

MedDRA[®] TERM SELECTION: POINTS TO CONSIDER

*Release 3.12
Based on MedDRA Version 12.0*

ICH-Endorsed Guide for MedDRA Users

**Application to Adverse Drug Reactions /Adverse Events
&
Medical and Social History & Indications**

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1.0 INTRODUCTION

The Medical Dictionary for Regulatory Activities (MedDRA)¹ was designed for the specific use of sharing regulatory information for human medical products. However, unless users can achieve consistency in the way they assign particular terms to particular symptoms, signs, diseases, etc., use of MedDRA terminology will yield little improvement over the divergent practices of the past.

This *MedDRA Term Selection: Points to Consider* document is an ICH-endorsed guide for MedDRA users. It is designed to be updated based on MedDRA changes, and is a companion document to the MedDRA terminology. It was developed and is maintained by a working group charged by the ICH steering committee consisting of regulatory and industry representatives of the European Union, Japan and the United States, as well as representatives from Canada, the MedDRA Maintenance and Support Services Organization (MSSO), and Japanese Maintenance Organization (JMO). (See appendix for members).

Specific examples contained in this document are based on MedDRA Version 12.0.

1.1 Objective of this document

The objective of this ICH *Term Selection: Points to Consider* document is to promote accurate and consistent term selection. Organizations are encouraged to document their term selection strategies, methods, and quality assurance procedures in organization-specific coding guidelines, which should be consistent with the *Term Selection: Points to Consider* document.

Consistency in term selection will promote medical accuracy when using MedDRA to share data worldwide. This will in turn facilitate a common understanding of data shared among academic, commercial, and regulatory entities. The document could also be used by healthcare professionals, researchers, and other interested parties outside of the regulated pharmaceutical/biological industry.

At the request of users, in some cases where there is more than one option for selecting terms, a “preferred option” is identified. **The fact that a “preferred option” is identified does not limit MedDRA users to using that option.**

The document is intended to provide term selection advice either for a business purpose or regulatory requirement. There might be examples that do not reflect practices or requirements in all regions; this document does not intend to communicate specific regulatory reporting requirements or address database issues. In addition, it is expected that as experience with MedDRA increases, there will be changes to the document.

¹ MedDRA refers to all sequential and translated versions of the terminology, which are maintained by either the Maintenance and Support Services Organization (MSSO) or the Japanese Maintenance Organization (JMO).

1.2 Purposes of Using MedDRA

To aggregate reported terms in medically meaningful groupings for the purpose of reviewing and/or analyzing safety data

To facilitate identification of common data sets for evaluation of clinical and safety information

To facilitate consistent retrieval of specific cases or medical conditions from a database

To improve consistency in comparing and understanding “safety signals” and aggregated clinical data

To facilitate electronic data interchange of clinical safety information

To report adverse reaction/adverse event (ADR/AE)² terms via individual case safety reports

To include ADR/AEs in tables, analyses, and line listings for reports

To identify frequency of medically similar ADR/AEs

To capture and present product indications, investigations, medical history, and social history data

1.3 Background

This *Points to Consider* document has been prepared to help all MedDRA users to begin on common ground, as the terminology itself does not contain specific guidelines for its use; it provides a framework to foster consistent use of MedDRA for data input and retrieval. The end result allows for medically meaningful review and analysis of clinical data.

The working group recognizes that this document is not able to address every situation. Medical judgment and common sense should also be applied.

This document is not a substitute for MedDRA training. It is considered essential that users have knowledge of the MedDRA structure and content. For optimal MedDRA term selection, it is suggested that the reader also refer to the *MedDRA Introductory Guide*³, which is provided with each MedDRA subscription.

² For ADR/AE definitions, refer to ICH Guidelines and CIOMS publications.

³ The *MedDRA Introductory Guide* can be found at the following link (Note: MedDRA user ID and password are required): <http://www.meddramsso.com/translations/translationdownloads.htm> (JMO website reference in Japanese version).

1.4 Scope of the Points to Consider

The current document addresses term selection for data entry of ADR/AEs, medical history, social history, indications, and investigations.

2.0 GENERAL PRINCIPLES

2.1 Quality of source data

Good MedDRA term selection is best accomplished with clear initial data. Clarification of data that are ambiguous, confusing, or unintelligible should be obtained. If clarification cannot be obtained, refer to Section 3.4, *Conflicting/ambiguous/vague information*. The quality of the information originally reported directly impacts the quality of data output. Proper term selection allows for systematic and consistent recording, interpretation, and comparison of data. It also provides for easy storage, retrieval, and analysis of the clinical information.

Example: The presence or absence of a single letter in the reported verbatim text can make a difference in the final term selected. If “lip sore” is reported, select “Lip sore” (PT “Lip pain”). If “lip sores” are reported, select “Sores lip” (PT “Cheilitis”). Similarly, if “sore gums” are reported, select “Sore gums” (PT “Gingival pain”) and if “sores gum” is reported, select “Sores gum” (PT “Gingivitis”).

2.2 Level of term selection

Lowest level term(s) that most accurately reflects the reporter’s words should be selected.

MedDRA users should be aware of the degree of specificity that MedDRA terms may have and the challenges this specificity may pose for appropriate term selection.

Below are examples that illustrate the specificity of MedDRA:

- Gender terms

MedDRA generally excludes demographic descriptors, such as gender and age, but some terms with gender qualifiers are included when the gender renders the concept unique.

Example: There are terms “Infertility”, “Infertility female” and “Infertility male” in MedDRA.

It is recommended that organization-specific coding guidelines address instances in which it is important to capture gender-specific concepts. MedDRA users should also consider the impact of gender-specific terms when comparing MedDRA coded data to data coded with older terminologies which may not have had corresponding gender-specific terms. For example, if the organization’s prior terminology had only a single term for “breast cancer”, consider the impact of selecting gender-specific terms for breast cancer for current data.

- Post-operative terms

MedDRA contains some post-operative terms. The most specific terms should be selected.

Example: If “Post-operative bleeding” is reported, “Postoperative bleeding” (not “Bleeding”) can be selected.

- Newly added terms

A new version of MedDRA is released every six months. When using a new version of MedDRA, additional, more specific LLTs may be available for term selection.

2.3 Use of “Current”/“Non-current” Lowest Level Terms (LLTs)

For term selection, only current LLTs should be used. The use of non-current terms should be restricted to the conversion of historical/legacy data.

2.4 Choice of term

2.4.1 In this document, more than one option for term selection is sometimes proposed. This is to allow a solution to accommodate different database configurations and historic working practices.

2.4.2 It is not considered appropriate to address deficiencies in MedDRA by developing organization-specific solutions. If the medical concept reported is not adequately represented in the latest version of MedDRA, it is appropriate to submit a change request to the MSSO. In general, the MSSO will add such terms if medical significance has been demonstrated (MedDRA *Introductory Guide*, Version 12.0).

Example: The term “HCV coinfection” was added to MedDRA following a user’s request.

2.4.3 Medical judgment should be used if an exact match cannot be found, but the medical concept can be adequately represented by an existing term.

Example: If “brittle hair” is reported, “Hair breakage” more accurately reflects the medical concept than the less specific term “Hair disorder”.

2.4.4 In situations where a specific medical concept is not represented by a **single** MedDRA term, a new term should be requested from the MSSO. While awaiting the addition of the new term, it is considered appropriate to select one or more existing terms. A consistent approach should be used. The impact on data retrieval, analysis, and reporting should be carefully considered.

Example: If “metastatic gingival cancer” were not represented in MedDRA by a single term, it would be appropriate to select “Gingival cancer” or “Metastatic carcinoma” or both “Gingival cancer” and “Metastatic carcinoma.”

- 2.4.5 Sometimes more than one choice of term selection is provided within the document. If only one term is selected, specificity might be lost, whereas the selection of two terms might lead to redundant counts. Organizations are encouraged to document their established procedures.

2.5 Do not subtract or add information

2.5.1 Do not omit reported information

Terms should be selected for every ADR/AE reported, regardless of perceived relationship to the drug product. No reported medical concept should be excluded from the term selection process.

Terms should be selected for each reported indication, investigation, medical history and social history concept, as appropriate.

If a diagnosis (medical concept) is reported with characteristic signs and symptoms, it is preferable to select a term for the diagnosis only (see Section 3.1 for more details and examples). As the diagnosis encompasses the signs and symptoms, this is not considered a loss of information.

2.5.2 Do not add information

No new medical concepts should be added. Neither a diagnosis nor a mechanism of action should be derived or inferred from reported signs or symptoms.

Example: If “abdominal pain, increased serum amylase, and increased serum lipase” are reported, it is considered inappropriate to assign a diagnosis of “pancreatitis”.

2.6 Quality Assurance

Tools such as auto-encoders can be helpful, but human intervention is necessary to assure the end result fully reflects the original information and makes medical sense.

To promote consistent term selection, organizations are encouraged to document their term selection strategies, methods, and quality assurance procedures in coding guidelines, which should be consistent with the *Term Selection: Points to Consider* document.

Data clarity can be promoted through internal procedures such as careful design of data collection forms and training of individuals involved in the

data collection and follow-up processes, e.g., clinical investigators/monitors, medical product sales representatives and others. For example, an organization may wish to make investigators and monitors aware of the issues of reporting “combination” terms (see Section 3.5).

The MedDRA terminology is multi-axial and more complex than common terminologies previously used. Therefore, term selection should be reviewed by a qualified individual, a person with medical background and/or training who is also trained in the use of MedDRA.

MedDRA is a standardized terminology. It is considered essential that *ad hoc* structural changes in MedDRA not occur. The assignment of terms across SOCs is pre-determined within the terminology and should not be altered by users. If MedDRA users believe that term(s) are inappropriately placed in the hierarchy, they should inform the MSSO by the change request process.

Example: In a previous version of MedDRA it was found that the primary SOC for the term “Factor VIII deficiency” was “Blood and lymphatic system disorders”. It was corrected by making “Congenital, familial and genetic disorders” the primary SOC and “Blood and lymphatic system disorders” the secondary SOC.

3.0 TERM SELECTION POINTS

3.1 Diagnoses and provisional diagnoses with or without signs and symptoms

The table below provides options for term selection regarding diagnoses and provisional diagnoses, with or without signs/symptoms reported. Examples of certain points are listed below the table.

A provisional diagnosis may be described by, “suspicion of”, “probable”, “presumed”, “likely”, “rule out”, “questionable”, “differential”, etc.

SINGLE DIAGNOSIS	
DEFINITIVE DIAGNOSIS	PROVISIONAL DIAGNOSIS
<p>Single diagnosis without signs/symptoms Diagnosis (only possible option)</p>	<p>Single provisional diagnosis without signs/symptoms Provisional diagnosis (only possible option)</p>
<p>Single diagnosis with signs/symptoms</p> <ul style="list-style-type: none"> • Preferred: Single diagnosis only • Alternate: Diagnosis and signs/symptoms <p><i>Note: Always include signs/symptoms not associated with diagnosis</i></p> <p>Example 1</p>	<p>Single provisional diagnosis with signs/symptoms</p> <ul style="list-style-type: none"> • Preferred: Single provisional diagnosis and signs/symptoms • Alternate: Signs/symptoms only (as provisional diagnosis may change) <p><i>Note: Always include signs/symptoms not associated with diagnosis</i></p> <p>Example 2</p>
MULTIPLE DIAGNOSES	
DEFINITIVE DIAGNOSES	PROVISIONAL DIAGNOSES
<p>Multiple diagnoses without signs/symptoms</p> <ul style="list-style-type: none"> • Multiple diagnoses (only possible option) 	<p>Multiple provisional diagnoses without signs/symptoms</p> <ul style="list-style-type: none"> • Multiple provisional diagnoses (only possible option)
<p>Multiple diagnoses with signs/symptoms</p> <ul style="list-style-type: none"> • Preferred: Multiple diagnoses only • Alternate: Diagnoses and signs/symptoms <p><i>Note: Always include signs/symptoms not associated with diagnoses</i></p> <p>Example 3</p>	<p>Multiple provisional diagnoses with signs/symptoms</p> <ul style="list-style-type: none"> • Preferred: Multiple provisional diagnoses and signs/symptoms • Alternate: Signs/symptoms only (as provisional diagnoses may change) <p><i>Note: Always include signs/symptoms not associated with diagnoses</i></p> <p>Example 4</p>

Example 1:

If “anaphylactic reaction” is reported with “rash, dyspnea, hypotension, and laryngospasm”, selecting “Anaphylactic reaction” alone is preferred.

Alternatively, “Anaphylactic reaction”, “Rash”, “Dyspnea”, “Hypotension”, and “Laryngospasm” can be selected.

If “myocardial infarction” is reported with “chest pain, dyspnea, diaphoresis, ECG changes, and jaundice”, it would be appropriate to select terms for both “Myocardial infarction” and “Jaundice.” Note that jaundice is not typically associated with myocardial infarction.

Example 2:

If “possible myocardial infarction with chest pain, dyspnea, diaphoresis” is reported, selecting “Myocardial infarction”, “Chest pain”, “Dyspnea”, and “Diaphoresis” is preferred.

Alternatively, “Chest pain”, “Dyspnea”, and “Diaphoresis” can be selected.

Example 3:

If multiple diagnoses that include “pulmonary embolism, myocardial infarction, and congestive heart failure” are reported along with “chest pain, cyanosis, shortness of breath, and blood pressure decreased”, selecting “Pulmonary embolism”, “Myocardial infarction”, and “Congestive heart failure” is preferred.

Alternatively, “Pulmonary embolism”, “Myocardial infarction”, “Congestive heart failure”, “Chest pain”, Cyanosis”, “Shortness of breath”, and “Blood pressure decreased” can be selected.

Example 4:

If a differential diagnosis that includes “pulmonary embolism, myocardial infarction, and congestive heart failure” is reported along with “chest pain, cyanosis, shortness of breath, and blood pressure decreased”, selecting “Pulmonary embolism”, “Myocardial infarction”, “Congestive heart failure”, “Chest pain”, Cyanosis”, “Shortness of breath”, and “Blood pressure decreased” is preferred.

Alternatively, “Chest pain”, Cyanosis”, “Shortness of breath”, and “Blood pressure decreased” can be selected.

3.2 Death and Other Patient Outcomes

When an ADR/AE is reported in association with a consequence of an event or a patient outcome, a term for the ADR/AE should be selected and the outcome should be captured in the appropriate field.

3.2.1 Death

3.2.1.1 Death is an outcome and is not usually considered to be an ADR/AE.

Example: If “death due to myocardial infarction” is reported, “Myocardial infarction” can be selected and death should be captured as the outcome.

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

Example: If “constipation, ruptured bowel, peritonitis, sepsis, and patient died” are reported, “Constipation”, “Perforated bowel”, “Peritonitis”, and “Sepsis” can be selected, and death should be captured as the outcome.

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

Example: If a reporter states only that “a patient was found dead”, “Found dead” can be selected.

If circumstances of the death are provided (e.g., natural, accidental, suicide, homicide), and the term exists, it should be selected. However, circumstances of death should not be inferred, but captured only if stated specifically by the reporter.

Example: If the autopsy report states, “the cause of death was natural”, “Death from natural causes” can be selected.

3.2.2 Other Patient Outcomes

Consequences of an event such as hospitalization and disability are not generally considered to be ADR/AEs.

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

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

Example: If a reporter states only that “a patient was hospitalised”, “Hospitalisation” can be selected.

3.3 Suicide and Self-harm

Accurate and consistent term selection for reports of suicide attempts, completed suicides and self-harm is necessary for appropriate data retrieval. Where the motive for the injury is unclear, attempts should be made to gain more specific information.

3.3.1 It is not acceptable to assume that an overdose is a suicide attempt. Only the appropriate term that describes the overdose can be selected.

3.3.2 Similarly, for reports of self-injury that do not mention suicide/suicide attempt, only the appropriate self-injury term should be selected.

Example: If “self slashing” or “cut her own wrists” is reported, select “Self inflicted laceration” which is linked to PT “Intentional self-injury.”

Example: If “cut wrists in a suicide attempt” is reported, select “Suicide attempt.” “Laceration of arm” can also be selected.

3.3.3 If a suicide attempt is successful, it is acceptable to select the term that reflects the outcome instead of the attempt only.

Example: If “suicide attempt resulted in death” is reported, select “Completed suicide” and capture death as a fatal outcome.

3.4 Conflicting/ambiguous/vague information

When conflicting, ambiguous, or vague information is provided, it can be difficult to select a term that will lead to appropriate data retrieval. In such circumstances, attempts should be made to obtain more specific information. (See Section 2.1, *General Principles: Quality of source data*). If clarification attempts have failed, the examples below might be helpful:

3.4.1 Conflicting information

Example: If only “hyperkalemia with a serum potassium of 1.6 mEq/L” is reported, “Serum potassium abnormal” can be selected because this single term conveys both medical concepts.

3.4.2 Ambiguous information

Example: If “GU pain” is reported, “GU” could refer to either “genito-urinary” or “gastric ulcer”. However, since pain was reported, “Pain” can be selected.

It may be advisable to seek clarification for some terms as the final result of term selection may be very different.

Example: COLD may refer to the common cold (PT “Nasopharyngitis”) or Chronic Obstructive Lung Disease.

3.4.3 Vague information

Example: If the only information reported is “patient experienced every listed adverse event”, and attempts to obtain more specific information are unsuccessful, “Unevaluable event” can be selected.

3.5 Combination terms

A combination term in MedDRA is a single medical concept combined with an additional medical term to provide important information on pathophysiology or etiology. A combination term represents an internationally recognized distinct and robust medical concept, e.g. PT *Diabetic retinopathy*, PT *Hypertensive cardiomegaly*, and PT *Eosinophilic pneumonia*.

When combination terms are reported, medical judgment should be applied and the following points should be considered:

- 3.5.1 If one of the terms is a diagnosis and the other is a characteristic sign and/or symptom, the diagnosis term can be selected (See Section 3.1).

Example: If “Chest pain due to myocardial infarction” is reported, “Myocardial infarction” can be selected.

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

Example: If “hepatic function disorder (acute hepatitis)” is reported, “Hepatitis acute” can be selected.

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

- 3.5.3 If a term exists that describes the combination, it should be used.

Example: If “retinopathy due to diabetes” is reported, “Diabetic retinopathy” can be selected.

Example: If “rash with itching” is reported, “Itchy rash” can be selected.

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

Example: If “diarrhea and vomiting” is reported, “Diarrhea” and “Vomiting” can be selected.

Example: If “DIC due to sepsis” is reported, “DIC” and “Sepsis” can be selected.

Example: If “wrist fracture due to fall” is reported, “Wrist fracture” and “Fall” can be selected.

However, be aware that splitting may occasionally result in loss of information unless one is attentive to the particular terms selected and especially where they lie in the MedDRA hierarchy.

Example: If “Hematoma due to an animal bite” is reported, “Animal bite” and “Traumatic hematoma” can be selected. Note that “Traumatic hematoma” is more appropriate than “Hematoma” based on the linkage in the MedDRA hierarchy (HLT Non-site specific injuries NEC and HLT Haemorrhages NEC for “Traumatic hematoma”; HLT Haemorrhages NEC for “Hematoma”).

3.5.5 If the reported term is a combination of an event and a pre-existing condition that has not changed (see Section 3.9) and the combination term does not exist in MedDRA, it is considered sufficient to select a term for the event.

Example: If “shortness of breath due to cancer” is reported in a patient with cancer, “Shortness of breath” can be selected

3.6 Age vs. Event Specificity

3.6.1 Some MedDRA terms describe the age group and the event. If available, the term with the specific age group and event should be selected.

Example: If “jaundice in a newborn” is reported, “Neonatal jaundice” can be selected.

3.6.2 If a term is not available to capture both concepts, the preferred option is to select the term for the event and capture the age group in a demographic field.

Example: If “oral candidiasis in a neonate” is reported, then it is preferable to select “Oral candidiasis”, and the neonatal status can be captured in a demographic field.

Alternatively, it is acceptable to select terms for both age and event.

Example: If “oral candidiasis in a neonate” is reported, “Oral candidiasis” and “Neonatal candida infection” can be selected.

3.7 Body site vs. Event specificity

3.7.1 Some MedDRA terms describe both the body site location and the event. If available, the term with both the specific body site and the event should be selected.

Example: If “skin rash on face” is reported, “Rash on face” can be selected.

3.7.2 Not all MedDRA terms describe body sites. If the suitable MedDRA term with the specific site description is not available, in general, the relevant medical event should have priority.

Example: If “skin rash on chest” is reported, “Skin rash” can be selected.

There will however be occasions when medical judgment is required and the body site description should have priority.

Example: If “cyanosis at injection site” is reported, “Injection site reaction” can be selected instead of “Cyanosis” as cyanosis implies a generalized disorder.

3.7.3 If a term contains multiple body sites, and all link to the same PT, the relevant medical event should have priority.

Example: If “skin rash on face and neck” is reported, “Skin rash” can be selected.

3.8 Location vs. Infectious agent

3.8.1 Some MedDRA terms have both the location and the specific organism/infection. If available, the term with both the specific location and the organism should be selected.

Example: If “pneumococcal pneumonia” is reported, “Pneumococcal pneumonia” can be selected.

3.8.2 Not all infection terms in MedDRA describe location. If the suitable MedDRA term with the organism description is not available, the preferred option would be to select the infective agent. It is also considered acceptable to select the infection site term alone or to select terms for both concepts.

Example: If “respiratory chlamydial infection” is reported, it is preferable to select “Chlamydial infection”.

Example: If “respiratory chlamydial infection” is reported, “Respiratory infection” can be selected.

Example: If “respiratory chlamydial infection” is reported, “Chlamydial infection” and “Respiratory infection” can be selected.

3.9 Pre-existing medical conditions

Pre-existing medical conditions that have not changed should generally be classified as medical and/or social history (See Section 3.24). Pre-existing medical conditions that have changed can be classified as ADR/AEs.

3.9.1 It is important to capture the concept that a pre-existing condition was modified, such as aggravated, exacerbated, worsened, intermittent, recurrent, progressive, or improved. If a pre-existing medical condition is modified, the specific MedDRA term should be selected, provided that it exists.

Example: If “exacerbation of myasthenia gravis” is reported, “Myasthenia gravis aggravated” can be selected.

3.9.2 In the absence of such a term, the following options are considered appropriate:

3.9.2.1 A term for the condition should be selected and the modification should be captured in a consistent, documented way. The non-specific modifier term alone should not be selected.

Example: If “halitosis worsened” is reported, “Halitosis” only can be selected.

3.9.2.2 A term for the condition and an additional term to describe the modification of the condition should be selected, e.g., “Condition aggravated”, “Disease progression.”

Example: If “progression of Addison’s disease” is reported, “Addison’s disease” and “Disease progression” can be selected.

Example: If “aggravation of jaundice” is reported, “Jaundice” and “Condition aggravated” can be selected.

3.9.3 If the reported term is a combination of an event and a pre-existing condition that has not changed and the combination term does not exist in MedDRA, it is considered sufficient to select a term for the event.

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

3.10 Exposures During Pregnancy and Breast Feeding

MedDRA contains various terms that address exposures to medical products (drug and nondrug) during pregnancy and breast feeding. To select the most

appropriate term(s) to capture the information, first determine if the subject/patient who experienced the event(s) was the mother or the child/fetus.

3.10.1 Events in the Mother

3.10.1.1 Patient became pregnant while receiving medication

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

If the occurrence of pregnancy is reported but no adverse event has occurred, it is appropriate to select both “*Pregnancy*” and “*No adverse effect*” (see Section 3.20).

If the occurrence of pregnancy is reported but there is no pregnancy outcome and it is not known yet whether any adverse event occurred, select “*Pregnancy*” only.

3.10.1.2 Pregnant patient experienced adverse event(s) while receiving medication.

Appropriate term(s) for the adverse event and “*Drug exposure during pregnancy*” can be selected. “*Pregnancy*” can also be selected for the medical history and/or concomitant medical condition.

3.10.2 Events in the child or fetus

It is helpful to first determine if the child or fetus was exposed or potentially exposed to the medical product from the mother or the father.

3.10.2.1 Child or fetus experienced adverse event(s) and was exposed to the drug in utero; mother received the product. (Note that the patient is the child or fetus).

Appropriate term(s) should be selected for the adverse event(s). In addition, “*Drug exposure in utero*” or “*Maternal drug exposure*” can also be selected.

3.10.2.2 Child or fetus experienced adverse event(s) and was exposed to the drug in utero; father received the product. (Note that the patient is the child or fetus).

Appropriate term(s) should be selected for the adverse event(s). In addition, “*Paternal drug exposure*” can also be selected.

3.10.2.3 Child experienced an adverse event and was exposed to the drug from breast milk.

Appropriate term(s) should be selected for the adverse event(s). (Note that the patient is the child). In addition, “*Drug exposure via breast milk*” can also be selected.

3.11 Congenital terms

The definition of “congenital” for MedDRA is “any condition present at birth, whether genetically inherited or occurring in utero” (MedDRA *Introductory Guide*, Version 12.0).

3.11.1 Terms from the SOC *Congenital, familial and genetic disorders* should be used when the condition is described as congenital by the reporter or when medical judgment establishes that the condition was present in the child at the time of birth.

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

3.11.2 If the condition is not specified as congenital and not stated to be present at birth, the non-specific term should be selected or in its absence, the acquired term should be selected.

Example: If “night blindness” is reported, the term “Night blindness” can be selected which links to the PT “Night blindness”.

Example: If “cholangiectasis” is reported, the term “Cholangiectasis acquired” can be selected.

3.12 Neoplasms

Given the wide variety of neoplasm types, it is not possible to provide specific guidance applicable to all situations. However, MedDRA users should be aware that the MedDRA *Introductory Guide* has rules and conventions for the way certain neoplasm and related terms are used in MedDRA. For example, in MedDRA:

- The words “cancer” and “carcinoma” are used synonymously. (Appendix B, MedDRA Concept Descriptions, of MedDRA *Introductory Guide*, Version 12.0).
- The word “tumo(u)r” is considered neoplastic.
- The words “lump” and “mass” are not considered neoplastic.

These points should be kept in mind for term selection.

Clarification from the reporter should be sought if the type of neoplasia described is not clear. When selecting terms for neoplastic conditions, medical experts should be consulted for difficult or unusual neoplasms.

3.12.1 Malignancy should not be inferred but captured only if stated specifically by the reporter. Reported events of “tumor” should not

be assigned a “cancer” or “carcinoma” term unless it is clear that a malignancy is present.

Example: If “Tumour growing on skin” is reported, “Skin tumour” can be selected.

Example: If “Cancer growing on tongue” is reported, “Malignant tongue cancer” can be selected.

3.13 Medical/Surgical Procedures

The use of the SOC *Surgical and medical procedures* is generally not appropriate for ADR/AEs. The terms in the SOC *Surgical and medical procedures* are not multi-axial in MedDRA. Users should be aware of the impact that use of these terms will have on data retrieval, data analysis, and reporting. When selecting terms for procedures, the following points might be helpful:

- 3.13.1 If the procedure represents the only information provided, a term should be selected for the procedure.

Example: If “patient had gallbladder surgery” is the only information reported, “Gallbladder operation” can be selected.

Example: If “patient had tonsillectomy in childhood” is reported, “Tonsillectomy” can be selected.

- 3.13.2 If a procedure is reported in combination with a diagnosis, it is preferable to select a term for the procedure in addition to a term for the diagnosis, since information concerning a procedure may indicate severity of the condition. Alternatively, it is considered sufficient to select a term for the diagnosis alone.

Example: If “liver transplantation due to liver injury” is reported, it is preferable to select both “Liver injury” and “Liver transplantation”. Alternatively, “Liver injury” alone can be selected.

3.14 Investigations

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

- 3.14.1 **Investigation terms without qualifiers**

Terms in SOC *Investigations* **without qualifiers** can be used to capture test names such as in the E2B field B.3.1c.

Example: If “bilirubin” test is performed, then “Bilirubin” can be selected.

Example: If “cardiac output” is measured, then “Cardiac output” can be selected.

Example: If “blood glucose increased” is reported, and the user wishes to capture laboratory results, the term “Blood glucose” can be selected for the test name and the free text “increased” can be entered in the result field. It is not appropriate to put “Blood glucose increased” as a test name.

- 3.14.2 The results of investigations might represent ADR/AEs. When selecting terms for results of investigations, the following points might be helpful:

3.14.2.1 Medical conditions vs. laboratory results.

Example: If “hypoglycemia” is reported, “Hypoglycemia” can be selected.

(Note: “Hypoglycemia” links to SOC Metabolism and nutrition disorders.)

Example: If “decreased glucose” is reported, “Glucose decreased” can be selected.

(Note: “Glucose decreased” links to SOC Investigations.)

3.14.2.2 Unambiguous laboratory results

Example: If a value is reported that is clearly below the reference range, e.g., glucose 40 mg/dL, “Glucose low” can be selected.

3.14.2.3 Ambiguous laboratory results

Example: If “his glucose was 40” is reported without units, and additional clarification cannot be obtained, “Glucose abnormal” can be selected.

- 3.14.3 It is not considered necessary to select terms for each diagnostic result that is consistent with the clinical diagnosis provided by the reporter. (See Section 3.1.)

Example: If “elevated potassium, K 7.0 mmol/L and hyperkalemia” are reported, “Hyperkalemia” can be selected. An additional term for elevated potassium (e.g., “Potassium increased”) is not necessary.

- 3.14.4 It is considered necessary to select terms for each diagnostic result that is not consistent with the clinical diagnosis provided by the reporter.

Example: If “alopecia, rash, and elevated potassium 7.0 mmol/L” are reported as adverse events, then “Alopecia”, “Rash”, and “Potassium increased” can be selected.

- 3.14.5 Non-specific investigation terms should only be used when more specific result terms are not available.

Example: If “abnormal liver function tests” is reported, “Abnormal liver function tests” can be selected.

Example: If “increased alkaline phosphatase, increased SGPT, increased SGOT, and elevated LDH” is reported, four individual terms should be selected. A single term such as “Liver function tests abnormal” should not be selected.

3.15 Medication/administration errors and accidental exposures

There are specific medication error terms in MedDRA. Information may be reported describing medication errors with or without clinical consequences.

- 3.15.1 If a medication error results in clinical consequences, term(s) for the medication error and the clinical consequences should be selected.

Example: If “hives due to medication error” is reported, “Hives” and “Medication error” can be selected.

Example: A patient was administered the wrong drug and experienced hypotension. The term “Hypotension” and “Wrong drug administered” can be selected

Explanations of the interpretations and uses of certain medication error terms (e.g., “dispensing error”) are found in The MedDRA *Introductory Guide* (Appendix B, MedDRA Concept Descriptions).

- 3.15.2 Medication errors in the absence of clinical consequences are not ADR/AEs; however, it is important to capture the occurrence or the potential occurrence of a medication error. The term closest to the type of medication error should be selected.

Example: If “medication was given intravenously instead of intramuscularly” is reported, “Intramuscular formulation administered by other route” can be selected.

Example: A patient was dispensed the wrong drug strength. The error was detected prior to patient administration. The term “Intercepted drug dispensing error” can be selected.

Additionally, information may be received describing the potential for a medication error.

Example: A pharmacist notices that the names of two drugs are similar and is concerned that this may result in a medication error. The term “Drug name confusion” can be selected.

Example: A patient reports that tablets of a different strength are the same color and shape and this may result in a medication error. The term “Circumstance or information capable of leading to medication error” can be selected.

3.15.3 The same principle applies to accidental exposures.

Example: If “nurse splashed an injectable drug in her own eye” is reported, “Inadvertent exposure to drug” can be selected.

Example: If “child exposed to maternal drug during breast feeding” is reported, “Drug exposure via breast milk” can be selected.

3.15.4 It is considered acceptable to select the additional term “No adverse effect”, if specifically so reported. (See Section 3.20)

Example: If “medication was given intravenously instead of intramuscularly without sequelae” is reported, “Intramuscular formulation administered by other route” and “No adverse effect” can be selected.

3.15.5 If the product label clearly states that co-administration with specified drugs, specified food or administration to patients with specified disease states have known effects, the appropriate term for “Labelled drug-drug interaction medication error”, “Labelled drug-food interaction medication error”, “Labelled drug-disease interaction medication error” or “Documented hypersensitivity to administered drug” can be selected.

Example: If “patient became pregnant whilst taking an antifungal drug and an oral contraceptive” is reported, and this interaction is clearly stated in the product data sheet, “Labelled drug-drug interaction medication error” can be selected.

Example: If “patient drank grapefruit juice whilst taking a calcium channel blocker” is reported and the calcium channel blocker is labelled for grapefruit juice interaction, “Labelled drug-food interaction medication error” can be selected.

Example: If “a patient with renal failure is prescribed a drug for which renal failure is contraindicated” is reported, “Labelled drug-disease interaction medication error” can be selected.

Example: If a patient is administered a sulfonamide-based drug when it was clearly noted in his medical file that he had a sulfa allergy, “Documented hypersensitivity to administered drug” may be selected

- 3.15.6 It is not considered appropriate to infer that a medication error has occurred unless specific information is provided. (See Section 2.5.2)

Example: If “antibiotic was prescribed for a week and the patient stopped treatment after 2 days because of bitter taste” is reported, “Prescribed dosing duration not completed” and “Taste bitter” can be selected.

Example: If “antibiotic was prescribed and the patient stopped treatment after 2 days because of bitter taste” is reported, only “Taste bitter” can be selected as it is not appropriate to assume the medication was prescribed for a longer period.

- 3.15.7 It is not considered appropriate to infer an extra dose, overdose or underdose if that is not explicitly reported. (See Section 3.17.1).

Example: If “incorrect dosing by patient” or “Inadvertent dose administered” is the only information reported, “Wrong dose administered” can be selected. It is not considered appropriate to select “Extra dose administered” or “Overdose” on the basis of this information only.

Example: If “patient took only half the prescribed dose,” is reported, then “Underdose” can be selected.

3.16 Transmission via medicinal product of infectious agent

If a report of transmission of infectious agent via medicinal product is received, it is considered appropriate to select a term for the transmission. In addition, if the infectious agent is specified, it is considered appropriate to select the specific infectious agent as a second term.

Example: If “suspected transmission of Hepatitis C via a blood product” is reported, “Suspected transmission of an infectious agent via a medicinal product” and “Hepatitis C” can be selected.

Example: If “confirmed transmission of Hepatitis C via a blood product” is reported, “Transmission of an infectious agent via a medicinal product” and “Hepatitis C” can be selected.

In some instances, the reporter may not have clearly stated that transmission of infection had occurred via a medical product. Medical judgment should be used as transmission may be implied by data within a single case. The term “*Suspected transmission of an infectious agent via a medicinal product*” may be selected.

Alternatively, “*Suspected transmission of an infectious agent via a medicinal product*” may be selected for the E2B field reserved for the sender’s diagnosis (B.5.3, “Sender’s diagnosis/syndrome and/or reclassification of reaction/event”).

3.17 Overdose/Toxicity/Poisonings

- 3.17.1 Overdose, toxicity, and poisoning terms exist within MedDRA. Overdose terms are grouped under the HLT *Overdoses*. Toxicity and poisoning terms are grouped under the HLT *Poisoning and toxicity* (for more information please refer to the MedDRA *Introductory Guide*, Version 12.0). If overdose, toxicity, or poisoning is explicitly reported, the appropriate term should be selected.

Example: If “overdose of pills” is reported, “Overdose” can be selected.

Example: If “A child was accidentally poisoned when she ingested a cleaning product” is reported, “Accidental poisoning” can be selected.

- 3.17.2 Terms for the clinical consequences reported in association with an overdose should be selected.

Example: If “stomach upset from study drug overdose” is reported, “Stomach upset” and “Overdose” can be selected.

- 3.17.3 If an overdose is reported and it was specifically stated that there were no clinical consequences, it is considered acceptable to select “Overdose” and the additional term “No adverse effect”. (See Section 3.20).

3.18 Device terms

- 3.18.1 Device information may be reported with or without clinical consequences. If a device term in the absence of clinical consequences is reported, the appropriate term should be selected

Example: If “medical device breakage” is reported, “Device breakage” can be selected.

Example: If “my patch is leaking on my arm” is reported, “Leaking patch” can be selected

3.18.2 Some MedDRA terms capture both the device event and the clinical consequence; if available, the term with both the event and consequences should be selected.

Example: If “patient with a vascular implant developed an infection of the implant ” is reported, “Vascular implant infection” can be selected.

3.18.3 If the appropriate MedDRA term is not available to capture the device and associated clinical consequences, then both concepts should be captured by selecting the appropriate term(s) for the device and clinical consequence.

Example: If “ventricular tachycardia due to malfunction of device” is reported, “Device malfunction” and “Ventricular tachycardia” can be selected.

3.19 Drug interactions

This term includes drug/drug⁴, drug/food, drug/device, and drug/alcohol interactions. With respect to interactions, MedDRA does not include specific product names.

3.19.1 When the reporter specifically states that an interaction occurred, an appropriate interaction term should be selected in addition to term(s) for any medical event(s) described.

Example: If “torsade de pointes with suspected drug interaction” is reported, “Torsade de pointes” and “Drug interaction” can be selected.

Example: If “patient drank grapefruit juice which interacted with lipid lowering drug causing muscle pain” is reported, “Food interaction” and “Muscle pain” can be selected.

3.19.2 If two products are used together and the reporter does not specifically state there is an interaction but does report a medical event, only an event term should be selected.

Example: If “patient was started on an anti-seizure medication and a heart medication and developed syncope” is reported, “Syncope” can be selected.

Example: If “patient was already on an anti-seizure medication and was started on a heart medication and anti-seizure medication levels increased” is reported, “Anticonvulsant drug level increased” can be selected.

⁴ In this document, the term “drug” includes biological products

Labeled drug interactions may constitute medication errors. (See Section 3.15.5)

3.20 No adverse effect

Some organizations might wish to use this term to maintain records for administrative purposes, e.g., for pregnancy registries, overdoses, and medication errors.

The term “*No adverse effect*” could be used when it is specifically reported that no ADR/AE occurred, despite exposure to a product (See Section 3.15.4 and 3.17.3).

Terms describing normal states and outcomes exist in MedDRA, such as “*Normal baby*”, “*Normal electrocardiogram*”, and “*Sinus rhythm*”, which can be used as needed.

3.21 Unexpected therapeutic effect

Some organizations might wish to use the term “Unexpected therapeutic effect” although such effects are not usually considered ADR/AEs. Reports occasionally describe a beneficial effect of a drug aside from the use for which it had been given.

Example: If “a bald patient was pleased that he grew hair while using a product” is reported, the term “Hair growth increased” can be selected. In addition, “Unexpected therapeutic effect” can be selected.

3.22 Modification of effect

Modifications of effect are not always considered ADR/AEs; however, it is important to capture this information, and in certain situations, lack of effect is a reportable event. MedDRA contains many terms that describe modifications of effect. The closest term(s) available to capture the reported medical concept(s) should be selected, unless this information is captured by other means.

- 3.22.1 It is considered appropriate to use lack of effect terms when the reporter specifically states that the drug was ineffective (or did not work, or similar wording) or that the expected effect was not obtained. The preferred option is to select only the lack of efficacy term, even if the consequences are reported.

Example: If “antibiotic didn’t work” is reported, “Lack of drug effect” can be selected.

Example: If “patient took drug and her headache didn’t go away, drug ineffective” is reported, “Drug ineffective” can be selected.

- 3.22.2 Some organizations may also wish to select the event resulting from the lack of effect. The term(s) describing the consequence(s) of lack of effect may be selected for one or more database field(s), for example, adverse event, medical history or drug indication).

Example: If “patient took drug, her headache didn’t go away, drug is ineffective” is reported, “Drug ineffective” can be selected. “Headache” can also be selected.

3.22.3 It is not considered appropriate to infer lack of effect.

Example: If “AIDS patient taking anti-HIV drug died” is reported, “Lack of drug effect” should not be assumed. A term for death should be selected, as described in Section 3.2 of this document.

3.22.4 Increased, Decreased, and Prolonged effects

It is considered appropriate to use this group of terms when the reporter specifically identifies a modification of effect.

Example: If “patient had increased effect from drug A” is reported, “Increased drug effect” can be selected.

Example: If “patient had decreased effect from drug A” is reported, “Drug effect decreased” can be selected.

Example: If “patient had prolonged effect from drug A” is reported, “Drug effect prolonged” can be selected.

3.23 Social circumstances

The terms in this SOC describe social factors and might be suitable for social and medical history data term selection. Use of the SOC *Social circumstances* is generally not considered appropriate for ADR/AEs. However, some terms currently contained within this SOC are the only option for capturing certain ADR/AEs.

Example: If “patient’s ability to drive was impaired” is reported, “Impaired driving ability” can be selected.

The terms in SOC *Social circumstances* are not multi-axial in MedDRA. This SOC contains terms that are similar to terms in the disorder SOCs; however, terms in SOC *Social circumstances* generally refer to a person, rather than a condition. Users should be aware of the impact that use of these terms will have on data retrieval, data analysis, and reporting. The following example is illustrative:

SOC Social circumstances	“Disorder” SOC
Alcoholic	Alcoholism
Drug abuser	Drug abuse
Tobacco user	Nicotine dependence
Glue sniffer	Glue sniffing

Note that abuse terms not associated with drugs/substances appear in SOC *Social circumstances* regardless of whether they refer to the person or the condition. The following example is illustrative.

SOC Social circumstances	
LLT	PT
Child abuse	Child abuse
Child abuser	Child abuse
Elder abuse	Elder abuse
Elder abuser	Elder abuse

3.23.1 Illegal acts and concepts of crime or abuse (excluding drug/substance related abuse terms)

All illegal acts of crime or abuse (excluding drug and/or other substance related abuse terms) link to the SOC *Social circumstances*.

Example: If “physical assault” is reported the selected term “Physical assault” links to the SOC Social circumstances

3.23.1.1 Perpetrator

LLT terms representing the perpetrator are directly related to the corresponding PT term describing the unlawful act/crime committed

Example: If the reported patient history indicates that the patient is a known sexual offender, “Sexual offender” can be selected which links to the PT “Sexual abuse”.

(Note: The LLT “Sexual offender” links to the SOC *Social circumstances*.)

3.23.1.2 Victim

PT terms representing the victims of unlawful acts are preceded by “Victim of”. Associated unqualified terms representing the victim are represented at the LLT level.

Example: If it was reported that the patient was a childhood sexual assault victim, “Childhood sexual assault victim” can be selected, which links to the PT “Victim of sexual abuse”.

(Note: The LLT “Childhood sexual assault victim” links to the SOC *Social circumstances*.)

3.24 Medical and/or social history

The examples below illustrate how MedDRA can be used to capture medical and/or social history.

Example: If “history of gastrointestinal bleed and hysterectomy” is reported, “Gastrointestinal bleed” and “Hysterectomy” can be selected.

Example: If “patient is a cigarette smoker with coronary artery disease” is reported, “Cigarette smoker” and “Coronary artery disease” can be selected.

3.25 Indication for product use

These principles can be applied to product indications collected either pre-market or post-market. Specific regulatory requirements are not addressed in this document.

Historically, indication data have not been collected in a complete or consistent way, nor has a controlled terminology been widely used for the entry of these data. Consideration should be given to the importance of accurate data collection, the use of auto-encoders and the impact on data retrieval.

Reported indications can include: medical conditions, prophylaxis of such conditions, diagnostic tests, replacement therapies, procedures such as anesthesia induction and terms such as “anti-hypertension”. Because of the nature of such data, terms from almost any SOC, including SOC *Investigations*, may be selected for an indication.

It might be unclear in the reporting of indication data whether a medical condition or a desired outcome is being reported.

Example: If the indication reported is “weight loss”, “Weight loss” can be selected, as it is unknown if the reporter is expressing that the drug was taken to induce weight loss (overweight patient) or to treat weight loss (underweight patient).

Example: If the indication reported is “immunosuppression”, “Immunosuppression” can be selected, as it is unknown if the reporter is expressing that the drug was taken to induce immunosuppression or to treat the condition of immunosuppression.

3.25.1 Medical Conditions

3.25.1.1 Where the indication is a medical condition, a term that expresses the medical condition should be selected.

Example: If the reported indication is “hypertension”, “Hypertension” can be selected.

Example: If the reported indication is “anti-hypertensive”, “Hypertension” can be selected.

Example: If the reported indication is “chemotherapy for breast cancer”, “Breast cancer” can be selected.

Example: If “medication for gastrointestinal problem” is reported as an indication, “Gastrointestinal disorder” can be selected.

3.25.1.2 If the only information reported is a type of therapy, then the most specific term available should be selected.

Example: If a reporter states only that “a patient had received chemotherapy”, “Chemotherapy” can be selected.

3.25.2 Prevention and Prophylaxis

3.25.2.1 When the concept of prevention or prophylaxis is expressed, the specific MedDRA term should be selected, provided that it exists. The terms prevention and prophylaxis can be used interchangeably.

Example: If “arrhythmia prophylaxis” is reported, “Arrhythmia prophylaxis” can be selected.

Example: If “prevention of migraine” is reported, “Migraine prophylaxis” can be selected.

3.25.2.2 In the absence of a specific prophylaxis term, the following options are considered appropriate:

The preferred option is to select the closest terms for both concepts.

Example: If “prevention of hepatotoxicity” is reported, it is preferable to select both “Prevention” and “Hepatotoxicity”.

Or a term for the condition can be selected.

Example: If “prevention of hepatotoxicity” is reported, “Hepatotoxicity” can be selected.

Or the closest prophylaxis or prevention term can be selected.

Example: If “prevention of hepatotoxicity” is reported, “Prevention” can be selected.

3.25.3 Diagnostic Testing

If the product is being used to perform a diagnostic test, a term for the test should be selected.

Example: If “contrast agent for angiogram” is reported, “Angiogram” can be selected.

Example: If “contrast agent for coronary angiogram” is reported, “Coronary angiogram” can be selected.

3.25.4 Procedures

If the product is being used to perform a procedure, a term for the procedure should be selected.

Example: If “induction of anesthesia” is reported, “Induction of anesthesia” can be selected.

3.25.5 Supplementation and Replacement Therapies

Supplement and replacement therapies can be found in SOC *Surgical and medical procedures*. (See Section 3.13)

If the product indication specifies or describes supplementation or replacement, the closest term should be selected.

Example: If “testosterone replacement therapy” is reported, “Androgen replacement therapy” can be selected.

Example: If “thyroid replacement therapy” is reported, “Thyroid hormone replacement therapy” can be selected.

Example: If “prenatal vitamin” is reported, “Vitamin supplementation” can be selected.

3.25.6 Indication not reported

If the indication is not known and no clarification is available, then the term “*Drug use for unknown indication*” can be selected.

Example: If “aspirin was taken for an unknown indication” is reported, “Drug use for unknown indication” can be selected.

3.26 Off label use

Use of a product for an indication for which it is not labeled is referred to as “off label use.”

3.26.1 Indications for use

If a medical condition is reported as an indication and “off label use” is also reported, the condition can be selected for the indication field. “*Off label use*” should only be selected if that is the only information available. Alternatively, both the indication and “*Off label use*” can be selected.

Example: If the reported indication is “hypertension and this is an off label use”, “Hypertension” can be selected, or “Hypertension” and “Off label use” can be selected.

Example: If the reported indication is “off label use”, “Off label use” can be selected.

3.26.2 ADR/AEs

If ADR/AEs are a consequence of use of a product for an indication for which it is not labeled, terms for the ADR/AEs should be

selected. Alternatively, terms for both the ADR/AEs and “*Off label use*” can be selected.

Example: If “a patient was administered a drug off label for pulmonary hypertension and the patient suffered a stroke,” “Stroke” can be selected. Alternatively, both “Stroke” and “Off label use” can be selected.

4 Appendices:

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