MedDRA® TERM SELECTION: POINTS TO CONSIDER

ICH-Endorsed Guide for MedDRA Users

Condensed Version

2018

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INTRODUCTION

The **Med**ical **D**ictionary for **R**egulatory **A**ctivities terminology (MedDRA) was designed for sharing regulatory information for human medical products. In order for MedDRA to harmonise the exchange of coded data, users should be consistent in the assignment of terms to verbatim reports of symptoms, signs, diseases, etc.

This condensed *MedDRA Term Selection: Points to Consider* (MTS:PTC) document is an ICH-endorsed guide for MedDRA users. Its focus is on the fundamental principles of term selection; for more detailed information and examples of additional term selection situations, users should refer to the full MTS:PTC document. The full MTS:PTC is available in English and Japanese, is updated in step with new MedDRA versions and is a companion document to MedDRA. In contrast, this condensed MTS:PTC is not updated with each MedDRA release.

Both the full and condensed MTS:PTC documents were developed and are maintained by a working group charged by the ICH Management Committee. The working group consists of representatives of ICH regulatory and industry members, the World Health Organization, the MedDRA Maintenance and Support Services Organization (MSSO) and the Japanese Maintenance Organization (JMO).

Objectives of this Document

The objective of this condensed 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 condensed 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.

Uses of MedDRA

This condensed MTS:PTC document addresses fundamental term selection principles, primarily for adverse reactions/adverse events (ARs/AEs).

Detailed information on term selection situations, including medication errors, product quality issues, exposures, medical history, social history, misuse and abuse, off label use, device-related events, and indications is provided in the full 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.

How to Use this Document

The condensed 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, refer to the full MTS:PTC document and the MedDRA Introductory Guide (see Appendix, Section 4.2).

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.

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.

GENERAL TERM SELECTION PRINCIPLES

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.

Quality Assurance

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

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.

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.

Example

Reported	LLT Selected	Comment

Reported	LLT Selected	Comment
Abscess on face	Facial abscess	LLT *Facial abscess* more accurately reflects the reported concept than the less specific LLT *Abscess*

More specific LLTs may be available in a new version of MedDRA. Explanations of the interpretations and uses of many MedDRA terms and concepts are found in the MedDRA Introductory Guide (Appendix B, MedDRA Concept Descriptions) and can be viewed in the MedDRA Web-Based Browser.

Select Only Current Lowest Level Terms

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

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.

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.

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).

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.

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.

In some situations, particularly for medication errors and product quality issues, familiarity with the relevant hierarchy is essential for term selection. Navigating down in the MedDRA hierarchy to the appropriate LLTs is the optimal approach for term selection.

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 medication errors, product quality issues, medical history, device-related events, 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

<table>
<tr><th>Reported</th><th>LLT Selected</th><th>Comment</th></tr>
<tr><td rowspan="3">Abdominal pain, increased serum amylase, and increased serum lipase</td><td>Abdominal pain</td><td rowspan="3">It is inappropriate to assign an LLT
for diagnosis
of “pancreatitis”</td></tr>
<tr><td>Serum amylase increased</td></tr>
<tr><td>Lipase increased</td></tr>
</table>

TERM SELECTION POINTS

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. Similar principles apply for when multiple definitive or provisional diagnoses with or without signs/symptoms are reported.

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

The **preferred option** for a provisional diagnosis is to select a term for the diagnosis *and* terms for reported signs and symptoms. This is because a provisional diagnosis may change while signs/symptoms do not.

SUMMARY OF PREFERRED AND ALTERNATE OPTIONS	
DEFINITIVE DIAGNOSIS	**PROVISIONAL DIAGNOSIS**
Definitive diagnosis without signs/symptoms • Diagnosis (only possible option)	**Provisional diagnosis without signs/symptoms** • Provisional diagnosis (only possible option)
Definitive diagnosis with signs/symptoms • **Preferred:** Diagnosis only • Alternate: Diagnosis and signs/symptoms ***Note: Always include signs/symptoms not associated with diagnosis*** **SEE EXAMPLE 1**	**Provisional diagnosis with signs/symptoms** • **Preferred:** Provisional diagnosis and signs/symptoms • Alternate: Signs/symptoms only ***Note: Always include signs/symptoms not associated with diagnosis*** **SEE EXAMPLE 2**

EXAMPLES			
Example	**Reported**	**LLT Selected**	**Preferred Option**
1	Anaphylactic reaction, rash dyspnoea, hypotension, and laryngospasm	Anaphylactic reaction	✓
		Anaphylactic reaction Rash Dyspnoea	

EXAMPLES			
Example	**Reported**	**LLT Selected**	**Preferred Option**
		Hypotension Laryngospasm	
2	Possible myocardial infarction with chest pain, dyspnoea, diaphoresis	Myocardial infarction Chest pain Dyspnoea Diaphoresis	✓
		Chest pain Dyspnoea Diaphoresis	
Always include signs/ symptoms not associated with diagnosis	Myocardial infarction, chest pain, dyspnoea, diaphoresis, ECG changes and jaundice	Myocardial infarction Jaundice (note that jaundice is not typically associated with myocardial infarction)	

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.

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

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

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.

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, LLT *Unevaluable event* or LLT *Ill-defined disorder* are examples of terms that may be selected to represent vague reported information.

Combining and Splitting Terms

Combining Terms
Combining terms for certain reported ARs/AEs may be appropriate (e.g., a condition "due to", "secondary to", "as a result of" another condition). Note: medical judgment should be applied.

Example

Reported	LLT Selected	Comment
Hepatic function disorder (acute hepatitis)	Hepatitis acute	If one term is more specific than the other, select a term for the more specific condition
Retinopathy due to diabetes	Diabetic retinopathy	A single MedDRA combination term* represents both conditions

* 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.

When to "split" into more than one MedDRA term

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

Example

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

Exercise medical judgment so that information is not lost when "splitting" a reported term.

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.

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*

Investigation terms without qualifiers
Terms in SOC *Investigations* **without qualifiers**, e.g., LLT *Blood glucose*, are intended to be used to record test names when entering diagnostic test data in the ICH E2B electronic transmission standard.

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

Test name terms without qualifiers are not intended for use in other data fields capturing information such as ARs/AEs and medical history. The use of the Unqualified Test Name Term List is optional and may be used to identify the inappropriate selection of these terms in data fields other than the test name data element. It is available for download from the MedDRA and JMO websites (see Appendix, Section 4.2).

3.7 Situations reported without clinical consequences

There are certain situations that may on occasion be reported without mention of any clinical consequences, i.e., no associated adverse event/adverse reaction. However, it is important to capture the reported information by selecting appropriate terms for the specific situation. Such situations include medication errors, product quality issues, lack of effect, off label use, exposures (including occupational, pregnancy and breastfeeding exposures), overdoses, drug interactions and device-related issues.

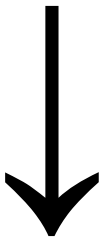
APPENDIX

Versioning

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

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

The table below summarises the types of versioning methods.

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

This list may not be inclusive; other versioning methods may be used. Depending on how MedDRA data are stored in the database, additional steps may be needed to ensure

consistency in data retrieval and reporting, including medical review of the data after the version method has been applied.

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

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

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 (MedDRA Best Practices. See Appendix, Section 4.2). 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 ICH regions, the MSSO recommends midnight GMT, Sunday to Monday, for the switchover. For example : • 1 March – MedDRA X.0 released • First Monday of May – MedDRA X.0 becomes the reporting version • 1 September – MedDRA X.1 released • First Monday of November – MedDRA X.1 becomes the reporting version

Links and References

The following documents and tools can be found on the MedDRA website: (www.meddra.org). Documents are available in all supported MedDRA languages except where noted.

- MedDRA Term Selection: Points to Consider document (full version available in English and Japanese)
- MedDRA Data Retrieval and Presentation: Points to Consider document (full version available in English and Japanese)
- Condensed MedDRA Data Retrieval and Presentation: Points to Consider document
- MedDRA Introductory Guide
- MedDRA Change Request Information document (English)
- MedDRA Web-Based Browser *
- MedDRA Desktop Browser
- MedDRA Version Report (lists all changes in new version) *
- MedDRA Version Analysis Tool (compares any two versions) *
- Unqualified Test Name Term List
- MedDRA Best Practices
- Transition Date for the Next MedDRA Version

* Requires user ID and password to access