

Complex Changes for MedDRA Version 14.0

The following decisions have been made in relation to the implementation of each complex change for MedDRA Version 14.0. All subscriber comments submitted via email to the MSSO were evaluated by the MSSO's International Medical Officers.

Out of the 12 originally proposed complex changes, 7 have been implemented for MedDRA v14.0.

1. Add a new HLT *Somatic mutation NEC* to HLGT *General system disorders NEC* in SOC *General disorders and administration site conditions*.

Subscriber rationale: This concept is being reported in our oncology trials. Currently MedDRA has the terms Gene mutation and Chromosomal mutation map to SOC *Congenital, familial, and genetic disorders*. Not all gene mutations are congenital by nature. Some mutations are acquired and can result from a variety of factors. Reference:
<http://www.britannica.com/EBchecked/topic/553940/somatic-mutation>

Terminology Impact: Based upon a review by the MSSO, the following PTs would be moved under new HLT *Somatic mutation NEC*.

- PT *Acquired gene mutation*
- PT *Acquired mitochondrial DNA mutation*
- PT *Mitochondrial DNA mutation*

Implementation Status: This proposal was implemented not as requested. The requested term *Somatic mutation NEC* will be rephrased to *Acquired mutations NEC* and added as an HLT under HLGT *General system disorders NEC*. HLT *Acquired mutations NEC* is intended to cover all mutations acquired by a somatic cell after conception.

In related changes, PT *Acquired gene mutation*, PT *Acquired mitochondrial DNA mutation* and PT *Acquired mitochondrial DNA deletion* will be moved to new HLT *Acquired mutations NEC*.

2. Add a new HLT *Electrical burns* to HLGT *Injuries by physical agents* in SOC *Injury, poisoning and procedural complications*.

Subscriber rationale: This concept is being reported in our clinical studies.

Terminology Impact: Based upon a review by the MSSO, only a single term – PT *Electrical burn* – would be moved under new HLT *Electrical burns*.

Implementation Status: This proposal was not implemented. Electrical burn is a sub concept of thermal burn. Dorland's Medical Dictionary includes electrical burn within the definition of thermal burn. PT *Electrical burn* was added under HLT *Thermal burns* in MedDRA v13.0.

3. Link HLT *Product label issues* to HLGT *Medication errors* in SOC *Injury, poisoning and procedural complications*.

Subscriber rationale: Product label issues could lead to medication errors

Terminology Impact: Currently HLT *Product label issues* is uni-axial to SOC *General disorders and administration site conditions*. Adding a link to HLGT *Medication errors* would create secondary links to SOC *Injury, poisoning and procedural complications* for the following PTs.

- PT *Physical product label issue*
- PT *Product barcode issue*
- PT *Product expiration date issue*
- PT *Product identification number issue*
- PT *Product label confusion*
- PT *Product label counterfeit*
- PT *Product label issue*
- PT *Product label on wrong product*
- PT *Product lot number issue*

Note: The MedDRA Introductory Guide 13.0 defines Medication errors and Product quality issues as follows:

Medication errors are defined as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in control of the health care professional, patient or consumer. Such events may be related to professional practice, health care products, procedures and systems, including prescribing, order communication, product labeling, packaging and nomenclature, compounding, dispensing, distribution, administration, education, monitoring and use.

Product quality issues are abnormalities that may be introduced during the manufacturing/labeling, packaging, shipping, handling or storage of the products.

The upcoming v13.1 MedDRA Term Selection: Points to Consider document will include a new section on product quality terms and their distinction from medication error terms.

Implementation Status: This proposal was not implemented. Medication errors and product quality issues are defined as separate concepts and are thus represented in MedDRA as separate HLGTS, with limited multi-axiality of subsumed PTs. A MedDRA user always has the option to search by combining terms from both HLGTS; however, it would be inappropriate for the terminology structure to force a combined scope of two different grouping concepts.

4. Link HLT *Product packaging issues* to HLGT *Medication errors in SOC Injury, poisoning and procedural complications*.

Subscriber rationale: Product packaging issues could lead to medication errors.

Terminology Impact: Currently HLT *Product packaging issues* is uniaxial to SOC *General disorders and administration site conditions*. Adding a link to HLGT *Medication errors* would create secondary links to SOC *Injury, poisoning and procedural complications* for the following PTs.

- PT *Failure of child resistant mechanism for pharmaceutical product*
- PT *Product blister packaging issue*
- PT *Product closure issue*
- PT *Product closure removal difficult*
- PT *Product commingling*
- PT *Product container issue*
- PT *Product container seal issue*
- PT *Product dropper issue*
- PT *Product outer packaging issue*
- PT *Product packaging counterfeit*
- PT *Product packaging issue*
- PT *Product packaging quantity issue*

Note: See the note for proposal # 3.

Implementation Status: This proposal was not implemented. Medication errors and product quality issues are defined as separate concepts and are thus represented in MedDRA as separate HLGTS, with limited multi-axiality of subsumed PTs. A MedDRA user always has the option to search by combining terms from both HLGTS; however, it would be inappropriate for the terminology structure to force a combined scope of two different grouping concepts.

5. Link HLT *Product quality issues NEC* to HLGTS *Medication errors in SOC Injury, poisoning and procedural complications*.

Subscriber rationale: Product quality issues could lead to medication errors.

Terminology Impact: Currently HLT *Product quality issues NEC* is uniaxial to SOC *General disorders and administration site conditions*. Adding a link to HLGTS *Medication errors* would create secondary links to SOC *Injury, poisoning and procedural complications* for the following PTs.

- PT *Incorrect product storage*
- PT *Incorrect storage of drug*
- PT *Medication residue*
- PT *Product adherence issue*
- PT *Product compounding quality issue*
- PT *Product counterfeit*
- PT *Product formulation issue*
- PT *Product measured potency issue*
- PT *Product name confusion*
- PT *Product quality issue*
- PT *Product substitution issue*
- PT *Product tampering*

Note: See the note for proposal # 3.

Implementation Status: This proposal was not implemented. Medication errors and product quality issues are defined as separate concepts and are thus represented in MedDRA as separate HLGTS, with limited multi-axiality of subsumed PTs. A MedDRA user always has the option to search by combining terms from both HLGTS; however, it would be inappropriate for the terminology structure to force a combined scope of two different grouping concepts.

6. Add new HLT *Nail and nail bed conditions* to HLGT *Infections - pathogen unspecified* in SOC *Infections and infestations*.

Subscriber rationale: Nails and nailfolds are subject to trauma, infection, vascular insufficiency, immune-mediated disease, neoplasia, defects in keratinization, and congenital abnormalities. A particular nail deformity may be caused by a variety of diseases. A single disease can present with various nail lesions. We suggest to add a new HLT *Nail and nail bed conditions* to regroup all the *Nail and nail bed conditions* related to infections such as *Nail bed infection*, *Paronychia*, *Nail infections*, *Onychomycosis*. For the clinical trial or spontaneous reporting within our company this allows the grouping of all events related *nail and nail bed conditions* under the same classification. Otherwise we can miss terms related *nail disease* under HLGT *Skin and subcutaneous tissue infections and infestations*.

Terminology Impact: Based upon a review by the MSSO, the following PTs would move to new HLT *Nail and nail bed conditions*.

- PT *Nail bed infection*
- PT *Nail bed infection bacterial*
- PT *Nail bed infection fungal*
- PT *Nail bed infection viral*
- PT *Nail discolouration*
- PT *Nail infection*
- PT *Onychomycosis*
- PT *Paronychia*

Note: Please note the HLGT *Infections - pathogen unspecified*, suggested by the subscriber as the placement for the new HLT, is "pathogen unspecified" and the proposed HLT would include terms such as PT *Nail bed infection fungal*, where the pathogen **is** specified - thus creating a conflict.

Implementation Status: This proposal was not implemented. The proposal to create a new HLT *Nail and nail bed conditions* encompassing organism specific terms such as PT *Nail bed infection bacterial* and PT *Nail bed infection fungal* under the existing HLGT *Infections - pathogen unspecified* in SOC *Infections and infestations* is not appropriate because organism specific terms would be grouped under an HLGT where the pathogens are not specified. To address terminology retrieval concerns, a subscriber may gather appropriate PTs related to nail infections in a specific query prepared and maintained by one's organization.

7. Add new HLT *Substance use*

[**Note:** This request was mistakenly posted as a request for HLT *Substance abuse* instead of HLT *Substance use*. The MSSO apologizes for the error.]

Subscriber rationale: Substance user is someone who smokes tobacco or cannabis, cigarette substitutes, or various other drugs. We believe this new HLT, different from the HLT *Drug and chemical use*, can cover such PT as Smoker, Non-smoker, Substance abuser.

Terminology Impact: Based upon a review by the MSSO, the following PTs would be moved under new HLT *Substance use*.

- PT *Caffeine consumption*

Implementation status: Implemented not as requested. *Substance use* will be added as a PT to HLT *Social issues*. Currently there are very few concepts that represent use of substances other than use of tobacco, alcohol, drugs and chemicals e.g., PT *Caffeine consumption*. Therefore, rather than adding a new HLT *Substance use*, PT *Caffeine consumption* and related concepts will be grouped under the existing HLT *Social issues*. Because HLT *Social issues* contains a variety of miscellaneous concepts that cannot be grouped elsewhere, it will be renamed to HLT *Social issues NEC*. In a related change, LLT *Recreational substance use* will be moved to new PT *Substance use*.

To address terminology retrieval concerns, a subscriber may gather appropriate PTs related to substance use including tobacco, alcohol and other substances, etc. in a specific query prepared and maintained by one's organization.

The following changes are proposed by the MSSO

The MSSO reviewed subscriber feedback on these proposed changes before making an implementation decision. The majority of comments received were in favor of the proposed changes.

8. Merge HLT *Picornaviral infections* under HLT *Viral infections NEC*

MSSO rationale: The HLT *Picornaviral infections* has one only PT under it (PT *Foot and mouth disease*), and the MSSO deems it appropriate to move the PT *Foot and mouth disease* under the HLT *Viral infections NEC* via a merge of HLT *Picornaviral infections* to under HLT *Viral infections NEC*.

Terminology Impact: PT *Foot and mouth disease*, the only PT under HLT *Picornaviral infections*, would move under HLT *Viral infections NEC*.

Implementation status: Implemented as requested. The HLT *Picornaviral infections* has only one PT under it (PT *Foot and mouth disease*), and it is appropriate to move the PT *Foot and mouth disease* under the HLT *Viral infections NEC* via a merge of HLT *Picornaviral infections* under HLT *Viral infections NEC*.

9. Add new HLT *Enteroviral infections NEC* and merge existing HLT *Enteroviral infections* under the new HLT.

MSSO rationale: The different serotypes of enteroviruses are grouped under different HLTs such as HLT *Coxsackie viral infections*, HLT *Echo viral infections*, HLT *Hepatitis viral infections* and HLT *Poliomyelitis viral infections*. HLT *Enteroviral infections* currently represents a miscellaneous HLT that houses infections that do not fit any of its serotypes. Therefore, a new HLT *Enteroviral infections NEC* is proposed to contain PTs that represent infections which cannot be attributed to the specific serotypes already represented at the HLT level. The existing HLT *Enteroviral infections* would be merged into the new HLT.

Terminology Impact: The following PTs would be moved under new HLT *Enteroviral infections NEC*.

PT *Acute haemorrhagic conjunctivitis*
PT *Central nervous system enteroviral infection*
PT *Encephalitis enteroviral*
PT *Enterovirus infection*

PT *Gastroenteritis enteroviral*
 PT *Meningitis enteroviral*

Implementation status: Implemented as requested. The different serotypes of enteroviruses are grouped under respective HLTs such as HLT *Coxsackie viral infections*, HLT *Echo viral infections*, HLT *Hepatitis viral infections* and HLT *Poliomyelitis viral infections*. HLT *Enteroviral infections* currently represents a miscellaneous HLT that houses infections that do not fit any of its serotypes. Therefore, a new HLT *Enteroviral infections NEC* will be added to contain PTs that represent infections which cannot be attributed to the specific serotypes already represented at the HLT level. The existing HLT *Enteroviral infections* will be merged into the new HLT.

10. Unlink HLT *Renal disorders congenital*, a multi-axial HLT, from HLGT *Renal disorders (excl nephropathies)* in SOC *Renal and urinary disorders*.

MSSO rationale: This change is proposed to allow a more specific placement for congenital disorders in their anatomical site of manifestation SOCs, specifically to group them with their counterpart “acquired” terms.

Terminology Impact: The following table lists PTs that currently have a secondary link to HLT *Renal disorders congenital*. The right column of the table shows proposed new secondary links that would be added if HLT *Renal disorders congenital* is unlinked from HLGT *Renal disorders (excl nephropathies)*.

PT	New Secondary HLT Links
Alport's syndrome	Glomerulonephritis and nephrotic syndrome
Benign familial haematuria	Glomerulonephritis and nephrotic syndrome
Fanconi syndrome ⁺	Metabolic acidoses (excl diabetic acidoses)
Liddle's syndrome ⁺	Metabolic alkaloses
Congenital nephrogenic diabetes insipidus	Nephropathies and tubular disorders NEC
Fanconi syndrome ⁺	Nephropathies and tubular disorders NEC
Liddle's syndrome ⁺	Nephropathies and tubular disorders NEC
Oculocerebrorenal	Nephropathies and tubular disorders

PT	New Secondary HLT Links
syndrome	NEC
Congenital nephrotic syndrome	Renal disorders congenital
Accessory kidney	Renal disorders NEC
Congenital renal disorder	Renal disorders NEC
Potter's syndrome	Renal disorders NEC
Solitary kidney	Renal disorders NEC
Congenital cystic kidney disease ⁺	Renal neoplasms
Congenital renal cyst ⁺	Renal neoplasms
Congenital cystic kidney disease ⁺	Renal neoplasms benign
Congenital renal cyst ⁺	Renal neoplasms benign
Congenital calyceal diverticulum	Renal structural abnormalities and trauma
Congenital hydrocele renalis	Renal structural abnormalities and trauma
Congenital pyelocaliectasis	Renal structural abnormalities and trauma
Kidney duplex	Renal structural abnormalities and trauma
Ectopic kidney	Renal structural abnormalities and trauma
Kidney malformation	Renal structural abnormalities and trauma
Kidney malrotation	Renal structural abnormalities and trauma
Pelvic kidney	Renal structural abnormalities and trauma
Renal aplasia	Renal structural abnormalities and trauma
Renal dysplasia	Renal structural abnormalities and trauma
Renal fusion anomaly	Renal structural abnormalities and trauma
Renal hypoplasia	Renal structural abnormalities and trauma

+ Represents a PT with more than one secondary link

In addition the following PTs would move:

PT	Current HLT	New HLT
Calyceal diverticulum	Renal disorders NEC	Renal structural abnormalities and trauma
Fanconi syndrome acquired	Amino acid metabolism disorders NEC	Metabolic acidoses (excl diabetic acidoses)
Nephrogenic diabetes insipidus	Renal disorders NEC	Nephropathies and tubular disorders NEC

Note: The link from HLT *Renal disorders congenital* to HLGT *Renal and urinary tract disorders congenital* in SOC *Congenital, familial and genetic disorders* would remain.

Implementation status: Implemented as requested. This change allows for specific placement of congenital renal disorders according to the SOC of the anatomical site of manifestation, and thus groups congenital renal disorders with their counterpart “acquired” terms.

11. Unlink HLT *Pyrimidine metabolism disorders congenital* from HLGT *Purine and pyrimidine metabolism disorders* in SOC *Metabolism and nutrition disorders*.

Unlink HLT *Purine metabolism disorders congenital* from HLGT *Purine and pyrimidine metabolism disorders* in SOC *Metabolism and nutrition disorders*.

Add a new HLT *Disorders of purine metabolism* to HLGT *Purine and pyrimidine metabolism disorders* and merge HLT *Purine metabolism disorders NEC* to HLT *Disorders of purine metabolism*.

Add a new HLT *Disorders of pyrimidine metabolism* to HLGT *Purine and pyrimidine metabolism disorders* and merge HLT *Pyrimidine metabolism disorders NEC* to HLT *Disorders of pyrimidine metabolism*.

MSSO rationale: This change is proposed to remove redundancy in HLT representation of purine and pyrimidine disorders in the SOC *Metabolism and nutritional disorders*.

Terminology Impact: The following table lists PTs that would have secondary links added if this change were implemented.

PT	Secondary HLT Link
Partial hypoxanthine-	Disorders of purine metabolism

PT	Secondary HLT Link
guanine phosphoribosyl transferase deficiency	
Total hypoxanthine-guanine phosphoribosyl transferase deficiency	Disorders of purine metabolism
Dihydropyrimidine dehydrogenase deficiency	Disorders of pyrimidine metabolism
Oroticaciduria congenital	Disorders of pyrimidine metabolism

Implementation Status: Implemented as requested. This change removes redundancies in the HLT representation of purine and pyrimidine disorders in the SOC *Metabolism and nutritional disorders*.

12. Add a new HLT *Peritoneal fluid and membrane function analyses* to HLG *Gastrointestinal investigations*.

MSSO rationale: The MSSO felt it is reasonable to have peritoneal investigations represented in a specific HLT in SOC *Investigations*. Terms related to peritoneal function (e.g., PT *Peritoneal permeability decreased* and PT *Peritoneal permeability increased*) have been added under HLT *Renal function analyses* as a “placeholder” (i.e., no other suitable grouping is currently available), but the terms do not reflect renal function. Furthermore, several peritoneal fluid/effluent terms are under HLT *Gastrointestinal histopathology procedures*. This proposed new HLT accommodates peritoneal fluid/effluent and function analyses concepts.

Terminology Impact: The following PTs would move to the new HLT *Peritoneal fluid and membrane function analyses*.

- PT *Effective peritoneal surface area increased*
- PT *Peritoneal effluent abnormal*
- PT *Peritoneal effluent analysis*
- PT *Peritoneal effluent erythrocyte count*
- PT *Peritoneal effluent erythrocyte count increased*
- PT *Peritoneal effluent leukocyte count*
- PT *Peritoneal effluent leukocyte count increased*
- PT *Peritoneal effluent platelet count*
- PT *Peritoneal effluent specific gravity*
- PT *Peritoneal equilibration test*
- PT *Peritoneal fluid analysis*
- PT *Peritoneal fluid analysis abnormal*
- PT *Peritoneal fluid analysis normal*

PT *Peritoneal fluid protein abnormal*
PT *Peritoneal fluid protein decreased*
PT *Peritoneal fluid protein increased*
PT *Peritoneal permeability decreased*
PT *Peritoneal permeability increased*

Implementation Status: Implemented as requested. This new HLT more appropriately accommodates peritoneal fluid/effluent and function analyses concepts. Terms related to peritoneal function (e.g., *PT Peritoneal permeability decreased* and *PT Peritoneal permeability increased*) have previously been added under HLT *Renal function analyses* as a “placeholder” (i.e., no other suitable grouping is currently available), but the terms do not reflect renal function. Furthermore, several peritoneal fluid/effluent terms are under HLT *Gastrointestinal histopathology procedures*.