Summary of Changes to

MedDRA® TERM SELECTION: POINTS TO CONSIDER

ICH-Endorsed Guide for MedDRA Users

Release 4.6
Based on MedDRA Version 16.1

1 October 2013

The following is a listing of changes made between releases 4.5 and 4.6 of *MedDRA Term Selection: Points to Consider*:

Throughout document

1) Correction of general spelling, punctuation, spacing, and format errors
2) Replacement of references to MedDRA Version 16.0 to Version 16.1
3) Update of examples based on MedDRA version changes
4) Deletion of specific links in body of document; all links and references are now in Appendix, Section 4.2

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

A title row, "Summary of Preferred and Alternate Options", was added to the first table in this section and the text was changed from "Example 1", etc. to "See Example 1", etc.

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

MULTIPLE DIAGNOSES	
DEFINITIVE DIAGNOSES	**PROVISIONAL DIAGNOSES**
Multiple definitive diagnoses without signs/symptoms • Multiple diagnoses (only possible option)	**Multiple provisional diagnoses without signs/symptoms** • Multiple provisional diagnoses (only possible option)
Multiple definitive diagnoses with signs/symptoms • **Preferred:** Multiple diagnoses only • Alternate: Diagnoses and signs/symptoms ***Note: Always include signs/symptoms not associated with diagnosis*** **SEE EXAMPLE 3**	**Multiple provisional diagnoses with signs/symptoms** • **Preferred:** Multiple provisional diagnoses and signs/symptoms • Alternate: Signs/symptoms only ***Note: Always include signs/symptoms not associated with diagnosis*** **SEE EXAMPLE 4**

A title row, “Examples”, was added to the second table in this section as follows:

EXAMPLES			
Example	**Reported**	**LLT Selected**	**Preferred Option**
1	Anaphylactic reaction, rash dyspnea, hypotension, and laryngospasm	Anaphylactic reaction	✓
		Anaphylactic reaction Rash Dyspnea Hypotension Laryngospasm	
2	Possible myocardial infarction with chest pain, dyspnea, diaphoresis	Myocardial infarction Chest pain Dyspnea Diaphoresis	✓
		Chest pain Dyspnea Diaphoresis	

EXAMPLES			
Example	**Reported**	**LLT Selected**	**Preferred Option**
3	Pulmonary embolism, myocardial infarction, and congestive heart failure with chest pain, cyanosis, shortness of breath, and blood pressure decreased	Pulmonary embolism Myocardial infarction Congestive heart failure	✓
		Pulmonary embolism Myocardial infarction Congestive heart failure Chest pain Cyanosis Shortness of breath Blood pressure decreased	
4	Chest pain, cyanosis, shortness of breath, and blood pressure decreased. Differential diagnosis includes pulmonary embolism, myocardial infarction, and congestive heart failure	Pulmonary embolism Myocardial infarction Congestive heart failure Chest pain Cyanosis Shortness of breath Blood pressure decreased	✓
		Chest pain Cyanosis Shortness of breath Blood pressure decreased	
Always include signs/ symptoms not associated with diagnosis	Myocardial infarction, chest pain, dyspnea, diaphoresis, ECG changes and jaundice	Myocardial infarction Jaundice (note that jaundice is not typically associated with myocardial infarction)	

3.6.2 No available MedDRA term includes both age and event information

The Example table in this section:

Example

Reported	LLT Selected	Preferred Option	Comment
Pancreatitis in a newborn	Pancreatitis	✓	Record patient age in a demographic field
	Pancreatitis		In addition, LLT *Neonatal disorder* can be selected

Was changed as follows (note the addition of another LLT Selected and a modification to the comment in the alternate option):

Example

Reported	LLT Selected	Preferred Option	Comment
Pancreatitis in a newborn	Pancreatitis	✓	Record patient age in a demographic field
	Pancreatitis Neonatal disorder		Record patient age in a demographic field. In addition, select LLT *Neonatal disorder*.

3.9 – Modification of Pre-existing Conditions

The wording and second table in this section:

If no such term exists, consider these options (Note: keep in mind possible database limitations):

- Option 1: Select a term for the pre-existing condition and record the modification in a consistent, documented way (narrative, check box on data collection form, etc.)

- Option 2: Select a term for the pre-existing condition **and** a second term for the modification of the condition (e.g., LLT *Condition aggravated*, LLT *Disease progression*)

Example

Options	Reported	LLT Selected	Comment
Option 1	Halitosis worsened	Halitosis	Record "worsened" in a consistent, documented way (e.g., check box on data collection form)
Option 2	Progression of Addison's disease	Disease progression Addison's disease	Use 2 terms to record pre-existing condition and modification
	Jaundice aggravated	Condition aggravated Jaundice	

Were changed as follows (note the wording change from "option" to "example" and the use of a single reported term, "Jaundice aggravated" to illustrate both approaches):

If no such term exists, consider these approaches:

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

Example

Examples	Reported	LLT Selected	Comment
Example 1	Jaundice aggravated	Jaundice	Record "aggravated" in a consistent, documented way
Example 2	Jaundice aggravated	Jaundice Condition aggravated	Record "aggravated" in a consistent, documented way. Select terms for the pre-existing

Examples	Reported	LLT Selected	Comment
			condition and the modification.

3.15.2.1 Accidental exposures

The Example table in this section:

Example

Reported	LLT Selected
Child accidentally took grandmother's pills and experienced projectile vomiting	Accidental drug intake by child Vomiting projectile
Father applying topical steroid to his arms accidentally exposed his child to the drug by carrying her	Exposure via skin contact

Was changed as follows (note addition of LLT *Accidental exposure to product by child* in the second example and addition of a comment):

Example

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

3.16.2 Abuse

The wording in the first sentence in this section:

For the purposes of term selection and analysis of MedDRA-coded data, **abuse** is the intentional, non-therapeutic use of a product – over-the counter or prescription – for a perceived reward or desired non-therapeutic effect including, but not limited to, “getting high”.

Was changed as follows (note “(euphoria)” was added after “getting high”):

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

3.16.3 Addiction

The Example table in this section:

Example

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

Was changed as follows (note the change for the first LLT Selected):

Example

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

3.17 – Transmission of Infectious Agent via Product

The wording and Example table in this section:

If a report of transmission of an infectious agent via medicinal product is received, select a term for the transmission. If the infection is identified, select a

second term for the specific infection; if appropriate, a product quality issue term can also be selected. (See Section 3.28).

Example

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

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

Were changed as follows (note the deletion of the word “medicinal”):

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

Example

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

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

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

The wording and Example table in this section:

If an overdose report specifically states that there were no clinical consequences, select LLT *Overdose* and the additional LLT *No adverse effect* can be selected. (See Section 3.21).

Example

Reported	LLT Selected	Comment
Patient received an overdose of medicine without any adverse consequences	Overdose No adverse effect	LLT *No adverse effect* can also be selected

Were changed as follows (note that a preferred option – to select only a term for the overdose – is now identified):

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

Example

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

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4.2 – Links and References

The table of links and references in this section was replaced as follows:

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

- MedDRA Introductory Guide
- MedDRA Change Request Information document
- MedDRA Web-based Browser

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

* Requires user ID and password to access

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

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

† Former Rapporteur