# MedDRA® TERM SELECTION: POINTS TO CONSIDER

## ICH-Endorsed Guide for MedDRA Users

***Release 4.10***

***Based on MedDRA Version 18.1***

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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 and Korean regulatory authorities, 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 considerations 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.** Users should always first consider regional regulatory requirements. An organisation should be consistent in the option that they choose to use and document that option in internal coding guidelines.

### 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 *Noninfective gingivitis*) |

- *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:<br>1. Select LLT *Gingival cancer* OR LLT *Metastatic carcinoma*<br>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.

<table>
<tr><th colspan="2">SUMMARY OF PREFERRED AND ALTERNATE OPTIONS</th></tr>
<tr><th colspan="2">SINGLE DIAGNOSIS</th></tr>
<tr><th>DEFINITIVE DIAGNOSIS</th><th>PROVISIONAL DIAGNOSIS</th></tr>
<tr><td>Single definitive diagnosis without signs/symptoms<ul><li>Diagnosis (only possible option)</li></ul></td><td>Single provisional diagnosis without signs/symptoms<ul><li>Provisional diagnosis (only possible option)</li></ul></td></tr>
<tr><td>Single definitive diagnosis with signs/symptoms<ul><li>Preferred: Diagnosis only</li><li>Alternate: Diagnosis and signs/symptoms</li></ul>Note: Always include signs/symptoms not associated with diagnosis<br>SEE EXAMPLE 1</td><td>Single provisional diagnosis with signs/symptoms<ul><li>Preferred: Provisional diagnosis and signs/symptoms</li><li>Alternate: Signs/symptoms only</li></ul>Note: Always include signs/symptoms not associated with diagnosis<br>SEE EXAMPLE 2</td></tr>
<tr><th colspan="2">MULTIPLE DIAGNOSES</th></tr>
<tr><th>DEFINITIVE DIAGNOSES</th><th>PROVISIONAL DIAGNOSES</th></tr>
<tr><td>Multiple definitive diagnoses without signs/symptoms<ul><li>Multiple diagnoses (only possible option)</li></ul></td><td>Multiple provisional diagnoses without signs/symptoms<ul><li>Multiple provisional diagnoses (only possible option)</li></ul></td></tr>
<tr><td>Multiple definitive diagnoses with signs/symptoms<ul><li>Preferred: Multiple diagnoses only</li><li>Alternate: Diagnoses and signs/symptoms</li></ul>Note: Always include signs/symptoms not associated with diagnosis<br>SEE EXAMPLE 3</td><td>Multiple provisional diagnoses with signs/symptoms<ul><li>Preferred: Multiple provisional diagnoses and signs/symptoms</li><li>Alternate: Signs/symptoms only</li></ul>Note: Always include signs/symptoms not associated with diagnosis<br>SEE EXAMPLE 4</td></tr>
</table>

| EXAMPLES | | | |
|---|---|---|---|
| **Example** | **Reported** | **LLT Selected** | **Preferred Option** |
| 1 | Anaphylactic reaction, rash dyspnoea, hypotension, and laryngospasm | Anaphylactic reaction | ✓ |
| | | Anaphylactic reaction<br>Rash<br>Dyspnoea<br>Hypotension<br>Laryngospasm | |
| 2 | Possible myocardial infarction with chest pain, dyspnoea, diaphoresis | Myocardial infarction<br>Chest pain<br>Dyspnoea<br>Diaphoresis | ✓ |
| | | Chest pain<br>Dyspnoea<br>Diaphoresis | |
| 3 | Pulmonary embolism, myocardial infarction, and congestive heart failure with chest pain, cyanosis, shortness of breath, and blood pressure decreased | Pulmonary embolism<br>Myocardial infarction<br>Congestive heart failure | ✓ |
| | | Pulmonary embolism<br>Myocardial infarction<br>Congestive heart failure<br>Chest pain<br>Cyanosis<br>Shortness of breath<br>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<br>Myocardial infarction<br>Congestive heart failure<br>Chest pain<br>Cyanosis<br>Shortness of breath<br>Blood pressure decreased | ✓ |
| | | Chest pain<br>Cyanosis<br>Shortness of breath<br>Blood pressure decreased | |
| **Always include signs/ symptoms not associated with diagnosis** | Myocardial infarction, chest pain, dyspnoea, diaphoresis, ECG changes and jaundice | Myocardial infarction<br>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 | Record death as an outcome |
| Constipation, ruptured bowel, peritonitis, sepsis; patient died | Constipation<br>Perforated bowel<br>Peritonitis<br>Sepsis | |

#### 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<br>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 | Self inflicted laceration<br>Suicide attempt | . |
| Took an overdose in an attempt to commit suicide | Intentional overdose<br>Suicide attempt | If overdose is reported in the context of suicide or a suicide attempt, the more specific LLT *Intentional overdose* can be selected (see also Section 3.18) |

#### 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*<br>PT *Hypertensive cardiomegaly*<br>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<br>(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<br>Vomiting |
| Wrist fracture due to fall | Wrist fracture<br>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<br>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 *Haematoma* 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<br>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<br>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<br>Recurrent<br>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<br><br>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 exposure 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

3.10.1.1 Pregnant patient exposed to medication with clinical consequences

If a pregnancy exposure is reported with clinical consequences, select terms for both the pregnancy exposure and the clinical consequences.

Example

| Reported | LLT Selected |
|---|---|
| Pregnant patient receiving drug X experienced a pruritic rash | Maternal exposure during pregnancy<br>Pruritic rash |

#### 3.10.1.2 Pregnant patient exposed to medication without clinical consequences

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

Example

| Reported | LLT Selected | Preferred Option |
|---|---|---|
| Patient received drug X while pregnant (no adverse effect) | Maternal exposure during pregnancy | ✓ |
| | Maternal exposure during pregnancy<br>No adverse effect | |

### 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<br>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<br>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<br>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 Congenital conditions

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 | Comment |
|---|---|---|
| Congenital heart disease | Heart disease congenital | |
| Child born with heart disease | | |
| Newborn with phimosis | Phimosis | A “congenital” term is not available but LLT/PT *Phimosis* links to primary SOC *Congenital, familial and genetic disorders* |

### 3.11.2 Acquired conditions (not present at birth)

If information is available indicating that the condition is not congenital or present at birth, i.e., it is acquired, select the non-qualified term for the condition, making sure that the non-qualified term does not link to SOC *Congenital, familial and genetic disorders.* If a non-qualified term is not available, select the “acquired” term for the condition.

Example

| Reported | LLT Selected | Comment |
|---|---|---|
| Developed night blindness in middle age | Night blindness | LLT/PT *Night blindness* links to primary SOC *Eye disorders*. Do not assume the condition is congenital (LLT/PT *Congenital night blindness*). |
| Developed phimosis at age 45 | Acquired phimosis | LLT/PT *Phimosis* should not be selected because it links to primary SOC *Congenital, familial and genetic disorders* |
| 34 year old patient with cholangiectasis | Cholangiectasis acquired | A non-qualified term “Cholangiectasis” is not available. It cannot be assumed that the condition was present at birth so it is appropriate to select the acquired term. |

### 3.11.3 Conditions not specified as either congenital or acquired

If a condition is reported without any information describing it as congenital or acquired, select the non-qualified term for the condition. For conditions or diseases existing in both congenital and acquired forms, the following convention is applied in MedDRA: the more common form of the condition/disease is represented at the PT level without adding a qualifier of either “congenital” or “acquired”.

Example

| Reported | LLT Selected | Comment |
|---|---|---|
| Pyloric stenosis | Pyloric stenosis | Pyloric stenosis is more commonly congenital than acquired; LLT/PT *Pyloric stenosis* links to primary SOC *Congenital, familial and genetic disorders* |
| Hypothyroidism | Hypothyroidism | Hypothyroidism is more commonly acquired than congenital; LLT/PT *Hypothyroidism* links to primary SOC *Endocrine disorders* |

## 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<br><br>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<br>Rash<br>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<br>SGPT increased<br>SGOT increased<br>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 Errors, Accidental Exposures and Occupational Exposures

### 3.15.1 Medication 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 | Comment |
|---|---|---|
| Patient was administered wrong drug and experienced hypotension | Wrong drug administered<br>Hypotension | |
| Because of similar sounding drug names, the wrong drug was dispensed; as a result, the patient took the wrong drug and experienced a rash | Drug name confusion<br>Wrong drug dispensed<br>Wrong drug administered<br>Rash | It is important to select terms for all medication error concepts, i.e., do not subtract information |
| Insulin was given using the wrong syringe resulting in the administration of an overdose. The patient developed hypoglycaemia. | Wrong device used<br>Accidental overdose<br>Hypoglycaemia | If an overdose is reported in the context of a medication error, the more specific term *LLT Accidental overdose* can be selected (see also Section 3.18) |

3.15.1.2 Medication errors and potential medication errors reported without 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.

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

Example

| Reported | LLT Selected | Preferred Option |
|---|---|---|
| Medication was given intravenously instead of intramuscularly but the patient did not experience any adverse effects | Intramuscular formulation administered by other route | ✓ |
| | Intramuscular formulation administered by other route<br>No adverse effect | |

Example

| 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 |
| Drug inadvertently administered. The error was noticed soon afterwards. | Drug administration error | |

#### 3.15.1.3 Medication monitoring errors

For the purposes of term selection and analysis of MedDRA-coded data, a medication monitoring error is an error that occurs in the process of monitoring the effect of the medication through clinical assessment and/or laboratory data. It can also refer to monitoring errors in following instructions or information pertinent to the safe use of the medication.

Example

| Reported | LLT Selected | Comment |
|---|---|---|
| The patient's liver enzymes were measured every six months instead of the recommended monthly schedule | Drug monitoring procedure incorrectly performed | The monthly monitoring schedule is in the label for this drug. This is an example of incorrect monitoring of laboratory tests recommended in the use of a drug. |
| Patient taking lithium-based drug did not have his lithium levels measured | Therapeutic drug monitoring analysis not performed | This is an example of not monitoring the therapeutic drug level to ensure that it is within the therapeutic range as recommended in the label for this drug. |

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, and if the report does not indicate that this is intentional misuse or intentional off label use, then select a medication error term for the type of interaction, such as those listed below:

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

Example

| Reported | LLT Selected | Comment |
|---|---|---|
| Patient became pregnant whilst taking an antifungal drug and an oral contraceptive | Labelled drug-drug interaction medication error<br>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 with known sulfa allergy is administered a sulfonamide-based drug and experienced wheezing | Documented hypersensitivity to administered drug<br>Wheezing | See Concept Description in Appendix B of the MedDRA Introductory Guide |

#### 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 |
|---|---|---|
| Patient took only half the prescribed dose | Underdose | Based on this report, it is not known whether the underdose is intentional or accidental. If information is available, select the more specific LLT *Accidental underdose* or LLT *Intentional underdose* as appropriate. |

### 3.15.2 Accidental exposures and occupational exposures

#### 3.15.2.1 Accidental exposures

The principles for Section 3.15.1 (Medication 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<br>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<br>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<br>Exposure via skin contact<br>Photosensitive rash | |
| Pathologist chronically exposed to formaldehyde developed nasopharyngeal carcinoma | Occupational exposure to toxic agent<br>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<br>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 |

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

Select the most specific term available and always check the MedDRA hierarchy above the selected term to be sure it is appropriate for the reported information. In some cases, it may be appropriate to select more than one MedDRA LLT to represent the reported information.

### 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 took the medication twice daily instead of once daily | Intentional misuse in dosing frequency |

### 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<br>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<br>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 illegal uses.

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<br>Inadvertent 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<br>Product contamination bacterial<br>Burkholderia cepacia infection |
| Patient received a blood transfusion and developed Hepatitis C | Transfusion-transmitted infectious disease<br>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

Accidental overdose terms are grouped under HLT *Maladministrations*; other overdose terms are grouped under HLT *Overdoses NEC*. Toxicity and poisoning terms are grouped under HLT *Poisoning and toxicity*. For more information, refer to the MedDRA Introductory Guide.

For the purposes of term selection and analysis of MedDRA-coded data, overdose is more than the maximum recommended dose (in quantity and/or concentration), i.e., an excessive dose (see Appendix B, MedDRA Introductory Guide.)

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

Example

| Reported | LLT Selected | Comment |
|---|---|---|
| Patient took an overdose | Overdose | Based on this report, it is not known whether the overdose is intentional or accidental. If information is available, select the more specific LLT *Accidental overdose* or LLT *Intentional overdose* as appropriate. |
| A child was accidentally poisoned when she ingested a chemical cleaning product | Accidental poisoning<br>Chemical poisoning | |
| Patient deliberately took an overdose of analgesic pills to treat his worsening arthritis | Intentional overdose | LLT *Arthritis aggravated* can be selected as the indication for treatment |
| The dose taken was above the recommended maximum dose in the label | Overdose | Based on this report, it is not known whether the overdose is intentional or accidental. If information is available, select the more specific LLT *Accidental overdose* or LLT *Intentional overdose* as appropriate. |
| 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 <u>with</u> 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<br>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<br>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<br>Ventricular tachycardia |
| Partial denture fractured leading to tooth pain | Dental prosthesis breakage<br>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 |

## 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<br>Torsade de pointes |
| Patient drank cranberry juice which interacted with anticoagulant drug causing an INR increase | Food interaction<br>INR increased |

### 3.20.2 Reporter does <u>not</u> 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<br>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<br>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<br>Hysterectomy |
| Patient is a cigarette smoker with coronary artery disease | Cigarette smoker<br>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<br>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. When recording off label use, consider that product information and/or regulations/requirements may differ between regulatory regions.

#### 3.27.1 Off label use when reported as an indication

If a medical condition/indication is reported **along with “off label use”**, the **preferred option** is to select terms for the medical condition/indication and 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<br>Hypertension | ✓ |
| | Hypertension | |

Example

| Reported | LLT Selected |
|---|---|
| Used off label | Off label use |

#### 3.27.2 Off label use when reported with an AR/AE

If an AR/AE occurs in the setting of off label use for a medical condition/indication, 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/indication in addition to a term for the AR/AE. Alternatively, select a term for the medical condition/indication 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<br>Pulmonary hypertension<br>Stroke | ✓ |
| | Pulmonary hypertension<br>Stroke | |

### 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/labelling, 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<br>Nauseous |
| I switched from one brand to another of my blood pressure medication, and I developed smelly breath | Product substitution issue brand to brand<br>Smelly breath |
| Consumer noted that the toothpaste they had purchased caused a stinging sensation in the mouth. Subsequent investigation of the product lot number revealed that the toothpaste was a counterfeit product. | Product counterfeit<br>Stinging mouth |

### 3.28.2 Product quality issue reported without 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<br>(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/labelling, 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 an underdose of antibiotic because the lines on the dropper were illegible | Product dropper calibration unreadable<br>Accidental underdose | Product quality issue and medication error. If underdose is reported in the context of a medication error, the more specific LLT *Accidental underdose* can be selected. |

## SECTION 4 – APPENDIX

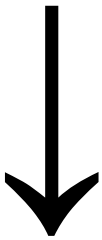
### 4.1 – Versioning

#### 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<br>and<br>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<br>and<br>Recode verbatim terms to new LLTs that are direct or lexical matches<br>and<br>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 :<br><br>• 1 March – MedDRA X.0 released<br>• First Monday of May – MedDRA X.0 becomes the reporting version<br><br>• 1 September – MedDRA X.1 released<br>• 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 using Semi-annual Version Control
- MSSO's Recommendations for MedDRA Implementation and Versioning for Clinical Trials
- 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 |
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| | Kavita Chadda |
| European Federation of Pharmaceutical Industries and Associations | Hilary Vass* |
| | Christina Winter† |
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| | Mitsuru Takano |
| Japan Pharmaceutical Manufacturers Association | Yo Tanaka |
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| Ministry of Health, Labour and Welfare/Pharmaceuticals and Medical Devices Agency | Daisuke Inoue |
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| Pharmaceutical Research and Manufacturers of America | Milbhor D'Silva |
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| Ministry of Food and Drug Safety, Korea | YuBin Lee |
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### 4.3.2 Former members of the ICH Points to Consider Working Group

| Affiliation | Member |
|---|---|
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| European Federation of Pharmaceutical Industries and Associations | Barry Hammond†; Reinhard Fescharek† |
| Health Canada | Alison Bennett; Heather Morrison; Polina Ostrovsky; Michelle Séguin; Heather Sutcliffe; Bill Wilson |
| Japanese Maintenance Organization | Osamu Handa; Akemi Ishikawa; Yasuo Sakurai; Yuki Tada; Reiji Tezuka |
| Japan Pharmaceutical Manufacturers Association | Takayoshi Ichikawa; Akemi Ishikawa; Satoru Mori; Yasuo Sakurai; Kunikazu Yokoi |
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| Pharmaceutical Research and Manufacturers of America | David Goldsmith; Sidney Kahn; Anna-Lisa Kleckner; Susan M. Lorenski; JoAnn Medbery; Margaret M. Westland† |
| US Food and Drug Administration | Miles Braun; Andrea Feight; John (Jake) Kelsey†; Brad Leissa; Toni Piazza-Hepp |

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