Summary of Changes to

MedDRA® TERM SELECTION: POINTS TO CONSIDER

ICH-Endorsed Guide for MedDRA Users

Release 4.8
Based on MedDRA Version 17.1

1 September 2014

The following is a listing of changes made between releases 4.7 and 4.8 of the *MedDRA Term Selection: Points to Consider* document:

Throughout document

1) Correction of general spelling, punctuation, spacing, and format errors
2) Replacement of references to MedDRA Version 17.0 to Version 17.1
3) Update of examples based on MedDRA version changes

SECTION 1 – INTRODUCTION

The last sentence of the second paragraph was modified to include representatives from the Korean regulatory authority in the list of working group members as follows:

> 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).

1.4 - Preferred Option

The text in this section:

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

Was changed as follows (note the addition of a sentence about regional regulatory requirements and the addition of a reference to documentation of the chosen option in the last sentence):

> 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.

3.3.2 If self-injury is reported

An additional (third) example was added to the Example table:

Example

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

As follows:

Example

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

3.11 Congenital Terms

There were extensive changes made to this section of the document to provide more detailed guidance and examples of term selection for congenital and acquired conditions.

First, the section name:

3.11.1 Condition described as congenital

Was changed as follows:

3.11.1 Congenital conditions

The wording and examples in this section were replaced with the following:

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

Secondly, the section name:

3.11.2 Condition not congenital/not present at birth

Was changed as follows:

3.11.2 Acquired conditions (not present at birth)

The wording and examples in this section were replaced with the following:

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.

Lastly, a **new** section that did not exist in the previous version of the document. was added as follows:

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*

3.15.1.1 Medication errors reported with clinical consequences

An additional (third) example was added to the Example table:

Example

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

As follows:

Example

Reported	LLT Selected	Comment
Patient was administered wrong drug and experienced hypotension	Wrong drug administered Hypotension	
Because of similar sounding drug names, the patient took the wrong drug and experienced a rash	Drug name confusion Wrong drug administered Rash	
Insulin was given using the wrong syringe resulting in the administration of an overdose. The patient developed hypoglycaemia.	Wrong device used Accidental overdose 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 <u>without</u> clinical consequences

The Example table:

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

Reported	LLT Selected	Comment
result in a medication error		tracking purposes). Note: this example is a potential medication error
Drug inadvertently administered. The error was noticed soon afterwards.	Drug administration error	

Was changed as follows (note changes to the third and fourth examples):

Reported	LLT Selected	Comment
Medication was given intravenously instead of intramuscularly	Intramuscular formulation administered by other route	
Medication was given intravenously instead of intramuscularly **without sequelae**	Intramuscular formulation administered by other route No adverse effect	See Section 3.21
The pharmacist selected the wrong drug strength but the error was detected prior to dispensing to the patient	Intercepted wrong drug strength selected	LLT *Intercepted wrong drug strength selected* links to PT *Intercepted drug dispensing error*
Pharmacist notices that the names of two drugs are similar and is concerned that this may result in a medication error	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 errors in the context of labelled interactions

There were several changes made to this sub-section of the document to accommodate new examples of medication monitoring errors in addition to the

existing examples of medication errors occurring in the context of labelled interactions.

The sub-section name:

3.15.1.3 Medication errors in the context of labelled interactions

Was changed as follows:

3.15.1.3 Medication monitoring errors

New wording and an Example table were added to the beginning of the sub-section as follows (note the addition of a Concept Description for medication monitoring error):

> 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 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

The previous Example table in this sub-section:

Example

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

Was changed as follows (in the fourth example, note the addition of the event of wheezing and the addition of a reference to the Concept Description):

Example

Reported	LLT Selected	Comment
Patient became pregnant whilst taking an antifungal drug and an oral contraceptive	Labelled drug-drug interaction medication error Pregnancy on oral contraceptive	Interaction must be stated in product data sheet (see also Section 3.20)
Patient drank grapefruit juice whilst taking a calcium channel blocker	Labelled drug-food interaction medication error	Product is labelled for grapefruit juice interaction
Patient with renal failure is prescribed a drug that is contraindicated in renal failure	Labelled drug-disease interaction medication error	
Patient with known sulfa allergy is administered a sulfonamide-based drug and experienced wheezing	Documented hypersensitivity to administered drug Wheezing	See Concept Description in Appendix B of the MedDRA Introductory Guide

3.16.4 Drug diversion

The wording in this section:

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

Was changed as follows (note the deletion of text at the end of the sentence):

> 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.

The Example table:

Example

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

Was changed as follows (note the change to the LLT Selected in the second example):

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 Inadvertent exposure to drug

3.18 – Overdose, Toxicity and Poisoning

A second paragraph was added to this section:

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

As follows:

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

The Example table:

Example

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

Was changed as follows (note changes to the third example):

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

3.27.2 Off label use when reported with an AR/AE

The text in the first sentence of this section:

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

Was changed as follows:

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

The Example table:

Example

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

Was changed as follows (for clarity, the terms listed in the LLT Selected column follow the order in which they are listed in the Reported column):

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

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

The Example table:

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

Was changed as follows (note change to the third example):

Reported	LLT Selected
New bottle of drug tablets have unusual chemical smell that made me nauseous	Product odour abnormal Nauseous
I switched from one brand to another of my blood pressure medication, and I developed smelly breath	Product substitution issue brand to brand Smelly breath
Consumer noted that the toothpaste they had purchased did not taste like normal. Subsequent investigation of the product lot number revealed that the toothpaste was a counterfeit product.	Product counterfeit Product taste abnormal

4.3.1 Current members of the ICH Points to Consider Working Group

The table of current members was replaced and updated as follows:

Affiliation	Member
Commission of the European Communities	Maria Luisa Casini
	Sarah Vaughan
European Federation of Pharmaceutical Industries and Associations	Hilary Vass*
	Christina Winter†
Health Canada	Polina Ostrovsky
	Lynn Macdonald
Japanese Maintenance Organization	Yutaka Nagao
	Kazuyuki Sekiguchi
	Mitsuru Takano
	Reiji Tezuka
Japan Pharmaceutical Manufacturers Association	Yo Tanaka
	Hitomi Takeshita
MedDRA MSSO	Judy Harrison
Ministry of Health, Labour and Welfare/Pharmaceuticals and Medical Devices Agency	Yuhei Fukuta
	Miki Ohta
	Daisuke Sato
	Makiko Isozaki
Pharmaceutical Research and Manufacturers of America	Milbhor D'Silva
	JoAnn Medbery
US Food and Drug Administration	Sonja Brajovic#
	Christopher Breder
Ministry of Food and Drug Safety, Korea	YuBin Lee
	Kyung-Eun Yoon

* Current Rapporteur
\# Regulatory Chair
† Former Rapporteur

4.3.2 Former members of the ICH Points to Consider Working Group

The table of former members was replaced and updated as follows:

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

† Former Rapporteur