Papworth Hospital NHS
NHS Foundation Trust

GD051

MedDRA Coding

This guidance document describes the process for manually coding in OpenClinica using MedDRA.

Coding is used to apply standard coding to the verbatim terms that have been reported in free text data fields within CRFs. There is probability for ambiguity, and coding facilitates the presentation and comparison of the data. OpenClinica CRFs allow for the creation of tables to facilitate the capture of medical coding. The example used within this guide is for the coding of Adverse Events (AEs) however, there are other instances where medical coding maybe used.

The **Med**ical **D**ictionary for **R**egulatory **A**ctivities (MedDRA) is a clinically validated international medical terminology dictionary. It includes and organises a wide range of medical terms and is used in clinical trials for the documentation and monitoring of safety data by coding the medical terms, such as adverse events, to a standardised format. MedDRA includes medical conditions (diagnosis, signs and symptoms), indications, investigations (tests and results), medical procedures, medical history, medication errors and device-related and product use issues.

The Data Management Plan will reference the version of MedDRA that will be used and how often the coding is reviewed.

1. Preparing the OpenClinica data

a) The eCRF that usually requires coding in OpenClinica is for Adverse Events (AEs). The usual design of the eCRF will have data fields for the location staff to enter the reportable AE, alongside a start /end date, severity etc. In addition, there are four fields requiring coding. The Data Management Plan (DMP) will advise on what is being coded. Section 3 shows the OpenClinica 3 format of coding requirements (OpenClinica 4 layout may differ however the content is the same).

b) Prior to coding, it is important that AE event is reviewed. Unclear medical terminology, abbreviations and any other ambiguous, confusing, or unintelligible information should be queried with the location staff (via a discrepancy or query note) and clarified.

c) Only one medical term must be represented per AE row, MedDRA codes only included one term. For example, an AE recorded as ‘nausea and vomiting’ cannot be coded with those terms together. Hence, it should be split into two separate AEs, one for ‘nausea’ and the other one for ‘vomiting’, even if they occurred for the same event.

d) All event terms should be a diagnosis, where possible, as opposed to signs and symptoms. Event terms should not be recorded as procedures, but rather the medical reason for the procedure. Ensure that the protocol is followed for events that do not need coding. The protocol may specify adverse events that do not need recording or reporting to Sponsor (e.g. anticipated disease related symptoms, common side effects of the IMP).

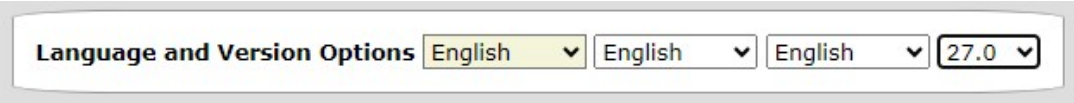
e) All adverse events must be recorded and reported within the time period defined in the trial protocol.

f) It is important to communicate with the study team early and often, so they understand any complexities of completing the eCRF for example points above.

2. Accessing MedDRA

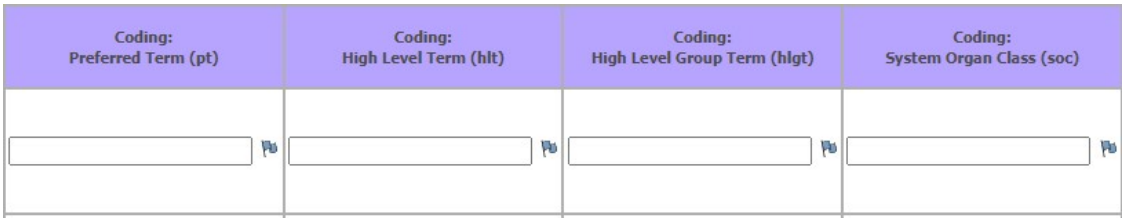
a) To access the MedDRA Web-Based Browser, the user should navigate to the following URL: https://tools.meddra.org/wbb/login.aspx. The login credentials can be obtained from the Senior Clinical Trial Data Manager. The login credentials are shared within the data management team, the password should not be changed unless you are prompted to do so (the password in changed annually in line with the registration renewal).

b) When entering the initial page of the MedDRA browser, the version of MedDRA to be used can be set. The most current version is used at the onset of the study, and this version should be used throughout and not be changed**.** The version of MedDRA used for a study is recorded in the FRM046 DMP Prior to going live and in the studies AE MedDRA coding spreadsheet.



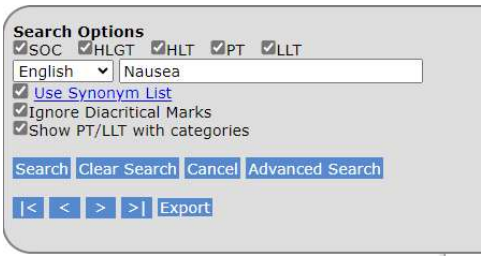
3. Medical coding

a) Appendix A provides further guidance on the MedDRA coding structure, you should ensure you have read the appendix prior to beginning coding. Adverse Events (one AE term per row) will be coded with the 8-digit numeric code for the Preferred Term (PT), High Level Term (HLT), High Level Group Term (HLGT) and System Organ Class (SOC) levels. This will be added directly in the coding columns of the CRF table; the screen shot below shows the layout within OpenClinica 3 (OpenClinica 4 layout may differ however the content is the same), where the columns to be coded are in purple.



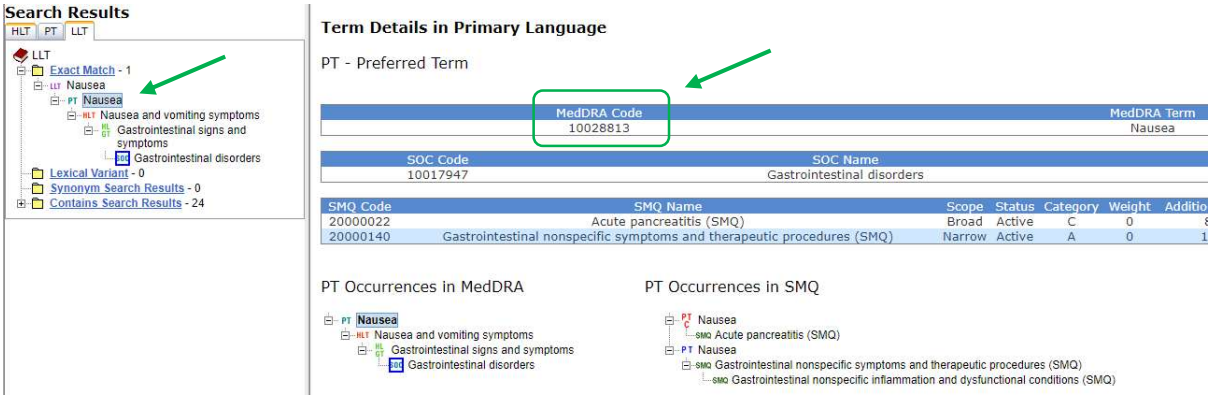
b) Choose the correct MedDRA version to use (see the **Accessing MedDRA** section).

c) Type the adverse event term in the Search box field and click on Search (in this example we have used the term nausea).



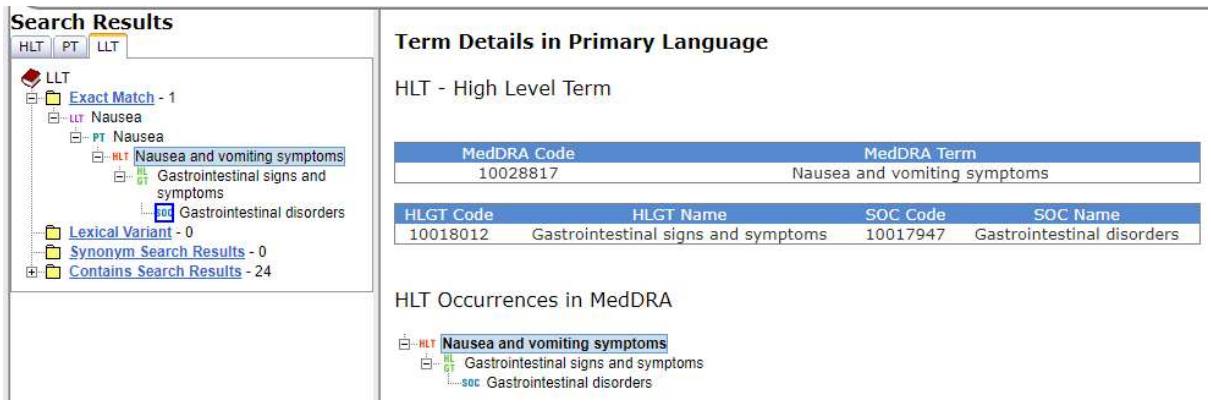
d) The 'Search Results' window will show all the results available. Look at the Exact Match results, but also at the Contains Search Results section to see if a more precise option can be appropriate. Choose the option that is linked to the most accurate PT term.

e) Click on the PT term and on the ⊞ symbols to show the different levels associated with this PT. The right-sided window will show the complete path and the MedDRA code linked to this PT term.



f) The SMQ section can be ignored.

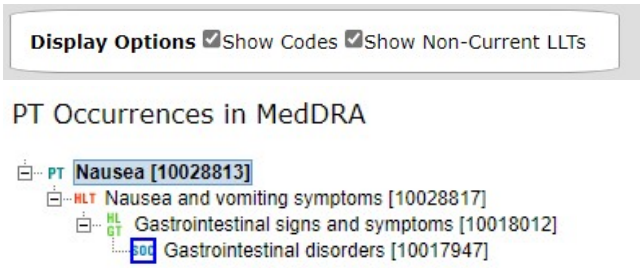
g) Click on the HLT term to see the MedDRA codes associated with all the next levels.



h) These numeric MedDRA codes are the ones to copy and paste into the AE row in the database.

Coding: Preferred Term (pt)	Coding: High Level Term (hlt)	Coding: High Level Group Term (hlgt)	Coding: System Organ Class (soc)
10028813	10028817	10018012	10017947

i) You can also click on 'Show Codes' in the Display Options bar before typing your AE term in the Search box field. The codes will be easier to copy/paste as they will be visible all at the same time.

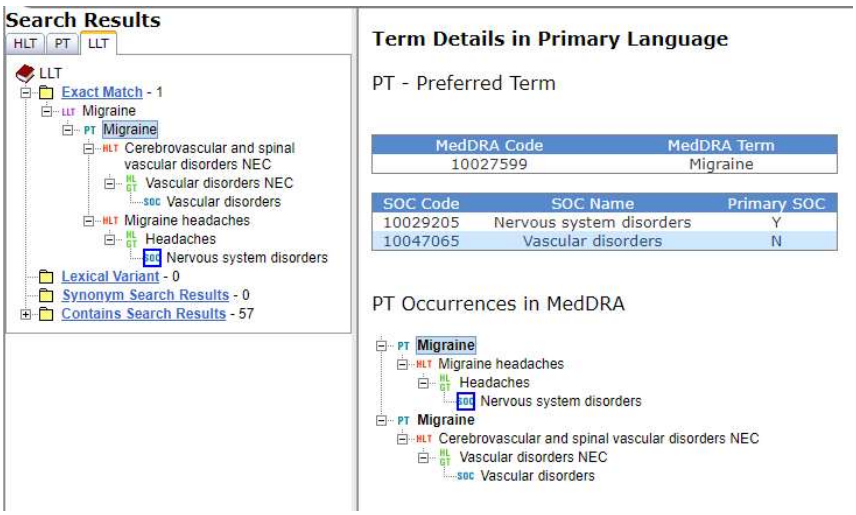


j) In some instances, MedDRA may provide more than one HLT, HLGT or SOC option for the adverse event term you have entered. An example of this is for 'migraine'.

k) For an AE recorded as 'Migraine, follow the same steps as previously until you find the correct PT term.

l) Click on the PT term and on the symbols to show the different levels associated with this PT. There are two different HLT terms that can be linked to 'migraine', leading to different SOC.

m) The right-sided window will also show the different options.



n) A decision should be made by the Chief Investigator (CI) (or any other delegated clinical member of the study team) regarding which one of these options should be used for medical coding. A list should be provided to the CI clearly outlining the coding options (via email or face to face), they should choose the most appropriate coding option. The communications with Chief Investigators (CI) or other medical professionals with regards to decisions made for which codes to use, should be save as PDFs in the eTMF and printed and stored in the relevant section of the TMF (Trial Master File).

o) Once the path is chosen, the same steps as described previously can be followed to complete the coding process in the database.

4. Approvals

a) All coding must be approved by a designated clinical professional, this role is appointed by the Chief Investigator. Each time coding is allocated to a reported event, the coding must be approved by the clinician.

b) The study data manager will collate a written record (either an email or a paper written document) of the verbatim event and the coding that has been allocated to this. The clinician will review the coding and give their approval that it is a correct reflection of the event. This will be done via a return email confirming the approval or, if seen in person, the signing and dating of the paper communication.

c) The approvals for coding must be saved as PDFs in the relevant section of the eTMF and, if necessary, printed and stored in the relevant section of the TMF (Trial Master File).

d) During a study, some adverse events are often expected and can occur more than once or to more than one participant. Keeping an excel spreadsheet with the AEs and the MedDRA codes can facilitate and accelerate the coding process. The EXCEL template can be found at S:\Shared\R&D\Data Management\AEs\Study Template AE Coding MedDRA.xlsx).

e) This spreadsheet will also record the version number of MedDRA and approvals for any coding; with the authorising initials and date of approval.

4. General guidance

a) Select the LLT that most accurately reflects the reported verbatim information. If an exact match cannot be found in MedDRA, medical judgment should be used to adequately represent the medical concept with an existing MedDRA term.

b) If a diagnosis is reported with characteristic signs and symptoms, the preferred option is to select a term for the diagnosis only.

c) When selecting terms, no reported information should be excluded from the term selection process (AE may need to be separated); similarly, do not add information by selecting a term for a diagnosis if only signs or symptoms are reported.

d) Death, disability, and hospitalisation are considered outcomes in the context of safety reporting and not usually considered Adverse Reactions/Adverse Events. An AE verbatim representing an outcome should only be selected if it is the only information reported or provides significant clinical information.

e) If a procedure is reported with a diagnosis, the preferred option is to select terms for both the procedure and diagnosis (and for the location staff to separate the AEs).

f) More information about the MedDRA naming conventions can be found in the Introductory Guide of each MedDRA Version.

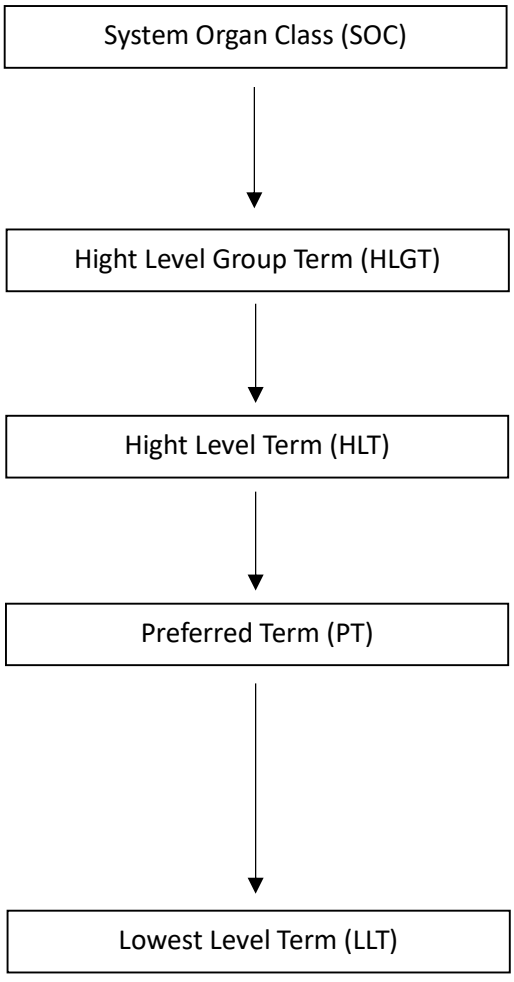
g) MedDRA is updated twice a year: once in March for the complex changes, and once in September for the minor changes. **It is important to ensure that the same MedDRA version is used during the whole life of a particular study, the version is recorded in the DMP.**

Appendix 1

MedDRA structure

MedDRA is structured as a pre-defined hierarchy of descriptive terms.

Starting from the System Organ Class, each subsequent level reflects an increasing level of specificity. All levels use British English apart from the LLT that can include American English terms.



The **System Organ Class (SOC)** is the highest level of the hierarchy. The 27 system organ classes group the terms based on their manifestation site, aetiology or purpose.

The **High Level Group Term (HLGT)** group the HLTs based on their anatomy, pathology, physiology, aetiology or function.

The **High Level Term (HLT)** is another group level which links Preferred Terms related to it by anatomy, pathology, physiology, aetiology or function.

The **Preferred Term (PT)** is the medical concept of the AE term. PTs should be unambiguous and as specific and self-descriptive as possible. A PT will be linked to at least one SOC (its primary SOC) but can be linked to more than one SOC (Secondary SOCs) via other HLT > HLGT > SOC routes.

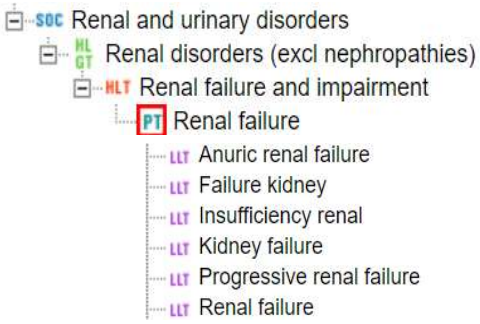
The **Lowest Level Term (LLT)** is the lowest level of the terminology and represents the AE recorded. Some of the LLTs have a "non-current" flag status LLT. These should not be used as they are vague, ambiguous, truncated, abbreviated, out-dated, or misspelled.
Each LLT is linked to only one PT, but one PT can include many LLTs that are synonyms or lexical variants.
We currently do not code the LLTs in the database.

Terms including 'NOS' (not otherwise specified) are found on the LLT level and represent concepts for which no further specific information is available. Similarly, terms including 'NEC' (not elsewhere classified) on the HLT and HLGT levels denote groupings of miscellaneous terms that do not readily fit into other hierarchical classifications.

Structure examples

a) All these **LLTs** are linked to the **PT** 'Renal failure' as they are synonyms or lexical variants.

The **PT** 'Renal failure' is then linked to only one **SOC** via the **HLT** 'Renal failure and impairment', which is linked to the **HLGT** 'Renal disorders (excl. nephropathies)', which is linked to the **SOC** 'Renal and urinary disorders.



b) The **PT** 'Migraine' is linked to more than one **SOC**.

When looking for 'Migraine', MedDRA will show the different paths leading to all the SOC that apply.

'Migraine' is here linked to the **SOC** 'Vascular disorders' via the route **HLT** 'Cerebrovascular and spinal vascular disorders NEC' and the **HLGT** 'Vascular disorders NEC'.

It is also linked to its primary **SOC** 'Nervous system disorders' via the **HLT** 'Migraine headaches' and the **HLGT** 'Headaches'.

Each MedDRA term from each level is assigned an 8-digit numeric code. These codes are non-expressive – we cannot determine the level or significance of the term by looking only at the code. These are the codes that will be recorded in the database for analysis and standardisation purposes.

Appendix 2

MedDRA supporting documentation/learning resources

MedDRA MSSO - YouTube

Support Documentation | MedDRA

Training Materials | MedDRA