# MedDRA®
# POINTS TO CONSIDER
# COMPANION DOCUMENT
## ICH-Endorsed Guide for MedDRA Users

***Release 2.0***

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## 1. INTRODUCTION

The *MedDRA Term Selection: Points to Consider* and *MedDRA Data Retrieval and Presentation: Points to Consider* documents provide valuable guidance to MedDRA users worldwide on general term selection and data retrieval principles as well as providing specific examples of approaches to coding and analysis. However, there are certain topics where users could benefit from having more detailed information pertaining to the use of MedDRA than can be covered in the existing documents.

The purpose of this Companion Document is to supplement the Points to Consider (PtC) documents by providing additional details, examples, and guidance on specific MedDRA-related topics of global regulatory importance. It was developed and is maintained by the same working group that was charged by the ICH Management Committee to develop the PtC documents. The working group consists of representatives of ICH regulatory and industry members, the World Health Organization, the MedDRA Maintenance and Support Services Organization (MSSO), and the Japanese Maintenance Organization (JMO).

The Companion Document is intended to be a “living” document and is updated based on users’ needs, rather than being tied to MedDRA releases. Like the PtC documents, the Companion Document is available in English and Japanese; however, if certain examples are not relevant or are difficult to translate, these will not be included in the Japanese version.

The contents of the document are agreed by all ICH parties; it does not specify regulatory requirements, nor does it address database issues. Organisations are encouraged to document their own coding and data retrieval conventions in organisation-specific guidelines which should be consistent with the PtC documents and this Companion Document.

Users are invited to contact the MSSO Help Desk with any questions or comments about the MedDRA Points to Consider Companion Document.

## 2. DATA QUALITY

This section will discuss important data quality and data entry principles related to the use of MedDRA in the clinical trial and postmarketing environments. It will not address specific regulatory requirements, database structure issues, file format conventions, data workflow applications, or other topics which are beyond the scope of MedDRA.

In both the development and marketing of human medicinal products, data collection is a critical and ongoing process. As noted in the *MedDRA Term Selection: Points to Consider* (MTS:PTC) document, the quality of original reported information directly impacts the quality of data output.


Data are applied to make inferences, test hypotheses, draw conclusions, make statements, and report findings about the safety and efficacy of biopharmaceutical products. Since data are used for activities ranging from coding to information categorisation, retrieval, analysis, and presentation, ensuring access to high quality data is paramount. Quality data support safety functions including signal detection, data analysis, and product label development. This section will describe some of the practices and processes which should be part of an organisational data quality strategy.

### 2.1 THE IMPORTANCE OF DATA QUALITY

As the regulated biopharmaceutical industry strives for greater harmonisation of safety reporting regulations and standards, there is an increasing emphasis on safety surveillance and data quality. In addition to supporting patient/subject safety, increased data quality facilitates communication of complete and accurate information to those involved in clinical research and post-marketing processes (including regulatory bodies, sponsoring companies, study site personnel and marketing authorisation holders). Collection of high quality data can also result in greater time and cost efficiency during product development and marketing (e.g. less querying of incomplete data, decrease site monitoring costs and reduce the risk of delayed regulatory approval).

The quality of adverse event data is central to safety monitoring in clinical trials, to the risk assessment of marketing applications and in the evaluation of safety signals within postmarketing data. Adverse events are typically generated by complaints from study subjects, patients or their caregivers. These verbatim terms may be either coded manually or coded automatically with autoencoder tools by selecting MedDRA Lowest Level Terms (LLTs). Users need to be aware that some LLTs are rather non-specifc and that further clarification of the reported information may be necessary. Small deviations in coding can result in significant issues and produce misleading analyses. Coding selections may vary even in apparently simple cases.Given this variability, it is important to thoughtfully evaluate adverse event data rather than relying on any specific recommendation or guidance.

## 2.2 CHARACTERISTICS OF GOOD QUALITY DATA

Quality data have several common features. Foremost, these data should be both complete and accurate. Whenever possible, the most concise form of data should be collected, provided that this can be done without sacrificing either completeness or accuracy. Within an organisation, data quality is fostered by comprehensive, consistent, transparent and documented data handling processes. Quality data is, by definition, supported by the available information. For example, clinical diagnoses should be consistent with the available medical history, physical findings, laboratory and investigational results. Furthermore, quality data should be capable, when appropriate, of supporting data-related associations (e.g. when performing a causality assessment of an adverse event which could be related to a product).

## 2.3 THE ROLE OF MEDDRA IN A DATA QUALITY STRATEGY

As a standardised and validated clinical terminology used in both clinical development and postmarketing surveillance, MedDRA should play an important role in a sound data quality strategy. Since MedDRA is used to “code” information during data entry, it is important to consider the principles in the MTS:PTC document to ensure the selection of coding terms with the highest specificity and analytical quality. The large number of available LLTs provides a high degree of granularity. However, even the granularity of MedDRA cannot overcome “low quality” primary information.

## 2.4 COMPONENTS OF AN ORGANISATIONAL DATA QUALITY STRATEGY

The development and implementation of an organisational data quality strategy is a complex task which involves the input, support and collaboration of many stakeholders. Many of the principles of high quality data collection are the same in both the clinical trial and postmarketing environments. This section will discuss a framework for acquiring data of high quality.

### 2.4.1 Data collection

Whether in a clinical trial, a postmarketing safety call center, or a healthcare professional’s office, there is often only one opportunity to capture complete and accurate information. Since data output quality is determined by data input quality in a database, there are important consequences from these initial steps. For those collecting information (e.g. a study site physician/nurse, a postmarketing call center employee, a dispensing pharmacist, an emergency room physician), certain practices will help to maximise the quality of the collected data:

- During data collection, completeness and accuracy need to be weighed against the risk of collecting “unimportant” information. This is particularly true if time limitations are present. It is advisable to minimise the amount of unimportant information placed in dedicated data fields for key concepts such as adverse events. Otherwise, the data coding and management can be further complicated.

- In clinical trials, reporters should be encouraged to use consistent medical terminology to describe similar medical concepts. The best strategy is to carefully train study site personnel (especially investigators) about the importance of consistency in data collection.

- In clinical trials, data collection instruments (whether they are electronic or paper case report forms) should be carefully designed to be easy to use, enduring and sufficiently comprehensive to gather all the necessary information. Since individual trials or clinical projects can span years, it is never possible to spend “too much” time developing quality data collection tools. Appropriate “subject matter experts” in data management, information technology, statistics, quality assurance, and regulatory compliance should be involved throughout the planning process. After years into development, it is difficult, if not impossible, to compensate for needed data which has not been adequately collected.

- With the passage of time, the ability to seek clarification of incomplete information becomes limited and very often, a reporter’s recollection of important facts can change dramatically. Therefore, it is crucial to start the “query” process as soon as possible to obtain clarification from the data source.

- When a report contains multiple diagnoses (such as a report of “broken finger and hand abrasion” or “urinary bladder obstruction and cystitis”), it is usually appropriate to record these as separate concepts on the data collection form

- Attempt to minimise spelling errors and the use of abbreviations and acronyms. The table below illustrates the difficulty of interpreting such poor or ambiguous data:

| Reported | Data Quality Challenge |
|---|---|
| Had MI | Does MI stand for myocardial infarction, mitral insufficiency, mental illness or mesenteric ischaemia? |
| Interperial | Was this word intended to represent “intraperitoneal” or “intraperineal”? |
| Nitro drip | Did this drip contain nitroglycerin or nitroprusside? |

- Furthermore, without proper context, it is impossible to interpret other “vague” terms as shown in the table below:

| Reported | Data Quality Challenge |
|---|---|
| Congestion | Nasal, hepatic, venous, etc.? |
| Obstruction | Bronchial, intestinal, ureteral, etc.? |
| Infarction | Myocardial, cerebral, retinal, etc.? |

Clarification of such terms should be requested at the time of data collection.

### 2.4.2 MedDRA coding considerations

MedDRA can be used to accurately code many types of reported information. This includes not only diagnoses, signs and symptoms representing adverse reactions/adverse events but also concepts such as medical and social history, indications for product use, device-related events, surgical and medical procedures, investigations, exposures, misuse and abuse, off label use, medication errors, and product quality issues. For meaningful data review, it is important to ensure that all required information is coded consistently. Important data quality issues to consider include:

- Steps should be taken to ensure that individuals responsible for MedDRA coding have familiarity with the terminology as well as the requisite training to utilise it effectively. Particular attention should be paid to the relevant coding principles outlined in the MTS:PTC document. In environments where MedDRA coding is performed by a number of individuals, it is important to have a consistent organisational approach.

- Appropriately trained individuals should review MedDRA coding

- It is an important concept that all adverse events and adverse reactions from a report should be coded, regardless of causal association. Similarly, do not add information by selecting a term for a diagnosis if only signs or symptoms are reported (MTS:PTC Section 2.10)

- It is important that reported information is coded accurately; it is not appropriate to select terms for concepts which are less specific or less severe than the reported term (e.g., coding a convulsive seizure with LLT *Shakiness* or coding peritonitis with LLT *Belly ache*)

- It is advisable to follow the “preferred” coding options specified in the MTS:PTC document, especially for issues like the coding of provisional and definitive diagnoses with associated signs and symptoms. If one chooses to use an “alternate” coding option from the MTS:PTC, it is a good practice to document why this was done and to be consistent in the use of this alternate choice.

- It is important to distinguish medical conditions (typically found in the SOC of the primary manifestation site) from laboratory and test terms (which are found in SOC *Investigations*)

- Verbatim terms may contain more than one medical concept (such as a report of “fall and contusion”). It is important to consider each of the reported events and code as appropriate.

- Consider the use of “split coding” (selecting more than one term) where there is no single LLT within MedDRA which captures all of the concepts (MTS:PTC Section 2.8 and Section 3.5.4)

- Organisations may wish to create “synonym” lists of verbatim terms which can then be coded to pre-determined LLTs. An example of a synonym list is shown below:

| Reported Verbatim | LLT |
|---|---|
| Throbbing above temple<br>Aching all over head<br>Pulsing pain in head | In a synonym list, each of these verbatim reports would be coded using LLT *Headache* |

Synonym lists may be particularly helpful in some circumstances, e.g. when those involved in report coding have limited medical expertise, when coding is in several geographical sites or when an autoencoder is being extensively used. It is also important to ensure that terms selected for a synonym are true synonyms for the coded medical concept.

- Medical and surgical procedures are generally not adverse events. However, if only a procedure is reported, then an appropriate term is used to code the procedure (MTS:PTC Section 3.13.1). On the other hand, if a procedure is reported with a diagnosis, then the preferred option is to select an appropriate term to code both the procedure and diagnosis. The alternate option is to code only the reported diagnosis (MTS:PTC Section 3.13.2). Some organisations have data collection forms with separate data fields for adverse events and for procedures; this aids entry of data in the appropriate category.

- In the context of safety reporting, death, disability and hospitalisation are outcomes, not adverse events. Therefore, they are generally not coded with MedDRA. Instead, they are recorded in the appropriate data collection field for outcomes. One exception to this recommendation is when death, disability, or hospitalisation is the only reported verbatim. These concepts are coded with MedDRA while clarification of the underlying cause is sought (see MTS:PTC Section 3.2 for further information). In addition, death terms that add important clinical information (e.g. LLT *Sudden unexplained death in epilepsy*, LLT *Foetal death*) should be selected along with any reported ARs/AEs.

- When vague, ambiguous, or conflicting information is reported, MedDRA has codes which can be utilised while attempts are made to clarify the information. For example:

**Vague information (see also MTS:PTC Section 3.4.3):**

| Reported | LLT Selected | Comment |
|---|---|---|
| Appeared red | Unevaluable event | "Appeared red" reported alone is vague; this could refer to a patient's appearance or even that of a product (i.e., a pill, a solution, etc.) |

**Ambiguous Information (see also MTS:PTC Section 3.4.2):**

| Reported | LLT Selected | Comment |
|---|---|---|
| Patient had medical history of AR | Ill-defined disorder | It is not known what medical condition the patient had (aortic regurgitation, arterial restenosis, allergic rhinitis?), so LLT *Ill-defined disorder* can be selected |

**Conflicting Information (See also MTS:PTC Section 3.4.1):**

| Reported | LLT Selected | Comment |
|---|---|---|
| Severe anaemia with a haemoglobin of 19.1 g/dL | Haemoglobin abnormal | LLT *Haemoglobin abnormal* covers both of the reported concepts (note: haemoglobin value of 19.1 g/dL is a high result, **not** a low result as would be expected in severe anaemia |

### 2.4.3 Training

Appropriate ongoing training is a key part of a good data quality strategy. Training should be given to all persons involved in the collection, transcription, categorisation, entry, coding, and review of information. Organisational training practices and procedures should be documented in writing and continually reviewed for updates. Training should be performed by appropriately qualified individuals who are knowledgeable about the organisation's standardised procedures and focused on compliance. Cross-training of key functions is

advisable to ensure a consistent approach and to preserve data quality standards during periods of unexpected personnel changes.
Given that organisations may commonly use unfamiliar or remote study sites for clinical trial conduct, it is also important to ensure that study site personnel (e.g., investigators, study nurses, clinical study coordinators, clinical research associates, site pharmacists) are well trained in all relevant aspects of clinical trial conduct including:

- Correct use of the assigned data collection instruments
- Training in appropriate techniques for interviewing of study subjects/patients [e.g. the use of non-directed questioning, reporting of adverse events as diagnoses (when possible) rather than lists of signs and symptoms, precautions to avoid unblinding]
- Knowledge of relevant regulatory considerations related to quality data collection
- Adequate knowledge of the use of MedDRA for coding purposes, as applicable. This is particularly important for concepts such as coding of definitive versus provisional diagnoses (with or without symptoms) and not inferring diagnoses
- A thorough understanding of and compliance with an organisation's agreed-upon "data query" process to clarify information

The "Data Quality, Coding and MedDRA" presentation in the 'General/Basics' section of the "Training Materials" page of the MedDRA website (https://www.meddra.org/training-materials) is another useful resource. This customisable slide set is intended for use at investigator meetings and for training personnel involved with data collection (such as clinical research associates and clinical coordinators). It provides an overview of the importance and benefits of good quality data as it relates to MedDRA.

### 2.4.4 Quality assurance checks

A thoughtful and thorough quality assurance (QA) process supports the goal of maximising data quality. QA checks during the data management process ensure compliance with established organisational procedures and metrics. Examples of inaccurate MedDRA coding which QA checks could identify include:

| Reported | Inaccurately Selected LLT | QA Review Outcome |
|---|---|---|
| Allergic to CAT scan | Allergic to cats | This inaccurate LLT was selected by an autoencoder which matched the words "**Allergic to CAT s**can" from the reported term |
| Feels pressure in eye | | This inaccurate LLT refers to the name of the test for intraocular |

| | | |
|---|---|---|
| | Intraocular pressure | pressure; the appropriate term to reflect the symptom being described in the report would be LLT *Sensation of pressure in eye* |

These checks can identify coding errors with MedDRA before the database is locked and erroneous data become part of a data analysis.
The MSSO-maintained Unqualified Test Name Term List is a comprehensive collection of all unqualified test name terms at the Preferred Term (PT) and Lowest Level Term (LLT) levels in SOC *Investigations*. The Unqualified Test Name Term List can be found on the "Support Documentation" page on the MedDRA website. It may be applied by regulatory authorities and industry as a QA check of data quality in clinical trial and pharmacovigilance databases. Test name terms without qualifiers (e.g., LLT *Blood glucose*, LLT *CAT scan*) do not represent ARs/AEs but are intended to point to an actual value in a specific database field. For example, in the section for Results of Tests and Procedures in the ICH E2B ICSR electronic transmission standard, unqualified terms may be used in the data element capturing the test name. Unqualified Test Name terms are not intended for use in other data fields capturing information such as ARs/AEs. The Unqualified Test Name Term List is intended as a recommendation only, providing a standard tool for checking coding quality.

### 2.4.5 MedDRA versioning strategy

Given the twice-yearly releases of new MedDRA versions, organisations should have a documented versioning strategy to address these updates. The MSSO has created a Best Practice document which contains sections entitled "Recommendations for MedDRA Implementation and Versioning for Clinical Trials" and "Recommendations for Single Case Reporting Using Semi-annual Version Control". This document is found on the "Support Documentation" page on the MedDRA website.
In addition, the MSSO has provided a MedDRA Version Analysis Tool (MVAT) which facilitates the identification and understanding of the impact of changes between any two MedDRA versions, including non-consecutive ones (see the "Tools" Page on the MedDRA website).

## 3. MEDICATION ERRORS

The purpose of this section is to expand on the section on medication errors in the *MedDRA Term Selection: Points to Consider* (MTS:PTC) document and to provide guidance on scenarios that are medication errors as well as scenarios informative for medication errors or scenarios that are confused with medication errors. Additionally, guidance and examples of coding of some scenarios are provided. This section has two main sub-sections; the first sub-section provides answers to commonly asked questions about coding medication errors. The second sub-section provides examples for coding medication errors. Examples are based on MedDRA Version 23.0.
The document is a living document and the content of this section will be updated based on user feedback. Users are invited to contact the MSSO Help Desk with any questions or comments about the MedDRA Points to Consider Companion

Document.

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**Background**
For coding purposes, terms that reflect medication errors are grouped in the High Level Group Term (HLGT) *Medication errors and other product use errors and issues* (from MedDRA Version 20.0 onwards). However, terms located elsewhere in the MedDRA hierarchy can also be used to code cases describing medication errors. To aid data retrieval of the widely dispersed coding terms, the Standardised MedDRA Query (SMQ) *Medication errors* was developed, with a narrow and a broad scope, as a tool for standardised retrieval of suspected medication error cases.
The HLGT *Medication errors and other product use errors and issues* contains numerous terms:

- Types of errors (e.g., LLT *Wrong drug*),
- Terms combining the type of error with a stage of the medication use system (e.g., LLT *Wrong drug prescribed*)
- Describing the potential for error
- Intercepted errors that did not reach the patient
- This HLGT also contains terms for situations when it is uncertain whether the reported incident is an error

Each PT is grouped into one of the High Level Terms (HLTs), either for accidental exposures, stages of the medication use system*, product confusion, or the HLT grouping for various other PTs not elsewhere classified.
*For the purposes of this document, the medication use system encompasses a continuum of activities after release of the product into the healthcare system during which a medication error can occur, including procurement, storage, prescribing, transcribing, selecting, preparing, dispensing, administering, and monitoring. The medication use system excludes activities related to the entire manufacturing process including manufacturer distribution and storage.

## 3.1 CODING MEDICATION ERRORS – QUESTIONS AND ANSWERS

This sub-section provides answers to commonly asked questions about coding medication errors.

### 3.1.1 Use of LLT Medication error

**When is it acceptable to use the Lowest Level Term (LLT) *Medication error*? Can the term be selected if there is no appropriate MedDRA term for the error?**

- The use of LLT *Medication error* should be avoided unless there is NO other information reported about the medication error

- Check all the LLTs in HLGT *Medication errors and other product use errors and issues* for the most specific term possible

- If a specific error is reported but no suitable LLT is available, the procedure for a change request should be followed (see the Change Requests page on the MedDRA website). In the interim, select the closest available term to code the reported error. There may be rare instances when LLT *Medication error* is the closest term and can be selected.

### 3.1.2 Selecting more than one term

**Should terms for all reported errors related to the same incident be selected?**

Sometimes the 'originating error' (also referred to as the initial error) results in consequent errors. For example, it was reported that "a prescribing error for the wrong drug consequently resulted in the wrong drug being dispensed and administered."

- The 'originating' error should be coded as the priority. Additional or 'consequent' errors can be coded if they are stated in the report. In the above example, the priority is to code LLT *Wrong drug prescribed*; LLT *Wrong drug dispensed* and LLT *Wrong drug administered* are terms for consequent errors and can also be added.

- Avoid 'double coding' the same error. In other words, do not use multiple LLTs to capture a singular error that is reported with both a general and a specific verbatim; code only the specific error. For example, if it is reported that there was an administration error in that the wrong drug was administered, select only LLT *Wrong drug administered* for the specific error. Do not use an additional LLT *Drug administration error* for the general description because this would not add any meaningful information (even though the two LLTs are linked to different PTs).

- Bear in mind that some organisations will have their database configured in a way that counts at LLT level and therefore if two LLTs which map to the same PT are used this may impact on signal detection.

### 3.1.3 Medication error vs. off label use

**It is reported that "a prescriber ordered a much higher dose than per label", but it is not stated if this was a mistake or off label use; should terms for both possibilities be selected, as in differential diagnoses?**

- Do not double code a singular event by selecting a term for an error and a term for off label use when neither is stated but both are possible; this approach is not helpful.

- When a scenario is unclear, try to obtain clarification; if still unknown, select the most applicable term for what is reported without inferring what is *not* reported. For example, if it is only reported that Drug X was prescribed at a much higher dose than per label (no information that it was in error or off label use), select LLT *Prescribed overdose* (HLT *Overdoses NEC*).

- Off-label use terms should only be selected when off label use is specifically mentioned in the reported verbatim information.

### 3.1.4 Potential medication errors

**How should terms be selected for reports that describe the potential for error?**

For example, a report stated that 'two drug labels look alike and could result in someone getting the wrong drug'.

- Potential errors should be designated as such by selecting the LLT *Circumstance or information capable of leading to medication error* or LLT *Circumstance or information capable of leading to device use error*.

- Also, select terms that represent information about the error that could potentially occur. For the above example, select three terms:
    - For the potential error (LLT *Circumstance or information capable of leading to medication error*)
    - For the contributing scenario (LLT *Drug label look-alike*)
    - For the type of error that could occur (LLT *Wrong drug*)

### 3.1.5 Selecting the most specific term

**How should terms that have overlapping concepts with other terms be used?**

For example, a report described a patient who did not allow a product adequate time to reconstitute before self-administering.

- The most specific available LLT should be selected for the reported information. For the above example, select LLT *Inappropriate reconstitution technique* (PT *Product preparation error*) because it is more specific than LLT *Wrong technique in product usage process (PT Wrong technique in product usage process)*. Coding a

singular error by selecting two error terms is useful only when this provides meaningful additional information, i.e. when the single LLT cannot describe the entire reported scenario.

### 3.1.6 MedDRA Concept Description for medication error

**Does the MedDRA Concept Description for medication error include abuse, misuse, or off label uses?**

The MedDRA Concept Description for medication error is taken from the National Coordinating Council for Medication Error Reporting and Prevention (US)* and is as follows:

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

* National Coordinating Council for Medication Error Reporting and Prevention (US); 2001. About medication errors. https://www.nccmerp.org/about-medication-errors. Accessed 1 March, 2020.

As a general principle, intentional uses such as abuse, intentional misuse, off-label use, and intentional overdose are not medication errors. However, whether a scenario is an error or not may depend on the reason or cause.
For example:

- If confusion with some aspect of the product causes or results in incorrect product use or misuse (e.g. the device was confusing so the person administered an extra dose to make sure he got a full dose), it would usually be considered an error, and not intentional misuse
- Occurrence of an adverse drug reaction (ADR) may cause the patient to stop therapy; this is not intentional misuse or an error. Therapy cessation due to an ADR is usually captured elsewhere in the database, and only the ADR is coded in the case.
- Patient may decide to take their medication less frequently than prescribed; this is usually classified as intentional misuse, not a medication error

Drug abuse and details describing how the drug is abused (route of administration, preparation) do not constitute medication errors
Note that situations such as product quality or product supply issues outside one's control are also not usually classified as medication errors, but can **result in** medication errors. For example, device malfunction or packaging defect (product quality issues) can result in an incorrect dose administered.

### 3.1.7 Stages of the medication use system

**When is it appropriate to use a medication error term without the stage of the medication use system?**
Some MedDRA terms have both the type of error and stage of the medication use system (e.g., LLT *Wrong drug prescribed*); some terms have only the type of error (e.g., LLT *Wrong drug*); and some terms have only the stage (e.g., LLT *Drug prescribing error*).

- Using a single LLT

For example, a report stated that 'the pharmacy dispensed the wrong drug'. It is important to highlight both the stage and the type of error where it is known. In this example, this is possible using a single LLT *Wrong drug dispensed* (instead of two LLTs: LLT *Wrong drug* and LLT *Wrong drug dispensed*).

- Using more than one LLT

For example, a report of 'mistakenly prescribed the wrong strength' should be coded with LLT *Wrong strength* and LLT *Drug prescribing error* because no available single term captures the reported information in full.
If the stage is not known, there are terms for the type of error only, such as LLT *Wrong drug*, LLT *Wrong schedule*, LLT *Wrong strength*, etc.

### 3.1.8 Coding the root cause

**Is it recommended to code the root cause if stated in the case report?**
When the root cause is provided, select a term for the root cause if possible because root causes are critical to understanding why an error occurred and identifying interventions that can be undertaken to prevent the error.

- For example, a product quality issue may lead to a medication error; in such a case, the product quality issue is the root cause of the error. Select terms for both the quality issue and the error.

- For example, a communication issue may lead to a medication error; in such a case, the communication issue is the root cause of the error. Select terms for both the communication issue (e.g., LLT *Patient misunderstanding health care provider instructions for product use)* and the error.

- For the broader patient safety concepts, the root cause may not be represented in MedDRA and should be documented in free text (e.g. narrative field) if known. These include issues such as human factors (stress, fatigue) or system issues (training deficiencies, unclear instructions).

### 3.1.9 Do not infer a medication error

**Is it acceptable to use specific medication error codes for information not explicitly stated in the case report?**

The selected LLTs should reflect only the information stated in the case report; it

should not be assumed that a medication error occurred if this is not clearly reported as such.

For example, the report that only stated ‘The nurse administered 50 mg of Drug X’ is not an informative report and should not be submitted as such; further information should be sought or a dose qualification referencing the prescribing information should be provided in the narrative.

Ideally, at the point of data capture, the reason for reporting as a medication error should be included in the narrative, e.g. ‘the patient was accidentally given 50 mg which is more than the prescribed dose’. Alternatively, if it is not possible to clarify with the reporter but the prescribing information recommends a smaller dose, then the report should reference the prescribing information in the narrative, e.g. “the nurse administered 50 mg of Drug X, whereas the recommended dose in the prescribing information is 5 mg.”

### 3.1.10 Device use errors, wrong technique, and device malfunction.

**What is the difference between a device use error, wrong technique, and device malfunction?**

When evaluating medication errors involving devices, it is important to capture the specific device related event that led to the error. Such events can be problems with the device itself (including device malfunctions), or they can be problem with the way the device is used by the person (device use error or wrong technique). In MedDRA, device use errors refer to broad errors in using the device appropriately, e.g., LLT *Unintentional device use beyond labelled duration*. In contrast, the wrong technique in device usage process concepts refer specifically to the *technical* aspect of not properly using the device (e.g., LLT *Incorrect needle gauge used*, LLT *Wrong injection technique*). Device malfunction refers to failure of the device to perform as intended when used in accordance with the labelling. A malfunction of a device is not considered a device use error or a wrong technique error.

Sometimes the reports do not have enough information to determine if the incident is related to a device issue/malfunction, device use error, or wrong technique. Clarification should be sought since these are very important distinctions. Attempt to code the verbatim information and avoid inferences.

## 3.2 EXAMPLES FOR CODING MEDICATION ERRORS

This sub-section provides examples for coding medication errors in various categories.
The tables are organised in the following way:

- The first column describes a scenario

- The second column indicates whether this scenario is considered a medication error in the context of the MTS:PTC or not, or if this is unknown from the provided information

- The third column provides the selected LLT(s) and, if helpful, the relevant PT(s) or HLT(s)

- The fourth column provides additional comments and explanations regarding the term selection

The LLTs may fall into more than one category and the concepts presented may overlap across tables.

### 3.2.1 **Accidental exposures to products**

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| Person tried to commit suicide by overdosing on prescription opioids and heroin | No | Multiple drug overdose intentional<br><br>Attempted suicide | This is not a medication error as the person intended to overdose |
| Person took street heroin to get high but died of a heroin overdose | No | Overdose<br><br>Opioid abuse | It is not known that the overdose was intentional; do not code as accidental overdose because the scenario is in the context of drug abuse, not a medication error. Death would be captured as an outcome. |
| Parent accidentally injected himself in the thumb while using an auto-injector to administer the drug to the child | Yes | Accidental exposure while administering drug | The parent was not the intended patient and was accidentally exposed to the drug. The selected LLT captures the reported information with specificity, e.g., that the accidental exposure occurred while administering the drug. |

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| Patient with visual impairment experienced choking after accidentally swallowing a desiccant tube that was the same colour and similar size as the tablets in the bottle | Yes | Accidental ingestion of product desiccant<br><br>Product appearance confusion<br><br>Choking | Accidental exposure is captured as well as the contributing factor of look-alike product confusion.<br>LLT *Visual impairment* would be captured in medical history. |
| 2-year-old child took some antibiotics that were accidentally left on the kitchen counter | Yes | Accidental drug intake by child | |
| Adolescent died of overdose after taking 200 doses of a nasal inhalant in under 15 minutes, in an attempt to get high | No | Drug abuse<br><br>Overdose | Overdose in the context of abuse is not a medication error nor<br>Intentional misuse (which implies therapeutic use according to the table in MTS:PTC, Section 3.16). Death would be captured as an outcome. |
| Adult ingested 2 tablets of 100 mg strength | Unknown | | This is not an informative report and further information should be sought. There is nothing to code in the provided text. |
| Adult intentionally ingested 2 tablets of 100 mg strength for his back pain instead of the recommended 1 tablet | No | Intentional misuse by dose change | This is an example of intentional misuse and is not a medication error |

### 3.2.2 Miscellaneous medication errors/issues

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| Pharmacist reported that the product label was | Yes | Circumstance or information | This is an example of a potential medication error |

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| confusing and that it could result in a patient receiving the wrong dosage form | | capable of leading to medication error<br><br>Product label confusion<br><br>Wrong dosage form | since the report does not state that the wrong product was actually dispensed or administered. The LLT *Circumstance or information capable of leading to medication error* captures that the error is a potential one. The most specific code for the reported type of potential medication error should be selected and the contributing factor, label confusion. |
| Patient drew her insulin out of the pen with a syringe because she was confused by the numbers marked on the pen, and did not want to mistakenly take too much insulin using the pen | Yes | Wrong device used<br><br>Product design confusion | The patient uses a wrong device to prevent an error, due to her initial confusion with the pen markings. The confusion and the consequent use of the wrong device are both within a scenario of a medication error, so there is no need to add Intentional device misuse. |
| Patient experienced hypoglycaemia after he used his insulin pen cartridge as a vial. He reported that he did so because he had leftover insulin syringes and did not want to waste them. | No | Intentional device misuse<br><br>Hypoglycaemia | This is an example of Intentional misuse: there is a therapeutic purpose but there is no mention of a medication error |
| The pharmacist selected a wrong adapter device that was incompatible with the drug; the device started dissolving when it was used to transfer the drug from the vial to the bag for administration | Yes | Wrong device used<br><br>Drug-device incompatibility | Capture both that the wrong device was used and that it is incompatible with the drug |
| Patient did not wait the recommended 10 seconds when using the | Yes | Wrong technique in device usage process | Do not select LLT *Device use error*, since this is a broader term than the |

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| autoinjector pen because he misunderstood how to use the pen | | | selected LLT *Wrong technique in device usage process.* The selected LLT represents a technical error with using the device. |
| The patient forgot to have her hormonal IUD replaced after the recommended 5 years. In the 7th year after device was originally inserted, she became pregnant. | Yes | Unintentional device use beyond labelled duration<br><br>Pregnancy with IUD | LLT *Unintentional device use beyond labelled duration* (PT *Device use error*) represents a broad error in using the device appropriately according to recommendations for its intended use. |
| Pharmacy software had a built-in dose calculator that was misprogrammed by the pharmacy. The error resulted in a child getting the wrong dose. | Yes | Device programming error<br><br>Dose calculation error associated with device<br><br>Wrong dose administered | |
| While hospitalized, patient experienced an unspecified medication error but no adverse event | Yes | Medication error | This is not an informative report but is an example where the verbatim is captured with LLT *Medication error*.<br>According to the MTS:PTC, if a medication error report specifically states that there were no clinical consequences, the preferred option is to select only a term for the medication error. Alternatively, a term for the medication error and the additional LLT *No adverse effect* can be selected (see MTS:PTC, Section 3.21). |
| Nurse administered the wrong dose after using a | Yes, consequent | Mobile medical application issue | The issue with the mobile application is the cause of |

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| faulty mobile medical device (app) that miscalculated the patient's insulin needs | to a device issue | Dose calculation error associated with device<br><br>Wrong dose administered | the dose calculation error and the subsequent administration of the wrong dose |
| Patient split their tablet (labelling doesn't advise against splitting the tablet) | No | | The report does not mention an error, instead it confirms that this is not a medication error because the label does not advise not to split. There is nothing to code in the provided text. |
| Provider prescribed half a tablet once daily, unaware that the labelling states to swallow the tablets whole. Patient split the tablets. | Yes | Product prescribing error<br><br>Tablet split by mistake | This is a prescribing error that resulted in the patient splitting the tablet. This is not a case of off label use, as the prescriber was unaware that the tablet should not be split. |
| Prescriber advised patient to split tablet. The labelling states that tablets should be swallowed whole. | Unknown | Product prescribing issue | Select LLT *Product prescribing issue* since it is not known whether this is unintentional (a medication error) or intentional (off label use). The report does not indicate whether the prescriber was aware that the tablets should be swallowed whole. |
| Patient should be on Drug A but instead got Drug B; it is unclear where the error occurred | Yes | Wrong drug | This is a "Wrong drug" medication error; the stage where the error occurred is not stated (e.g., at prescribing, dispensing, selection, or administration) |
| A generic was incorrectly substituted for the brand name product although the physician specifically prescribed the brand | Yes | Product substitution error (HLT *Medication errors, product* | |

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| name product with no substitution | | *use errors and issues NEC*) | |
| Patient had thrown medicated opioid patches in the open waste bin instead of disposing as recommended in the label. Their child experienced an overdose after playing with the patches. | Yes | Incorrect disposal of medication<br><br>Accidental exposure to product by child<br><br>Accidental overdose | The route of exposure is not specified in the verbatim information and therefore cannot be coded |

### 3.2.3 Product administration errors/issues

#### 3.2.3.1 Dose omission

As per the MedDRA Concept Description, dose omission is 'the failure to administer an ordered dose to a patient before the next scheduled dose, if any. This excludes patients who refuse to take a medication, a clinical decision (e.g., contraindication), or other reasons not to administer (e.g., patient sent for test)."

For the purposes of retrieval and analysis, in general, a dose omission should be considered to be a suspected medication error. However, there are scenarios where doses are missed which are not considered medication errors. The cause or contributing factors for the dose omission are necessary to determine if the omission is a medication error or not, and consequently to select the appropriate MedDRA terms. Scenarios where dose omission occurs can be generally grouped as follows:

- Dose omission unintentional (error) (e.g., patient misunderstood instructions; pen device jammed and patient could not deliver the dose; patient forgot to take dose)
- Dose omission intentional (e.g., patient skips a dose of an antidiabetic because of low blood sugar, medicine held one day prior to surgery)
- Dose omission that is unspecified (cause / contributing factors unknown)
- Therapy interruption (neither an error nor intentional. Due to non-clinical or external factors such as supply, insurance, financial issues, etc.)

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| Health provider reported a problem that resulted in leakage where the two syringes were connected. This led to the dose not being given. | Yes | Syringe connection issue<br><br>Device leakage<br><br>Drug dose omission by device | This is an example of a device issue leading to a medication error. |
| Patient was not given the dose of the drug, as the nurse accidentally administered the diluent to the patient instead of using the diluent to reconstitute the vial containing the active ingredient | Yes | Missed dose in error<br><br>Active ingredient not added to diluent (PT *Product preparation error*)<br><br>Single component of a two-component product administered | In this scenario, dose omission is an error caused by failure to reconstitute the vial with the diluent. The specific term LLT *Missed dose in error* should be selected if the report indicates that the dose omission is an error. |
| Missed dose | Unknown | Missed dose (PT *Product dose omission*) | |
| Patient couldn't take medication for a week because the pharmacy was out of the medication | No | Temporary interruption of therapy<br><br>Product availability issue | This event is neither intentional nor a medication error. Use LLT *Temporary interruption of therapy* and capture that external factors caused the interruption of therapy. |
| Patient missed her dose because she did not notice that one of the dosage units in the package was empty | Yes | Missed dose in error<br><br>Package empty units (PT *Product packaging quantity issue*) | This event of missing a dose is due to a product packaging quantity issue |
| Patient did not take medication this week because he could not afford it | No | Inability to afford medication<br><br>Temporary interruption of therapy | This is neither a dose omission in error nor an intentional dose omission. Use LLT *Temporary* |

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| | | | *interruption of therapy* and capture that external factors caused the interruption of therapy. |
| The afternoon dose was held because the patient was scheduled for a medical procedure | No | Intentional dose omission | This is an example of an intentionally omitted dose |
| Patient's blood sugar was low so he decided to skip the prescribed evening dose of insulin | No | Intentional dose omission | This is an example of an intentionally omitted dose by the patient |
| Patient took the drug as prescribed but broke out in a red itchy rash and did not take the remaining doses | No | Itchy rash | Stopping therapy because of an adverse event does not represent an error or intentional misuse. Discontinuation of therapy is typically captured as an outcome. |
| Patient habitually skipped prescribed antipsychotic | No | Treatment noncompliance | |
| The on-body infuser fell off the patient's arm and she missed the dose | Yes | Missed dose in error<br><br>Drug delivery device fell off skin | Capture the unintentional missed dose and that it occurred because the delivery device fell off. In this case it is not stated whether this is an adhesion issue. |
| Patient forgot to take his medication on one day during the week | Yes | Forgot to take product | |

#### 3.2.3.2 Other administration errors/issues

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| Patient accidentally took 1 tablet twice daily instead of the prescribed 1 tablet once daily | Yes | Once daily dose taken more frequently | When available, it is important to select a specific LLT for the reported scenario, rather than just the LLT that matches the PT *Inappropriate schedule of product administration*, allowing further sub-analyses on the LLT level.<br>Although the LLT does not capture that it was accidental, it falls under HLT *Product administration errors and issues*. |
| Tablet was crumbled, but was still administered to the patient | Yes, consequent to a product quality issue | Tablet physical issue<br><br>Poor quality drug administered | "Tablet was crumbled" in this scenario is a product quality issue (LLT *Tablet physical issue*); do not select a medication error term such as LLT *Tablet crushed incorrectly*. The error is that a product with a known quality issue ("crumbled") was still administered to the patient. |
| Patient had difficulty removing the tablet from the thick blister pack; she managed to force it out but the tablet crumbled into many pieces that fell to the floor. She found and took only one piece of the dose. | Yes | Product blister packaging issue<br><br>Incorrect dose administered | "Tablet crumbled" in this scenario is not a product quality issue and does not need to be coded. Code the reported blister packaging issue and the consequent partial dose administration. |
| Syringe plunger couldn't be completely pushed down so the patient | Yes, consequent to a delivery device issue | Device delivery system malfunction | Capture both the device issue and the consequent medication error. LLT *Device* |

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| received only half of his scheduled dose | | Incorrect dose administered by device | *delivery system malfunction* is more specific than LLT *Syringe issue.* |
| A patient reported that he followed the directions for use, but the device jammed and most of the injection sprayed all over his hands | Yes, consequent to a delivery device issue | Device delivery system malfunction<br><br>Accidental exposure while administering drug<br><br>Exposure via skin contact | Do not infer a missed dose, since it is not reported in the narrative |
| Patient taking contraindicated drug | Unknown | Contraindicated drug administered | The report states that the patient is taking a contraindicated drug; circumstances are not provided |
| The drug was administered in the abdomen rather than the arm muscle as recommended | Unknown | Drug administered at inappropriate site | |
| Patient inquired about possible overdose symptoms because she accidentally took an extra dose | Yes | Extra dose administered | The patient is only inquiring about overdose symptoms (not reporting an overdose).<br>Although the LLT does not capture that it was accidental, it falls under HLT *Product administration errors and issues*. |
| Patient reported taking an expired drug for his headache | Unknown | Expired drug used | |
| Patient experienced respiratory arrest after the nurse misprogrammed the infusion pump to deliver the drug over 5 minutes | Yes | Drug administration rate too fast<br><br>Pump programming error | |

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| instead of the intended 50 minutes | | Respiratory arrest | |
| The patient used a cracked insulin cartridge which resulted in a partial dose administered | Yes | Partial dose delivery by device<br><br>Cartridge cracked | |

### 3.2.4 Product confusion errors/issues

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| Patient was dispensed Drug Y instead of Drug X. The two drugs had similar looking packaging. | Yes | Look alike packaging<br><br>Wrong drug dispensed | |
| Patient purchased over the counter (OTC) Drug X 10 g instead of intended Drug X 5 g because of label confusion | Yes | Product label confusion<br><br>Wrong drug strength selected | |
| Patient accidentally took the wrong drug for a week because the tablets looked identical to his daily vitamin tablets | Yes | Look alike pill appearance<br><br>Wrong drug administered | |
| Mix-up of 5 mg/ml with 50 mg/ml product | Yes | Wrong strength | It is unclear whether the patient was administered the drug. 'Strength' pertains to the product itself; 'dose' is the amount of drug the patient receives / should receive. |
| Patient was dispensed 'Drillo' instead of 'Millo', as the pharmacist misheard the name of the drug as 'Drillo" when | Yes | Drug name sound-alike<br><br>Wrong drug dispensed | |

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| the physician ordered it over the telephone | | | |
| Patient experienced skin ulceration after applying the wrong topical cream. Error attributed to the creams packaged in the same size tube with similar red font and black background. | Yes | Look alike packaging<br><br>Wrong drug administered<br><br>Skin ulceration | |

### 3.2.5 Dispensing errors/issues

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| Patient complained that the generic didn't work as well as the innovator drug | No | Product substitution issue brand to generic<br><br>Drug effect decreased | This is a product quality complaint |
| A generic was substituted for the brand name product | Unknown | Product substitution (HLT *Therapeutic procedures NEC)* | Code only what is stated. The report does not specify an error. |
| Patient received expired patches from the pharmacy | Yes | Expired drug dispensed | |
| Patient took the drug daily instead of on the intended weekly schedule because the clinic wrote the wrong directions on the vial | Yes | Wrong directions typed on label (PT Product *dispensing error*)<br><br>Once weekly dose taken more frequently | |
| Drug was not dispensed in the original container, although the labelling advises that the drug must be kept in the original container | Yes | Drug not dispensed in original container | |

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| The prescription was illegible and resulted in the pharmacy dispensing the wrong strength | Yes | Wrong drug strength dispensed<br><br>Written prescription illegible | |
| Pharmacy dispensed drug with the pharmacy label obscuring the recommended storage information. Product stored at wrong temperature. | Yes | Drug dispensing error<br><br>Pharmacy label placed incorrectly (PT *Product dispensing error*)<br><br>Product storage error | |

### 3.2.6 Monitoring errors/issues

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| Patient was hospitalized with thromboembolism because his INR wasn't monitored as recommended in the labelling | Yes | Drug monitoring procedure not performed<br><br>Thromboembolism | |
| Literature report hypothesised a possible drug interaction caused the patient to experience hypotension | No | Drug interaction<br><br>Hypotension | |

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| Patient experienced type I hypersensitivity after receiving amoxicillin during surgery. The patient's e-health record had a documented history of amoxicillin allergy. The error was attributed to the lack of interoperability between the anaesthesia software and the hospital's e-health record. | Yes | Hypersensitivity type I<br><br>Documented hypersensitivity to administered drug<br><br>Device computer software issue | |
| Patient on anticoagulant undergoing surgery but due to an oversight, it was not stopped prior to surgery as recommended in the labelling and patient experienced postoperative bleeding | Yes | Medication monitoring error<br><br>Failure to suspend medication<br><br>Postoperative bleeding | |
| Provider prescribed two drugs with known drug interaction because he was unaware of the interaction potential | Yes | Labelled drug-drug interaction medication error<br><br>Drug prescribing error | |

### 3.2.7 Preparation errors/issues

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| Caregiver wasn't aware to remove the inner cover from an insulin pen needle when preparing the pen | Yes | Product assembly error during preparation for use | |
| Product was reconstituted with the wrong diluent | Yes | Wrong solution used in drug reconstitution | |

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| Pharmacy compounded the wrong strength product | Yes | Product compounding error<br><br>Wrong strength | |
| Patient received only one component of a two-component product because the nurse wasn't aware that the two components needed to be mixed together before administration | Yes | Product preparation error<br><br>Single component of a two-component product administered | |
| Pharmacy prepared incorrect concentration because of confusion related to the way the strengths for the two active ingredients were stated on the label | Yes | Wrong concentration prepared<br><br>Product label confusion | |
| The technician didn't follow the instructions to mix the contents of the vial for 5 minutes after reconstitution | Yes | Product preparation error | LLT *Product preparation error* (HLT *Product preparation errors and issues*) is more specific than LLT *Wrong technique in product usage process* (HLT *Medication errors, product use errors and issues NEC*) |
| Respiratory therapist put the canister in an inhaler the wrong way | Yes | Product assembly error during preparation for use | |

### 3.2.8 Prescribing errors/issues

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| Drug prescribed in error for unauthorised use | Yes | Drug prescribing error | This is a prescribing error. Off label use should not be coded in addition. Off label use is |

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| | | | an intentional act not an error. |
| Unintentionally prescribed Drug X instead of Drug Y because the names sounded alike | Yes | Drug prescribing error<br><br>Drug name sound-alike | It is important to be able to identify the confusion as a root cause |
| Prescribed 4 mg/kg instead of 0.4 mg/kg. Prescriber realised immediately and called nurse but nurse had already administered the drug. | Yes | Drug dose prescribing error<br><br>Wrong dose administered | Even though the error was detected it was not intercepted in time |
| Patient was switched to different insulin product but dose adjustment was not written on the prescription. Patient administered the wrong dose and experienced hypoglycaemia. | Yes | Drug dose prescribing error<br><br>Wrong dose administered<br><br>Hypoglycaemia | |
| Patient was prescribed 2 times the appropriate dose due to computerised prescriber order entry (CPOE) error | Yes | Drug dose prescribing error<br><br>CPOE error | |
| Patient with intractable seizures and taking multiple drugs was prescribed a contraindicated drug | Unknown | Contraindicated drug prescribed | LLT *Seizures* should be captured as medical history |
| Patient was prescribed 0.5 mg to be taken by splitting the 1 mg tablet | Unknown | | No event to code based on the stated information. It is not known if this is a prescribing error, off label use, or neither. If this is the ONLY information, this is not a case and should not be recorded. |
| Patient prescribed 1 tablet daily for insomnia for many years. The product directions state | Unknown | Medically prescribed prolongation of labelled treatment | The selected LLT captures both the "prescribing" concept and the "duration" concept |

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| that the product should not be taken for more than 2 weeks. | | duration (PT *Product prescribing issue*) | |
| An elderly man felt dizzy and fell after he was inappropriately prescribed Drug A | Unknown | Inappropriate prescribing<br><br>Dizzy<br><br>Fall | Select LLT *Inappropriate prescribing* only when specifically stated in the narrative; otherwise, select LLT *Product prescribing issue* or a similar term when it is unknown if the product was prescribed off label or in error |
| Patient hospitalised for withdrawal symptoms after his unspecified opioids were inappropiately downtitrated | Unknown | Opiate withdrawal symptoms<br><br>Inappropriate drug titration | |
| Patient prescribed 0.25 mg (off-label starting dose) | No | Off label dosing | |
| Physician ordered the wrong rate of administration for the IV drug, and the patient experienced hypotension | Yes | Incorrect drug administration rate<br><br>Hypotension<br><br>Drug prescribing error | |
| Drug indicated for IV administration was used off label via the oral route | No | Off label use<br><br>Intravenous formulation administered by other route | LLT *Intravenous formulation administered by other route* (PT *Incorrect route of product administration,* HLT *Product administration errors and issues*) provides additional information about the specific type of off label use. The term is not an off label use term itself; it is a general product use issue term that can be used in combination with other terms to capture |

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| | | | detail about off label use, misuse, medication errors, etc. |
| Patient accidentally received duplicate therapy because the prescriber didn't realise the 2 drugs had the same active ingredient | Yes | Duplicate drug prescription error<br><br>Duplicate therapy with same active substance | |

### 3.2.9 Product selection errors/issues

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| The elderly patient confirmed that due to the cataract, the patient did not see well and ended up buying the infant formulation | Yes | Product selection error | This is not a product name confusion.<br>Cataract would be captured as medical history. |
| Pharmacist selected the wrong drug because of name confusion, but the error was caught and corrected before the drug was dispensed | Yes | Intercepted wrong drug selected<br><br>Drug name confusion | It is important to capture the cause of the error |
| The hospital selected the wrong bag and the patient received a transfusion of the wrong blood type prior to and during surgery | Yes | Wrong product selected<br><br>Transfusion with incompatible blood | |
| Clerk ordered the wrong drug from the wholesaler because the drugs were listed next to each other in the catalogue and the names looked very similar | Yes | Wrong drug selected<br><br>Drug name look-alike | |

### 3.2.10 Product storage errors/issues

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| Healthcare facility reported storing reconstituted drug in syringes past the recommended 30 days, and administering it to patients. One of these syringes was used by a patient who reported that the drug didn't work. | Yes | Improper storage of unused product<br><br>Expired drug administered<br><br>Lack of drug effect | LLT *Poor quality drug administered* should not be selected because the selected LLT *Expired drug administered* is more specific |
| Vaccine product was stored in the pharmacy at excessive temperatures | Yes | Product storage error temperature too high | This is a medication error, as the error occurred in the product use system |
| The pharmacy staff member could not find drug as it had inadvertently been placed on the wrong shelf | Yes | Drug stored in wrong location | |
| Boxes of the drug sent from the manufacturer were left outside at excessive temperatures over the weekend when the wholesaler was closed | No | Manufacturing product storage issue (HLT *Product distribution and storage issues*, SOC *Product issues*). | This storage problem is not a medication error because it occurred under manufacturing distribution and storage activities, prior to the product reaching the medication use system |
| Pharmacy delivered the drug to the patient's home while the patient was hospitalised. The package was outside at temperatures below freezing for two days (drug should not be frozen). | Yes | Product storage error temperature too low | This is a medication error, as the error occurred in the product use system |
| Manufacturer issued a recall of certain lots of Drug X that were found to be exposed to inappropriate storage conditions by the wholesaler | No | Manufacturing product storage issue<br><br>Recalled product | This storage problem is not a medication error because it occurred under manufacturing distribution and storage activities, prior to the product |

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| | | | reaching the medication use system |
| Pharmacy mistakenly stocked the wrong drug in the automated dispensing system. Reporter attributed the error to both drugs being packaged in similar sized vials with look-alike container labels. | Yes | Drug label look-alike<br><br>Wrong drug stocked<br><br>Product packaging confusion | |

### 3.2.11 Product transcribing errors/communication issues

| Scenario | Medication error? | LLT | Comment |
|---|---|---|---|
| Healthcare provider called in a prescription for Drug A, but pharmacy wrote down the prescription as Drug B | Yes | Transcription medication error | |
| Pharmacy dispensed 800 mg strength instead of 600 mg due to data entry error | Yes | Product data entry error<br><br>Wrong drug strength dispensed | |
| Physician ordered insulin pens, but a transcription error transpired with the pharmacy and the patient was dispensed insulin in a vial with syringes instead | Yes | Transcription medication error<br><br>Wrong device dispensed | |
| Patient had an issue communicating and was given the possible diagnosis of autism | No | Communication disorder<br><br>Autism | Despite the terms “issue” and “communicating” in the example, this is not a medication error and should not be captured under LLT *Product communication issue*, but rather should be captured under LLT *Communication disorder* |

# 4. PRODUCT QUALITY ISSUES

The purpose of this section is to expand on the section on product quality issues in the MedDRA Term Selection: Points to Consider (MTS:PTC) document. This particular section is intended to facilitate term selection for product quality issues for distributed products reported in the **clinical** setting. This section does not provide suggestions for the use of the MedDRA terminology which covers specific manufacturing deviations or non-conformances. Additionally, guidance and examples for coding of some scenarios are provided. This section has three main sub-sections:

- Background: concept of product quality issues in medical products
- Examples for coding product quality issues (based on MedDRA Version 23.0)
- Data search and retrieval strategies: guidance and considerations

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## 4.1 BACKGROUND

It is important to recognise product quality issues as they may have implications for patient safety. Product quality issues are defined as abnormalities, also known as non-conformances (failures to conform with established product specifications), that may be introduced in any phase of the supply chain. These include the manufacturing, labelling, packaging, shipping, handling or storage of the products. Product quality terms may be used to report product defects to regulatory authorities and may also be used in organisations' internal databases to track and trend quality issues or deviations. Product quality issues may occur with or without clinical consequences. Not all product quality issues are readily detectable to the user.

Product quality issues may be reported in the context of adverse events or as part of a product quality monitoring system. Likewise, patient safety data may facilitate surveillance for evidence of product quality issues. MedDRA coding conventions for product quality issues promote consistency in data entry, facilitating data retrieval that is required to support health risk assessment when a non-conforming product is detected in the marketplace.

Other important concepts that may be reported into a product quality monitoring system include consumer preference complaints in which the reporter makes no allegation against the product quality, but communicates dissatisfaction with the product or packaging design. Examples include request for a liquid form of a solid dosage form, a suggestion to change the package configuration from bottle

to blister or to increase the quantity of tablets per bottle, and a request for a dye-free version of a children's suspension. While these may not represent product quality non-conformance and/or there is no discrete clinical consequence, these may be valuable to inform enhancements to the product and packaging design and labelling, and may influence the product benefit-risk profile.

Familiarity with HLGT *Product quality, supply, distribution, manufacturing and quality system issues* (in SOC *Product issues*) is essential for term selection. Under this HLGT are categories of specific product quality issues such as HLT *Product packaging issues*, HLT *Product physical issues*, HLT *Counterfeit, falsified and substandard products*, and HLT *Product contamination and sterility issues*. MedDRA Lowest Level Terms (LLT) that most accurately reflects the reported verbatim information should be selected. This may be achieved by use of the search function or by use of the SOC window of a browser to navigate the MedDRA hierarchy down to the appropriate LLT.

SOC *Product issues* 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 may be multi-axial 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*. The fact that most product quality terms are single-axial and are located in SOC *Product issues* should be taken into account when designing queries and other retrieval strategies.

Explanations of the interpretations and uses of certain product quality issue terms (e.g., "Product coating incomplete") are found in the MedDRA Introductory Guide (Appendix B, MedDRA Concept Descriptions).

## 4.2 EXAMPLES FOR CODING PRODUCT QUALITY ISSUES

### 4.2.1 Product physical issues

| Scenario | LLT | Comment |
|---|---|---|
| Pharmacist opened bottle of tablets and detected an irregular odour that was due to mould | Product odour abnormal<br><br>Product contamination mould | A term has been added for the reporter's statement that the abnormal odour is the result of contamination with mould. This is also a form of biocontamination (see Section 4.2.2). |
| Patient stated chewable tablets were excessively hard and he suffered a broken tooth. He suspects the product was defective. | Medication too hard to chew<br><br>Tooth fracture<br><br>Tablet physical issue | Note, product quality issue, LLT *Tablet physical issue*, is based on reporter verbatim. In the absence of this information, a product quality issue should not be inferred. |

| Scenario | LLT | Comment |
|---|---|---|
| Mother states she gave her child a suspension labelled as cherry flavoured and it had a distinct taste of mint instead | Product taste abnormal | These reports only refer to a discrepancy between labelled taste/colour and actual taste/colour. Either the product content is incorrect or the label is incorrect. An event within the HLT *Product label issues* should be coded only if the reporter indicates that the label is incorrect. |
| When the nurse opened the vaccine carton, the vial was observed to contain yellow liquid. The product label states it should be colourless. | Product colour issue | |
| The pharmacist opened the medication bottle and discovered some of the tablets were broken | Tablet chipped | |
| Patient found intact tablets in her stool and complained that the tablet must be of poor quality | Tablet in stool<br><br>Product quality complaint | This LLT is under PT *Product residue present* and located in the SOC *Investigations*. Although this is not typically a product non-conformance, it is the patient perception that something is wrong, or that the tablet is of poor quality. |
| A female patient noticed that her contraceptive medication smelled bad and tasted differently than before | Product smell abnormal<br><br>Product taste abnormal | |

### 4.2.2 Product contamination/sterility issues

| Scenario | LLT | Comment |
|---|---|---|
| Upon opening the sterile packaging for a venous catheter, the surgeon noticed an insect present in the inner packaging. She discarded the unit and retrieved an alternate package that was clean and intact. | Product contamination insect | This information may require collection and reporting by the user facility, with or without evidence of patient involvement. |
| Upon inspection of a prefilled syringe, the nurse detected particles floating in | Particle present in liquid product | LLT *Product availability issue* is a more general term, as it does not specify the reason for unavailability. |

| Scenario | LLT | Comment |
|---|---|---|
| the liquid. This was the last available prefilled syringe for this drug at the clinic. The patient's treatment was delayed until the following week when the syringe was available again. | Temporary interruption of therapy<br><br>Product availability issue | LLT *Product supply issue* is not appropriate in this example, because there is no mention of a supply issue. |
| A consumer reported that while examining the drug provided in an ampoule, she noticed that there was a piece of glass inside | Product contamination glass | |
| The patient reported contracting fusarium keratitis of her left eye. She suspected contamination of her contact lens solution was the source. | Fusarium infection<br><br>Keratitis fungal<br><br>Suspected product contamination<br><br>Suspected transmission of an infectious agent via product | LLT/PT *Suspected transmission of an infectious agent via product* is multi-axial, linking to SOC *Infections and infestations* as primary and SOC *Product issues* as secondary. |

### 4.2.3 Product distribution issues

| Scenario | LLT | Comment |
|---|---|---|
| A patient complained that the medication shipment to her home was delayed. As a result, she ran out of medication, missed several doses and developed hyperglycaemia. | Product shipment delay<br><br>Therapy interrupted<br><br>Hyperglycaemia | |

### 4.2.4 Product label issues

| Scenario | LLT | Comment |
|---|---|---|
| The patient was unable to read the expiration date on the medication bottle because it had faded in colour | Product expiration date illegible | |

| Scenario | LLT | Comment |
|---|---|---|
| A consumer opened a carton containing infant suspension in a bottle. The accompanying package insert was for the adult tablet form. | Product package insert incorrect | |
| A patient stated he read the dosing schedule on a tube of ophthalmic ointment incorrectly because the print was illegible. As a result, he used product twice a day instead of the recommended once a day. He developed irritation in his eyes. | Product label text illegible<br><br>Once daily dose taken more frequently<br><br>Irritation of eyes | |

### 4.2.5 Counterfeit

| Scenario | LLT | Comment |
|---|---|---|
| A patient was contacted by the infusion facility to inform her that she had been treated with counterfeit medication. She was advised to return for treatment. | Counterfeit product administered | This LLT links to SOC *Injury, poisoning and procedural complications* as the primary SOC and to SOC *Product issues* as the secondary SOC. LLT *Counterfeit product administered* should only be selected if counterfeit has been confirmed. Otherwise, LLT *Suspected counterfeit product* should be selected. |
| When inspecting a carton of vaccines from a new supplier, the clinic manager noted that the product branding was different from previous cartons. He suspected that the material was not authentic. | Suspected counterfeit product | |
| A consumer had been using a drug for several years. The newly purchased unit was ineffective compared to past experience. She suspected that the product was counterfeit. | Suspected counterfeit product<br><br>Drug ineffective | |

### 4.2.6 Product supply and availability

| Scenario | LLT | Comment |
|---|---|---|
| A patient was told by her pharmacist that her medication was not available due to a shortage in supply following closure of several manufacturing facilities. Her physician prescribed an alternative therapy. | Product supply issue<br><br>Drug therapy changed | |
| The pharmacist informed the patient that his medication was not available due to the COVID-19 pandemic | Product unavailable due to pandemic | |

### 4.2.7 Packaging issues

| Scenario | LLT | Comment |
|---|---|---|
| When the patient removed the medication bottle from the carton, the tamper evident seal was absent | Product container seal issue | |
| On inspection of a medication bottle, a customer noticed that the child resistant cap did not work | Failure of child resistant product closure | |
| A nurse noticed that the blister package was not completely sealed | Product blister packaging separated | |
| A woman reported that her contraceptive medication was missing the placebo tablets | Package dosage units missing | |

## 4.3 DATA SEARCH AND RETRIEVAL OF PRODUCT QUALITY ISSUES

Product quality issues may result in patient safety concerns, but these are not always detectable to the manufacturer or the patient. When detected, an opportunity is created to remediate the non-conformance and restore product safety.

Appropriate data entry practices facilitate detection and retrieval of product quality issues in safety data. It is also important to be aware that multiple databases might be used to capture product quality complaints, e.g., a safety

database and a quality database. Consider potential database specifics including differences in data coding of adverse events and quality complaints between the databases (e.g., different dictionaries or data that is not coded).

Broadly, medical safety data review may detect product quality deviations on a continuous, periodic and ad hoc basis. During continuous, real-time review product quality issues can be detected based on single Individual Case Safety Reports (ICSRs) or based on batches/lots when these have a disproportionate number of adverse event reports.

The periodic review for product quality issues is generally product specific. Dependent on the scope of the review this can be done by means of aggregate adverse event review performed on a fixed schedule, or by a review of events reported to the quality system. If data is coded in MedDRA, the retrieval and data output may be enhanced by developing and applying a customised data filter based on MedDRA product quality issue terms. When creating and maintaining a data review strategy, it is important to document the review strategy and terms, and to also document review and update of the terms with each MedDRA release. Periodic review is usually performed to find anomalies in the data. Thus, an increase in certain quality complaints might lead to the generation of a new hypothesis. Further validation could then become necessary by searching for adverse event terms suspected to occur with this type of quality issue.

Data review may be lot specific (i.e., all adverse events for the material in scope) and/or problem specific (i.e., all material, with or without a lot number, for a defined list of adverse event terms). Distribution dates and locations may also be incorporated into this type of data review strategy. The adverse event term list should reflect the medical conditions that may result from exposure to non-conforming product. For example, assessment of a product containing an undocumented potential allergen should include MedDRA terms reflecting hypersensitivity concepts. SMQ *Hypersensitivity* could be applied to achieve this with efficiency. Assessment of a product subject to biocontamination should include MedDRA terms reflecting infection concepts, both broad and specific to the contaminant, if known.

Whether data assessment for product quality is continuous, periodic, or for cause, description of quality issues using MedDRA facilitates detection and retrieval. This improves the integrity of the medical assessment.