguous, or vague information is reported, term selection to support appropriate data retrieval may be difficult. When this occurs, attempt to obtain more specific information. If clarification cannot be achieved, select terms as illustrated in the examples below (Sections 3.4.1 through 3.4.3).

3.4.1 Conflicting information

Example

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)

3.4.2 Ambiguous information

Example

Reported	LLT Selected	Comment
GU pain	Pain	Effort should be made to obtain clarification of the meaning of "GU" from the source so that more specific term selection may be possible. "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*

3.4.3 Vague information

For information that is vague, attempt to obtain clarification. If clarification cannot be achieved, select an LLT that reflects the vague nature of the reported event.

Example

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

3.5 – Combination Terms

A **combination term** in MedDRA is a single medical concept combined with additional medical wording that provides important information on pathophysiology or aetiology. A combination term is an internationally recognised, distinct and robust medical concept as illustrated in the examples below.

Example

MedDRA Combination Terms
PT Diabetic retinopathy
PT Hypertensive cardiomegaly
PT Eosinophilic pneumonia

A combination term may be selected for certain reported ARs/AEs (e.g., a condition "due to" another condition), keeping the following points in mind (NOTE: medical judgment should be applied):

3.5.1 Diagnosis and sign/symptom

If a diagnosis and its characteristic signs or symptoms are reported, select a term for the diagnosis (See Section 3.1). A MedDRA combination term is not needed in this instance.

Example

Reported	LLT Selected
Chest pain due to myocardial infarction	Myocardial infarction

3.5.2 One reported condition is more specific than the other

If two conditions are reported in combination, and one is more specific than the other, select a term for the more specific condition.

Example

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

3.5.3 A MedDRA combination term is available

If two conditions are reported in combination, and a single MedDRA combination term is available to represent them, select that term.

Example

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

3.5.4 When to "split" into more than one MedDRA term

If "splitting" the reported ARs/AEs provides more clinical information, select more than one MedDRA term.

Example

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

Exercise medical judgment so that information is not lost when "splitting" a reported term. Always check the MedDRA hierarchy above the selected term to be sure it is appropriate for the reported information.

Example

Reported	LLT Selected	Comment
Haematoma due to an animal bite	Animal bite Traumatic haematoma	LLT *Traumatic haematoma* is more appropriate than LLT *Haematoma* (LLT *Traumatic haematoma* links to HLT *Non-site specific injuries NEC* and HLT *Haemorrhages NEC* while LLT Ha*ematoma* links only to HLT *Haemorrhages NEC*)

3.5.5 Event reported with pre-existing condition

If an event is reported along with a pre-existing condition **that has not changed**, and if there is not an appropriate combination term in MedDRA, select a term for the event only. (See Section 3.9 for pre-existing conditions that have changed).

Example

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 condition that has not changed

3.6 – Age vs. Event Specificity

3.6.1 MedDRA term includes age and event information

Example

Reported	LLT Selected
Jaundice in a newborn	Jaundice of newborn
Developed psychosis at age 6 years	Childhood psychosis

3.6.2 No available MedDRA term includes both age and event information

The **preferred option** is to select a term for the **event** and record the age in the appropriate demographic field.

Alternatively, select terms (more than one) that together reflect both the age of the patient and the event.

Example

Reported	LLT Selected	Preferred Option
Pancreatitis in a newborn	Pancreatitis	✔
	Pancreatitis Neonatal disorder	

3.7 – Body Site vs. Event Specificity

3.7.1 MedDRA term includes body site and event information

Example

Reported	LLT Selected
Skin rash on face	Rash on face

3.7.2 No available MedDRA term includes both body site and event information

Select a term for the **event**, rather than a term that reflects a non-specific condition at the body site; in other words, the **event** information generally has priority.

Example

Reported	LLT Selected	Comment
Skin rash on chest	Skin rash	In this instance, there is no available term for a skin rash on the chest

However, medical judgment is required, and sometimes, the body site information should have priority as in the example below.

Example

Reported	LLT Selected	Comment
Cyanosis at injection site	Injection site reaction	Cyanosis implies a generalised disorder. In this example, selecting LLT *Cyanosis* would result in loss of important medical information and miscommunication

3.7.3 Event occurring at multiple body sites

If an event is reported to occur at more than one body site, and if all of those LLTs link to the same PT, then select a single LLT that most accurately reflects the event; in other words, the **event** information has priority.

Example

Reported	LLT Selected	Comment
Skin rash on face and neck	Skin rash	LLT *Rash on face,* LLT *Neck rash,* and LLT *Skin rash* all link to PT *Rash*
Oedema of hands and feet	Oedema of extremities	LLT *Oedema hands* and LLT *Oedematous feet* both link to PT *Oedema peripheral*. However, LLT *Oedema of extremities* most accurately reflects the event in a single term

3.8 – Location-Specific vs. Microorganism-Specific Infection

3.8.1 MedDRA term includes microorganism and anatomic location

Example

Reported	LLT Selected	Comment
Pneumococcal pneumonia	Pneumococcal pneumonia	In this example, the implied anatomic location is the lung

3.8.2 No available MedDRA term includes both microorganism and anatomic location

The **preferred** option is to select terms for both the microorganism-specific infection **and** the anatomic location.

Alternatively, select a term that reflects the anatomic location **or** select a term that reflects the microorganism-specific infection. Medical judgment should be used in deciding whether anatomic location or the microorganism-specific infection should take priority.

Example

Reported	LLT Selected	Preferred Option	Comment
Respiratory chlamydial infection	Chlamydial infection Respiratory infection	✔	Represents both microorganism-specific infection **and** anatomic location
	Respiratory infection		Represents location-specific infection
	Chlamydial infection		Represents microorganism-specific infection

3.9 – Modification of Pre-existing Conditions

Pre-existing conditions that have changed may be considered ARs/AEs, especially if the condition has worsened or progressed. (See Section 3.5.5 for pre-existing conditions that have not changed, and Section 3.22 for an unexpected improvement of a pre-existing condition).

Ways That Pre-existing Conditions May Be Modified
Aggravated, exacerbated, worsened Recurrent Progressive

Select a term that most accurately reflects the modified condition (if such term exists).

Example

Reported	LLT Selected
Exacerbation of myasthenia gravis	Myasthenia gravis aggravated

If no such term exists, consider these approaches:

- ➢ Example 1: Select a term for the pre-existing condition and record the modification in a consistent, documented way in appropriate data fields
- ➢ Example 2: Select a term for the pre-existing condition **and** a second term for the modification of the condition (e.g., LLT *Condition aggravated*, LLT *Disease progression*). Record the modification in a consistent, documented way in appropriate data fields.

Example

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.

3.10 – Exposures during Pregnancy and Breast Feeding

To select the most appropriate term (or terms), first determine if the subject/patient who experienced the event is the mother or the child/foetus.

3.10.1 Events in the mother

- ➢ Patient became pregnant while receiving product

Pregnancy is not normally considered an adverse event, but organisations may wish to record this information in their databases.

Example

Reported	LLT Selected	Comment
Pregnancy (no adverse effect)	Pregnancy No adverse effect	Select LLT *No adverse effect* (in addition to LLT *Pregnancy*) if no adverse event has occurred. (See Section 3.21)
Pregnancy (outcome unknown)	Pregnancy	Select LLT *Pregnancy* **only** if neither outcome nor occurrence of AE is known

> ➢ Pregnant patient receiving medication experienced adverse event

Example

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

3.10.2 Events in the child or foetus

Select terms for both the type of exposure and any adverse event(s).

Example

Setting/Patient	Reported	LLT Selected
Foetus with AE; exposed *in utero*; **mother** took product	Pregnant woman taking drug X; foetal tachycardia noted on routine examination	Drug exposure in utero Foetal tachycardia
Baby with AE; exposed *in utero*; **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

3.11 – Congenital Terms

"Congenital" = any condition present at birth, whether genetically inherited or occurring *in utero*. (See the MedDRA Introductory Guide).

3.11.1 Condition described as congenital

Select terms from SOC *Congenital, familial and genetic disorders* when the reporter describes the condition as congenital or when medical judgment establishes that the condition was present at the time of birth.

Example

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

3.11.2 Condition not congenital/not present at birth

If the condition is not described as congenital or present at birth, select the non-qualified term for the condition; if a non-qualified term is not available, select the "acquired" term for the condition.

Example

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

3.12 – Neoplasms

Due to the large number of neoplasm types, specific guidance cannot be provided for all situations. The MedDRA Introductory Guide describes the use and placement of neoplasm terms and related terms in MedDRA.

Keep in mind the following points:

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 not neoplasia

If the type of neoplasia is not clear, seek clarification from the reporter. Consult medical experts when selecting terms for difficult or unusual neoplasms.

3.12.1 Do not infer malignancy

Select a malignancy term only if malignancy is stated by the reporter. Reports of "tumo(u)r" events should not be assigned a "cancer", "carcinoma" or another malignant term unless it is clear that malignancy is present.

Example

Reported	LLT Selected
Tumour growing on skin	Skin tumour
Cancer growing on tongue	Malignant tongue cancer

3.13 – Medical and Surgical Procedures

Terms in SOC *Surgical and medical procedures* are generally not appropriate for ARs/AEs. Terms in this SOC are not multiaxial. Be aware of the impact of these terms on data retrieval, analysis, and reporting.

Keep in mind the following points:

3.13.1 Only the procedure is reported

If only a procedure is reported, select a term for the procedure.

Example

Reported	LLT Selected
Patient had transfusion of platelets	Platelet transfusion
Patient had tonsillectomy in childhood	Tonsillectomy

3.13.2 Procedure and diagnosis are reported

If a procedure is reported with a diagnosis, the **preferred option** is to select terms for both the procedure and diagnosis. Alternatively, select a term only for the diagnosis.

Example

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

3.14 – Investigations

SOC *Investigations* includes test names with qualifiers (e.g., increased, decreased, abnormal, normal) and without qualifiers. Corresponding medical conditions (such as "hyper-" and "hypo-" terms) are in other "disorder" SOCs (e.g., SOC *Metabolism and nutrition disorders*).

SOC *Investigations* is not multiaxial; always consider the terms in this SOC for data retrieval.

3.14.1 Results of investigations as ARs/AEs

Keep in mind the following points when selecting terms for results of investigations:

➤ Selecting terms for a medical condition vs. an investigation result

Example

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*

➤ Unambiguous investigation result

Example

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

➤ Ambiguous investigation result

Example

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

3.14.2 Investigation results consistent with diagnosis

When investigation results are reported with a diagnosis, select only a term for the diagnosis **if investigation results are consistent with the diagnosis**.

Example

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

3.14.3 Investigation results <u>not</u> consistent with diagnosis

When investigation results are reported with a diagnosis, select a term for the diagnosis **and also** select terms for any investigation results that are **not** consistent with the diagnosis.

Example

Reported	LLT Selected	Comment
Alopecia, rash, and elevated potassium 7.0 mmol/L	Alopecia Rash Potassium increased	Elevated potassium is not consistent with the diagnoses of alopecia and rash. Terms for all concepts should be selected

3.14.4 Grouped investigation result terms

Select a term for each investigation result as reported; do not "lump" together separate investigation results under an inclusive term **unless reported as such**.

Example

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 *Liver function tests abnormal* should **not** be selected

3.14.5 Investigation terms without qualifiers

Terms in SOC *Investigations* **without qualifiers** may be used to record test names when entering diagnostic test data in the ICH E2B electronic transmission standard.

Example

Information/Reported (Verbatim)	LLT Selected for Test Name	Comment
Cardiac output measured	Cardiac output	
Haemoglobin 7.5 g/dL	Haemoglobin	LLT *Haemoglobin decreased* should **not** be selected as it is both a test name and a result*

* MedDRA is used only for test names, not test results, in the E2B data elements for Results of Tests and Procedures

3.15 – Medication/Administration Errors, Accidental Exposures and Occupational Exposures

3.15.1 Medication/administration errors

Medication errors are defined as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient or consumer.

Appendix B of the MedDRA Introductory Guide contains descriptions of the interpretation and use of certain medication error terms (e.g., "Dispensing error").

Reports of medication errors may or may not include information about clinical consequences.

3.15.1.1 Medication errors reported with clinical consequences

If a medication error is reported with clinical consequences, select terms for both the medication error and the clinical consequences.

Example

Reported	LLT Selected
Patient was administered wrong drug and experienced hypotension	Wrong drug administered Hypotension
Because of similar sounding drug names, the patient took the wrong drug and experienced a rash	Drug name confusion Wrong drug administered Rash

3.15.1.2 Medication errors and potential medication errors reported <u>without</u> clinical consequences

Medication errors without clinical consequences are not ARs/AEs. However, it is important to record the occurrence or **potential** occurrence of a medication error. Select a term that is closest to the description of medication error reported.

Also, if specifically reported that no adverse effect has occurred, it is acceptable to select LLT *No adverse effect*.

In instances where the medication did not reach the patient, it is acceptable to select LLT *Drug not taken in context of intercepted medication error*.

Example

Reported	LLT Selected	Comment
Medication was given intravenously instead of intramuscularly	Intramuscular formulation administered by other route	
Medication was given intravenously instead of intramuscularly **without sequelae**	Intramuscular formulation administered by other route No adverse effect	See Section 3.21
Patient was dispensed the wrong drug. The error was detected prior to patient administration	Intercepted drug dispensing error	
Pharmacist notices that the names of two drugs are similar and is concerned that this may result in a medication error	Circumstance or information capable of leading to medication error	LLT *Drug name confusion* could be an optional additional term to select (for tracking purposes). Note: this example is a potential medication error
Drug inadvertently administered. The error was noticed soon afterwards.	Drug administration error	

3.15.1.3 Medication errors in the context of labelled interactions

If the label describes **known effects** when the product is co-administered with specific drugs, with specific foods, or to patients with specific disease states, then select a medication error term for the type of interaction, such as those listed below:

Medication Error Terms – Labeled Interactions
Labelled drug-drug interaction medication error
Labelled drug-food interaction medication error
Labelled drug-disease interaction medication error
Documented hypersensitivity to administered drug

Example

Reported	LLT Selected	Comment
Patient became pregnant whilst taking an antifungal drug and an oral contraceptive	Labelled drug-drug interaction medication error Pregnancy on oral contraceptive	Interaction must be stated in product data sheet (See also Section 3.20)
Patient drank grapefruit juice whilst taking a calcium channel blocker	Labelled drug-food interaction medication error	Product is labelled for grapefruit juice interaction
Patient with renal failure is prescribed a drug that is contraindicated in renal failure	Labelled drug-disease interaction medication error	
Patient is administered a sulfonamide-based drug	Documented hypersensitivity to administered drug	Medical file clearly indicates patient has a sulfa allergy

3.15.1.4 Do not infer a medication error

Do not infer that a medication error has occurred unless specific information is provided. This includes inferring that extra dosing, overdose, or underdose has occurred. (See Section 3.18)

Example

Reported	LLT Selected	Comment
Antibiotic was prescribed for a week, and the patient stopped treatment after 2 days because of bitter taste	Prescribed dosing duration not completed Taste bitter	LLT *Taste bitter* represents a sensory perception issue. LLT *Medication after taste* refers to a product quality issue
Incorrect dosing by patient	Incorrect dose administered	Do not select *Extra dose administered* or *Overdose* based on this information alone
Patient took only half the prescribed dose	Underdose	

3.15.2 Accidental exposures and occupational exposures

3.15.2.1 Accidental exposures

The principles for Section 3.15.1 (Medication/administration errors) also apply to accidental exposures.

Example

Reported	LLT Selected	Comment
Child accidentally took grandmother's pills and experienced projectile vomiting	Accidental drug intake by child Vomiting projectile	
Father applying topical steroid to his arms accidentally exposed his child to the drug by carrying her	Accidental exposure to product by child Exposure via skin contact	The "exposure to" term captures the agent of exposure, i.e., a product, and the "exposure via" term captures the route/vehicle of exposure, i.e., skin contact

3.15.2.2 Occupational exposures

For the purposes of term selection and analysis of MedDRA-coded data, occupational exposure encompasses the "chronic" exposure to an agent (including therapeutic products) during the normal course of one's occupation, and could include additional scenarios in specific regulatory regions. For example, occupational exposure may additionally relate to a more acute, accidental form of exposure that occurs in the context of one's occupation. In

these regions, occupational exposure for healthcare workers could be of particular interest.

Example

Reported	LLT Selected	Comment
Physical therapist developed a photosensitivity rash on hands after exposure to an NSAID-containing pain relief cream that she applied to a patient	Occupational exposure to drug Exposure via skin contact Photosensitive rash	
Pathologist chronically exposed to formaldehyde developed nasopharyngeal carcinoma	Occupational exposure to toxic agent Nasopharyngeal carcinoma	Exposure to formaldehyde is a known risk factor for this type of malignancy
Nurse splashed injectable drug in her own eye resulting in excessive tearing	Inadvertent exposure to drug Excess tears	An additional term for occupational exposure – e.g., LLT *Occupational exposure to drug* – could also be selected, if applicable to regional requirements

3.16 – Misuse, Abuse and Addiction

The concepts of misuse, abuse and addiction are closely related and can pose challenges for term selection since the terms may overlap to some extent; the specific circumstances of each case/reported event may help in consideration for term selection of these concepts. Medical judgment and regional regulatory considerations need to be applied.

It may also be useful to consider these concepts as shown in the table below.

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

3.16.1 Misuse

For the purposes of term selection and analysis of MedDRA-coded data, **misuse** is the intentional and inappropriate use of a product – over-the-counter or prescription – other than as prescribed or not in accordance with the authorised product information.

Example

Reported	LLT Selected
Patient deliberately ingested the topical medication	Intentional use by incorrect route
Patient deliberately took the medication for two days longer than instructed on the product label	Intentional use beyond labelled duration

3.16.2 Abuse

For the purposes of term selection and analysis of MedDRA-coded data, **abuse** is the intentional, non-therapeutic use of a product – over-the counter or prescription – for a perceived reward or desired non-therapeutic effect including, but not limited to, "getting high"(euphoria). Abuse may occur with a single use, sporadic use or persistent use of the product.

Example

Reported	LLT Selected
Athlete used anabolic steroid preparation to enhance performance	Steroid abuse
Patient occasionally uses opioid product to get high	Opioid abuse, episodic use
Patient deliberately ingested the topical medication for its psychoactive effect	Drug abuse Intentional use by incorrect route

See Section 3.24.1 and 3.24.2 for additional references to "abuse" terms in MedDRA.

3.16.3 Addiction

For the purposes of term selection and analysis of MedDRA-coded data, **addiction** is an overwhelming desire to take a drug for non-therapeutic purposes together with inability to control or stop its use despite harmful consequences. Addiction can occur because drug induces physical dependence and consequently a withdrawal syndrome, but this is not an essential feature; and addiction can occur because of a desire to experience the drug's psychological, behavioral or physical effects.

Example

Reported	LLT Selected
Patient became dependent on crack cocaine	Dependence on cocaine
Patient became addicted to a deliberately ingested topical medication for its psychoactive effect	Drug addiction Intentional use by incorrect route

See Section 3.24.1 for additional references to "addict/addiction" terms in MedDRA.

3.16.4   Drug diversion

For the purposes of term selection and analysis of MedDRA-coded data, drug diversion means that a drug is diverted from legal and medically necessary uses toward uses that are illegal and typically not medically authorised or necessary.

Example

Reported	LLT Selected
Pharmacist stole medications from the pharmacy and sold them to others for recreational use	Drug diversion
A person put a sedative into the patient's drink	Drug diversion Accidental exposure to drug

3.17 – Transmission of Infectious Agent via Product

If a report of transmission of an infectious agent via a product is received, select a term for the transmission. If the infection is identified, select a second term for the specific infection; if appropriate, a product quality issue term can also be selected. (See Section 3.28).Example

Reported	LLT Selected
Patient received a nasal spray product and later developed a severe nasal infection with *Burkholderia cepacia.* Cultures of unopened containers of the nasal spray grew B. cepacia	Transmission of an infectious agent via product Product contamination bacterial Burkholderia cepacia infection
Patient received a blood transfusion and developed Hepatitis C	Transfusion-transmitted infectious disease Hepatitis C

Medical judgment should be used if the reporter does not explicitly state transmission of an infectious agent via a product but this could be implied by other data within the report. In this instance, select LLT *Suspected transmission of an infectious agent via product.*

3.18 – Overdose, Toxicity and Poisoning

Overdose terms are grouped under HLT *Overdoses*. Toxicity and poisoning terms are grouped under HLT *Poisoning and toxicity*. For more information, refer to the MedDRA Introductory Guide.

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

Example

Reported	LLT Selected	Comment
Overdose of pills	Overdose	
A child was accidentally poisoned when she ingested a chemical cleaning product	Accidental poisoning Chemical poisoning	
Patient intentionally took many more than the prescribed number of pills	Intentional overdose	
The dose of drug X taken was above the recommended maximum dose in the label	Drug overdose	
Nurse inadvertently administered an additional vaccine dose to an already vaccinated child	Inappropriate dose of vaccine administered	Please note that LLT *Inappropriate dose of vaccine administered* is a maladministration term, not specifically an overdose term

3.18.1 Overdose reported with clinical consequences

Select terms for overdose and for clinical consequences reported in association with an overdose.

Example

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

3.18.2 Overdose reported <u>without</u> clinical consequences

If an overdose report specifically states that there were no clinical consequences, the **preferred option** is to select only a term for the overdose. Alternatively, a term for the overdose and the additional LLT *No adverse effect* can be selected. (See Section 3.21).

Example

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

3.19 – Device-related Terms

3.19.1 Device-related event reported <u>with</u> clinical consequences

If available, select a term that reflects both the device-related event and the clinical consequence, if so reported.

Example

Reported	LLT Selected
Patient with a vascular implant developed an infection of the implant	Vascular implant infection
Patient noted the prosthesis caused pain	Medical device pain

If there is no single MedDRA term reflecting the device-related event and the clinical consequence, select separate terms for both.

Example

Reported	LLT Selected
Ventricular tachycardia due to malfunction of device	Device malfunction Ventricular tachycardia
Partial denture fractured leading to tooth pain	Dental prosthesis breakage Tooth pain

3.19.2 Device-related event reported <u>without</u> clinical consequences

If a device-related event is reported in the absence of clinical consequences, select the appropriate term.

Example

Reported	LLT Selected
Medical device breakage	Device breakage
My patch is leaking on my arm	Leaking patch
My patch is not sticking to my skin	Medicinal patch adhesion issue

3.20 – Drug Interactions
This term includes reactions between drugs and other drugs, food, devices and alcohol. In this document, "drug" includes biologic products.

Labelled drug interactions may be medication errors. (See Section 3.15.1.3).

3.20.1 Reporter specifically states an interaction

Select an interaction term and additional term(s) for any reported medical event.

Example

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

3.20.2 Reporter does not specifically state an interaction

Two products may be used together, but if the reporter does not specifically state that an interaction has occurred, select terms only for the medical events reported.

Example

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

3.21 – No Adverse Effect and "Normal" Terms

3.21.1 No adverse effect

LLT *No adverse effect* can be used when absence of an AR/AE is specifically reported, despite exposure to a product. (See Sections 3.15.1.2 and 3.18.2).

Some organisations may want to record LLT *No adverse effect* for administrative purposes (e.g., pregnancy registries, overdose and medication error reports).

3.21.2 Use of "normal" terms

Terms for normal states and outcomes can be used as needed.

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

3.22 – Unexpected Therapeutic Effect

Some organisations may want to record LLT *Unexpected therapeutic effect* for reports of a beneficial effect of a product apart from the reason it had been given. (Such effects are not usually considered ARs/AEs).
Example

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

3.23 – Modification of Effect

It is important to record modification of effect (e.g., increased, prolonged) although it is not always an AR/AE.

3.23.1 Lack of effect

The **preferred option** is to select only the "lack of effect" term even if consequences are also reported. However, terms may also be selected for events associated with the lack of effect.

Example

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	

3.23.2 Do not infer lack of effect

Example

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)

3.23.3 Increased, decreased and prolonged effect

Example

Reported	LLT Selected
Patient had increased effect from drug A	Increased drug effect
Patient had decreased effect from drug A	Drug effect decreased
Patient had prolonged effect from drug A	Drug effect prolonged

3.24 – Social Circumstances

3.24.1 Use of terms in this SOC

Terms in SOC *Social circumstances* represent social factors and may be suitable to record social and medical history data. Such terms are not generally suitable for recording ARs/AEs; however, in certain instances, terms in SOC *Social circumstances* are the only available terms for recording ARs/AEs or may add valuable clinical information.

Example

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

Terms in SOC *Social circumstances* are not multiaxial and, unlike terms in other "disorder" SOCs in MedDRA (e.g., SOC *Gastrointestinal disorders*), they generally refer to a **person**, not to a medical condition.

Be aware of the impact that terms in SOC *Social circumstances* may have on data retrieval, analysis and reporting as illustrated in the table below:

Term in SOC *Social circumstances* ("person")	Similar term in "Disorder" SOC ("condition")
Alcoholic	Alcoholism
Drug abuser	Drug abuse
Drug addict	Drug addiction
Glue sniffer	Glue sniffing
Smoker	Nicotine dependence

Note that "abuse" terms not associated with drugs/substances are in this SOC*, regardless of whether they refer to the person or to the condition, as illustrated in the table below:

LLT	PT
Child abuse	Child abuse
Child abuser	
Elder abuse	Elder abuse
Elder abuser	

(See Section 3.24.2 concerning illegal/criminal acts).

3.24.2 Illegal acts of crime or abuse

Terms for illegal acts of crime and abuse (excluding those related to drug/substance abuse) are in SOC *Social circumstances*, such as LLT *Physical assault*.

LLTs representing the **perpetrator** are linked to PTs describing the unlawful act committed. PTs representing the **victim** of unlawful acts generally begin with "*Victim of…*".

Example

Reported	LLT Selected	Comment
Patient's history indicates that patient is a known sexual offender	Sexual offender	**Perpetrator;** LLT *Sexual offender* links to PT *Sexual abuse* in SOC *Social circumstances*
Patient was a childhood sexual assault victim	Childhood sexual assault victim	**Victim;** LLT *Childhood sexual assault victim* links to PT *Victim of sexual abuse* in SOC *Social circumstances*

3.25 – Medical and Social History

Example

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

3.26 – Indication for Product Use

Indications can be reported as medical conditions, prophylaxis of conditions, replacement therapies, procedures (such as anesthesia induction) and verbatim terms such as "anti-hypertension". Terms from almost any MedDRA SOC – including SOC *Investigations* – may be selected to record indications.

Regulatory authorities may have specific requirements for certain aspects of term selection for indications (e.g., for indications within regulated product information). Please refer to the regulatory authority's specific guidance for such issues.

3.26.1 Medical conditions

Example

Reported	LLT Selected
Hypertension	Hypertension
Anti-hypertensive	
Chemotherapy for breast cancer	Breast cancer
I took it for my cold symptoms	Cold symptoms

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

Example

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

It may not be clear if the reported indication is a medical condition or a desired outcome of therapy. The term selected in either case may be the same.

Example

Reported	LLT Selected	Comment
Weight loss	Weight loss	Unclear if the purpose is to induce weight loss or to treat an underweight patient
Immunosuppression	Immunosuppression	Unclear if the purpose is to induce or to treat immunosuppression

3.26.2 Complex indications

Term selection for some indications (e.g., in regulated product information) may be complex and require selection of more than one LLT to represent the information completely, depending on the circumstances.

Example

Reported	LLT Selected	Comment
Treatment of aggression in autism	Aggression	The products do not treat the underlying autism, thalassaemia, or myocardial infarction, but they *do* address the associated signs/symptoms (aggression, chronic iron overload, atherothrombosis). It may be necessary to select LLT *Autism,* LLT *Thalassaemia major*, or LLT *Myocardial infarction* based on regional regulatory requirements.
Treatment of chronic iron overload in thalassaemia major	Chronic iron overload	
Prevention of atherothrombotic events in patients with myocardial infarction	Atherothrombosis prophylaxis	

3.26.3 Indications with genetic markers or abnormalities

For indications that describe a genetic marker or abnormality associated with a medical condition, select a term for both the medical condition and the genetic marker or abnormality.

Example

Reported	LLT Selected
Non small cell lung cancer with K-ras mutation	Non-small cell lung cancer K-ras gene mutation

3.26.4 Prevention and prophylaxis

When an indication for prevention or prophylaxis is reported, select the specific MedDRA term, if it exists. (Note: the words "prevention" and "prophylaxis" are synonymous in the context of MedDRA).

Example

Reported	LLT Selected
Prophylaxis of arrhythmia	Arrhythmia prophylaxis
Prevention of migraine	Migraine prophylaxis

If there is no MedDRA term containing "prevention" or "prophylaxis", choose one of the following options (Note: the **preferred option** is to select a general prevention/ prophylaxis term **and** a term for the condition):

Example

Reported	LLT Selected	Preferred Option	Comment
Prevention of hepatotoxicity	Prevention Hepatotoxicity	✔	Select the closest term for both concepts
	Hepatotoxicity		Select a term for the condition
	Prevention		Select the closest prevention/prophylaxis term

3.26.5 Procedures and diagnostic tests as indications

Select the appropriate term if the product is indicated for performing a procedure or a diagnostic test.

Example

Reported	LLT Selected
Induction of anaesthesia	Induction of anaesthesia
Contrast agent for angiogram	Angiogram
Contrast agent for coronary angiogram	Coronary angiogram

3.26.6 Supplementation and replacement therapies

Terms for supplemental and replacement therapies are in SOC *Surgical and medical procedures*. (See Section 3.13). If the product indication is for supplementation or replacement therapy, select the closest term.

Example

Reported	LLT Selected
Testosterone replacement therapy	Androgen replacement therapy
Prenatal vitamin	Vitamin supplementation

3.26.7 Indication not reported

If clarification cannot be obtained, select LLT *Drug use for unknown indication.*

Example

Reported	LLT Selected
Aspirin was taken for an unknown indication	Drug use for unknown indication

3.27 – Off Label Use

The concept of "off label use" relates to situations where the product is intentionally used for a medical purpose not in accordance with the authorised product information.

3.27.1 Off label use when reported as an indication
If a medical condition is reported as an indication **along with "off label use"**, the **preferred option** is to select terms for the medical condition and LLT *Off label* use or other appropriate LLTs linked to PT *Off label use*. Alternatively, select a term for the medical condition/indication alone*.* Select LLT *Off label use* alone **only** if it is the only information available.

Example

Reported	LLT Selected	Preferred Option
Hypertension; this is off label use	Off label use Hypertension	✔
	Hypertension	

Example

Reported	LLT Selected	Comment
Used off label	Off label use	
Off label use in paediatric patients	Drug use in unapproved population	Refers to a population of patients
Drug X given to a 10 year old boy; the drug is not indicated for use below 18 years	Adult product administered to child	LLT *Adult product administered to child* is linked to PT *Off label use*

3.27.2 Off label use when reported with an AR/AE

If an AR/AE occurs as a result of off label use, the **preferred option** is to select LLT *Off label use*, or other appropriate LLTs linked to PT *Off label use,* and a term for the medical condition in addition to a term for the AR/AE. Alternatively, select a term for the medical condition and a term for the AR/AE.

Example

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

3.28 – Product Quality Issues

It is important to recognise product quality issues as they may have implications for patient safety. They may be reported in the context of adverse events or as part of a product quality monitoring system.

Product quality issues are defined as abnormalities that may be introduced during the manufacturing/labeling, packaging, shipping, handling or storage of the products. They may occur with or without clinical consequences. Such concepts may pose a challenge for term selection.

Familiarity with HLGT *Product quality issues* (in SOC *General disorders and administration site conditions*) is essential for term selection. Under this HLGT are categories of specific product quality issues such as HLT *Product packaging*

issues, *Product physical issues*, etc. Navigating down to the appropriate LLTs from the MedDRA hierarchy is the optimal approach for term selection.

Explanations of the interpretations and uses of certain product quality issue terms (e.g., "Product coating incomplete") are found in the MedDRA Introductory Guide (Appendix B, MedDRA Concept Descriptions).

3.28.1 Product quality issue reported <u>with</u> clinical consequences

If a product quality issue results in clinical consequences, term(s) for the product quality issue and the clinical consequences should be selected.

Example

Reported	LLT Selected
New bottle of drug tablets have unusual chemical smell that made me nauseous	Product odour 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

3.28.2 Product quality issue reported <u>without</u> clinical consequences

It is important to capture the occurrence of product quality issues even in the absence of clinical consequences.

Example

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

3.28.3 Product quality issue vs. medication error

It is important to distinguish between a product quality issue and a medication error.

Product quality issues are defined as abnormalities that may be introduced during the manufacturing/labeling, packaging, shipping, handling or storage of the products. They may occur with or without clinical consequences.

Medication errors are defined as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient or consumer.

Explanations of the interpretations of product quality issue terms are found in the MedDRA Introductory Guide (Appendix B, MedDRA Concept Descriptions).

Example

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 insufficient amount of prescribed antibiotic because the lines on the dropper were hard to read	Product dropper calibration unreadable Insufficient dosage	Product quality issue and medication error

Section 4 – APPENDIX

4.1 – Versioning

4.1.1 Versioning methodologies

Each organisation should have a versioning strategy that should be documented. The versioning strategy may differ between safety databases and clinical trial databases. For example, there may be no need to update clinical trial data from older trials if the data are not presently used or will not be used in the future. On the other hand, postmarketing safety data may be required to be reported in the current (or near-current) version of MedDRA, and version update recommendations then apply.

Users should choose the most optimal approach based on their organisation's characteristics.The optional methods described below can be used to document the extent to which an organisation has applied a new version of MedDRA. These methods should not be interpreted as regulatory requirements but may be used to communicate effectively between and within organisations.

The table below summarises the types of versioning methods.

Method	Description	Resource Intensity	Data Accuracy
1	Begin to use new version for coding new data; no recoding of existing data	Least	Least
2	Identify verbatim terms linked to non-current LLTs and recode existing data		
3	Identify verbatim terms linked to non-current LLTs and recode existing data and Recode verbatim terms to new LLTs that are direct or lexical matches	↓	↓
4	Identify verbatim terms linked to non-current LLTs and recode existing data and Recode verbatim terms to new LLTs that are direct or lexical matches and Recode verbatim terms to new LLTs that are more accurate concepts	Most	Most

This list may not be inclusive; other versioning methods may be used. Depending on how MedDRA data are stored in the database, additional steps may be needed to ensure consistency in data retrieval and reporting, including medical review of the data after the version method has been applied.

Note that Method 4 is the most resource intense and Method 1 is the least. There are additional points to consider: recoding to LLTs that are new direct matches or more accurate concepts (Method 4) provides the most accurate data compared to the other methods.

The MSSO and JMO provide tools to assist the user in comparing the changes between MedDRA versions. The Version Report (provided by the MSSO and JMO) is a spreadsheet listing all changes between the current version of MedDRA and the one previous to it; this spreadsheet is provided with each new release of MedDRA. The MSSO also provides the MedDRA Version Analysis Tool (MVAT) that facilitates identification and understanding of the impact of changes between any two MedDRA versions, including non-consecutive ones. (See Appendix, Section 4.2).

4.1.2 Timing of version implementation

For single case reporting, the sender and receiver of the data need to be in synchrony regarding MedDRA versions. There are MSSO recommendations for the timing of the implementation of a new MedDRA release for both individual case safety reporting and clinical trial data. Specific transition dates for single

case reporting for the next MedDRA versions are provided. (See Appendix, Section 4.2).

Date of New Reporting Version for Individual Case Safety Reporting
A new release version of MedDRA should become the reporting version on the first Monday of the second month after it is released. To synchronise this event over the three ICH regions, the MSSO recommends midnight GMT, Sunday to Monday, for the switchover. For example : • 1 March – MedDRA X.0 released • First Monday of May – MedDRA X.0 becomes the reporting version • 1 September – MedDRA X.1 released • First Monday of November – MedDRA X.1 becomes the reporting version

4.2 – Links and References

The following documents and tools can be found on the MedDRA website: (www.meddra.org):

- MedDRA Introductory Guide
- MedDRA Change Request Information document
- MedDRA Web-based Browser
- MedDRA Desktop Browser
- MedDRA Version Report (lists all changes in new version) *
- MedDRA Version Analysis Tool (compares any two versions) *
- MSSO's Recommendations for Single Case Reporting
- MSSO's Recommendations for Clinical Trial Versioning
- Transition Date for the Next MedDRA Version

*   Requires user ID and password to access

4.3 – Membership of the ICH Points to Consider Working Group

4.3.1 Current members of the ICH Points to Consider Working Group

Affiliation	Member
Commission of the European Communities	Sarah Vaughan
	Maria Luisa Casini
European Federation of Pharmaceutical Industries and Associations	Hilary Vass*
	Christina Winter†
Health Canada	Lynn Macdonald
Japanese Maintenance Organization	Yutaka Nagao
	Kazuyuki Sekiguchi
	Reiji Tezuka
Japan Pharmaceutical Manufacturers Association	Yo Tanaka
MedDRA MSSO	Judy Harrison
Ministry of Health, Labour and Welfare/Pharmaceuticals and Medical Devices Agency	Sonoko Ishihara
	Makiko Isozaki
	Yuuhei Fukuta
Pharmaceutical Research and Manufacturers of America	Anna-Lisa Kleckner
	JoAnn Medbery
US Food and Drug Administration	Sonja Brajovic#
	Christopher Breder

*   Current Rapporteur
#   Regulatory Chair
†   Former Rapporteur

4.3.2 Former members of the ICH Points to Consider Working Group

Affiliation	Member
Commission of the European Communities	Dolores Montero
	Carmen Kreft-Jais
	Morell David
European Federation of Pharmaceutical Industries and Associations	Barry Hammond[†]; Reinhard Fescharek[†]
Health Canada	Alison Bennett, Heather Morrison; Michelle Séguin; Heather Sutcliffe; Bill Wilson
Japanese Maintenance Organization	Osamu Handa; Akemi Ishikawa; Yasuo Sakurai; Yuki Tada
Japan Pharmaceutical Manufacturers Association	Takayoshi Ichikawa; Akemi Ishikawa; Satoru Mori; Yasuo Sakurai; Kunikazu Yokoi
MedDRA MSSO	JoAnn Medbery; Patricia Mozzicato
Ministry of Health, Labour and Welfare/Pharmaceuticals and Medical Devices Agency	Tamaki Fushimi; Wakako Horiki; Kazuhiro Kemmotsu; Tatsuo Kishi; Chie Kojima; Emiko Kondo; Hideyuki Kondou; Kemji Kuramochi; Tetsuya Kusakabe; Kaori Nomura; Izumi Oba; Shinichi Okamura; Yoshihiko Sano; Nogusa Takahara; Kenichi Tamiya; Daisuke Tanaka; Shinichi Watanabe; Takashi Yasukawa; Go Yamamoto; Manabu Yamamoto; Nobuhiro Yamamoto
Pharmaceutical Research and Manufacturers of America	David Goldsmith; Sidney Kahn; Susan M. Lorenski; Margaret M. Westland[†]
US Food and Drug Administration	Miles Braun; Andrea Feight; John (Jake) Kelsey[†]; Brad Leissa; Toni Piazza-Hepp

[†] Former Rapporteur