

Implemented MedDRA Version 20.0 Complex Changes

(December 2016)



1. Proposed revisions to the medication error and product use issues hierarchies

Two options for revisions to the medication error and product use issues hierarchies are presented for user comment. The first option, 1.a, is the MSSO's recommended option as it addresses issues raised by users concerning the current hierarchy. Various expert groups provided input to the MSSO and support posting this option for user feedback. The alternate option, 1.b, represents a modification of the current hierarchy and is presented for purposes of comparison.

1.a Recommended option

The proposed hierarchy is shown in the table below. To aid users in understanding the impact in more detail, a spreadsheet showing the proposed hierarchy populated with existing PTs from MedDRA Version 19.0 can be downloaded from [here](#). This detailed spreadsheet represents only an overview of potential changes as applied to MedDRA v19.0 PTs and does not consider placement of LLTs. Once the proposals are finalized and approved, the HLGTS and HLTs will be populated with appropriate PTs and LLTs for MedDRA Version 20.0.

Primary SOC	HLGT	HLT	Notes
Injury, poisoning and procedural complications	Medication errors and other product use errors and issues		New HLGTS
		Accidental exposures to product	
		Medication errors, product use errors and issues NEC	New HLT
		Product administration errors and issues	New HLT
		Product confusion errors and issues	New HLT
		Product dispensing errors and issues	New HLT
		Product monitoring errors and issues	New HLT

	New
	Existing

Primary SOC	HLGT	HLT	Notes
		Product preparation errors and issues	New HLT
		Product prescribing errors and issues	New HLT
		Product selection errors and issues	New HLT
		Product storage errors and issues in the product use system	New HLT. Represents storage issues by end-users such as pharmacists, patients, etc. Distinct from storage issues during manufacturing or distribution phases; these concepts are in SOC <i>Product issues</i> .
		Product transcribing errors and communication issues	New HLT. New area to be expanded with additional terms.
		Off label uses and intentional product misuses/use issues	New HLGT. <i>The original proposal for this HLGT was HLGT Off label uses, intentional product misuses and intentional product use issues. The name was adjusted based on MedDRA user feedback</i>
		Off label uses	
		Intentional product misuses	New HLT
		Intentional product use issues	New HLT
	Overdoses and underdoses NEC		New HLGT
		Overdoses NEC	
		Underdoses NEC	

Rationale:

- Addition of HLGT *Product use issues* in v18.0 has caused confusion for some users
- The current hierarchy forces a distinction between medication errors and product use issues, but there may be an overlap between these concepts
 - Some terms in HLGT *Medication errors* don't specify error or accidental

- There are neutral terms in HLT *Product use issues NEC* that could represent medication errors, misuse, or off label use depending on the circumstances, e.g., Drug administered to patient of inappropriate age

Advantages of revision:

- By grouping errors and issues, terms, particularly “neutral” ones, would not be force-classified as medication errors vs. product use issues by their placement in the hierarchy as is the current situation
- Terms for intentional concepts such as off label use, misuse and intentional product use would be separated from errors and “neutral” or unspecified product use issues
- Unspecified and intentional overdose and underdose concepts would be in a separate HLGTT from accidental and other intentional concepts
- By using the word “product” in grouping term names, they can accommodate not only medication, i.e., drug concepts, but other types of product concepts such as the device use and error PTs currently in HLT *Device issues NEC* in SOC *Product issues*
- HLT *Device issues NEC* in SOC *Product issues* will only contain terms for issues relating to the device itself, the device use and error terms having been moved to the new product use errors and issues hierarchy
- Errors and issues can be classified according to the stage in the medication/product process. (Prescribing, storage in clinical practice, dispensing, preparation for administration, and administration. See EMA [Good Practice Guide on Recording, Coding, Reporting and Assessment of Medication Errors](#). Section 5.5.1.)
- HLT *Intercepted medication errors* would be removed and the intercepted medication errors terms would be moved under the relevant stage HLTs
- There are other mechanisms for identifying concepts besides relying on the hierarchy
 - In the future, E2B R3 will have code lists for Additional information on drug – G.k.10.r
 - Include: medication error, misuse, off label use, overdose
 - SMQ *Medication errors* can aid in identifying potential medication error cases independent of the hierarchy

Implementation Status: The revisions to the medication error and product use issues hierarchies will be implemented as proposed in the recommended option 1a with one exception. Based on MedDRA user feedback, the proposed HLGTT *Off label uses, intentional product misuses and intentional product use issues* will be added as HLGTT *Off label uses and intentional product misuses/use issues*.

1.b Alternate option



This alternate option represents modifications to the existing hierarchy as suggested by MedDRA users with the following features:

- Maintain separate HLG *Medication errors* and HLG *Product use issues*
- Add stages of the medication process to HLG *Medication errors* (Prescribing, storage in clinical practice, dispensing, preparation for administration, and administration. See EMA [Good Practice Guide on Recording, Coding, Reporting and Assessment of Medication Errors](#).)
- Remove existing HLT *Intercepted medication errors* and move the PTs to the appropriate stage HLTs
- Add stage of product use process to HLT *Product use issues* where appropriate
- Where possible, move PTs that do not explicitly mention error, accidental, or otherwise imply a medication error from HLG *Medication errors* to HLG *Product use issues*

Considerations

- The names of the HLG *Medication errors* and some of its HLTs which specify “medication” do not reflect the contents; there are PTs referring to the broader concept of “product” as well as “device” PTs
- The separation of medication errors and product use issues does not address users’ concerns with appropriate coding and retrieval of overlapping concepts
- It is difficult to determine the appropriate placement of some terms that don’t explicitly mention or infer a medication error. For example, PT *Counterfeit drug administered* may refer to a situation where the drug was taken in error or intentionally.
- The word “wrong” such as in PT *Wrong drug administered* has different meanings in different languages. In some languages, it implies “in error” but in other languages it has a neutral meaning.

The proposed revisions to the existing hierarchy are shown in the table below. To aid users in understanding the impact in more detail, a spreadsheet showing the proposed revisions based on existing PTs in MedDRA Version 19.0 can be downloaded from [here](#). This detailed spreadsheet represents only an overview of potential changes as applied to MedDRA v19.0 PTs and does not consider placement of LLTs. Terms for which it is difficult to determine placement are highlighted in the spreadsheet.

Primary SOC	HLGT	HLT	Notes
Injury, poisoning and procedural complications	Medication errors		
		Accidental exposures to product	
		Medication prescribing errors	New HLT
 New  Existing		Medication dispensing errors	New HLT
		Medication administration errors	New HLT
		Medication preparation errors	New HLT
		Medication errors NEC	
		Medication storage errors in medication use system	New HLT. Represents storage issues by end-users such as pharmacists, patients, etc. Distinct from storage issues during manufacturing or distribution phases; these concepts are in SOC <i>Product issues</i> .
		Medication monitoring errors	
			New HLT. Represents storage issues by end-users such as pharmacists, patients, etc. Distinct from storage issues during manufacturing or distribution phases; these concepts are in SOC <i>Product issues</i> .
	Product use issues		
		Product administration issues	New HLT for product administration issues. There are no PTs for product dispensing, prescribing issues, etc. so no HLTs are needed for these stages.
		Product use issues NEC	
		Overdoses NEC	
		Underdoses NEC	
		Off label uses	

Implementation Status: The revisions to the medication error and product use issues hierarchies will be implemented as proposed in the recommended option 1a with one exception. Based on MedDRA user feedback, the proposed HLG *Off label uses, intentional product misuses and intentional product use issues* will be added as HLG *Off label uses and intentional product misuses/use issues*.

MedDRA User Submitted Requests:

2. Replace HLT *Accidental exposures to product* with HLT *Accidental exposures to medication*

Submitter rationale: Currently HLT *Accidental exposures to product* is placed under HLT *Medication errors*. However "product" is a wide concept which contains not only drugs but also medical devices. Therefore this HLT should be renamed to more appropriate wording. If the HLT is not renamed, it could move from HLT *Medication errors* to HLT *Exposures, chemical injuries and poisoning*.

Terminology Impact: If approved, HLT *Accidental exposures to product* would be replaced by HLT *Accidental exposures to medication*; however, the underlying PTs would still refer to "product" or "device". If moved from HLT *Medication errors* to HLT *Exposures, chemical injuries and poisoning*, the PT concepts in the HLT which all refer to accidental product or device exposures would be separated from other medication/product error and use issue terms.

Note that this request is impacted by the set of complex change proposals to revise the medication error and product use issues hierarchies discussed in item 1. Under option 1a, the recommended option, HLT *Accidental exposures to product* would be added to new HLT *Medication errors and other product use errors and issues* in SOC *Injury, poisoning and procedural complications*. HLT *Medication errors* and HLT *Product use issues* would be merged under new HLT *Medication errors and other product use errors and issues*. Thus, the new HLT would cover both medication errors and the broader concept of product use errors; HLT *Accidental exposures to product* would not need to be renamed. Option 1b, the alternate option, would keep HLT *Accidental exposures to product* under HLT *Medication errors* in SOC *Injury, poisoning and procedural complications*.

Implementation Status: This proposal will not be approved. This request is impacted by the set of complex change revisions to the medication error and product use issues hierarchies. See option 1a above. HLT *Accidental exposures to product* will be moved to new HLT *Medication errors and other product use errors and issues* in SOC *Injury, poisoning and procedural complications*. HLT *Medication errors* and HLT *Product use issues* will be merged under new HLT *Medication errors and other product use errors and issues*. Thus, the new HLT *Medication errors and other product use errors and issues* would cover both medication errors and the broader concept of product use errors and therefore HLT *Accidental exposures to product* would not need to be replaced with a new HLT *Accidental exposures to medication*.

3. Move HLT *Upper respiratory tract signs and symptoms* from HLGT *Respiratory disorders NEC* to HLGT *Upper respiratory tract disorders (excl infections)*

Move HLT *Lower respiratory tract signs and symptoms* from HLGT *Respiratory disorders NEC* to HLGT *Lower respiratory tract disorders (excl obstruction and infection)*

Submitter rationale: These HLT are linked to an unnecessary general HLGT as there are more specific HLGTs available which reflects "Upper respiratory tract" and "Lower respiratory tract".

Terminology Impact: Currently all three "respiratory tract signs and symptoms" HLTs – HLT *Lower respiratory tract signs and symptoms*, HLT *Respiratory signs and symptoms NEC* and HLT *Upper respiratory tract signs and symptoms* reside under HLGT *Respiratory disorders NEC*. If approved, the three "respiratory tract signs and symptoms" HLTs would be represented together with respiratory disorders under three different HLGTs – HLGT *Respiratory disorders NEC*, HLGT *Upper respiratory tract disorders (excl infections)*, and HLGT *Lower respiratory tract disorders (excl obstruction and infection)*.

Note: In MedDRA, disorders are generally separated from signs and symptoms because there is not always a clear association between the two concepts. The MSSO proposal would be to add a new HLGT *Respiratory tract signs and symptoms* to include the following HLTs: HLT *Upper respiratory tract signs and symptoms*; HLT *Lower respiratory tract signs and symptoms*; HLT *Respiratory signs and symptoms NEC*. This would be consistent with the HLGT groupings in SOC *Cardiac disorders*, SOC *Gastrointestinal disorders*, and SOC *Renal and urinary disorders* where signs and symptoms are separated from disorder concepts at the HLGT level.

Implementation Status: This request will be implemented, but not as requested. In MedDRA, disorders are generally separated from signs and symptoms because there is not always a clear association between the two concepts. Based on this convention, the MSSO will add new HLGT *Respiratory tract signs and symptoms* to include the following HLTs: HLT *Upper respiratory tract signs and symptoms*; HLT *Lower respiratory tract signs and symptoms*; HLT *Respiratory signs and symptoms NEC*. These changes are consistent with the HLGT groupings in SOC *Cardiac disorders*, SOC *Gastrointestinal disorders*, and SOC *Renal and urinary disorders* where signs and symptoms are separated from disorder concepts at the HLGT level.

4. Add New HLT *Extended-spectrum beta-lactamase-producing bacteria infection* to HLGT *Bacterial infectious disorders* in SOC *Infections and infestations*

Submitter rationale: This is a growing clinical issue due to antibiotic resistance mechanisms and limited treatment options for the patients.

Terminology Impact: New LLT *Extended-spectrum beta-lactamase-producing bacteria infection* has been added to PT *Pathogen resistance* in HLT *Infections NEC* in MedDRA Version 19.1.

Note: The HLT groupings in HLGT *Bacterial infectious disorders* are based on genus, e.g., HLT *Enterobacter infections*, HLT *Klebsiella infections*, etc. The proposed new HLT would introduce a separate grouping that is not based on genus. In addition, adding an HLT for Extended-spectrum beta-lactamase (ESBL)-producing bacteria infections (presumably with PT concepts for the specific genus such as ESBL *Klebsiella infection*) would lead to the introduction of combination terms and double representation of concepts.

In the current structure of MedDRA, the approach to coding a report of an ESBL infection would be to split code and select LLT *Extended-spectrum beta-lactamase-producing bacteria infection* and a term for the appropriate organism, e.g., LLT *Klebsiella infection*.

Implementation Status: This proposal will not be approved based upon further review and MedDRA user feedback. The HLT groupings in HLGT *Bacterial infectious disorders* are based on genus, e.g., HLT *Enterobacter infections*, HLT *Klebsiella infections*, etc. The proposed new HLT would introduce a separate grouping that is not based on genus. In addition, adding an HLT for Extended-spectrum beta-lactamase (ESBL)-producing bacteria infections (presumably with PT concepts for the specific genus such as ESBL *Klebsiella infection*) would lead to the introduction of combination terms and double representation of concepts.

The approach to coding a report of an ESBL infection would be to split code and select LLT *Extended-spectrum beta-lactamase-producing bacteria infection* and a term for the appropriate organism, e.g., LLT *Klebsiella infection*.

5. Add New HLT *Non-substance related addictions*

Submitter rationale Conditions that are not 'substance' related are bucketed into what we feel is an inappropriate HLT.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3164585/>

https://en.wikipedia.org/wiki/Behavioral_addiction

Terminology Impact: If approved, PT *Gambling disorder* would move from HLT Substance-related disorders to new HLT Non-substance related addictions.

Note: See a related request in item # 7 proposed by the MSSO to add HLT *Substance related and addictive disorders*

Implementation Status: This proposal will not be approved. Instead, a similar request proposed by the MSSO to add new HLT *Substance related and addictive disorders* to HLGT *Psychiatric disorders NEC* and merge existing HLT *Substance-related disorders* to new HLT *Substance related and addictive disorders* (see item # 7 of this document or change request # 2015324041) will be implemented. The definition of addictions was modified in the latest Diagnostic and Statistical Manual of Mental Disorders (DSM-V) to include not only substances but other addictive disorders such as gambling. Therefore, the existing HLT *Substance-related disorders* is no longer an appropriate grouping term for the expanded definition of addictive disorders.

6. Add New HLT *Structural valve deterioration* to HLGT *Cardiac valve disorders* in SOC *Cardiac disorders*

Submitter rationale: This will be a proper and consistent alignment for the LLT / PT of Structural Valve Deterioration. Also align this HLT secondarily to the PT *Aortic valve incompetence*, and PT *Aortic valve stenosis* (these are specific deterioration involving the operated valve, as occurs as during structural valve deterioration) and Device material Issue

Note: PT *Structural valve deterioration* was added in MedDRA Version 19.1. This PT is primary to HLT *Cardiac and vascular procedural complications* in SOC *Injury, poisoning and procedural complications*; secondary to HLT *Cardiac valve disorders NEC* in SOC *Cardiac disorders*.

Terminology Impact: There are several technical and medical considerations relating to this proposal. Firstly, groupings of procedure related complications are placed in SOC *Injury, poisoning and procedural complications*, not in the anatomical SOC; the PTs within the complications HLTs have links to HLTs in the anatomical SOC as appropriate. For example, new PT *Structural valve deterioration* and existing PT *Cardiac valve replacement complication* are linked to primary HLT *Cardiac and vascular procedural complications* in SOC *Injury, poisoning and procedural complications*; and secondary HLT *Cardiac valve disorders NEC* in SOC *Cardiac disorders*.

From a technical perspective, individual PTs cannot be linked to more than one HLT within an individual SOC. For example, PT *Aortic valve incompetence*, and PT *Aortic valve stenosis* could not be linked to both HLT *Aortic valve disorders* and a new HLT *Structural valve deterioration* in SOC *Cardiac disorders*.

From a medical perspective, PT *Aortic valve incompetence* and PT *Aortic valve stenosis* as stand-alone concepts generally refer to the native valve and don't necessarily refer to an issue with a prosthetic or repaired valve. The approach to capturing the specific results of valve deterioration would to be split code and select terms for both the specific valve defect (e.g., stenosis or incompetence) and the valve deterioration or valve replacement complication concept.

If a new HLT *Structural valve deterioration* were to be added, it would have to be in HLT *Cardiac and vascular procedural complications* and it would have to be named HLT *Structural valve deteriorations* to be consistent with MedDRA rules for plural concepts at the grouping term level to distinguish them from single concepts at the PT level.

Consideration should also be given as to whether the proposed HLT with only one PT *Structural valve deterioration* is too specific or whether the concept can be represented by the PT *Structural valve deterioration* in its placement in the broader HLT *Cardiac and vascular procedural complications*.

Implementation Status: This proposal will not be approved based upon further review and MedDRA user feedback. The submitter's rationale is that this change would be a proper and consistent alignment for the PT *Structural valve deterioration*. The proposal would also align this new HLT secondarily to the PT *Aortic valve incompetence* and PT *Aortic valve stenosis*.

The MSSO notes that individual PTs cannot be linked to more than one HLT within an individual SOC. For example, PT *Aortic valve incompetence*, and PT *Aortic valve stenosis* could not be linked to both HLT *Aortic valve disorders* and a new HLT *Structural valve deterioration* in SOC *Cardiac disorders*.

PT Structural valve deterioration is linked to HLTs two separate SOCs, not within the same SOC. It is primarily linked to HLT Cardiac and vascular procedural complications in SOC Injury, poisoning and procedural complications with a secondary link to HLT Cardiac valve disorders NEC in SOC Cardiac disorders.

7. Remove the secondary link of PT *Respiratory moniliasis* from HLT *Fungal lower respiratory tract infections* in SOC *Respiratory, thoracic and mediastinal disorders*

Submitter rationale: Mapping this way assumes a secondary HLT link of Fungal lower respiratory tract infections. 'Lower' RTI is not ALWAYS the case. For example, LLT *Candidiasis of trachea*, LLT *Candidiasis respiratory*, and LLT *Moniliasis respiratory system* are linked to PT *Respiratory moniliasis* and are therefore also hierarchically assumed to be of the lower respiratory tract because of the linkage. Suggestions: A new HLT *Fungal upper respiratory tract infections*, New LLT *Upper respiratory moniliasis* and LLT *Lower respiratory moniliasis*. If not approved then suggest the re-mapping of PT *Respiratory moniliasis* to secondary pathway HLT *Fungal respiratory infections NEC* so that neither upper or lower are specified.

Implementation Status: This request will be implemented, but not as requested. Rather than remove the secondary link of PT *Respiratory moniliasis* from HLT *Fungal lower respiratory tract infections*, the MSSO will move this PT to new HLT *Fungal upper respiratory tract infections* for a more specific grouping similar to bacterial and viral infection concepts. New HLT *Fungal upper respiratory tract infections* will be added under HLGT *Respiratory tract infections* in SOC *Respiratory, thoracic and mediastinal disorders* as a counterpart to the existing HLT *Fungal lower respiratory tract infections*. Furthermore, the following PTs will will be moved from HLT *Upper respiratory tract infections NEC* to the new HLT *Fungal upper respiratory tract infections*:

<i>PT Fungal pharyngitis</i>	<i>PT Fungal rhinitis</i>	<i>PT Fungal tracheitis</i>
<i>PT Laryngitis fungal</i>	<i>PT Oropharyngitis fungal</i>	<i>PT Sinusitis fungal</i>
<i>PT Tonsillitis fungal</i>	<i>PT Upper respiratory fungal infection</i>	

Also, LLT *Candidiasis of trachea* will be promoted to a PT under primary HLT *Candida infections* and secondary HLT *Fungal upper respiratory tract infections*.

MSSO Proposed Requests:

8. Add HLT *Substance related and addictive disorders* to HLGT *Psychiatric disorders NEC*

Merge HLT *Substance-related disorders* to HLT *Substance related and addictive disorders*

MSSO rationale: In the latest Diagnostic and Statistical Manual of Mental Disorders (DSM-V), the definition of addictions was modified to include not only substances but other additive disorders such as gambling. Therefore, the existing HLT *Substance-related disorders* is no longer an appropriate grouping term for the expanded definition of addictive disorders.

Terminology Impact: All PTs under HLT *Substance-related disorders* would be moved under new HLT *Substance related and addictive disorders*.

Note: See a related request in item # 5 proposed by a MedDRA user to add HLT *Non-substance related addictions*.

Implementation Status: This request will be implemented as proposed. In the latest Diagnostic and Statistical Manual of Mental Disorders (DSM-V), the definition of addictions was modified to include not only substances but other addictive disorders such as gambling. Therefore, the existing HLT *Substance-related disorders* is no longer an appropriate grouping term for the expanded definition of addictive disorders.

9. Merge existing HLTs – HLT *Sleep disorders related to another mental condition* and HLT *Sleep disorders due to general medical condition* to existing HLT *Sleep disorders NEC*

MSSO rationale: The concepts of Sleep disorders related to another mental condition and Sleep disorders due to general medical condition were removed from DSM-V. Therefore to better align MedDRA with DSM-V, the MSSO proposes to consolidate HLT *Sleep disorders related to another mental condition* and HLT *Sleep disorders due to general medical condition* to existing HLT *Sleep disorders NEC*.

Terminology Impact: The PTs under HLT *Sleep disorders related to another mental condition* and HLT *Sleep disorders due to general medical condition*

would be moved under existing HLT *Sleep disorders NEC*. See the information below.

- PTs moved from HLT *Sleep disorders due to general medical condition*:

PT *Sleep disorder due to a general medical condition*
PT *Sleep disorder due to general medical condition, hypersomnia type*
PT *Sleep disorder due to general medical condition, insomnia type*
PT *Sleep disorder due to general medical condition, mixed type*
PT *Sleep disorder due to general medical condition, parasomnia type*

- PT s move from HLT *Sleep disorders related to another mental condition*:

PT *Hypersomnia related to another mental condition*
PT *Insomnia related to another mental condition*

- PTs that remain under HLT *Sleep disorders NEC*:

PT *Hypersomnia-bulimia syndrome*
PT *Sleep disorder*
PT *Sopor*

Implementation Status: This request will be implemented as proposed. The concepts of *Sleep disorders related to another mental condition* and *Sleep disorders due to general medical condition* were removed from DSM-V. Therefore to better align MedDRA with DSM-V, the MSSO will consolidate HLT *Sleep disorders related to another mental condition* and HLT *Sleep disorders due to general medical condition* to existing HLT *Sleep disorders NEC*.