Introductory Guide
MedDRA Version 26.1

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Notice to Reader

This Introductory Guide is written in English and is intended only for use with the English version of MedDRA. Additional Introductory Guides have been developed to support languages other than English and are included with their specific translation copies.

The Introductory Guide is intended for use in conjunction with the MedDRA Browsers, available with each MedDRA subscription.

Changes which are version specific or changes in documentation may be found in the What's New document. This document is included with the MedDRA release and is also posted on the MSSO Web site under Support Documentation.

The MedDRA terminology is maintained under an ISO 9001:2015 registered quality management system.

There are no changes of note in the MedDRA Introductory Guide Version 26.1

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1. INTRODUCTION

The Medical Dictionary for Regulatory Activities (MedDRA) Terminology is the international medical terminology developed under the auspices of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). This guide describes the development, scope, and structure of the terminology.

1.1 BACKGROUND

Prior to the development of MedDRA, there had been no internationally accepted medical terminology for biopharmaceutical regulatory purposes. Most organizations processing regulatory data used one of the international adverse drug reaction terminologies in combination with morbidity terminology. In Europe, most of these organizations used a combination of the World Health Organization's Adverse Reaction Terminology (WHO-ART©) and the International Classification of Diseases Ninth Revision (ICD-9). In the United States, the Food and Drug Administration's (FDA) Coding Symbols for a Thesaurus of Adverse Reaction Terms (COSTART©) was usually used in conjunction with Clinical Modification of ICD-9 (ICD-9-CM©). The Japanese developed their own versions of these international terminologies, Japanese Adverse Reaction Terminology (J-ART) and Medical Information System (Japan) (MEDIS). In addition, many organizations modified these terminologies to suit their needs. Established terminologies lacked specificity of terms at the data entry level, provided limited data retrieval options (e.g., too few levels in the hierarchy, or capacity to retrieve data via one axis only), and did not handle syndromes effectively. Organizations with sufficient resources developed their own “in-house” terminologies to address some or all of these deficiencies.

The use of multiple terminologies raised several problems. Using different terminologies at various stages in a product's life complicates data retrieval and analysis, making it difficult to cross-reference data. For example, safety data had frequently been classified for pre-registration clinical trials using ICD terminology and for post-marketing surveillance using J-ART, WHO-ART, or COSTART. Furthermore, using different terminologies in separate geographic regions impaired international communication and necessitated the conversion of data from one terminology to another. This data conversion had the potential to cause time delays and loss or distortion of data. In particular, these problems affected multinational pharmaceutical companies whose subsidiaries used multiple terminologies to fulfill the different data submission requirements of regulators. The use of multiple terminologies also affected communication between companies and clinical research organizations.

It became increasingly difficult to manage the information required for product registration applications and to meet the time scale requirements for data exchange between regulatory authorities and the medical product industries. These difficulties prompted an industry-wide commitment to exploit developments in communication and information technology. However, electronic communication still required a standardized data set and structure to be successful.

1.2 ADOPTION OF MEDICAL TERMINOLOGY AS AN ICH TOPIC

In October 1994, the ICH Steering Committee introduced multi-disciplinary regulatory communication initiatives to complement the ongoing safety, quality, and efficacy harmonization topics. These initiatives focused on a medical terminology for regulatory purposes (M1) and electronic standards for the transfer of regulatory information (ESTRI, M2). The ICH adopted these initiatives to recognize the increasing importance of electronic communication of regulatory data and the need for internationally agreed standards.

The aim of the ICH M1 initiative was to standardize the international medical terminology for regulatory communication. This includes communication in the registration, documentation, and safety monitoring of medical products for use in both pre- and post-marketing phases of the regulatory process. The objective was to agree on a unified medical terminology for regulatory activities that overcomes the limitations of current terminologies, is internationally accepted, and is supported by long-term maintenance. Regulators and industries benefit from such a terminology because it improves the quality, timeliness, and availability of data for analysis. The terminology also facilitates the electronic exchange of data relating to medical products and results in long-term savings in resources.

The M1 Expert Working Group (EWG) was established and was composed of representatives of the six ICH sponsors, an observer for the WHO, and the European Union acting as rapporteur. The EWG defined the “deliverables” of the initiative as a terminology of agreed content and structure (the implementable version) and an agreed maintenance framework.

1.3 DEVELOPMENT OF THE MEDICAL DICTIONARY FOR REGULATORY ACTIVITIES (MedDRA) TERMINOLOGY

The ICH terminology was developed from a pre-existing terminology. The MEDDRA Working Party enhanced the United Kingdom MCA's (now MHRA - Medicines and Healthcare products Regulatory Agency) medical terminology to produce MEDDRA Version 1.0. This was adopted as the basis for the new ICH terminology.

MedDRA Version 2.0 was signed off as the implementable version of the terminology at the ICH-4 conference in July 1997. A change in name and modified acronym were agreed upon at this meeting. Hence, MEDDRA is used for versions up to Version 1.5, while the implementable version (Version 2.0) and future versions are known as the MedDRA terminology.

1.4 IMPLEMENTATION OF THE TERMINOLOGY

The success of the terminology depends on its long-term maintenance and its evolution in response to medical/scientific advances and changes in the regulatory environment. This is why the MedDRA Maintenance and Support Services Organization (MSSO) is a necessary element to implementing the MedDRA terminology. The MSSO was appointed by ICH through an open competitive tender.

1.5 SCOPE OF THE TERMINOLOGY

The MedDRA terminology applies to all phases of development of medical products for human use, excluding animal toxicology. The scope of MedDRA encompasses medical, health-related, and regulatory concepts pertaining to such products. The terminology also addresses the health effects and malfunction of devices (e.g., PT *Device related infection* and PT *Device failure*). Furthermore, the terminology may also support other types of products which are regulated in at least one region such as food or cosmetics.

The categories of terms classified as “medical and health-related” for these purposes are as follows:

- signs
- symptoms
- diseases
- diagnoses
- therapeutic indications – including signs, symptoms, diseases, diagnoses, diagnosis or prophylaxis of disease, and modification of physiologic function
- names and qualitative results of investigations – e.g., increased, decreased, normal, abnormal, present, absent, positive, and negative
- medication errors and product quality terms
- surgical and medical procedures
- medical/social/family history

Although social circumstances are not usually regarded as medical terms, they fall within the “medical” scope if they are relevant to the evaluation of regulatory data (e.g., in the assessment of clinical outcome of treatment in the light of exposure to risk factors). Examples are: PT *Foreign travel*, PT *Substance use*, HLT *Tobacco use*, and HLT *Bereavement issues*. The terminology, as defined above, was developed for regulators and the regulated medical product industry. These groups can utilize the terminology for data entry, retrieval, evaluation, and presentation, and in both pre- and post-marketing phases of the regulatory process as follows:

- clinical studies
- reports of spontaneous adverse reactions and events
- regulatory submissions
- regulated product information

In consultation with the MedDRA Management Committee, the terminology may be expanded in scope to accommodate additional medical/health-related and regulatory concepts that are developed based on collaborative efforts involving relevant experts. The addition of new topic areas will undergo the usual MSSO change request process.

1.6 INCLUSION OF TERMS FROM ESTABLISHED TERMINOLOGIES

The initial release of MedDRA (v2.1) in March 1999 included numeric and symbol codes from earlier terminologies in specific fields of the MedDRA files associated with term names. The codes were links from other terminologies to similar or identical terms in MedDRA and included codes from COSTART (5th Edition), WHO-ART© (3rd Quarter,

1998), ICD9, ICD9-CM, HARTS© (Release 2.2), and J-ART (1996). For example, PT *Nausea* in MedDRA has a corresponding term NAUSEA in COSTART.

MedDRA was not developed as a metathesaurus, and the hierarchies of these other terminologies are not subsets of it. Thus, data entry terms from other terminologies do not necessarily have the same PT in MedDRA as they did in their "parent" terminology. The hierarchies used for data retrieval and presentation are unique to MedDRA.

Inclusion of terms from other terminologies is restricted to those within the scope of MedDRA as defined above.

The ICH M1 Expert Working Group – who created the original version of MedDRA – included the numeric and symbol codes with the text of the terms; the codes were intended to be useful in the transition to MedDRA. Since most organizations have converted their data from older terminologies to MedDRA, and the codes have not been maintained or updated since the original release of MedDRA, the MSSO has removed them from the MedDRA files as of MedDRA v15.0.

Note that no MedDRA term names or codes have been modified or removed as a result of this action, and the structure of the MedDRA extended ASCII files has not changed.

1.7 EXCLUSION CRITERIA

The exclusion criteria used in the development of the terminology do not necessarily limit the terminology's expansion scope. Since this is a medical terminology, the following terms used in regulatory affairs are out of scope:

- Drug/product terminology (Note: The generic names of some commonly used products, such as digoxin, that are included with their associated adverse events)
- Equipment/device/diagnostic product terminology
- Study design
- Demographics (including patient sex, age, race, and religion).

As its focus is on health effects in individual patients, the following are excluded:

- Qualifiers that refer to populations rather than individual patients (e.g., rare, frequent)
- Numerical values associated with laboratory parameters are not included (e.g., serum sodium 141 mEq/L). See Section 4.9 for more details.
- Descriptors of severity are not included in the terminology. Descriptors such as "severe" and "mild" are used only when pertinent to the specificity of the term (e.g., severe vs. mild mental retardation).

2. STRUCTURAL ELEMENTS OF THE TERMINOLOGY

The MedDRA terminology was developed as a medically validated medical terminology for utilization throughout the regulatory process. The developers of the terminology designed a structure that promotes specific and comprehensive data entry and flexible data retrieval. Figure 2-1 represents the hierarchical structure of the terminology. Relationships between terms in the terminology fall into the following two categories:

2.1 EQUIVALENCE

The equivalence relationship groups synonymous terms, or equivalent terms, under Preferred Terms.

2.2 HIERARCHICAL

The hierarchy provides degrees or levels of superordination and subordination. The superordinate term is a broad grouping term applicable to each subordinate descriptor linked to it. Hierarchical levels thus represent vertical links in the terminology.

Hierarchies are an important mechanism for flexible data retrieval and for the clear presentation of data. The five-level structure of this terminology provides options for retrieving data by specific or broad groupings, according to the level of specificity required. The Lowest Level Term (LLT) level provides maximum specificity.

The terminology was not developed as a formal classification or taxonomy; each level in the hierarchy may reflect a variable degree of specificity or “granularity” from one System Organ Class to another. High Level Terms (HLTs) and High Level Group Terms (HLGTs) facilitate data retrieval and presentation by providing clinically relevant grouping of terms. Collectively, the HLT and HLGT levels are sometimes referred to as the “grouping terms” in MedDRA.

The 27 System Organ Classes (SOCs) represent parallel axes that are not mutually exclusive. This characteristic, called “multi-axiality,” allows a term to be represented in more than one SOC and to be grouped by different classifications (e.g., by etiology or manifestation site), allowing retrieval and presentation via different data sets. Grouping terms are pre-defined in the terminology and not selected on an ad hoc basis by data entry staff. Rather, the terminology is structured so that selection of a data entry term leads to automatic assignment of grouping terms higher in the hierarchy. Multi-axial links of terms are pre-assigned in MedDRA, ensuring comprehensive and consistent data retrieval, irrespective of which SOC is selected at data retrieval.

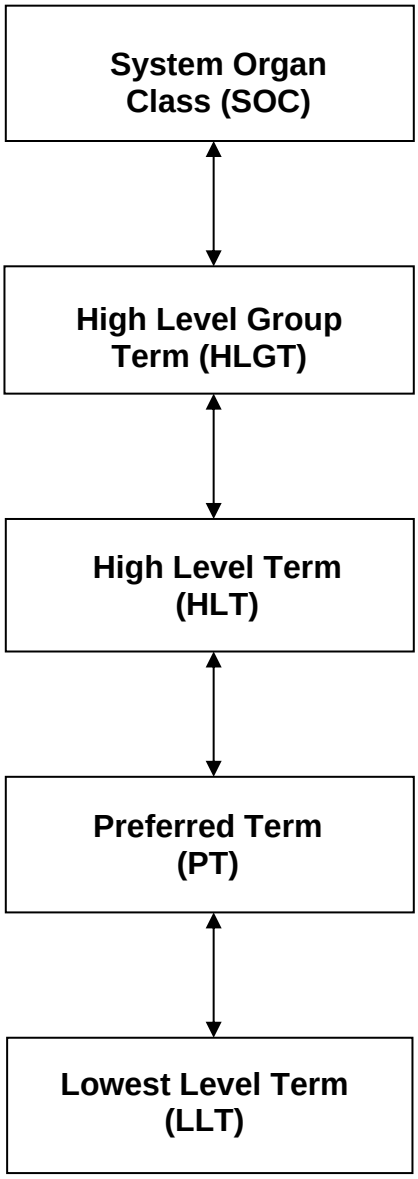

Figure 2-1. Structural Hierarchy of the MedDRA Terminology

3. LEVELS OF STRUCTURAL HIERARCHY

The levels of structural hierarchy are characterized as follows:

3.1 LOWEST LEVEL TERMS

LLTs constitute the lowest level of the terminology. Each LLT is linked to only one PT.

LLTs have any of the following relationships to their parent PT:

Synonyms: Different terms for the same concept inherent in the PT (e.g., PT *Arthritis* and its subordinate LLT *Joint inflammation*)

Lexical variants: Different word forms for the same expression. These include full names vs. abbreviations and direct vs. inverted word order (e.g., PT *Acquired immunodeficiency syndrome* and its subordinate LLT *AIDS* or PT *Biopsy tongue* and its subordinate LLT *Tongue biopsy*).

Quasi-synonyms: Quasi-synonyms are terms that are not precisely the same meaning as another term, but are treated as synonymous in a given terminology. These include site and laterality descriptions (e.g., PT *Otitis externa* and its subordinate LLT *Bilateral otitis externa*).

Sub-concept: Sub-concepts (of the parent PT concept) are represented by LLTs with more detailed information such as anatomic specificity (e.g., PT *Contusion* with LLT *Bruising of face* or LLT *Bruising of leg*).

Identical LLT: One LLT is identical to its PT for data entry purposes (e.g., PT *Dementia Alzheimer's type* and its subordinate LLT *Dementia Alzheimer's type*). In this instance, the LLT and parent PT have the same MedDRA code but appear at both levels.

Since LLTs may accommodate colloquial or culturally unique terms, every LLT may not have a unique translation in every language.

The LLT level plays an important role in facilitating the transfer of historical data because many of the terms from other terminologies incorporated, are represented at this level.

LLTs facilitate data entry and promote consistency by decreasing subjective choices made at this stage. LLTs may also be used as the basis for auto-encoding. Since LLTs may be more specific than the PT to which they are linked, users can retrieve data at the most specific level of the terminology.

LLTs carry a “current” or “non-current” flag status. Terms that are very vague, ambiguous, truncated, abbreviated, out-dated, or misspelled carry a non-current flag. These terms may derive from terminologies incorporated into MedDRA. The terminology retains LLTs with a non-current flag to preserve historical data for retrieval and analysis. The flag also allows users to implement the terminology within a database and prevent the inadvertent use of non-current LLTs in post-implementation coding.

3.2 PREFERRED TERMS

A **PT** is a distinct descriptor (single medical concept) for a symptom, sign, disease, diagnosis, therapeutic indication, investigation, surgical, or medical procedure, and medical, social, or family history characteristic.

PTs should be unambiguous and as specific and self-descriptive as possible in the context of international requirements. Therefore, eponymous terms are only used when they are recognized internationally.

The granularity/specificity of the PT level is such that clinical pathologic or etiologic qualifiers of the descriptors are represented at the PT level. For example, a variety of rhinitis and meningitis terms exist as separate entities at this level (e.g., PT *Rhinitis ~~perennial~~allergic*, PT *Rhinitis ulcerative*, PT *Rhinitis atrophic*, PT *Meningitis aseptic*, PT *Meningitis cryptococcal*, PT *Meningitis viral*, PT *Meningitis bacterial*, etc.). This level of specificity in PTs ensures that the multi-axial nature of the terminology can be maximally exploited.

There is no limit to the number of LLTs that can be linked to a PT, however, a PT must have at least one LLT linked to it. When a new PT is added to the terminology, an identical LLT is created automatically for data entry purposes.

PTs are subordinate to HLTs.

A PT must be linked to at least one SOC. A PT can be linked to as many SOCs as is appropriate. It can only be linked to each SOC via one HLT=>HLGT=>SOC route. Each PT has a primary SOC that determines under which SOC the term appears in cumulative data outputs.

3.3 HIGH LEVEL TERMS

An **HLT** is a superordinate descriptor for the PTs linked to it. It is an inclusive category which links PTs related to it by anatomy, pathology, physiology, etiology, or function. The terminology is not a taxonomy, so the specificity of HLTs is not uniform throughout the terminology (or between SOCs).

HLTs are intended for data retrieval and presentation purposes; they are a grouping level and are not intended to be a coding level.

HLTs are subordinate to HLGTs. An HLT must be linked to at least one SOC via an HLGT. It can only be linked to a particular SOC via one route (i.e., linked to only one HLGT per SOC). All HLTs linked to a particular HLGT will appear in every SOC to which the HLGT is linked.

3.4 HIGH LEVEL GROUP TERMS

An **HLGT** is a superordinate descriptor for one or more HLTs related by anatomy, pathology, physiology, etiology, or function.

HLGTs are intended for data retrieval and presentation purposes. HLGTs group HLTs to aid retrieval by broader concepts.

HLGTs are subordinate to SOCs. An HLGT must be linked to at least one SOC and to at least one HLT (the next levels up and down in the hierarchy, respectively).

There is no limit to the number of SOCs to which an HLGT can be linked.

3.5 SYSTEM ORGAN CLASS

A **SOC** is the highest level of the hierarchy that provides the broadest concept for data retrieval. SOCs comprise groupings by:

- Etiology (e.g., SOC *Infections and infestations*)
- Manifestation site (e.g., SOC *Gastrointestinal disorders*)
- Purpose (e.g., SOC *Surgical and medical procedures*)

The exception from the above categories is SOC *Social circumstances* which contains information about the person, not the adverse event and provides a grouping for those factors that may give insight into personal issues that could have an effect on the event being reported.

A SOC is related directly (superordinated) to at least one HLGT with no restriction on the number of links to HLGTs.

To avoid “double counting” while retrieving information from all SOCs, each PT is assigned a primary SOC. This is required because PTs can be represented in more than one SOC (multi-axiality). It prevents an individual PT from being displayed more than once in cumulative SOC-by-SOC data outputs, which would result in over-counting of terms. All PTs in MedDRA are assigned a primary SOC that determines the SOC in which the term is displayed in these outputs. This property does not prevent display and counting of the term in any of the SOCs in which it is represented for data retrieval purposes that do not involve all SOCs.

The following rules are used for the allocation of the primary SOC:

- PTs that are only represented in one SOC are automatically assigned that SOC as primary.
- PTs relating to diseases or signs and symptoms are assigned to the prime manifestation site SOC with the following exceptions:
  - Terms for congenital and hereditary anomalies are assigned to SOC *Congenital, familial and genetic disorders* as the primary SOC.

- Terms for neoplasms are assigned to SOC *Neoplasms benign, malignant and unspecified (incl cysts and polyps)* as primary SOC. This does not apply to cyst and polyp terms. These terms have as their primary SOC the manifestation site SOC. For example, PT *Aural polyp* has SOC *Ear and labyrinth disorders* as its primary SOC and SOC *Neoplasms benign, malignant and unspecified (incl cysts and polyps)* as its secondary SOC.
- Terms for infections are assigned to SOC *Infections and infestations* as the primary SOC.

If a PT links to more than one of these three "exceptions" SOCs, the following priority is used to determine the primary SOC:

- SOC *Congenital, familial and genetic disorders*
- SOC *Neoplasms benign, malignant and unspecified (incl cysts and polyps)*
- SOC *Infections and infestations*

As an example, PT *Congenital teratoma* is linked to SOC *Congenital, familial and genetic disorders* as the primary SOC with a secondary link to SOC *Neoplasms benign, malignant and unspecified (incl cysts and polyps)*.

The decision was made during the development of MedDRA to abrogate the general rule of manifestation site (rather than etiology) when determining the primary SOC allocation for neoplasms, congenital abnormalities, and infections. This was done to facilitate signal identification, since all PTs relating to such categories are grouped together on routine cumulative data outputs.

Other considerations for primary SOC allocation are as follows:

- Not all SOCs in MedDRA express multi-axiality. Terms contained within SOC *Investigations*, SOC *Social circumstances*, and SOC *Surgical and medical procedures* reside within those SOCs and nowhere else in the terminology because they lack multi-axial linkages.
- The majority (but not all) of injury, poisoning and procedural complications terms are represented in SOC *Injury, poisoning and procedural complications* as the primary SOC.
- Application, implant, and injection site reactions are assigned the primary SOC *General disorders and administration site conditions*, while infections at these sites have the primary SOC *Infections and infestations*.

The Alphabetical Listing of MedDRA SOCs is presented in Table 3-1 (in English). Presented in Table 3-2 are the MedDRA SOCs listed in the internationally agreed order. The original MedDRA Expert Working Group determined there is not a standard alphabetic order of SOCs due to the multi-lingual nature of MedDRA. As a result, they developed the international order to facilitate consistency irrespective of language or alphabet.

SOC *Blood and lymphatic system disorders*
SOC *Cardiac disorders*
SOC *Congenital, familial and genetic disorders*
SOC *Ear and labyrinth disorders*
SOC *Endocrine disorders*
SOC *Eye disorders*
SOC *Gastrointestinal disorders*
SOC *General disorders and administration site conditions*
SOC *Hepatobiliary disorders*
SOC *Immune system disorders*
SOC *Infections and infestations*
SOC *Injury, poisoning and procedural complications*
SOC *Investigations*
SOC *Metabolism and nutrition disorders*
SOC *Musculoskeletal and connective tissue disorders*
SOC *Neoplasms benign, malignant and unspecified (incl cysts and polyps)*
SOC *Nervous system disorders*
SOC *Pregnancy, puerperium and perinatal conditions*
SOC *Product issues*
SOC *Psychiatric disorders*
SOC *Renal and urinary disorders*
SOC *Reproductive system and breast disorders*
SOC *Respiratory, thoracic and mediastinal disorders*
SOC *Skin and subcutaneous tissue disorders*
SOC *Social circumstances*
SOC *Surgical and medical procedures*
SOC *Vascular disorders*

Table 3-1. The MedDRA Terminology SOC List – Alphabetical Listing

SOC *Infections and infestations*

SOC *Neoplasms benign, malignant and unspecified (incl cysts and polyps)*

SOC *Blood and lymphatic system disorders*

SOC *Immune system disorders*

SOC *Endocrine disorders*

SOC *Metabolism and nutrition disorders*

SOC Psychiatric disorders

SOC *Nervous system disorders*

SOC *Eye disorders*

SOC *Ear and labyrinth disorders*

SOC *Cardiac disorders*

SOC *Vascular disorders*

SOC *Respiratory, thoracic and mediastinal disorders*

SOC *Gastrointestinal disorders*

SOC *Hepatobiliary disorders*

SOC *Skin and subcutaneous tissue disorders*

SOC *Musculoskeletal and connective tissue disorders*

SOC *Renal and urinary disorders*

SOC *Pregnancy, puerperium and perinatal conditions*

SOC *Reproductive system and breast disorders*

SOC *Congenital, familial and genetic disorders*

SOC *General disorders and administration site conditions*

SOC *Investigations*

SOC *Injury, poisoning and procedural complications*

SOC *Surgical and medical procedures*

SOC *Social circumstances*

SOC *Product issues*

Table 3-2. The MedDRA Terminology SOC List – Internationally Agreed Order

3.6 STANDARDISED MedDRA QUERY (SMQ)

Standardised MedDRA Queries (SMQs) are groupings of MedDRA terms, ordinarily at the Preferred Term (PT) level that relate to a defined medical condition or area of interest. SMQs are intended to aid in the identification and retrieval of potentially relevant individual case safety reports. The included terms may relate to signs, symptoms, diagnoses, syndromes, physical findings, laboratory and other physiologic test data, etc. The only Lowest Level Terms (LLTs) represented in an SMQ are those that link to a PT used in the SMQ; all others are excluded.

For detailed information about the SMQs, please refer to the Introductory Guide for Standardised MedDRA Queries (SMQs), which is a separate document. It can be found along with the other supporting user documentation with this release.

4. RULES AND CONVENTIONS ADOPTED IN THE TERMINOLOGY (INCLUDING PRESENTATION AND FORMATTING OF TERMS)

This section, and sections 5 and 6 contain the rules and conventions used in the terminology. Each rule holds true in the majority of cases, but many rules will have exceptions. Some of those exceptions are listed within each rule, however, it is not possible to notate all exceptions. MedDRA is a medical terminology not a taxonomy and medically must be balanced, pragmatic, reflect actual medical practice, and have consideration for how different cultures interpret specific terms.

4.1 SPELLING

Terminology spelling consistently follows *Dorland's Illustrated Medical Dictionary (30th edition)*©, Dorland's online and standard medical literature for all medical terms. Nonmedical terms included in the terminology follow *Merriam-Webster® English Dictionary*.

Use of the hyphen is consistent with its most prevalent use in *Dorland's Illustrated Medical Dictionary* and standard medical literature. “Non” in a word will always be used with a hyphen unless it is a term not found in Dorland's but is accepted in the *Merriam-Webster English Dictionary* as one word (e.g., nontoxic, nonspecific, noninvasive, nondependent, nonmedical, nonproductive, noncompliance, nondominant, etc).

In accordance with *Dorland's Illustrated Medical Dictionary*, “post” terms are separated by a space with the following exceptions: hyphenated terms include “post-traumatic,” “postero-lateral,” and “post-term.” Examples of single word terms include forms of “postabortal,” “postpartum,” “postmature,” “postmenopausal,” “postmastoid,” “postvaccinal,” “postvaccinial,” “postnasal,” “postauricular,” “postictal,” “postmastectomy,” and “postnatal.”

British spellings are used at the PT level and above. At the LLT level, both the British spelling and the American spelling counterpart of the same term are included (e.g., LLT *Diarrhoea* and LLT *Diarrhea* under PT *Diarrhoea*). Misspelled terms that come from inherited terminologies are flagged as non-current.

4.2 ABBREVIATIONS

In general, abbreviations are excluded from levels above LLT. Exceptions to this rule are: 1) when including the full term makes the phrase very long (over 100 characters); and 2) when the term has a well-established abbreviation. Below are some examples:

CDC Centers for Disease Control (USA)

CNS central nervous system

CSF cerebrospinal fluid

ECG electrocardiogram

The following abbreviation is limited to the HLT and HLGT levels (with the exception of a few non-current LLTs)**:**

NEC not elsewhere classified

The following abbreviation is limited to the LLT level:

NOS not otherwise specified

Abbreviation letters are not punctuated by full stops (periods). Abbreviations or acronyms that may represent different meanings in the various ICH regions are excluded from the terminology to prevent ambiguity. Abbreviations and acronyms exhibiting multiple interpretations in standard text books of acronyms are generally not accepted for addition into the terminology. However, an acronym will be added, despite multiple interpretations, at the LLT level for its most common usage worldwide e.g.,LLT *CVA* for Cerebrovascular accident and LLT *Raised LFTs* for Raised liver function tests.

Based upon advice from the MedDRA Expert Panel, the majority of abbreviated virus LLTs (and related terms without abbreviations and a qualifier), which can be interpreted as either an investigation or infection terms such as LLT *HAV*, LLT *HBV,* and LLT *Hepatitis B virus,* are non-current. As of MedDRA 12.1, the MSSO will refrain from adding new abbreviated terms without the qualifier of “test” or “infection.”

The chemical elements are represented in MedDRA with their official chemical symbols on LLT level such as “Cl” for chloride and “Cu” for copper.

4.3 CAPITALIZATION

Most of the terminology is presented in lower case letters. Upper case letters are used only for the initial letter in each term, with the exception of proper names (e.g., PT *Non-Hodgkin's lymphoma*), and components of microorganism taxonomic names and abbreviations.

Terminologies, dictionaries, and thesauri traditionally use a mixture of lower and upper case letters to indicate the correct orthography of terms. However, organizations have complete flexibility regarding how they implement term case in their databases. Upper case terms can be used exclusively if desired.

4.4 PUNCTUATION

Apostrophes are used in proper names (e.g., PT *Gilbert's syndrome*).

Diacritical marks, for example the French “accent aigu” or “é”, (e.g., PT *Guillain-Barre syndrome*) are excluded from the English version of the terminology.

4.5 SINGLE WORD VS. MULTIPLE WORD TERMS

Each LLT or PT represents a single concept, but the concept may be expressed in one or more words.

Terms describing two or more concepts were “inherited” from other terminologies (e.g., LLT *Nausea vomiting and diarrhoea*). These compound terms are linked as LLTs to the PT that denotes the primary or most clinically relevant effect. For example, the term LLT *Nausea vomiting and diarrhoea* is linked to PT *Vomiting*. Additionally, this term has been flagged non-current.

4.6 WORD ORDER

In general, the PT, HLT, HLGT, and SOC levels use natural language word order which means the term is expressed in the way it is generally spoken (e.g., PT *Myocardial infarction*, not "Infarction myocardial"*).* The exception is when reversing the words in a PT facilitates grouping of similar terms for alphabetical display in SOC hierarchies. For example: PT *Meningitis aseptic,* PT *Meningitis chemical,* PT *Meningitis eosinophilic,* and PT *Meningitis toxoplasmal.*

4.7 MedDRA CODES

In contrast to the typical use of the word "code" in the regulatory milieu, within MedDRA, the "code" refers to the eight-digit number assigned to each term and is not to be confused with the text string of the term itself. Each term in MedDRA has a unique non-expressive code. Non-expressive, in this context, means that no information can be derived from the digits within the code (e.g., SOC assigned level within the hierarchy, etc.). A code is assigned to all terms across all categories. Initially, the codes were assigned in alphabetical order starting with 10000001. New terms added to the terminology are assigned the next sequential number. Previously used MedDRA codes are usually not reused for new terms, however, in some circumstances, when terms are renamed (e.g., the correction of misspellings), codes may be reused.

4.8 BODY SITE CONSIDERATIONS IN MedDRA

Abdominal wall – In general, the abdominal wall is classified in MedDRA as a gastrointestinal structure. There is not a formal definition for abdominal wall in MedDRA but, for the purpose of term placement, the MSSO considers the abdominal wall to comprise the peritoneum, muscles and fascia enclosing the abdominal cavity, thus classifying it as a gastrointestinal structure. The umbilicus and periumbilical area are considered to be skin structures and therefore are linked to SOC *Skin and subcutaneous tissue disorders*.

Cardiac and vascular anomalies – Certain congenital anomalies include both cardiac and vascular components; these terms are linked to HLT *Congenital cardiovascular disorders NEC* (with HLGT *Congenital cardiac disorders* linking it to SOC *Cardiac disorders*).

Chest wall - The chest wall is classified as a musculoskeletal structure. In general, terms related to the chest wall are linked to SOC *Musculoskeletal and connective tissue disorders*.

Eyelid - The eyelid is classified as a structure of the eye. In general, terms related to the eyelid are primarily linked to SOC *Eye disorders* and secondarily to SOC *Skin and subcutaneous tissue disorders*.

Pharynx and diaphragm - The pharynx and diaphragm are classified in MedDRA as respiratory structures.

Pinna - The pinna, including the ear lobe, is considered part of the ear and has a primary link to SOC *Ear and labyrinth disorders*.

4.9 NUMERICAL VALUES

Some MedDRA LLTs contain numerical values associated with certain clinical parameters (e.g., LLT *Foetal growth retardation, unspecified, 1,500-1,749 grams*); usually these are terms incorporated from other terminologies, and are flagged non-current since they do not fit MedDRA rules. Numerical values associated with laboratory parameters are also excluded (e.g., serum sodium 141 mEq/L). Numerals may be incorporated into LLTs and PTs when they are part of a name or inherent to the concept (e.g., PT *5-alpha-reductase deficiency*).

4.10 AGGRAVATION OF UNDERLYING CONDITIONS

The majority of terms expressing "aggravated" concepts (e.g., LLT *Allergy aggravated*) have been inherited from other terminologies. As a result of the modified term review, several similar concepts were added in MedDRA Version 9.1. However, in the future the MSSO will add new terms containing "aggravated," "worsen/-ed/-ing," or "exacerbated," only if they demonstrate medical significance.

4.11 NOS AND NEC TERMS

Terms including "NOS" (not otherwise specified) are a common feature of medical terminologies used within drug regulatory affairs. In MedDRA, "NOS" terms are only found on the LLT level and are meant to represent concepts for which no further specific information is available (e.g., during coding of adverse events). Terms carrying "NOS" reflect nonspecific terms and can only be interpreted with reference to other terms specified in the terminology. The specified concept is not a constant throughout this terminology (e.g., it may relate to acute vs. chronic conditions, body site, or infective organism). For coding, users should employ the most specific term available (e.g., LLT *Cluster headaches* vs. LLT *Headache NOS*). At the direction of the MedDRA Management Committee, as of MedDRA Version 6.1, no additional "NOS" terms will be accepted into the terminology. Additionally, all "NOS" terms previously existing at the PT level have been demoted to the LLT level in the terminology.

Similarly, "NEC" (not elsewhere classified) is a standard abbreviation used to denote groupings of miscellaneous terms that do not readily fit into other hierarchical classifications within a particular SOC. The "NEC" designation is used only with HLTs and HLGTs for grouping purposes. For example, HLT *Bladder disorders NEC* includes a diverse range of PTs including PT *Bladder stenosis,* PT *Bladder granuloma* and PT *Bladder telangiectasia*. All "NEC" terms previously existing at the PT level have been demoted to the LLT level and flagged non-current.

4.12 GENDER SPECIFIC TERMS

In general, gender specific terms are not included in MedDRA because patient gender is traditionally considered a database variable. However, a special case has been made for instances in which the gender of the patient makes the concept clinically distinct as for certain breast and reproductive tract disorders (e.g., PT *Breast cancer male* and PT *Breast cancer female*). In general, there is also a corresponding gender-neutral term (PT *Breast cancer*).

4.13 HIERARCHY NAMING CONVENTIONS

Plurality

Terms at the HLT and HLGT levels are normally in the plural form since they are groupings of medical concepts (e.g., HLT *Malignant hepatobiliary neoplasms*). Generally, terms at the PT and LLT levels are in the singular form since they are not groupings of medical concepts.

Use of Adjectives

The adjective form, e.g., “cardiac” or “hepatic” is used whenever possible instead of the noun (e.g., “heart” or “liver”). The exceptions are when there is a naming conflict (i.e., two terms at different levels that could potentially be represented by the same text string) or when the term is not normally stated as such in common practice. For example, “heart attack” is normally used in common practice rather than “cardiac attack.”

“Excl” and “Incl”

In order to be consistent with the conventions for the grouping terms, the standard use of terms with “including” or “excluding” are represented as the following:

1. “excl” represents excluding, “except,” and “excl.”
2. “incl” represents including and “incl.”

“Signs and symptoms;” “infections and inflammations”

In the text of terms where such phrases are used, the word order is “signs and symptoms” and “infections and inflammations.”

Benign and malignant

Generally, words “benign” and “malignant” are placed at the end of the text strings in SOC *Neoplasms benign, malignant and unspecified (incl cysts and polyps)* and at the beginning of the text strings in other SOCs. This convention provides information as to which SOC and HLGT the term belongs to by reading its name only.

Congenital

Generally, the word “congenital” is placed at the end of the text string in SOC *Congenital, familial and genetic disorders* and at the beginning of the term in other SOCs. This convention provides information as to which SOC and HLGT the term belongs by only reading its text string. The term “congenital” has been used to describe any condition present at birth, whether genetically inherited or occurring in utero.

Disorder, disease, and disturbance

In MedDRA, the concept of “disturbance” is subordinate to “disease” which is subordinate to “disorder.” “Disorder” is generally used in the HLT, HLGT, and SOC levels since it is more of a general term (e.g., HLGT *Gallbladder disorders*). As an exception, “disease” is sometimes used at the HLT level when this is the most common way of stating the concept e.g., HLT *Parkinson's disease and parkinsonism*. “Parkinson's disease” is the most common way of stating the term, not “Parkinson's disorder.”

“Disturbance” is synonymous with “disorder” and will be only added if that is the preferred wording for a concept. If a “disorder” term exists at the PT/LLT level, the “disturbance” concept will no longer be added.

5. PT AND LLT NAMING CONVENTIONS

5.1 GENERAL WORD USAGE

Alcohols: Single word names are used for alcohols (e.g., “ethanol,” not “ethyl alcohol”). The symbol –OH is spelled out (e.g., LLT *17-hydroxycorticosteroid activity*).

Anastomosis: This is classified as a surgical procedure and is single-axial linked to SOC *Surgical and medical procedures*. Alternative terms are used to describe related disorders outside of the surgical realm.

Cervical (neck) and Cervix (uterus): In general, the word “cervical” is used to identify the neck location whereas “cervix” is used to identify the uterine location. When a “cervical” term refers to the uterus, it carries the qualifier of “uterine” to differentiate it from cervical spine conditions. Exceptions to this latter convention are concepts that could only relate to the uterine location (e.g., PT *Cervical dysplasia*) and thus require no further qualification.

Dilation and Dilatation: Standard medical definitions of “dilation” and “dilatation” indicate that they are synonyms. The MSSO recognizes that there are some common usages in certain cultures for these types of terms. However, for purposes of distinction in MedDRA, the term “dilation” is considered a procedure and the term “dilatation” is considered a disorder. The word “procedure” is normally added to “dilation,” e.g., PT *Stomach dilation procedure* to make it self-explanatory. An exception to this convention is PT *Uterine dilation and curettage,* since it is recognized as a procedure without the addition of the qualifying word.

Drainage (surgical/procedural term) and Discharge (non-surgical secretion term): “Drainage” is a term used as a procedure (systematic withdrawal of fluids), whereas “discharge” and “secretion” are terms used for the excretion of liquids from the body. “Drainage” terms that fall outside of the realm of surgical procedures are considered exceptions and dealt with by using the word “discharge.” These terms are linked appropriately based on their particular meaning (e.g., PT *Post procedural discharge* links to SOC *Injury, poisoning and procedural complications*). In addition, all surgical terms retain “drainage” and link to SOC *Surgical and medical procedures*. Finally, if a term can be either a surgical procedure or a non-surgical term, then both the “term+drainage” (PT *Post procedural drainage* linked to SOC *Surgical and medical procedures*) and the “term+discharge” (PT *Post procedural discharge* linked to SOC *Injury, poisoning and procedural complications*) are present in the terminology and linked as indicated above. The MSSO recognizes that there are some common usages in certain cultures for these types of terms that may not be reflected by this MedDRA rule. Subscribers are advised to make clear which concept applies – surgical, non-surgical, or both – when submitting Change Requests.

Failure and Insufficiency: In MedDRA, for the major body systems of cardiac, hepatic, pulmonary, and renal, the words “failure” and “insufficiency” are used synonymously. In SOC *Cardiac disorders,* SOC *Hepatobiliary disorders,* SOC *Renal and urinary disorders,* and SOC *Respiratory, thoracic and mediastinal disorders,* the “failure” term is generally at the PT level and the “insufficiency” term is at the LLT level (e.g., PT *Cardiac failure* and LLT *Cardiac insufficiency*).
Interpretations of the words “failure” and “insufficiency” can be problematic; some users may interpret the concepts as synonymous while others interpret them as similar, but differing in severity (with “insufficiency” being less severe than “failure”). In order to reconcile this, MSSO decided to make the terms essentially synonyms for the major body systems as described above. The MSSO realizes this means that many subscribers will have a different interpretation of these words than MedDRA's, but MSSO found this was the most practical solution for consistency in the terminology.

Gangrene Terms: Terms with “gangrene” or “gangrenous” have a primary link to SOC *Infections and infestations,* except those specifically representative of a noninfective concept (e.g., PT *Dry gangrene*).

Drug Product Names: Generic drug names are used (e.g., “digoxin,” not “Lanoxin®”) but only appear in MedDRA because they give further clarification to their parent PT (e.g., PT *Toxicity to various agents*) in the early days of the terminology.

Greek Letters: Greek letters are spelled out (“alpha,” not “α;” “beta,” not “β”).

Eponymous Terms: Eponymous terms are only used if recognized internationally (e.g., LLT *Paul Bunnell test* linked to PT *Mononucleosis heterophile test*).

Lesion: Lesion terms may be considered for inclusion in MedDRA when the word “lesion” is part of a medical concept, e.g., PT *Glomerulonephritis minimal lesion* or a well-documented medical concept, e.g., LLT *Brain lesion.* However, the term will not be added when adding a broad “lesion” term only adds an additional imprecise term to existing “disorder” concepts, e.g., “renal lesion,” when one could use for coding the existing LLT *Renal disorder* under PT *Renal disorder*.

Lump (non-neoplastic): For MedDRA terms, the word “lump” is not considered neoplastic. Terms with “lump” are linked primarily to the SOC that represents the site of manifestation.

Mass (non-neoplastic): For MedDRA terms the word “mass” is not considered neoplastic. Terms with “mass” are linked primarily to the SOC that represents the site of manifestation. ”Mass” terms which have no inherent anatomic site (e.g., PT *Mass*) are linked as primary to SOC *General disorders and administration site conditions*.

Nodule: In general, new terms containing “nodule” are not added to MedDRA, except when a nodule represents a full diagnostic expression, e.g., PT *Milker’s nodules*.

Tumor (neoplastic): Terms containing the word "tumo(u)r" are considered neoplastic. PTs that represent tumors are linked primarily to SOC *Neoplasms benign, malignant and unspecified (incl cysts and polyps)*. The secondary link is to the site of manifestation when identified. If malignancy is not specified in a tumor term, it is linked to an HLT that contains the wording " …malignancy unspecified."

Congenital and Acquired: For conditions or diseases existing in both congenital and acquired forms, the following convention is applied: the more common form of the condition/disease is represented at the PT level without adding a qualifier of either "congenital" or "acquired." For example, hypothyroidism is more commonly acquired than congenital; therefore, the unqualified term is at the PT level (PT *Hypothyroidism*). The less common form of the condition or disease will also be at the PT level but with a qualifier added. Using again the example of hypothyroidism, the less common congenital form has the qualifier "congenital" at the PT level (PT *Congenital hypothyroidism*). The addition of qualified LLTs under the unqualified PT term is limited in MedDRA. The qualified LLTs will only be added in instances where the likelihood of occurrence of congenital and acquired condition is close to being the same. The alignment of existing affected terms along the lines described above (i.e., the "acquired," "congenital," and unqualified terms) has already been carried out in MedDRA Version 8.0. The subscriber Change Request process will drive the remainder of alignments of possible term sets.

Polyp Terms: The existing unqualified polyp terms in MedDRA (e.g., PT *Gastric polyps*) currently default to a benign classification within SOC *Neoplasms benign, malignant and unspecified (incl cysts and polyps)*. Newly accepted polyp terms will not include a qualifier of "benign." Polyps are secondarily linked to SOC *Neoplasms benign, malignant and unspecified (incl cysts and polyps)* and primarily linked to the appropriate site of manifestation SOC. Polyp terms with the qualifier of "malignant" will no longer be added to MedDRA. Instead, it is recommended that subscribers use available "malignant neoplasm" terms for their coding needs.

Death: Death terms are in SOC *General disorders and administration site conditions* and may have additional secondary links to related site or etiology SOCs. For example, PT *Death* is only linked to SOC *General disorders and administration site conditions*, while PT *Death neonatal* is linked primarily to SOC *General disorders and administration site conditions* and secondarily to SOC *Pregnancy, puerperium and perinatal conditions.*
Foetal and maternal death terms are linked primarily to SOC *Pregnancy, puerperium and perinatal conditions* as they are considered a special population.
"Death of a relative" is considered a social issue, and terms will be found linked only to SOC *Social circumstances*.
"Cell death" is considered an exception and is linked primarily to SOC *Metabolism and nutrition disorders* because it is an event on a cellular, not organism, level.

Occlusion and obstruction: In general, whenever referring to blood vessels, stents, shunts, and catheters, the word "occlusion" is used at the PT level (PT *Hepatic artery occlusion*). The word "obstruction" is generally used in association with non-vascular

terms, such as the gastrointestinal tract or respiratory system (e.g., PT *Large intestinal obstruction* and PT *Tracheal obstruction*).

Injury and damage: Injury and damage concepts were discussed by a MedDRA Expert Panel which resulted in new guidelines for MedDRA. Based on this, injury and damage terms in MedDRA are considered generally as synonymous. Injury or damage to a major organ that has a low probability for a traumatic causality will be placed primary to the site of manifestation, unless causality "due to accident" is the more obvious or the most probable. In this case, the term will be linked primary to SOC *Injury, poisoning and procedural complications*. Following this guidance some liver injury terms were re-aligned. PT *Cholestatic liver injury*, PT *Mixed liver injury*, and PT *Liver injury* are considered non-traumatic and are primarily linked to SOC *Hepatobiliary disorders* while PT *Traumatic liver injury* is primarily linked to SOC *Injury, poisoning and procedural complications*.

Intestine and Intestinal: Terms with a combination of small/large and intestine/intestinal refer to the anatomical site and not the severity of concepts, e.g., PT *Small intestinal haemorrhage* and PT *Large intestine polyp* refer to the site of haemorrhage and polyp respectively and not the severity of the two events.

Spine and Spinal: For the purposes of MedDRA, spine and spinal terms are considered synonymous with vertebral and spinal column concepts rather than with the spinal cord, unless "spinal" clearly represents a neurological concept such as PT *Spinal claudication*.

Unapproved and Unlabelled: For the purposes of MedDRA, the words "unapproved" and "unlabelled"/"unlabeled" are considered synonymous and refer to the use of products in a manner that is not specified in the product information (label) that has been approved by a regulatory authority. For example, the concepts of unapproved indication and unlabelled indication are similar in the following terms: PT *Unintentional use for unapproved indication* and LLT *Intentional use for unlabelled indication*.

5.2 GENERAL SEARCH STRATEGIES

Single-axial SOC search: SOC *Investigations*, SOC *Social circumstances*, and SOC *Surgical and medical procedures* are single-axial SOCs. The terms in these SOCs are only represented in these SOCs, i.e., they do not have links to any other SOCs in MedDRA. If a search of MedDRA-coded data is to include laboratory test results, social issues, or therapeutic procedures, these individual SOCs should be represented in the query. For example, increased blood glucose is associated with diabetes mellitus; however, PT *Diabetes mellitus* is represented in SOC *Metabolism and nutrition disorders* and SOC *Endocrine disorders*, whereas PT *Blood glucose increased* is represented only in SOC *Investigations*. (Please refer to Section 6 - System Organ Classes - for additional information.)

6. SYSTEM ORGAN CLASSES

Explanatory Notes

Explanatory notes are provided for each SOC and cover its structure and the basis for classification (e.g., anatomic, pathologic, or etiologic). These notes provide guidance on use of the terminology to ensure effective and comprehensive data retrieval.

6.1 BLOOD AND LYMPHATIC SYSTEM DISORDERS

6.1.1 Basis for Classification

- The terms within this SOC are primarily divided pathologically at the HLGT level
- At the HLT level, terms are further subdivided by etiology and pathology wherever possible. For example:
  - HLTs concerning hemolysis are divided by etiology
  - HLTs concerning spleen, lymphatic, and reticuloendothelial system disorders are divided on an anatomic basis
  - HLTs concerning hematologic neoplasms have been classified according to histologic criteria

6.1.2 Conventions and Exceptions

- The representation of hematologic neoplasms is identical to the hierarchy developed for the same terms within SOC *Neoplasms benign, malignant and unspecified (incl cysts and polyps)*
- Lymphoma terms in MedDRA generally follow the Revised European-American Lymphoma (R.E.A.L.) classification and the revised WHO lymphoma classification
- All lymphatic system-related disorders have their primary link to SOC *Blood and lymphatic system disorders* except infective and congenital disorders. (Lymphoma terms do not follow this convention).

6.1.3 Search Strategies

- If a search is intended to cover an overall classification of various types of blood disorders such as a search for anemias or a search for “bleeding diatheses”, multiple HLGTs should be considered because relevant terms are divided in different groupings

6.2 CARDIAC DISORDERS

6.2.1 Basis for Classification

- The division of HLGTs within this SOC has been done partly on an anatomic basis (e.g., myocardial disorders) and partly by pathophysiology (e.g., arrhythmias)
- HLTs are grouped by pathophysiology, with the exception of valve disorders, which are grouped anatomically by the valve affected

6.2.2 Conventions and Exceptions

- All congenital cardiac disorders are placed within a specific HLGT. This includes terms for certain congenital anomalies that include both cardiac and vascular components.
- Electrocardiogram (ECG) results and auscultatory abnormalities are not included in SOC *Cardiac disorders*; they are grouped within SOC *Investigations*
- For the major body systems of cardiac, hepatic, pulmonary, and renal, the terms “failure” and “insufficiency” are used synonymously. In SOC *Cardiac disorders*, the “failure” term is at the PT level and the “insufficiency” term is at the LLT level.

6.3 CONGENITAL, FAMILIAL AND GENETIC DISORDERS

6.3.1 Basis for Classification

- The terms within this SOC are primarily divided anatomically at the HLGT level. Where possible, these divisions at the HLGT level reflect the system organ classes used in MedDRA as a whole.
- At the HLT level, terms are further subdivided by anatomy wherever possible
- For those HLGTs that cannot be divided by anatomy, PTs are grouped in HLTs by disease process or by type of organism
- This SOC covers gene concepts, conditions, variants, and alterations regardless of whether they are acquired or congenital

6.3.2 Conventions and Exceptions

- In MedDRA, the term “congenital” is used to describe any condition present at birth, whether genetically inherited or occurring in utero
- Most MedDRA terms representing congenital, familial, and genetic disorders have manifestations in more than one system organ class. Since a term can only appear in one HLT within a SOC, the HLT for these terms has been selected according to the most clinically significant manifestation of that disorder. Additionally, these terms typically have SOC *Congenital, familial and genetic disorders* as their primary SOC. However, they will have links to secondary SOCs as usual in the multi-axial structure.
- For conditions or diseases existing in both congenital and acquired forms, the following convention is applied: the more common form of the condition/disease is represented at the PT level without adding a qualifier of either “congenital” or “acquired”
- The addition of qualified LLTs under the unqualified PT is limited in MedDRA. The qualified LLTs will only be added in instances where the likelihood of occurrence of congenital and acquired conditions is close to being the same.

6.4 EAR AND LABYRINTH DISORDERS

6.4.1 Basis for Classification

- The terms within this SOC are primarily divided at the HLGT level by anatomic site (external, middle, and inner ear)
- At the HLT level, terms are further subdivided anatomically, but the disease process may also be reflected at this level
- Congenital problems are grouped in a separate HLGT which is subdivided into HLTs by anatomic criteria

6.4.2 Conventions and Exceptions

- The PTs for neoplasms appear in the appropriate HLT by anatomic site
- Site-specific infections and inflammations are grouped at the HLT level in the appropriate HLGT by anatomic site
- The pinna, which includes the ear lobe, is considered part of the ear structure and is primarily linked to SOC *Ear and labyrinth disorders*

6.5 ENDOCRINE DISORDERS

6.5.1 Basis for Classification

- Endocrine disorders are classified using two general approaches:
  - The first approach groups HLTs specific to the dysfunction of a specific endocrine gland under an HLGT specific to that gland
  - The second type of classification includes HLGTs that group disorders affecting multiple endocrine glands
- Many of the terms related to gonadal function disorders are primarily linked to the body system SOC that is affected, with secondary links to SOC *Endocrine disorders*

6.5.2 Conventions and Exceptions

- There are two separate HLGTs that relate to diabetes: HLGT *Glucose metabolism disorders (incl diabetes mellitus)*, with HLTs for diabetes mellitus and both hypo- and hyperglycemic conditions; and HLGT *Diabetic complications*, which subdivides the complications of the disease anatomically. These two HLGTs are multi-axial and are primarily linked to SOC *Metabolism and nutrition disorders* and secondarily to SOC *Endocrine disorders*.
- Pancreatic endocrine disorders are linked primarily to SOC *Endocrine disorders*, whereas pancreatic exocrine disorders are linked primarily to SOC *Gastrointestinal disorders*. If the term does not distinguish between endocrine and exocrine, then the primary link defaults to SOC *Gastrointestinal disorders.*

6.6 EYE DISORDERS

6.6.1 Basis for Classification

- SOC *Eye disorders* is subdivided along pathophysiologic and anatomic lines:
  - The primary ordering of the HLGTs is according to pathophysiology. These HLGTs are subdivided using anatomically classified HLTs.
  - Both pathophysiology and anatomy are used to approach the classification of other HLGTs, which are disorders occurring in specific tissues of the eye. HLTs are also further classified anatomically.
- Eyelid, lash, and lacrimal disorders are included in this SOC
- Ocular neoplasms are subdivided pathophysiologically according to tumor type
- Note that there are hierarchical classifications in other SOCs that include terms of relevance to ophthalmologic concepts. Such terms merit consideration when designing search strategies and data retrieval and analysis criteria for terms pertaining to eye disorders. Examples include:
  - SOC *Nervous system disorders*
  - SOC *Surgical and medical procedures*
  - SOC *General disorders and administration site conditions*
  - SOC *Injury, poisoning and procedural complications*
  - SOC *Investigations*

6.6.2 Conventions and Exceptions

- Terms that represent blindness as a disability are linked to SOC *Social circumstances*
- Terms that represent blindness as a medical disorder are linked to SOC *Eye disorders* and to SOC *Nervous system disorders*
- The eyelid is classified as a structure of the eye. In general, terms related to the eyelid are primarily linked to SOC *Eye Disorders* and secondarily to SOC *Skin and subcutaneous tissue disorders*.

6.7 GASTROINTESTINAL DISORDERS

6.7.1 Basis for Classification

- There are three principles for classification in this SOC:
  - Terms are grouped at the HLGT level by a mix of disease process, etiology, and pathologic groupings such as hernias, infections, and ulcerations. These HLGTs are subdivided into HLTs by anatomic site or subtypes of the disease process.
  - Neoplasm terms are grouped into separate HLGTs for benign neoplasms and for malignant and unspecified neoplasms
  - The remaining HLGTs are based on anatomic site, disease process, or a combination of both

6.7.2 Conventions and Exceptions

- Gastrointestinal infections and gastrointestinal inflammatory conditions are in separate HLGTs in SOC *Gastrointestinal disorders*. In other SOCs, inflammatory and infectious conditions are often within a single HLGT.
- Pancreatic endocrine disorders are linked primarily to SOC *Endocrine disorders*. Pancreatic exocrine disorders are linked primarily to SOC *Gastrointestinal disorders*. If the term does not distinguish between endocrine and exocrine, then the primary link defaults to SOC *Gastrointestinal disorders*.

6.8 GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS

6.8.1 Basis for Classification

- This SOC contains terms that do not readily fit into the hierarchy of any one SOC or are nonspecific disorders that impact several body systems or sites
- HLGTs within it are divided by etiology (e.g., administration site reactions) or pathology (e.g., fatal outcomes)
- The HLTs within each HLGT are mainly divided by disease process. Exceptions are terms related to administration site reactions, which are divided by type of administration (e.g., application, implant, and injection site); and terms related to therapeutic and nontherapeutic effects, which are grouped by type of effect (e.g., interactions).

6.8.2 Conventions and Exceptions

- Representing PTs in SOC *General disorders and administration site conditions* in each potential secondary SOC would create an inordinately large number of multi-axial links. Therefore, most of the PTs in this SOC are primarily linked to SOC *General disorders and administration site conditions*, and have limited representation in secondary SOCs.
- Certain temperature concepts such as high temperature and spiking temperature are LLTs in SOC *General disorders and administration site conditions*. Although the concepts should appear in SOC *Investigations* by convention (i.e., they could be interpreted as a measured parameter), it is most frequently used as an expression for fever (PT *Pyrexia*). Thus, these terms are represented in SOC *General disorders and administration site conditions*.
- Terms related to complications associated with devices are used to capture patient reactions that occur during the use of a medical device (may or may not be directly attributable to the use of the device) and events that are a direct consequence of use of the medical device. In general, medical device event concepts are represented at the PT level, while corresponding sub-concepts pertaining to events with specific types of widely used devices are usually represented at the LLT level.

6.9 HEPATOBILIARY DISORDERS

6.9.1 Basis for Classification

- The terms in this SOC are grouped as follows:
  - HLGTs that are grouped by anatomic location and are subdivided into HLTs reflecting the etiology or disease process
  - Hepatobiliary neoplasms are in a separate HLGT which distinguishes between benign, malignant, and neoplasms with unspecified characteristics at the HLT level
- Two spellings, “hepato-biliary” and “hepatobiliary,” are used frequently in practice. MedDRA uses “hepatobiliary,” following *Dorland's Illustrated Medical Dictionary*
- For the major body systems of cardiac, hepatic, pulmonary, and renal, the terms “failure” and “insufficiency” are used synonymously. In SOC *Hepatobiliary disorders*, the “failure” term is at the PT level and the “insufficiency” term is at the LLT level.

6.10 IMMUNE SYSTEM DISORDERS

6.10.1 Basis for Classification

- The terms within this SOC are divided by disease process. Further sub-classification at the HLT level is by pathologic groupings, with some anatomically based subdivision.

6.10.2 Conventions and Exceptions

- Due to the systemic nature of SOC *Immune system disorders*, multi-axial terms are especially frequent. For instance, conditions related to the group of "connective tissue disorders" are found in SOC *Immune system disorders* as well as in SOC *Musculoskeletal and connective tissue disorders*, with still a possible third link in the related anatomic SOCs (generally the primary link).
- Other pathologic groupings within SOC *Immune system disorders*, in which a similar multi-axial richness can be found, are transplant rejection terms. The concept of transplant rejection is recognized as an effect of the immune system; therefore, related terms have SOC *Immune system disorders* as the primary link and SOC *Injury, poisoning and procedural complications* as well as the site of manifestation as secondary links.
- Only very well defined secondary immunodeficiencies have been included in an HLT for immunodeficiency disorders. The link of all possible immunodeficiencies under this HLT would result in too large a group for analytical purposes.

6.11 INFECTIONS AND INFESTATIONS

6.11.1 Basis for Classification

- SOC *Infections and infestations* was developed to provide a unique location for infectious disorders and related conditions
- The organization of this SOC at the HLGT level is based on broad, commonly used taxonomic classifications of pathogens (e.g., bacterial, viral, fungal, and ectoparasitic infections)
- At the HLT level, these groups are further sub-classified by genus in most cases for bacterial, protozoal, fungal, and viral disorders
- Within this SOC there is a general “pathogen unspecified” HLGT that is used to group together infections by anatomic location rather than pathogen class. The HLTs under this HLGT are named according to general anatomic location. However, diseases of specific anatomic locations caused by specified pathogens are classified under the name of the pathogen, and not under the corresponding anatomic location in this HLGT.

6.11.2 Conventions and Exceptions

- Most PTs in SOC *Infections and infestations* are primarily linked to this SOC. Exceptions are PTs that have a primary link to either SOC *Congenital, familial and genetic disorders* or SOC *Neoplasms benign, malignant and unspecified (incl cysts and polyps)*. For these terms, the link to SOC *Infections and infestations* is secondary.
- Additionally, PTs under HLT *Inflammatory disorders following infection* within HLGT *Ancillary infectious topics* also generally have a secondary link to SOC *Infections and infestations*. This HLGT does not include PTs representing infections or infestations but instead includes PTs that are very closely related such as infectious disease carriers; it also has terms representing types of infectious transmission or the above-mentioned inflammatory conditions following an infection.
- Terms ending with “-itis” are linked to SOC *Infections and infestations* only if they most frequently represent infectious conditions. Those terms that most frequently represent inflammatory conditions are linked to their corresponding site of manifestation SOCs without a primary link to SOC *Infections and infestations*.
- In general, pathogen genus is represented at the HLT. The PT level generally combines genus and anatomic site of infection in a single term. Genus, anatomic site, and species are designated in a single term at the LLT level.
- When the concepts of “sepsis” and “septic(a)emia” are paired in the terminology, the “sepsis” terms are PTs and the corresponding “septic(a)emia” terms are LLTs
- Terms with “gangrene” or “gangrenous” have a primary link to SOC *Infections and infestations*, except those specifically representative of a noninfective concept such as dry gangrene

- Within SOC *Infections and infestations,* PT level “cellulitis” terms are linked to the appropriate bacterial infection HLTs rather than the site of manifestation HLTs

6.11.3 Search Strategies

- For a search of opportunistic infections, the underlying disease, drug class, and other aspects possibly relevant to the question should be considered. For example, the most likely pathogen or the body site affected may differ depending on the cause of immunosuppression (e.g., HIV infection, solid organ transplant, hematopoietic stem cell transplant, malignancy, chemotherapy, TNF-alpha blockers, etc.), geographical region, and calendar year/decade (due to changes of prominence of pathogens over time).
- *Opportunistic infections (SMQ)* includes terms from SOC *Infections and infestations* for pathogens causing opportunistic infections as well as relevant terms from SOC *Investigations*
- Additional terms may be relevant for inclusion in a search strategy for specific conditions as in the following examples:
  - For an underlying HIV infection, many PTs containing "HIV," "AIDS," "CD4," or "T-lymphocyte" may be included
  - For an underlying solid organ transplant or hematopoietic stem cell transplant, certain PTs containing "transplant" or "graft" may be relevant
  - For an underlying malignancy, SOC *Neoplasms benign, malignant and unspecified (incl cysts and polyps)* may be reviewed; certain PTs indicating neutropenia and resulting complications secondary to chemotherapy may be added to the search

6.12 INJURY, POISONING AND PROCEDURAL COMPLICATIONS

6.12.1 Basis for Classification

- This SOC provides a grouping for those medical concepts where an injury, poisoning, procedural, or device complication factor is significant in the medical event being reported
- Terms that represent events directly attributed to trauma, poisoning, and procedural complications are primarily linked to SOC *Injury, poisoning and procedural complications*, with the exception of terms related to birth trauma which is primary to SOC *Pregnancy, puerperium and perinatal conditions*
- Bone fractures, which in most cases are frequently attributed to trauma, are primary to this SOC, whereas pathologic and osteoporotic fractures are primary to SOC *Musculoskeletal and connective tissue disorders*
- Terms for poisoning and toxicity are generally primarily linked to this SOC. When the body system is identified by the text string of the term associated with poisoning or toxicity, the SOC representing the site of manifestation is primary SOC in these scenarios. Based upon the common usage of the words “poisoning” and “toxicity” interchangeably, a distinction is not made between poisoning and toxicity in MedDRA.
- Injury and damage terms in MedDRA are generally considered as synonymous. Injury or damage to a major organ that has a low probability for a traumatic causality will be placed primary to the site of manifestation and its relevant anatomic SOC. If causality ”due to accident” is the more obvious or the most probable, the term will be linked primary to SOC *Injury, poisoning and procedural complications*.
- A distinction has been made between exposure “to” versus exposure “via” terms because this distinction is relevant to the representation of different exposure concepts and is of particular significance to toxicologic elements of pharmacovigilance. The “via” terms indicate the vehicle by which the patient is exposed whereas “to” concepts identify the specific agent of exposure. The “via” terms are meant to be used in combination with one or more additional term(s), for example, to code the agent of exposure and any resulting clinical consequences.
- Surgical and medical procedure related injuries and complications are included in this SOC. HLGT *Administration site reactions* is a multi-axial HLGT. It is primarily linked to SOC *General disorders and administration site conditions* and secondarily to SOC *Injury, poisoning and procedural complications.*
- Medication errors and other product use errors and issues are included in this SOC. Terms include the types of errors and issues and include the various stages in the medication/product use process (e.g., prescribing, storage, dispensing, and administration).
- Intentional product use issues are grouped separately and include off label use and misuse concepts

- Overdose and underdose terms are also included in this SOC.

6.12.2 Conventions and Exceptions

- Bone and joint injuries are grouped in a separate HLGT from other body system injury terms. This has been done for two reasons: 1) the skeletal system is frequently and significantly impacted by traumatic injuries; and 2) this additional level of classification allows a better linking to SOC *Musculoskeletal and connective tissue disorders*.
- Although terms for acute alcohol intoxication or poisoning are found in this SOC, the concept of ”alcoholism” is represented in SOC *Psychiatric disorders*.

6.13 INVESTIGATIONS

6.13.1 Basis for Classification

- The most significant characteristics of SOC *Investigations* are: 1) its content (i.e., investigations, not conditions); and 2) its single-axial nature.
- For MedDRA, an “investigation” is a clinical laboratory test concept (including biopsies), radiologic test concept, physical examination parameter, and physiologic test concept (e.g., pulmonary function test).
- Only PTs representing investigation procedures and qualitative results (e.g., increased/decreased, normal/abnormal) appear in SOC *Investigations*. Terms representing conditions (e.g., hyperglycemia and glycosuria) are excluded from this SOC and can be found in the respective “disorder” SOC.
- Terms in SOC *Investigations* are present only in this SOC and in no other SOC (i.e., SOC *Investigations* is single-axial). Therefore, it is important that queries of MedDRA-coded data encompass terms from both the “disorder” SOCs as well as the supporting investigation concepts in SOC *Investigations* since one cannot exploit multi-axial links to bridge these types of terms.
- Several classification approaches to HLGTs are used in this SOC:
  - Some HLGTs group investigations according to body system or according to the clinical discipline commonly specializing in a particular body system
  - Other HLGTs group (by type of substance, or by type of procedure) those analyses or investigations that do not fit readily into a single body system
- Where possible, PTs in this SOC are those included in IUPAC, LOINC®, and IFCC standards. However, in some cases, texts of terms from these standard terminologies are not the commonly used wording by practitioners. In these instances, the text strings used in MedDRA are the ones more commonly used in practice. Vitamins are represented by their common names rather than by the chemical names used in IUPAC.

6.13.2 Conventions and Exceptions

- The qualifier “increased” in MedDRA terms refers to changes from normal state to high, from low to normal, from low to high, and from low normal to high normal. Similar considerations apply to results that are “decreased.” MedDRA investigation terms use the qualifiers of “low” and “high” at the LLT level only; these LLTs with “low” and “high” are linked to PTs with qualifiers of “decreased” and “increased” respectively. Additionally, qualifiers "low/decreased" and “high/increased” in SOC *Investigations* are considered synonyms.

- "High and "low" terms in MedDRA are generally considered to be laboratory/investigation type of terms and are found in the SOC *Investigations.* Exceptions to this rule are as follows:
  - LLT *Blood pressure high* and LLT *Low blood pressure* are linked to PT *Hypertension* or PT *Hypotension*; these PTs are in SOC *Vascular disorders*
  - PTs representing "low grade" neoplasms are linked to SOC *Neoplasms benign, malignant and unspecified (incl cysts and polyps)*
  - PT *Sputum decreased* and PT *Sputum increased* are in SOC *Respiratory, thoracic and mediastinal disorders*. This is because these terms commonly express a medical condition rather than an investigation finding.
- Certain temperature concepts such as high temperature and spiking temperature are LLTs in SOC *General disorders and administration site conditions*. Although the concepts should appear in SOC *Investigations* by convention (i.e., they could be interpreted as a measured parameter), it is most frequently used as an expression for fever (PT *Pyrexia*). Thus, these terms are represented in SOC *General disorders and administration site conditions*.
- The qualifier "abnormal" in a MedDRA term represents a situation where the "direction" (i.e., increased or decreased) of the abnormal result is not specified. Other qualifiers used in SOC *Investigations* are "normal," "present," or "absent" for descriptive laboratory tests, "positive" or "negative" for qualitative, "prolonged," or "shortened" for tests measured in time, and "toxic," "therapeutic," or "subtherapeutic" for drug level monitoring tests.
- Unqualified terms (e.g., PT *Blood glucose*) are intended to be used to record test names and point to an actual value in a separate database field
- Terms containing the prefixes "hyper-" and "hypo-" are found in their respective "disorder" SOCs and not in SOC *Investigations*
- If an analyte is not normally present in a specimen, the PT describing that abnormality may be used in some cases (e.g., PT *Glucose urine present*)
- Blood is no longer the default/assumed specimen when a Change Request does not specify the specimen type. Newly added terms will include the specimen type if it is medically significant. When new terms without specimen type are added as PTs, any corresponding existing terms with specimen type will be demoted to LLT and linked to this new term.
- For non-laboratory procedures (e.g., radiology), anatomic site replaces specimen type in the term and is stated in the text string
- Generally, the descriptors "direct" and "indirect" are used only at the LLT level; one exception is the placement of Coombs direct/indirect tests at the PT level

6.14 METABOLISM AND NUTRITION DISORDERS

6.14.1 Basis for Classification

- There are three broad approaches to group terms at the HLGT level in this SOC:
  - The first type groups HLTs into HLGTs that describe disorders in the handling of specific substances by the body
  - The second type of grouping assembles HLGTs describing conditions associated with nutritional disorders in general
  - The third type of HLGT covers medical conditions that may not be associated with a specific metabolic or nutritional pathogenesis

6.14.2 Conventions and Exceptions

- Due to the multiplicity of etiologies and effects of many imbalances and disorders, most of these conditions have been assembled within HLT *Metabolic disorders NEC*
- It should be noted that there are two separate HLGTs that relate to diabetes: HLGT *Glucose metabolism disorders (incl diabetes mellitus)* and HLGT *Diabetic complications.* These two HLGTs are multi-axial and are primarily linked to SOC *Metabolism and nutrition disorders* and secondarily to SOC *Endocrine disorders*.

6.15 MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS

6.15.1 Basis for Classification

- SOC *Musculoskeletal and connective tissue disorders* is classified at the HLGT level by tissue type such as bone, or by disease entity such as neoplasms

6.15.2 Conventions and Exceptions

- Fracture terms in this SOC are closely aligned with bone and joint injury concepts SOC *Injury, poisoning and procedural complications*. Terms that are directly attributed to trauma, poisoning, and procedural complications are primarily linked to SOC *Injury, poisoning and procedural complications*. For example, bone fractures, which in most cases are attributed to trauma, are primary to SOC *Injury, poisoning and procedural complications*, whereas pathologic and osteoporotic fractures are primary to SOC *Musculoskeletal and connective tissue disorders*.
- There is also a grouping for those general soft tissue terms that cannot be linked to other specific body system organ classes within this SOC

6.16 NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)

6.16.1 Basis for Classification

- This SOC is classified anatomically, with pathologic sub-classifications for staging of both benign and malignant neoplasms. The reference for PT names is the PDQ (*Physicians Data Query*) *Terminology Guide*, a publication of the United States National Cancer Institute, except in the area of non-Hodgkin's lymphomas.
- Lymphoma terms in MedDRA generally follow the Revised European-American Lymphoma (R.E.A.L.) classification and the revised WHO lymphoma classification.
- For cysts and polyps, the primary linkage is to the site of manifestation with secondary linkage to SOC *Neoplasms benign, malignant and unspecified (incl cysts and polyps)*. All other neoplasm terms have a primary linkage to this SOC with secondary linkages to the site of manifestation.
- At the present time, the words “cancer” and “carcinoma” are used synonymously within the anatomically classified HLGTs at the PT and LLT levels of the MedDRA hierarchy, even though it is recognized that there is a distinction between such concepts. In addition to the terms that relate to classifications by stage of therapy, there has been an attempt to include PTs to capture terms that are less specific and do not provide staging information.
- Breast neoplasms HLGTs make a distinction between male and female malignant neoplasms. This is one of the few instances in MedDRA where a distinction is made for gender.
- Primary site malignant neoplasms that have metastasized are qualified by the word “metastatic” (e.g., PT *Bone cancer metastatic* represents a primary malignant neoplasm of bone which has metastasized to a site elsewhere in the body). Neoplastic lesions at secondary sites are qualified by the phrase “metastases to” (e.g., PT *Metastases to gallbladder* represents a malignant neoplasm from somewhere in the body that has established a metastatic focus in the gallbladder).

6.16.2 Conventions and Exceptions

- Sarcomas are classified outside the strict anatomic classification due to the ubiquitous nature of these neoplasms
- Malignant melanomas which do not specify an anatomical site, by convention are classified as skin melanomas, which is the most prevalent location
- When staging for a malignant neoplasm is included in the text string, the naming convention of “site/malignancy/stage” is maintained as much as possible in this SOC
- Terms for staging information are not included for malignancies for which therapy is not stage-dependent.

- HLGT *Neoplasm related morbidities* contains terms for disorders that are associated with neoplastic conditions. Some, but not all, PTs in this grouping that are specific to sites of manifestation have primary links to that site with SOC *Neoplasms benign, malignant and unspecified (incl cysts and polyps)* as a secondary link.
- HLGT *Metastases* contains terms for both specific site involvement and unknown or unspecified sites. The specific site terms generally have a primary link to SOC *Neoplasms benign, malignant and unspecified (incl cysts and polyps)* and a secondary link to the site of manifestation SOC.
- "Metastatic" terms are present at the PT level in MedDRA and are distinct from other PTs indicating a "stage IV" of malignancy. This has been done because metastasis can occur at different stages of disease and is not exclusively associated with stage IV, thus a linkage of "metastatic" terms to "stage IV" terms would not always be appropriate.
- "High" and "low" terms in MedDRA are generally considered to be laboratory/investigation type of terms and are found in SOC *Investigations*. An exception to this rule is PTs representing "low grade" neoplasms which are linked to SOC *Neoplasms benign, malignant and unspecified (incl cysts and polyps)*.
- The existing unqualified polyp terms in MedDRA currently default to a benign classification. Newly accepted polyp terms do not include a qualifier of "benign." Polyps are secondarily linked to SOC *Neoplasms benign, malignant and unspecified (incl cysts and polyps)*, and primarily linked to the appropriate site of manifestation SOC. Within SOC *Neoplasms benign, malignant and unspecified (incl cysts and polyps)*, polyp terms are linked to HLTs that represent the benign form rather than the malignant/unspecified form. Polyp terms with the qualifier of "malignant" will no longer be added to MedDRA. Instead, it is recommended that MedDRA users consider available "malignant neoplasm" terms for their coding needs.

6.17 NERVOUS SYSTEM DISORDERS

6.17.1 Basis for Classification

- Neurologic disorders are classified using three broad approaches at the HLGT level:
  - Anatomy
  - Etiology
  - Pathophysiology
- In MedDRA, signs and symptoms uniquely associated with disorders are generally included as HLGTs covering those disorders. However, neurologic signs and symptoms that could be associated with a variety of disorders are classified under HLGT *Neurological disorders NEC.*

6.17.2 Conventions and Exceptions

- Headaches have their own HLGT

6.18 PREGNANCY, PUERPERIUM AND PERINATAL CONDITIONS

6.18.1 Basis for Classification

- Disorders are grouped in a variety of ways in this SOC to distinguish between maternal, fetal, and neonatal disorders, and to delineate disorders according to the timeline of pregnancy (e.g., labor, delivery, postpartum, etc.)
- Others are classified at the HLGT level according to anatomy

6.18.2 Conventions and Exceptions

- This SOC includes terms that represent both normal and high-risk conditions related to pregnancy that are not complications or adverse events
- Abnormalities of fetal presentation, which could be considered both a maternal and fetal complication, are included
- HLGT *Neonatal and perinatal conditions* represents the only specific “pediatric” grouping within the terminology. Terms for other pediatric conditions are dispersed amid terms for adult conditions.
- Terms relating to fetal and neonatal issues are generally primarily linked to the site of manifestation SOC with a secondary link to this SOC
- Terms involving fetal exposure to drugs and other substances (e.g., tobacco) have a primary link to SOC *Injury, poisoning and procedural complications* and a secondary link to SOC *Pregnancy, puerperium and perinatal conditions*
- For terms related to “abortion,” the following are points of note:
  - Both “spontaneous” and “not specified” abortions are single-axial terms linked to SOC *Pregnancy, puerperium and perinatal conditions*
  - All “induced” forms of abortion are linked only to SOC *Surgical and medical procedures*
  - Complications of induced abortion are primarily in SOC *Injury, poisoning and procedural complications*
  - Complications of both “spontaneous” and “not specified” abortions are primarily linked to SOC *Pregnancy, puerperium and perinatal conditions*
- When searching for terms describing toxic exposures related to pregnancy, delivery, lactation and other circumstances potentially impacting the fetus or newborn, the user may need to consider selected PTs in certain HLTs in this SOC as well as various “exposure” concepts located in SOC *Injury, poisoning and procedural complications*
- “Perineum” terms may be linked to several SOCs including SOC *Reproductive system and breast disorders* and SOC *Pregnancy, puerperium and perinatal conditions*

- Fetal and maternal death terms are linked primarily to SOC *Pregnancy, puerperium and perinatal conditions* as they are considered a special population
- However, PT *Death neonatal* is linked primarily to SOC *General disorders and administration site conditions* and secondarily to SOC *Pregnancy, puerperium and perinatal conditions*

6.19 PRODUCT ISSUES

6.19.1 Basis for Classification

- The MedDRA Management Committee endorsed the recommendation of the Blue Ribbon Panel on the scope of MedDRA (April 2014) for the addition of a 27th SOC to MedDRA to accommodate non-clinical/non-patient related concepts pertaining to products. These concepts are important from regulatory and public health perspectives as they may affect patient safety.
- This SOC *Product issues* has been added in MedDRA Version 19.0 and includes terms relevant for issues with product quality, devices, manufacturing quality systems, product supply and distribution, and counterfeit products. One of the goals of incorporating product quality terms into MedDRA is to support the recording of product quality issues and any associated adverse events using a single terminology. It is envisaged that the product quality terms, including those relating to manufacturing and distribution, may be used to report product defects to regulatory authorities and may also be used in organizations' internal databases to track and trend quality issues or deviations.
- SOC *Product issues* contains two HLGTs: HLGT *Device issues* and HLGT *Product quality, supply, distribution, manufacturing and quality system issues*

6.19.2 Conventions and Exceptions

- This SOC is focused on issues related to products rather than clinical or patient related concepts and, therefore, the majority of terms are single-axial and have no need for multi-axial links to other patient related “disorder” SOCs. However, product terms that also denote a patient related issue express multi-axiality to preserve the link to patient safety. For example, PT *Transmission of an infectious agent via product* is linked to primary SOC *Infections and infestations* and has a secondary link to SOC *Product issues*.
- Device terms are generally event based, not device type based. However, MedDRA has evolved in response to users' requests to add certain device type terms when these devices are widely used or have a particular clinical relevance. Therefore, exceptions have been made for generic types of devices and device components (in widespread use) such as stents, pumps, needles, and syringes. In general, medical device event concepts are represented at the PT level, while corresponding sub-concepts pertaining to events with specific types of widely used devices are usually represented at the LLT level.
- HLT *Product distribution and storage issues* is intended to cover issues with the storage of products by manufacturers, distributors, wholesalers, etc. In contrast, product storage issues by end-users such as healthcare professionals, patients, and consumers are considered to be medication errors and are represented by appropriate medication error terms in SOC *Injury, poisoning and procedural complications*.

- Product supply and availability concepts are distinct from distribution, shipping and storage concepts, and cover issues such as supply chain interruption, product not available on formulary, product withdrawn from market, etc.

6.20 PSYCHIATRIC DISORDERS

6.20.1 Basis for Classification

- The primary guideline used for the classification of psychiatric disorders is the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, (DSM-5)©* published by the American Psychiatric Association. Associated symptoms are grouped at the HLGT levels according to the classification scheme suggested by the DSM-5. The disorders specifically named by DSM-5, or those in the vocabulary that are very closely related disorders, are placed together in the appropriate HLT.
- Signs and symptoms uniquely associated with disorders under an HLGT are grouped at the HLT level
- Signs and symptoms that are applicable to multiple DSM-5 classifications may be found in separate groupings
- Terms that have a basis in a central nervous system disorder are linked primarily to SOC *Nervous system disorders* and secondarily to SOC *Psychiatric disorders*
- Congenital disorders such as PT *Tourette's disorder* that have a basis in SOC *Psychiatric disorders* have a primary link to SOC *Congenital, familial and genetic disorders* in accordance with MedDRA rules. These terms have secondary links to SOC *Psychiatric disorders*, as well as to the body system of manifestation.
- Conditions associated with substance abuse are included in this SOC
- According to DSM-5, the official psychiatric term for addiction is “substance dependence.” Therefore, the word “addiction,” in general, only appears at the LLT level in MedDRA.
- For new “abuse” terms in MedDRA, the text string is devised to distinguish terms in SOC *Social circumstances* from those in SOC *Psychiatric disorders*. “Abuse” terms are linked to SOC *Psychiatric disorders* and kept independent of “dependence” counterpart PTs. Terms that refer to a person, such as PT *Drug abuser*, are in SOC *Social circumstances*.

6.20.2 Conventions and Exceptions

- An attempt is made to name disorders that are included in DSM-5 using the conventions established by the American Psychiatric Association. However, these disorders are associated with a specific set of criteria for diagnosis, while the more general names in the existing vocabulary do not always map in a one-to-one manner. For this reason, they are all included as disorders under the same HLT.

6.21 RENAL AND URINARY DISORDERS

6.21.1 Basis for Classification

- The majority of HLGTs in this SOC are based on anatomic classification
- Further subdivision on the HLT level has PTs grouped by disease process wherever possible
- Where a site is specified, the terms for neoplasms and congenital disorders are gathered at the HLT level within the HLGT of the appropriate anatomic site

6.21.2 Conventions and Exceptions

- HLT *Urinary abnormalities* gathers most of the "-uria" terms present in the terminology. This decision was made to avoid conflicts with respect to underlying etiology as in the case of PT *Proteinuria*, which may have several intrarenal and extrarenal etiologies. The corresponding terms with the phrase or concept "in urine" (e.g., PT *Protein urine present*) are found in SOC *Investigations.*
- For the major body systems of cardiac, hepatic, pulmonary, and renal, the terms "failure" and "insufficiency" are used synonymously. In SOC *Renal and urinary disorders,* the "failure" term is at the PT level and the "insufficiency" term is at the LLT level.

6.22 REPRODUCTIVE SYSTEM AND BREAST DISORDERS

6.22.1 Basis for Classification

- The terms within this SOC are classified using two general approaches: anatomic and functional
  - HLGTs based on anatomy are subdivided mainly by disease process at the HLT level. Signs and symptoms for the anatomic part may form an HLT.
  - HLGTs that reflect functional disorders are subdivided by subtypes of functional disorder at the HLT level
- This SOC contains terms for conditions present at birth (i.e., congenital conditions) irrespective of whether the conditions are hereditary or acquired in utero. The HLTs allocate terms on the basis of gender (male, female, or unspecified).
- Infections and inflammations are not linked to the HLGTs by anatomic location but by gender where this is specified

6.22.2 Conventions and Exceptions

- Unlike other anatomically based HLGTs in this SOC, which exclude terms for infections and inflammations, HLGT *Breast disorders* contains an HLT for these concepts
- "Perineum" terms may be linked to several SOCs including SOC *Reproductive system and breast disorders* and SOC *Pregnancy, puerperium and perinatal conditions*

6.23 RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS

6.23.1 Basis for Classification

- There are three broad approaches to group terms at the HLGT level in this SOC:
  - HLGTs that reflect the anatomic site contain HLTs based on pathologic classification. HLGTs that describe a larger anatomic site, e.g., the upper respiratory tract, are further divided at the HLT level into more specific anatomic locations, disease processes, or a combination of parameters.
  - HLGTs that are based on disease processes are subdivided by anatomic site at the HLT level
  - Specific HLGTs have been created for congenital disorders, neonates, and miscellaneous respiratory disorders which contain HLTs that are not based on anatomic sites or specific disease processes

6.23.2 Conventions and Exceptions

- Pleural infections and neoplasms are grouped together in HLGT *Pleural disorders*, not in the respective HLGTs for respiratory tract infections and neoplasms
- PT *Sputum decreased* and PT *Sputum increased* are in SOC *Respiratory, thoracic and mediastinal disorders*. This is because these terms commonly express a medical condition rather than an investigation finding.
- For the major body systems of cardiac, hepatic, pulmonary, and renal, the terms “failure” and “insufficiency” are used synonymously. In SOC *Respiratory, thoracic and mediastinal disorders,* the “failure” term is at the PT level and the “insufficiency” term is at the LLT level.

6.24 SKIN AND SUBCUTANEOUS TISSUE DISORDERS

6.24.1 Basis for Classification

- The principal division at the HLGT level in this SOC is by pathophysiology or etiology
- The exceptions are HLGTs for skin appendage conditions, which is a microanatomic grouping, and epidermal and dermal conditions, which groups skin conditions that do not belong to any of the other HLGTs
- At the HLT level, the division is mainly pathologic

6.24.2 Conventions and Exceptions

- In general, terms related to the eyelid are primarily linked to SOC *Eye disorders* and secondarily to SOC *Skin and subcutaneous tissue disorders*

6.25 SOCIAL CIRCUMSTANCES

6.25.1 Basis for Classification

- SOC *Social circumstances* is one of the three single-axial SOCs in MedDRA. The purpose of this SOC is to provide a grouping for those factors that may give insight into personal issues that could have an effect on the event being reported. Essentially, SOC *Social circumstances* contains information about the person, not the adverse event. As an example, PT *Drug abuser* is found in this SOC, whereas its respective disorder term, PT *Drug abuse*, is found in SOC *Psychiatric disorders*.
- The terms within this SOC do not fall into any anatomic or pathologic classification. The HLGTs are broad groupings of social factors (e.g., family issues or economic circumstances). At the HLT level, these HLGTs are further subdivided into groups of social factors with a common theme. (e.g., Family issues include bereavement issues).
- In this SOC, terms representing the crime or action of abuse and the perpetrator of the crime or abuse are kept in a PT/LLT relationship, with the crime/action of abuse at the PT level and the perpetrator of the crime or abuse at the LLT level (e.g., PT *Sexual abuse* and its LLT *Sexual abuser*). Terms representing the victim of these crimes are qualified with "victim of" at the PT level.
- For new “abuse” terms in MedDRA, the text string is devised to distinguish terms in SOC *Social circumstances* from those in SOC *Psychiatric disorders*. "Abuse" terms are linked to SOC *Psychiatric disorders* and kept independent of “dependence” counterpart PTs.

6.25.2 Conventions and Exceptions

- HLT *Drug and chemical abuse* excludes alcohol-related terms. HLT *Alcohol product use* captures all aspects, including alcoholic, abstention, and social use. PT *Alcoholism* is found in SOC *Psychiatric disorders*.
- HLGT *Legal issues* makes a distinction between being a victim of a crime and being the person who committed the crime
- To make a distinction between blindness as a disability and blindness as a medical disorder, PT *Sight disability* is linked to SOC *Social circumstances* (blindness as a disability) and PT *Blindness* is linked to SOC *Eye disorders* (blindness as a medical disorder) and to SOC *Nervous system disorders***.** The concept of deafness follows the same principles.

6.26 SURGICAL AND MEDICAL PROCEDURES

6.26.1 Basis for Classification

- This SOC is one of the three single-axial SOCs in MedDRA. It contains only those terms that are surgical or medical procedures. There are no multi-axial links between terms in this SOC and other SOCs.
- The nature of this SOC makes it more of a “support” SOC for recording case information and for developing queries. Surgical and medical procedures may occur in the treatment of an adverse event, as an associated condition related to the indication for a medical product, or as medical history. A comprehensive search strategy needs to consider that this is a single-axial SOC whose terms are not found elsewhere in the terminology.
- The terms within this SOC are primarily divided by anatomic region at the HLGT level, except for general or miscellaneous therapeutic procedures and soft tissue procedures which are grouped in separate HLGTs
- There is a distinction between the term “abortion,” which is frequently used as a procedure term, and a disorder term such as “spontaneous abortion.” In MedDRA, the term “induced abortion” is used to identify the term as a procedure; therefore, it is in this SOC. The term “spontaneous abortion” is used as the disorder term and is in SOC *Pregnancy, puerperium and perinatal conditions*. When an abortion term is not identified as being either a procedure or a disorder, it is assumed to be a disorder term and is categorized in SOC *Pregnancy, puerperium and perinatal conditions*.

6.26.2 Conventions and Exceptions

- The anatomic breakdown at HLGT level is similar to the SOC organization (represented body systems) in MedDRA, with a few exceptions where treatment of certain body systems is closely related. The result is groupings that are similar to surgical subspecialties:
  - Ear, nose, and throat procedures are grouped together since procedures in these areas constitute a single surgical speciality
  - Skull and vertebrae procedures are grouped with brain and spinal cord therapy
- At the PT and LLT level, terms with the words “operation” and “surgery” are used interchangeably.
- Standard medical definitions of "dilation” and "dilatation" indicate that they are synonyms. The MSSO recognizes that there are some common usages in certain cultures for these types of terms. However, for purposes of distinction in MedDRA, the term "dilation" is considered a procedure and the term "dilatation" is considered a disorder. The word "procedure" is normally added to "dilation," e.g., PT *Stomach dilation procedure* to make it self-explanatory. An exception to

this convention is PT *Uterine dilation and curettage* since it is recognized as a procedure without the addition of the qualifying word.

- Anastomosis is classified as a surgical procedure and is single-axial linked to SOC *Surgical and medical procedures*
- "Drainage" is a term used as a procedure (systematic withdrawal of fluids), whereas "discharge" and "secretion" are terms used for the excretion of liquids from the body. "Drainage" terms that fall outside of the realm of surgical procedures are considered exceptions and dealt with by using the word "discharge." These terms are linked appropriately based on their particular meaning. In addition, all surgical terms retain "drainage" and link to SOC *Surgical and medical procedures*.
- Revision procedures are generally represented in MedDRA as sub-concept LLTs of the basic procedure

6.27 VASCULAR DISORDERS

6.27.1 Basis for Classification

- The terms within this SOC are primarily divided by pathology or clinical disease entity at the HLGT level. Most vascular disorder terms are already grouped anatomically by their representation within the anatomic “disorder” SOCs; this division allows more flexible data retrieval.
- At the HLT level, terms are further subdivided anatomically

6.27.2 Conventions and Exceptions

- In general, terms related to thrombosis are primarily linked to the site of manifestation, when applicable, and are secondarily linked to SOC *Vascular disorders*
- Arterioscerosis, stenosis, and vascular insufficiency concepts represent “chronic” impairments developed progressively whereas embolism and thrombosis concepts represent “acute” conditions
- “High” and “low” terms in MedDRA are generally considered to be laboratory/investigation type of terms and are found in SOC *Investigations*. Exceptions to this rule are LLT *Blood pressure high* and LLT *Low blood pressure* under PT *Hypertension* and PT *Hypotension*, respectively, which are in SOC *Vascular disorders*.

APPENDIX A: ACRONYMS

A

ASCII	American Standard Code for Information Interchange

C

CIOMS	Council for International Organizations of Medical Sciences
COSTART	Coding Symbols for a Thesaurus of Adverse Reaction Terms

E

EWG	Expert Working Group
EXCL	Excluding, except, excl

F

FDA	Food and Drug Administration (United States)

H

HARTS	Hoechst Adverse Reaction Terminology System
HLGT	High Level Group Term
HLT	High Level Term

I

ICD-9	International Classification of Diseases – 9th Revision
ICD-9-CM	International Classification of diseases – 9th Revision Clinical Modification
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IFCC	International Federation of Clinical Chemistry and Laboratory Medicine
IFPMA	International Federation of Pharmaceutical Manufacturers and Associations
INCL	Including, incl
IUPAC	International Union of Pure and Applied Chemistry

J

J-ART	Japanese Adverse Reaction Terminology
JPMA	Japan Pharmaceutical Manufacturer Association

L

LLT	Lowest Level Term
LOINC	Logical Observation, Identifiers, Names and Codes

M

MCA	Medicines Control Agency (United Kingdom)
MEDIS	Medical Information System (Japan)
MedDRA	Medical Dictionary for Regulatory Activities
MEDDRA	Medical Dictionary for Drug Regulatory Affairs
MHLW	Ministry of Health, Labour and Welfare (Japan)
MHRA	Medicines and Healthcare products Regulatory Agency (United Kingdom)
MSSO	Maintenance and Support Services Organization

P

PT	Preferred Term

S

SMQ	Standardised MedDRA Query
SOC	System Organ Class

W

WHO	World Health Organization
WHO-ART	World Health Organization Adverse Reaction Terminology

For a list of MedDRA term abbreviations and acronyms, please visit our Web site (https://www.meddra.org/how-to-use/support-documentation).

APPENDIX B: MedDRA CONCEPT DESCRIPTIONS

This appendix provides a link to the online list of MedDRA concept descriptions. A concept description is a description of how a concept is interpreted, used, and classified within the MedDRA terminology and is not a definition. The concept descriptions are intended to aid the consistent and accurate use of MedDRA in coding, retrieval, and analysis and to overcome the differences of medicine practice worldwide. The MSSO expects this to be a working document and grow as subscribers request additional concepts to be documented.

Online MedDRA Concept Descriptions:
(http://mssotools.com/mssoweb/mdb/english_intguide_appendix_B.htm).