

Implemented MedDRA Version 19.0 Complex Changes

(Update November 2015)

Proposed Complex Changes for SOC *Product issues*



1. Add new SOC *Product issues*

Rationale and Background: The ICH MedDRA Management Board has endorsed the creation of an additional (27th) System Organ Class for implementation in MedDRA Version 19.0. SOC *Product issues* will include terms relevant for issues with product quality, devices, product manufacturing and quality systems, supply and distribution, and counterfeit products.

As defined in the MedDRA Introductory Guide, for the purposes of MedDRA, product can refer to various types of products intended for human use such as drugs (prescription and over the counter), biologics, vaccines, combination products, devices, nutraceuticals, dietary supplements, etc. Furthermore, the terminology may also support other types of products which are regulated in at least one region such as food or cosmetics.

An Expert Working Group comprising the MSSO, JMO, and representatives from regulatory authorities and industry with expertise in MedDRA and in product quality provided input on the hierarchy proposals for the new SOC.

Terminology Impact: The addition of SOC *Product issues* to MedDRA will bring the total number of SOCs to 27. The new SOC will have the same five level hierarchical structure as the existing SOCs and it will express multi-axiality, i.e., where appropriate, terms in the SOC can also be represented in other SOCs via multi-axial links. The proposed hierarchy is presented in the table below. Once the proposals are finalized and approved, the HLGs and HLTs will be populated with existing PTs and LLTs (some of which will be moved from existing grouping terms to new, more specific groupings). In addition, new PTs and LLTs - including relevant terms for manufacturing and quality system issues that are not currently represented in MedDRA - will be added to the hierarchy through the ongoing Change Request process. See the table below for the proposed hierarchy.

Primary SOC	HLGT	HLT	Notes
Product issues			New SOC
	Device issues		HLGT moved from SOC <i>General disorders and administration site conditions</i>
		Device computer issues	HLT moved from SOC <i>General disorders and administration site conditions</i>
 New  Existing		Device electrical issues	HLT moved from SOC <i>General disorders and administration site conditions</i>
		Device incompatibility issues	HLT moved from SOC <i>General disorders and administration site conditions</i>
		Device information output issues	HLT moved from SOC <i>General disorders and administration site conditions</i>
		Device issues NEC	HLT moved from SOC <i>General disorders and administration site conditions</i>
		Device malfunction events NEC	HLT moved from SOC <i>General disorders and administration site conditions</i>
		Device operational issues NEC	HLT moved from SOC <i>General disorders and administration site conditions</i>
		Device physical property and chemical issues	HLT moved from SOC <i>General disorders and administration site conditions</i>
	Product quality, supply, distribution, manufacturing and quality system issues		New HLGT
		Counterfeit, falsified and substandard products	New HLT
		Manufacturing facilities and equipment issues	New HLT
		Manufacturing issues NEC	New HLT. Could potentially include terms used in root cause analysis for product quality defects, including human error concepts.
		Manufacturing laboratory controls issues	New HLT
		Manufacturing materials issues	New HLT
		Manufacturing production issues	New HLT
		Product contamination and sterility issues	HLT moved from SOC <i>General disorders and administration site conditions</i>

Primary SOC	HLGT	HLT	Notes
		Product distribution and storage issues	New HLT. Would include stage issues related to manufacturers, transport companies, wholesalers, etc. Storage issues resulting from errors on the part of healthcare professionals or patients/consumers are considered to be separate medication error concepts and would not be represented in this HLT.
		Product label issues	HLT moved from SOC <i>General disorders and administration site conditions</i>
		Product packaging issues	HLT moved from SOC <i>General disorders and administration site conditions</i>
		Product physical issues	HLT moved from SOC <i>General disorders and administration site conditions</i>
		Product quality issues NEC	HLT moved from SOC <i>General disorders and administration site conditions</i>
		Product supply and availability issues	New HLT. Could include terms for supply chain interruptions, product not available on formulary, product withdrawn from market, etc.

Implementation Status: This hierarchy for new SOC *Product issues* will be implemented as proposed. The HLGTs and HLTs will be populated with existing PTs and LLTs (some of which will be moved from existing grouping terms to new, more specific groupings). In addition, new PTs and LLTs - including relevant terms for manufacturing and quality system issues that are not currently represented in MedDRA - will be added to the hierarchy through the ongoing Change Request process.

MedDRA User Submitted Requests:

2. Add New HLT *Respiratory auscultatory investigations* to HLT *Respiratory and pulmonary investigations (excl blood gases)*

Submitter rationale: This term requested in accordance with the already existing HLTs *Cardiac auscultatory investigations* and HLT *Vascular auscultatory investigations*.

Terminology Impact: If approved the following PTs are examples of terms that would be moved to new HLT *Respiratory auscultatory investigations*:

PT <i>Breath sounds</i>	PT <i>Pulmonary physical examination</i>
PT <i>Breath sounds abnormal</i>	PT <i>Pulmonary physical examination abnormal</i>
PT <i>Breath sounds absent</i>	PT <i>Pulmonary physical examination normal</i>
PT <i>Breath sounds normal</i>	PT <i>Rales</i>
PT <i>Crepitations</i>	PT <i>Rhonchi</i>
PT <i>Pleural rub</i>	

Implementation Status: This proposal will not be approved based upon further review and MedDRA user feedback. The elements of a pulmonary physical examination include not only auscultation but visual inspection and percussion; moving broad concepts such as the pulmonary physical examination terms under the specific proposed HLT *Respiratory auscultatory investigations* would not be appropriate. Furthermore, it is not always possible to clearly differentiate between those findings which are exclusive to auscultation and those which are not. Therefore, the placement of the current terms is considered appropriate.

3. Replace HLT *Obstructive bile duct disorders (excl neoplasms)* with HLT *Obstructive bile duct disorders*

Submitter rationale: Some PTs under HLT *Obstructive bile duct disorders (excl neoplasms)* can be used to code conditions related to neoplasms or not (e.g., Bile duct obstruction) therefore the "excl neoplasms" specification is misleading.

Terminology Impact: If approved, all PTs under HLT *Obstructive bile duct disorders (excl neoplasms)* would be moved under HLT *Obstructive bile duct disorders*.

Implementation Status: This proposal will not be approved based upon further review. All the PT concepts in HLT *Obstructive bile duct disorders (excl neoplasms)* may be the consequences of a neoplasm as well as other etiologies, but they are not neoplasms *per se*. The intent of this and other HLTs designated as (excl neoplasms) is to exclude concepts that are specifically identified as neoplasms. Thus HLT *Obstructive bile duct disorders (excl neoplasms)* does not need to be replaced.

4. Add New HLT *Anaphylactoid response*

Submitter rationale: Anaphylactoid reaction are IGE independent hypersensitivity reactions, they cannot be under Anaphylactic Responses that are IGE dependent hypersensitivity reactions.

Terminology Impact: If approved, the MSSO would name the new HLT *Anaphylactoid responses*. PT *Anaphylactoid reaction*, PT *Anaphylactoid shock*, PT *Anaphylactoid syndrome of pregnancy* and PT *Dialysis membrane reaction* would be moved under the new HLT *Anaphylactoid responses*. Note that in MedDRA Version 18.1, PT *First use syndrome* has been demoted to an LLT under new PT *Dialysis membrane reaction*.

Implementation Status: This proposal will be implemented, but not as requested. The MSSO will add new HLT *Anaphylactic and anaphylactoid responses* and merge the existing HLT *Anaphylactic responses* under the new HLT. This action groups anaphylactic and anaphylactoid responses together as they have similar clinical manifestations, but have different underlying mechanisms (IgE dependent vs. IgE independent, respectively).

5. Add New HLT *Device site reactions*

Submitter rationale: I was not able to find the appropriate change request option to recommend creating a secondary mapping for specific PTs. We recommend creating a secondary mapping to the Injury, poisoning and procedural complications SOC for Medical device site reaction PTs. This recommendation is consistent with the other 'site reaction' terms (e.g., Application site reaction).

Terminology Impact: If approved, the “medical device site” PTs under HLT *Complications associated with device NEC* could be secondarily linked to new HLT *Device site reactions*. Below are some examples of PTs that would be linked to proposed HLT *Device site reactions*.

PT <i>Medical device site abscess</i>	PT <i>Medical device site joint pain</i>
PT <i>Medical device site calcification</i>	PT <i>Medical device site lymphadenopathy</i>
PT <i>Medical device site erosion</i>	PT <i>Medical device site nerve damage</i>
PT <i>Medical device site granuloma</i>	PT <i>Medical device site paraesthesia</i>
PT <i>Medical device site hypersensitivity</i>	PT <i>Medical device site pustule</i>
PT <i>Medical device site joint effusion</i>	PT <i>Medical device site scab</i>

Implementation Status: The proposal will be approved as requested. The HLT *Device site reactions* will be added to HLGT *Procedural related injuries and complications NEC*. All medical device site terms will secondarily linked to this new HLT.

6. Add New HLT *Marginal zone lymphomas* to HLGT *Lymphomas non-Hodgkin's B-cell*

Submitter rationale: This is to be consistent with the other marginal type non-Hodgkin’s B-cell lymphomas already in the dictionary (e.g., HLT *Extranodal marginal zone B-cell lymphomas (low grade B-cell)*, HLT *Nodal marginal zone B-cell lymphomas*, HLT *Splenic marginal zone lymphomas*).

Terminology Impact: If approved, an “NEC” modifier would be added to the HLT name to distinguish this term from the other three specific marginal zone lymphomas HLTs: HLT *Extranodal marginal zone B-cell lymphomas (low grade B-cell)*, HLT *Nodal marginal zone B-cell lymphomas*, and HLT *Splenic marginal zone lymphomas*). In MedDRA Version 18.1, a new LLT *Marginal zone lymphoma* was added under PT *B-cell lymphoma*. The MSSO proposes promoting this LLT to a PT and moving it to the proposed HLT *Marginal zone lymphomas*. Additionally, the MSSO proposes adding new PTs under the proposed HLT *Marginal zone lymphomas NEC* to provide specific stage concepts similar to the other lymphomas HLTs. The proposed HLT would therefore include the following PTs:

PT *Marginal zone lymphoma*
 PT *Marginal zone lymphoma stage I*
 PT *Marginal zone lymphoma stage II*
 PT *Marginal zone lymphoma stage III*

PT *Marginal zone lymphoma stage IV*
PT *Marginal zone lymphoma recurrent*
PT *Marginal zone lymphoma refractory*

Implementation Status: This proposal will be implemented, but not as requested. The MSSO will add new HLT *Marginal zone lymphomas NEC* to HLG *Lymphomas non-Hodgkin's B-cell*. The new HLT will group undetermined marginal zone lymphomas that are not anatomically specified and which can not be classified per the existing Marginal zone lymphoma HLTs. The PTs listed above will be added to new HLT *Marginal zone lymphomas NEC*.

MSSO Proposed Requests:

7. Add New HLT *Intercepted medication errors* to HLG *Medication errors*

MSSO rationale: Intercepted medication errors represent a distinct category of medication errors and refer to situations where an error occurred but was identified and intercepted before reaching the patient, thus preventing a potential adverse drug reaction. The MedDRA Expert Panel has endorsed the proposal to add a new HLT *Intercepted medication errors* to facilitate the coding and retrieval of these concepts.

Terminology Impact: The following PTs would be moved from HLT *Medication errors NEC* to new HLT *Intercepted medication errors*: PT *Intercepted drug dispensing error*, PT *Intercepted drug prescribing error*, PT *Intercepted medication error*, PT *Intercepted product selection error*, PT *Intercepted wrong patient selected*. In addition, PT *Intercepted drug administration error* would be moved from HLT *Maladministrations* to new HLT *Intercepted medication errors*.

Implementation Status: The proposal will be approved as requested.

8. Replace HLT *Varicose veins non-site specific* with HLT *Varicose veins NEC*

MSSO rationale: Site specific terms such as PT *Nasal varices* and PT *Endocardial varices* are under HLT *Varicose veins non-site specific*.

Terminology Impact: All PTs under HLT *Varicose veins non-site specific* would be moved under HLT *Varicose veins NEC*. Additionally, PT *Urinary bladder varices* would move from HLT *Site specific vascular disorders NEC* to new HLT *Varicose veins NEC*.

Implementation Status: The proposal will be approved as requested.

9. The MSSO proposes to replace one HLG and three HLTs in SOC *Psychiatric disorders* due to changes in how these concepts are referenced in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) or changes in common use among medical, educational, and other professionals. Below are the list of proposed changes and a corresponding rationale.

- Replace the HLG *Somatoform and factitious disorders* with HLG *Somatic symptom and related disorders*

Rationale: In DSM-5, somatoform disorders are now referred to as somatic symptom and related disorders.

- **Replace HLT *Somatoform disorders* with HLT *Somatic symptom disorders***

Rationale: In DSM-5, somatoform disorders are now referred to as somatic symptom disorders.

- **Replace HLT *Mental retardations* with HLT *Intellectual disabilities***

Rationale: The term mental retardation was used in DSM-IV. However, *intellectual disability* is the term that has come into common use over the past two decades among medical, educational, and other professionals, and by the lay public and advocacy groups. Moreover, a federal statute in the United States (Public Law 111-256, Rosa's Law) replaces the term "mental retardation" with "intellectual disability."

Note: HLT *Mental retardations* is multi-axial and has a link to SOC *Nervous system disorders* and SOC *Psychiatric disorders*.

- **Replace HLT *Paraphilias* with HLT *Paraphilias and paraphilic disorders***

Rationale: In DSM-5, paraphilias are not ipso facto mental disorders. There is a distinction between paraphilias and paraphilic disorders.

Terminology Impact: If approved, all HLTs under HLGT *Somatoform and factitious disorders* would be moved under new HLGT *Somatic symptom and related disorders*.

All PTs under HLTs:

- HLT *Mental retardations*
- HLT *Somatoform disorders*
- HLT *Paraphilias*

would move under new respective HLTs:

- HLT *Intellectual disabilities*
- HLT *Somatic symptom disorders*
- HLT *Paraphilias and paraphilic disorders*

Implementation Status: The proposal will be approved as requested.