Summary of Changes to

**MedDRA® TERM SELECTION:
POINTS TO CONSIDER**

**ICH-Endorsed Guide for MedDRA Users**

***Release 4.9***

***Based on MedDRA Version 18.0***

**1 March 2015**

The following is a listing of changes made between releases 4.8 and 4.9 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 17.1 to Version 18.0
3. Update of examples based on MedDRA version changes

**2.4 – Always Select a Lowest Level Term**

The Example table:

Example

| **Reported** | **LLT Selected** |
| --- | --- |
| Lip sore | Lip sore (PT Lip pain) |
| Lip sore**s** | Sores lip (PT Cheilitis) |
| Sore gums | Sore gums (PT Gingival pain) |
| Sore**s** gum | Sores gum (PT Gingival inflammation) |

Was changed as follows (note the change of PT *Gingival inflammation* to PT *Noninfective gingivitis*, related to MedDRA version changes):

Example

| **Reported** | **LLT Selected** |
| --- | --- |
| Lip sore | Lip sore (PT *Lip pain*) |
| Lip sore**s** | Sores lip (PT *Cheilitis*) |
| Sore gums | Sore gums (PT *Gingival pain*) |
| Sore**s** gum | Sores gum (PT *Noninfective gingivitis*) |

**3.3.2** **If self-injury is reported**

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 |
| Took an overdose in an attempt to commit suicide | Intentional overdoseSuicide 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) |

Was changed as follows (note that Self inflicted laceration has been moved from the Comment column to the LLT Selected column for the second example):

Example

| **Reported** | **LLT Selected** | **Comment** |
| --- | --- | --- |
| Self slashing | Self inflicted laceration | LLT *Self inflicted laceration* is linked to PT *Intentional* *self-injury* |
| Cut her own wrists |
| Cut wrists in a suicide attempt | Self inflicted lacerationSuicide attempt | .  |
| Took an overdose in an attempt to commit suicide | Intentional overdoseSuicide 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) |

**3.10.1 Events in the mother**

There were several changes made to this section of the document to provide examples of term selection and to identify a preferred option for exposures without clinical consequences.

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

**3.10.1 Events in the mother**

3.10.1.1. Pregnant patient exposed to medication with clinical consequences

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

Example

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

 3.10.1.2 Pregnant patient exposed to medication without clinical consequences

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

Example

| **Reported** | **LLT Selected** | **Preferred Option** |
| --- | --- | --- |
| Patient received drug X while pregnant (no adverse effect) | Maternal exposure during pregnancy | **✓** |
| Maternal exposure during pregnancyNo adverse effect |  |

**3.15 – Medication Errors, Accidental Exposures and Occupational Exposures**

There were several changes made to this section of the document to provide examples of term selection and to identify a preferred option for medication errors and potential medication errors without clinical consequences.

First, the section name:

**3.15 – Medication Errors/Administration Errors, Accidental Exposures and Occupational Exposures**

Was changed as follows:

**3.15 – Medication Errors, Accidental Exposures and Occupational Exposures**

Second, the section name:

**3.15.1 Medication/administration errors**

Was changed as follows:

**3.15.1 Medication errors**

3.15.1.1 Medication errors reported with clinical consequences

The Example table:

Example

| **Reported** | **LLT Selected** | **Comment** |
| --- | --- | --- |
| Patient was administered wrong drug and experienced hypotension | Wrong drug administeredHypotension |  |
| Because of similar sounding drug names, the patient took the wrong drug and experienced a rash | Drug name confusionWrong drug administeredRash |  |
| Insulin was given using the wrong syringe resulting in the administration of an overdose. The patient developed hypoglycaemia. | Wrong device usedAccidental overdoseHypoglycaemia | 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) |

Was changed as follows (note the changes and the addition of a comment to the second example):

Example

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

3.15.1.2 Medication errors and potential medication errors reported without clinical consequences

The wording and Example tables in this section:

Medication errors without clinical consequences are not ARs/AEs. However, it is important to record the occurrence or **potential** occurrence of a medication error. Select a term that is closest to the description of medication error reported.

Also, if specifically reported that no adverse effect has occurred, it is acceptable to select LLT *No adverse effect*.

In instances where the medication did not reach the patient, it is acceptable to select LLT *Drug not taken in context of intercepted medication error*.

Example

| **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 routeNo 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 confusionCircumstance 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 |  |

Were changed as follows (note that a preferred option – to select only a term for the medication error – is now identified and examples of intercepted medication errors have been deleted):

Medication errors without clinical consequences are not ARs/AEs. However, it is important to record the occurrence or **potential** occurrence of a medication error. Select a term that is closest to the description of medication error reported.

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

Example

| **Reported** | **LLT Selected** | **Preferred Option** |
| --- | --- | --- |
| Medication was given intravenously instead of intramuscularly without sequelae | Intramuscular formulation administered by other route | **✓** |
| Intramuscular formulation administered by other routeNo adverse effect |  |

Example

| **Reported** | **LLT Selected** | **Comment** |
| --- | --- | --- |
| Pharmacist notices that the names of two drugs are similar and is concerned that this may result in a medication error | Drug name confusionCircumstance or information capable of leading to medication error  | Note: this example is a potential medication error and LLT *Drug name confusion* provides additional information about the nature of the potential medication error |
| Drug inadvertently administered. The error was noticed soon afterwards. | Drug administration error |  |

3.15.1.3 Medication monitoring errors

The 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.

Was changed as follows (note the addition of the word “monitoring” in the second sentence. This concept description has also been updated in the MedDRA Introductory Guide and the Web-Based Browser):

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

The wording and term examples for medication errors in the context of labelled interactions:

If the label describes **known effects** when the product is co-administered with specific drugs, with specific foods, or to patients with specific disease states, then select a medication error term for the type of interaction, such as those listed below:

| **Medication Error Terms – Labelled Interactions** |
| --- |
| Labelled drug-drug interaction medication errorLabelled drug-food interaction medication errorLabelled drug-disease interaction medication errorDocumented hypersensitivity to administered drug |

Were changed as follows (note the change of Documented hypersensitivity to administered drug to Documented hypersensitivity to administered product – a new term added in MedDRA Version 18.0):

If the label describes **known effects** when the product is co-administered with specific drugs, with specific foods, or to patients with specific disease states, and if the report does not indicate that this is intentional misuse or intentional off label use, then select a medication error term for the type of interaction, such as those listed below:

| **Medication Error Terms – Labelled Interactions** |
| --- |
| Labelled drug-drug interaction medication errorLabelled drug-food interaction medication errorLabelled drug-disease interaction medication errorDocumented hypersensitivity to administered product |

3.15.1.4 Do not infer a medication error

The Example table:

| **Reported** | **LLT Selected** | **Comment** |
| --- | --- | --- |
| Antibiotic was prescribed for a week, and the patient stopped treatment after 2 days because of bitter taste | Prescribed dosing duration not completedTaste bitter | LLT *Taste bitter* represents a sensory perception issue. LLT *Medication after taste* refers to a product quality issue |
| Incorrect dosing by patient | Incorrect dose administered | Do not select *Extra dose administered* or *Overdose* based on this information alone |
| Patient took only half the prescribed dose | Underdose |  |

## Was changed as follows (note the deletion of the first two examples and the addition of a comment to the underdose example):

Example

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

## 3.16 – Misuse, Abuse and Addiction

The table and wording in this section:

| **Concept** | **Intentional?** | **By Whom?** | **Therapeutic Use?** | **Additional Sections in this Document** |
| --- | --- | --- | --- | --- |
| Misuse | Yes | Patient/consumer | Yes | 3.16.1 |
| Abuse | Yes | Patient/consumer | No | 3.16.2 |
| Addiction | Yes | Patient/consumer | No | 3.16.3 |
| Medication error | No | Patient/consumer **or** healthcare provider | Yes | 3.15 |
| Off label use | Yes | Healthcare provider | Yes | 3.27 |

Was changed as follows (note the addition of a footnote regarding the definitions of misuse and additional wording regarding term selection):

| **Concept** | **Intentional?** | **By Whom?** | **Therapeutic Use?** | **Additional Sections in this Document** |
| --- | --- | --- | --- | --- |
| Misuse | Yes | Patient/consumer | Yes\* | 3.16.1 |
| Abuse | Yes | Patient/consumer | No | 3.16.2 |
| Addiction | Yes | Patient/consumer | No | 3.16.3 |
| Medication error | No | Patient/consumer **or** healthcare provider | Yes | 3.15 |
| Off label use | Yes | Healthcare provider | Yes | 3.27 |

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

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

**3.16.1 Misuse**

The Example table:

Example

| **Reported** | **LLT Selected** |
| --- | --- |
| Patient deliberately ingested the topical medication | Intentional use by incorrect route  |
| Patient deliberately took the medication for two days longer than instructed on the product label | Intentional use beyond labelled duration |

Was changed as follows (note the deletion of the first example and change to the second example):

Example

| **Reported** | **LLT Selected** |
| --- | --- |
| Patient deliberately took the medication twice daily instead of once daily | Intentional misuse in dosing frequency |

## 3.18 – Overdose, Toxicity and Poisoning

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 poisoningChemical 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 |

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

## Example

| **Reported** | **LLT Selected** | **Comment** |
| --- | --- | --- |
| Patient took an overdose  | Overdose | Based on this report, it is not known whether the overdose is intentional or accidental. If information is available, select the more specific LLT *Accidental overdose* or LLT *Intentional overdose* as appropriate. |
| A child was accidentally poisoned when she ingested a chemical cleaning product | Accidental poisoningChemical poisoning |  |
| Patient deliberately took an overdose of analgesic pills to treat his worsening arthritis  | Intentional overdose | LLT *Arthritis aggravated* can be selected as the indication for treatment |
| The dose taken was above the recommended maximum dose in the label | Overdose | Based on this report, it is not known whether the overdose is intentional or accidental. If information is available, select the more specific LLT *Accidental overdose* or LLT *Intentional overdose* as appropriate. |
| Nurse inadvertently administered an additional vaccine dose to an already vaccinated child | Inappropriate dose of vaccine administered | Please note that LLT *Inappropriate dose of vaccine administered* is a maladministration term, not specifically an overdose term |

## 3.19.2 Device-related event reported without clinical consequences

The Example table:

Example

| **Reported** | **LLT Selected** |
| --- | --- |
| Medical device breakage | Device breakage |
| My patch is leaking on my arm | Leaking patch |
| My patch is not sticking to my skin | Medicinal patch adhesion issue |

Was changed as follows (note the deletion of the third example):

Example

| **Reported** | **LLT Selected** |
| --- | --- |
| Medical device breakage | Device breakage |
| My patch is leaking on my arm | Leaking patch |

## 3.27 – Off Label Use

The wording in this section:

The concept of “off label use” relates to situations where the product is intentionally used for a medical purpose not in accordance with the authorised product information.

Was changed as follows (note the addition of a second sentence):

The concept of “off label use” relates to situations where the product is intentionally used for a medical purpose not in accordance with the authorised product information. When recording off label use, consider that product information and/or regulations/requirements may differ between regulatory regions.

## 3.27.1 Off label use when reported as an indication

The wording in this section:

If a medical condition is reported as an indication **along with “off label use”**, the **preferred option** is to select terms for the medical condition and LLT *Off label* use or other appropriate LLTs linked to PT *Off label use*. Alternatively, select a term for the medical condition/indication alone*.* Select LLT *Off label use* alone **only** if it is the only information available.

Was changed as follows (note the use of “medical condition/indication” to indicate that these are the same concept):

If a medical condition/indication is reported **along with “off label use”**, the **preferred option** is to select terms for the medical condition/indication and off label use. Alternatively, select a term for the medical condition/indication alone*.* Select LLT *Off label use* alone **only** if it is the only information available.

The Example table:

Example

| **Reported** | **LLT Selected** | **Comment** |
| --- | --- | --- |
| Used off label | Off label use |  |
| Off label use in paediatric patients | Drug use in unapproved population | Refers to a population of patients |
| Drug X given to a 10 year old boy; the drug is not indicated for use below 18 years | Adult product administered to child | LLT *Adult product administered to child* is linked to PT *Off label use* |

Was changed as follows (note the deletion of the second and third examples):

Example

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

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

The wording in this section:

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.

Was changed as follows (note the use of “medical condition/indication” to indicate that these are the same concept):

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

## 3.28.1 Product quality Issue reported with clinical consequences

The Example table:

Example

| **Reported** | **LLT Selected** |
| --- | --- |
| New bottle of drug tablets have unusual chemical smell that made me nauseous | Product odour abnormalNauseous |
| I switched from one brand to another of my blood pressure medication, and I developed smelly breath | Product substitution issue brand to brandSmelly 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 counterfeitProduct taste abnormal |

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

Example

| **Reported** | **LLT Selected** |
| --- | --- |
| New bottle of drug tablets have unusual chemical smell that made me nauseous | Product odour abnormalNauseous |
| I switched from one brand to another of my blood pressure medication, and I developed smelly breath | Product substitution issue brand to brandSmelly breath |
| Consumer noted that the toothpaste they had purchased caused a stinging sensation in the mouth. Subsequent investigation of the product lot number revealed that the toothpaste was a counterfeit product. | Product counterfeitStinging mouth |

## 3.28.3 Product quality Issue vs. medication error

The Example table:

Example

| **Reported** | **LLT Selected** | **Comment** |
| --- | --- | --- |
| Pharmacist dispensing Drug A inadvertently attached a product label for Drug B | Wrong label placed on medication during dispensing | Medication error |
| The drug store clerk noted that the wrong product label was attached to some bottles in a shipment of mouthwash | Product label on wrong product | Product quality issue |
| The mother administered insufficient amount of prescribed antibiotic because the lines on the dropper were hard to read | Product dropper calibration unreadableInsufficient dosage | Product quality issue and medication error |

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

Example

| **Reported** | **LLT Selected** | **Comment** |
| --- | --- | --- |
| Pharmacist dispensing Drug A inadvertently attached a product label for Drug B | Wrong label placed on medication during dispensing | Medication error |
| The drug store clerk noted that the wrong product label was attached to some bottles in a shipment of mouthwash | Product label on wrong product | Product quality issue |
| The mother administered an underdose of antibiotic because the lines on the dropper were hard to read | Product dropper calibration unreadableAccidental underdose | Product quality issue and medication error.If underdose is reported in the context of a medication error, the more specific LLT *Accidental underdose* can be selected. |

## 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  |
| Kavita Chadda |
| European Federation of Pharmaceutical Industries and Associations | Hilary Vass\* |
| Christina Winter† |
| Health Canada | Alison Bennett |
| 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 |
| Kiyomi Ueno |
| 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 |
| World Health Organization | Daisuke Tanaka |

\* 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; Sarah Vaughan |
| European Federation of Pharmaceutical Industries and 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; 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