

## Complex Changes for MedDRA Version 15.0 (December 2011 Update)

The following decisions have been made for the implementation of each set of complex changes for MedDRA Version 15.0. All MedDRA user comments submitted via e-mail to the MSSO were evaluated by the MSSO's International Medical Officers before making a decision on the requests. See the [note](#) at the end of item 2 for an update to an earlier posting of this document.

### 1. Rename HLT *Myasthenias* to Myasthenia gravis conditions

**Submitter rationale:** PTs under HLT *Myasthenias* are related to myasthenia gravis, and the current wording of HLT *Myasthenias* makes it difficult to differentiate from HLT *Muscle weakness conditions*.

**Note:** Renaming terms is reserved for correcting misspellings or other minor corrections. If this proposal were implemented, a new HLT Myasthenia gravis conditions would be added and the existing HLT *Myasthenias* would be merged under it.

**Implementation Status:** This proposal will be implemented but not as requested. Based upon MedDRA user feedback, a new HLT *Myasthenia gravis and related conditions* will be added to HLT *Muscle disorders*. HLT *Myasthenia gravis and related conditions* is a broader concept which better represents the nature of the concepts under this HLT than the proposed term HLT *Myasthenia gravis conditions*. Related to this change, existing HLT *Myasthenias* will be merged under the new HLT *Myasthenia gravis and related conditions*. This will result in all the PTs under HLT *Myasthenias* moving to the new HLT and the removal of HLT *Myasthenias* from MedDRA.

The following changes were proposed by the MSSO.

- 2. Add a new HLT *Exposures, chemical injuries and poisoning* to SOC *Injury, poisoning and procedural complications* and merge existing HLT *Chemical injury and poisoning* to the new HLT**

**Add new HLT *Exposures to various agents* to proposed HLT *Exposures, chemical injuries and poisoning* and merge existing HLT *Medication errors due to accidental exposures* to the new HLT.**

**Add new HLT *Exposures associated with pregnancy and lactation* to proposed HLT *Exposures, chemical injuries and poisoning* and merge existing HLT *Pregnancy related accidental exposures and injuries* to the new HLT.**

**Make proposed HLT *Exposures associated with pregnancy and lactation* biaxial by adding a link to HLT *Pregnancy, labour, delivery and postpartum conditions*. The primary SOC for the PTs under HLT *Exposures associated with pregnancy and lactation* would be SOC *Injury, poisoning and procedural complications* with a secondary link to SOC *Pregnancy, puerperium and perinatal conditions*.**

**MSSO rationale:** Based on suggestions from the ICH Points To Consider Working Group, new sets of pregnancy exposure terms have been added and existing terms reorganized for MedDRA v14.1 to make them more self explanatory and easier to use for pharmacovigilance purposes. The proposed complex changes complete the reorganization.

Both the new and existing terms were organized to refer to circumstances involving transmission of various agents through intimate contact (e.g., mother to fetus or newborn, between partners, etc). The two main circumstances considered are exposures related to pregnancy and lactation, and terms representing relevant forms of potential transmission of various agents through intimate contact (e.g., PT *Exposure via partner*).

Existing terms where an actual harm is proved were not part of this set, even if they convey the concept of a pregnancy or intimate related previous exposure (e.g., PT *Maternal drugs affecting foetus* and PT *Anaesthetic complication foetal*). Additionally, existing exposure terms related to an agent or form of contamination which does not involve intimate contact and is only applicable to one individual (e.g., PT *Exposure to toxic agent*) were not included in this reorganization. Terms related to exposures to communicable diseases or environmental occupational and non-occupational exposures were not included either.

Note that concepts of agent exposures are subject to multiple variables, such as timing and origin of exposure and therefore more than one MedDRA term may be needed for term selection in a particular situation.

**Implementation Status:** This proposal will be implemented but not as requested. Based upon MedDRA user feedback, there were three modifications implemented which deviate from the original proposal.

- *HLGT Exposures, chemical injuries and poisoning to SOC Injury, poisoning and procedural complications and the merge of existing HLGT Chemical injury and poisoning to the new HLGT will be implemented as proposed.*
- *Proposed HLT Exposures to various agents will be added as HLT Exposures NEC (excl medication errors due to accidental exposures) to better represent the nature of the terms under this HLT. There will be no merge of HLT Medication errors due to accidental exposures. Instead all PTs under HLT Medication errors due to accidental exposures will be moved to the new HLT Exposures NEC (excl medication errors due to accidental exposures) except PT Accidental drug intake by child and PT Accidental exposure. Additionally, the following PTs will move from SOC Social circumstances to new HLT Exposures NEC (excl medication errors due to accidental exposures).*
  - *PT Exposure to allergen*
  - *PT Exposure to chemical pollution*
  - *PT Exposure to communicable disease*
  - *PT Exposure to contaminated device*
  - *PT Exposure to vaccinated person*
  - *PT Occupational exposure to drug*
  - *PT Occupational exposure to radiation*
  - *PT Occupational exposure to toxic agent*
- *Proposed HLT Exposures associated with pregnancy and lactation will be added as HLT Exposures associated with pregnancy, delivery and lactation to better represent the nature of the terms under this HLT. Existing HLT Pregnancy related accidental exposures and injuries will be merged under the new HLT as proposed.*
- *HLT Exposures associated with pregnancy, delivery and lactation will be made biaxial by adding a link to HLGT Pregnancy, labour, delivery and postpartum conditions as proposed. The primary SOC for the PTs under HLT Exposures associated with pregnancy and lactation would be SOC Injury, poisoning and procedural complications with a secondary link to SOC Pregnancy, puerperium and perinatal conditions.*

**Terminology Impact:** See the summary of changes in the table below. Note that the PTs and LLTs shown under HLT *Exposures NEC (excl medication errors due to accidental exposures)* and HLT *Exposures associated with pregnancy, delivery and lactation* are new terms added or existing terms moved in MedDRA v14.1. New terms are in red font.

HLGT	HLT	PT	LLT	Notes
<b>Exposures, chemical injuries and poisoning</b>				Replaces HLGT Chemical injury and poisoning in the SOC Injury, poisoning and procedural complications
	<b>Exposures NEC (excl medication errors due to accidental exposures)</b>			HLT Medication errors due to accidental exposures is retained with PT Accidental drug intake by child and PT Accidental exposure under it.
		Exposure to allergen		Moved from SOC Social circumstances
		Exposure to chemical pollution		Moved from SOC Social circumstances
		Exposure to communicable disease		Moved from SOC Social circumstances
		Exposure to contaminated device		Moved from SOC Social circumstances
		Exposure to vaccinated person		Moved from SOC Social circumstances
		Occupational exposure to drug		Moved from SOC Social circumstances
		Occupational exposure to radiation		Moved from SOC Social circumstances
		Occupational exposure to toxic agent		Moved from SOC Social circumstances
		Radiation exposure		
			Non-occupational	

HLGT	HLT	PT	LLT	Notes
			radiation exposure	
	<b>Exposures associated with pregnancy, delivery and lactation</b>			<b>Replaces HLT Pregnancy related accidental exposures and injuries; HLT is biaxial primary to SOC Injury, poisoning and procedural complications; secondary to SOC Pregnancy, puerperium and perinatal conditions</b>
		Exposure during breast feeding		
			Drug exposure via breast milk	
			Transmission of drug via breast milk	
			Vaccine exposure via breast milk	
			Viral vaccine antibody exposure via breast milk	
			Viral vaccine exposure via breast milk	
		Exposure via father		
			Fetal exposure via father	
			Foetal exposure via father	
			Paternal drug exposure	
			Paternal drug exposure before pregnancy	
			Paternal drug exposure during pregnancy	
		Foetal exposure during delivery		
			Exposure via birth canal	
			Fetal exposure	

HLGT	HLT	PT	LLT	Notes
			during delivery	
		Foetal exposure during pregnancy		
			Drug exposure in utero	
			Exposure via placenta	
			Fetal exposure during pregnancy	
			Fetal exposure during pregnancy, first trimester	
			Fetal exposure during pregnancy, second trimester	
			Fetal exposure during pregnancy, third trimester	
			Fetal tobacco exposure	
			Foetal exposure during pregnancy, first trimester	
			Foetal exposure during pregnancy, second trimester	
			Foetal exposure during pregnancy, third trimester	
			Foetal tobacco exposure	
			Radiation exposure in utero	
			Unspecified agent exposure in utero	
		Foetal exposure timing unspecified		
			Drug exposure via mother	
			Fetal exposure timing unspecified	
		Maternal exposure before pregnancy		
			Drug exposure before pregnancy	
			Vaccine exposure before pregnancy	
		Maternal exposure during delivery		
		Maternal		

HLGT	HLT	PT	LLT	Notes
		exposure during pregnancy		
			Drug exposure during pregnancy	
			Radiation exposure during pregnancy	
			Unspecified agent exposure during pregnancy	
			Vaccine exposure during pregnancy	
		Maternal exposure timing unspecified		
			Maternal drug exposure	
			Maternal vaccine exposure	
		Thalidomide embryopathy		secondarily linked to HLT Pregnancy related accidental exposures and injuries

Note: Five PTs listed below were originally shown in the above table as terms moved from existing HLT *Medication errors due to accidental exposures* to new HLT *Exposures NEC (excl medication errors due to accidental exposures)*.

- PT *Exposure via blood*
- PT *Exposure via direct contact*
- PT *Exposure via partner*
- PT *Exposure via semen*
- PT *Exposure via vaginal fluid*

Recently, significant concerns were expressed by a MedDRA user about moving these terms to the new HLT *Exposures NEC (excl medication errors due to accidental exposures)*. For the time being, these terms will remain under HLT *Medication errors due to accidental exposures* pending a larger discussion with this user and other parties on the organization and placement of exposure terms in MedDRA.

### 3. Add new HLT *Gene analyses* to HLGT *Cytogenetic investigations*

Add new HLT *Acquired gene mutations and other alterations* to HLGT *General system disorders NEC*

Merge existing HLT *Acquired mutations NEC* to new HLT *Acquired gene mutations and other alterations*

Move HLT *Cell marker procedures* from HLGT *Immunology and allergy investigations* to HLGT *Cytogenetic investigations*

**MSSO rationale:** As a proactive Terminology Maintenance initiative, which was based on a MedDRA user change request, the MSSO has added to MedDRA an initial group of pharmacogenetic and pharmacogenomic (PG) concepts of relevance to MedDRA users. The criteria used to add new terms focus on those genetic concepts and factors that have a potential impact on drug therapy. The following are hierarchical relationship principles for the new terms.

Four HLTs were used for PG term placement:

- HLT *Cell marker procedures* in SOC *Investigations*; for example, PT *Oestrogen receptor assay*
- Proposed HLT *Gene analyses* in SOC *Investigations*; for example, PT *Gene mutation identification test*
- Proposed HLT *Acquired mutations and other alterations* in SOC *General disorders and administration site conditions*; for example, proposed PT *K-ras mutation*
- HLT *Cell metabolism disorders NEC* in SOC *Metabolism and nutrition disorders*; for example, PT *NAT2 polymorphism*

**Implementation Status:** This proposal will be implemented as requested. In addition, PT *Genetic polymorphism* will be moved to the new HLT *Acquired gene mutations and other alterations* based upon MedDRA user feedback.

**Terminology Impact:** The following terms will be added or moved under new HLT *Gene analyses* or new HLT *Acquired gene mutations and other alterations* in accordance with the nature of the respective concept. Note that there were pharmacogenetic and pharmacogenomic PT and LLT concepts added in MedDRA v14.1. Please go to the [announcements section](#) in the subscriber area of the MSSO Web site for specific details on these term additions and changes.

Key			
Existing Term		New PT	
New HLT		New LLT	

HLGT	HLT	PT	LLT	Notes
<b>Cytogenetic investigations</b>				HLGT in SOC Investigations
	<b>Cell marker procedures</b>			Moved from HLGT Immunology and allergy investigations
		Epidermal growth factor receptor decreased		moved from HLT Protein analyses NEC
		Epidermal growth factor receptor increased		moved from HLT Protein analyses NEC
	<b>Chromosome analyses</b>			
	<b>Gene analyses</b>			<b>New HLT</b>
		Anaplastic lymphoma kinase gene and nucleophosmin gene fusion assay		
			ALK-NPM gene fusion assay	
		BCL-2 gene status assay		
		BRCA1 gene mutation assay		

HLGT	HLT	PT	LLT	Notes
		BRCA2 gene mutation assay		
		Carbonic anhydrase gene mutation assay		
			Carbonic anhydrase II gene mutation assay	
			Carbonic anhydrase IV gene mutation assay	
		C-kit gene status assay		
		CYP2C19 gene status assay		
		CYP2D6 gene status assay		
		EGFR status assay		
		Gene mutation identification test		moved from HLT Chromosome analyses
		HERG gene status assay		
		HLA-B gene status assay		
		H-ras status assay		
		K-ras status assay		
		NAT2 gene status assay		
		N-ras status assay		
		PTEN gene mutation assay		
		RET gene mutation assay		
		Tyrosine kinase mutation assay		
		UGT1A1 gene mutation assay		
<b>General system disorders NEC</b>				HLGT in SOC General disorders and administration site conditions
	<b>Acquired gene mutations and other alterations</b>			<b>Replaces HLT Acquired mutations NEC</b>

HLGT	HLT	PT	LLT	Notes
		Acquired gene mutation		from merge of HLT Acquired mutations NEC
		Acquired mitochondrial DNA deletion		from merge of HLT Acquired mutations NEC
		Acquired mitochondrial DNA mutation		from merge of HLT Acquired mutations NEC
		Anaplastic lymphoma kinase gene mutation		
			ALK gene mutation	
		Anaplastic lymphoma kinase gene and nucleophosmin gene fusion overexpression		
			ALK-NPM gene fusion overexpression	
		Androgen receptor gene overexpression		
		BRCA1 gene mutation		
		BRCA2 gene mutation		
		Carbonic anhydrase gene mutation		
			Carbonic anhydrase II gene mutation	
			Carbonic anhydrase IV gene mutation	
		C-kit gene mutation		
		C-kit gene overexpression		
		EGFR gene mutation		
		EGFR gene overexpression		
		Genetic polymorphism		Moved from HLT Cell metabolism disorders NEC
		HERG gene mutation		

HLGT	HLT	PT	LLT	Notes
		H-ras gene mutation		
		K-ras gene mutation		Moved from HLT Cell metabolism disorders NEC
		N-ras gene mutation		
		Oestrogen receptor gene overexpression		
		Platelet-derived growth factor receptor overexpression		
		Progesterone receptor gene overexpression		
		PTEN gene mutation		
		RET gene mutation		
		Transmembrane receptor tyrosine kinase overexpression		
		Tyrosine kinase mutation		
		UGT1A1 gene mutation		
		Vascular endothelial growth factor overexpression		
			VEGF overexpression	

4. **Add a new HLT *Dialysis related complications* to HLGT *Procedural related injuries and complications NEC***

**MSSO rationale:** The proposed HLT *Dialysis related complications* would provide a more intuitive grouping for dialysis related terms and dialysis related complications.

**Terminology Impact:** The following PTs would be moved to the proposed HLT *Dialysis related complications*.

- PT *Bloody peritoneal effluent*
- PT *Dialysis amyloidosis*
- PT *Dialysis disequilibrium syndrome*
- PT *Peritoneal dialysis complication*
- PT *Haemodialysis complication*
- PT *Haemodialysis-induced symptom*
- PT *Peritoneal cloudy effluent*

**Implementation Status:** This proposal will be implemented as requested.

5. **Add New HLGT *Physical examination and organ system status topics* to SOC *Investigations* and merge existing HLGT *Physical examination topics* to the new HLGT.**

**Add new HLT *Physical examination procedures and organ system status* to new HLGT *Physical examination and organ system status topics* and merge existing HLT *Physical examination procedures* to the new HLT.**

**MSSO rationale:** Currently HLT *Physical examination procedures* is the only HLT under HLGT *Physical examination topics*. The proposed actions would broaden the scope of the HLGT and the HLT for capturing normal investigational concepts based on physical examination or organ system status. Such terms are intended for medical history and physical examination assessments.

**Terminology Impact:** New HLT *Physical examination procedures and organ system status* would reside under new HLGT *Physical examination and organ system status topics*. All PTs under HLT *Physical examination procedures* would reside under new HLT *Physical examination procedures and organ system status*. Existing HLGT *Physical examination topics* and HLT *Physical examination procedures* would be removed as a result of the merges.

**Implementation Status:** This proposal will be implemented as requested.