

**MedDRA[®] TERM SELECTION:
POINTS TO CONSIDER**

*Release 3.4
Based on MedDRA version 7.1*

ICH-Endorsed Guide for MedDRA Users

**Application to Adverse Drug Reactions /Adverse Events
&
Medical and Social History & Indications**

18 November 2004

© Copyright ICH Secretariat (c/o IFPMA)

Copying is permitted, with reference to source, but material in this publication may not be used in any documentation or electronic media which is offered for sale, without the prior permission of the copyright owner.

IFPMA
30 rue de St- Jean
P.O. Box 758
1211 Geneva 13
Switzerland

Tel: +41 (22) 338 32 00
Fax: +41 (22) 338 32 99

Table of Contents

1.0	INTRODUCTION.....	4
1.1	OBJECTIVE OF THIS DOCUMENT	4
1.2	PURPOSES OF USING MEDDRA	5
1.3	BACKGROUND	5
1.4	SCOPE OF THE POINTS TO CONSIDER.....	5
2.0	GENERAL PRINCIPLES.....	6
2.1	QUALITY OF SOURCE DATA.....	6
2.2	LEVEL OF TERM SELECTION	6
2.3	USE OF “CURRENT”/“NON-CURRENT” LOWEST LEVEL TERMS (LLTs)	6
2.4	CHOICE OF TERM.....	6
2.5	DO NOT SUBTRACT OR ADD INFORMATION.....	7
2.6	QUALITY ASSURANCE	8
3.0	TERM SELECTION POINTS	8
3.1	PROVISIONAL DIAGNOSES	8
3.2	DEATH AND OTHER PATIENT OUTCOMES	9
3.3	CONFLICTING/AMBIGUOUS/VAGUE INFORMATION	10
3.4	COMBINATION TERMS	10
3.5	BODY SITE VS. EVENT SPECIFICITY	11
3.6	LOCATION VS. INFECTIOUS AGENT	12
3.7	PRE-EXISTING MEDICAL CONDITIONS.....	12
3.8	CONGENITAL TERMS.....	13
3.9	MEDICAL/SURGICAL PROCEDURES	14
3.10	INVESTIGATIONS	14
3.11	MEDICATION/ADMINISTRATION ERRORS AND ACCIDENTAL EXPOSURES	16
3.12	OVERDOSE/TOXICITY/POISONINGS.....	17
3.13	DRUG INTERACTIONS	17
3.14	NO ADVERSE EFFECT	18
3.15	UNEXPECTED THERAPEUTIC EFFECT	18
3.16	MODIFICATION OF EFFECT	18
3.17	SOCIAL CIRCUMSTANCES	19
3.18	MEDICAL AND/OR SOCIAL HISTORY	19
3.19	INDICATION FOR PRODUCT USE	20
4.0	Appendices:	23
4.1	CURRENT MEMBERS OF THE ICH <i>POINTS TO CONSIDER</i> WORKING GROUP:.....	23
4.2	PAST MEMBERS/AFFILIATIONS OF THE ICH <i>POINTS TO CONSIDER</i> WORKING GROUP:.....	24

1.0 INTRODUCTION

The Medical Dictionary for Regulatory Activities (MedDRA)¹ was designed for the specific use of sharing regulatory information for human medical products. However, unless users can achieve consistency in the way they assign particular terms to particular symptoms, signs, diseases, etc., use of MedDRA terminology will yield little improvement over the divergent practices of the past.

This *MedDRA Term Selection: Points to Consider* document is an ICH-endorsed guide for MedDRA users. It is designed to be updated based on MedDRA changes, and is a companion document to the MedDRA terminology. It was developed and is maintained by a working group charged by the ICH steering committee consisting of regulatory and industry representatives of the European Union, Japan and the United States, as well as representatives from Canada, the MedDRA Maintenance and Support Services Organization (MSSO), and Japanese Maintenance Organization (JMO). (See appendix for members).

Specific examples contained in this document are based on MedDRA version 7.1.

1.1 Objective of this document

The objective of this ICH *Points to Consider* document is to promote consistent term selection. Organizations are encouraged to document their term selection strategies, methods, and quality assurance procedures in organization-specific coding guidelines, which should be consistent with the *Points to Consider* document.

Consistency in term selection will promote medical accuracy when using MedDRA to share data worldwide. This will in turn facilitate a common understanding of data shared among academic, commercial and regulatory entities. The document could also be used by healthcare professionals, researchers and other interested parties outside of the regulated pharmaceutical/biological industry.

The document is intended to provide term selection advice either for a business purpose or regulatory requirement. There might be examples that do not reflect practices or requirements in all regions; this document does not intend to communicate specific regulatory reporting requirements or address database issues. In addition, it is expected that as experience with MedDRA increases, there will be changes to the document.

¹ MedDRA refers to all sequential and translated versions of the terminology, which are maintained by either the Maintenance and Support Services Organization (MSSO) or the Japanese Maintenance Organization (JMO).

1.2 Purposes of Using MedDRA

To aggregate reported terms in medically meaningful groupings for the purpose of reviewing and/or analyzing safety data

To facilitate identification of common data sets for evaluation of clinical and safety information

To facilitate consistent retrieval of specific cases or medical conditions from a database

To improve consistency in comparing and understanding “safety signals” and aggregated clinical data

To facilitate electronic data interchange of clinical safety information

To report adverse reaction/adverse event (ADR/AE)² terms via individual case safety reports

To include ADR/AEs in tables, analyses, and line listings for reports

To identify frequency of medically similar ADR/AEs

To capture and present product indications, investigations, medical history and social history data

1.3 Background

This *Points to Consider* document has been prepared to help all MedDRA users to begin on common ground, as the terminology itself does not contain specific guidelines for its use; it provides a framework to foster consistent use of MedDRA for data input and retrieval. The end result allows for medically meaningful review and analysis of clinical data.

The working group recognizes that this document is not able to address every situation. Medical judgment and common sense should also be applied.

This document is not a substitute for MedDRA training. It is considered essential that users have knowledge of the MedDRA structure and content. For optimal MedDRA term selection, it is suggested that the reader also refer to the MedDRA Introductory Guide, which is provided with each MedDRA subscription.

1.4 Scope of the Points to Consider

The current document addresses term selection for data entry of ADR/AEs, medical history, social history, indications and investigations.

² For ADR/AE definitions, refer to ICH Guidelines and CIOMS publications.

2.0 GENERAL PRINCIPLES

2.1 Quality of source data

Good MedDRA term selection is best accomplished with clear initial data. Clarification of data that are ambiguous, confusing or unintelligible should be obtained. The quality of the information originally reported directly impacts the quality of data output. Proper term selection allows for systematic and consistent recording, interpretation and comparison of data. It also provides for easy storage, retrieval and analysis of the clinical information.

Data clarity can be promoted through internal procedures such as careful design of data collection forms and training of individuals involved in the data collection and follow-up processes, e.g., clinical investigators/monitors, medical product sales representatives and others.

If clarification cannot be obtained, refer to Section 3.3, Conflicting/ambiguous/vague information.

2.2 Level of term selection

Lowest level term(s) that most accurately reflects the reporter's words should be selected.

2.3 Use of "Current"/"Non-current" Lowest Level Terms (LLTs)

For term selection, only current LLTs should be used. The use of non-current terms should be restricted to the conversion of historical/legacy data.

2.4 Choice of term

2.4.1 It is not considered appropriate to address deficiencies in MedDRA by developing organization-specific solutions. If the medical concept reported is not adequately represented in the latest version of MedDRA, the solution that is considered appropriate is to submit a change request to the MSSO.

Example: The term "HIV viral load increased" was added to MedDRA following a user's request

2.4.2 Medical judgment should be used if an exact match cannot be found, but the medical concept can be adequately represented by an existing term.

Example: If "brittle hair" is reported, "Hair texture abnormal" more accurately reflects the medical concept than the less specific term "Hair disorder"

2.4.3 In situations where a specific medical concept is not represented by a **single** MedDRA term, a new term should be requested from the MSSO. While awaiting the addition of the new term, it is considered

appropriate to select one or more existing terms. A consistent approach should be used. The impact on data retrieval, analysis, and reporting should be carefully considered.

Example: If “metastatic gallbladder cancer” were not represented in MedDRA by a single term, it would be appropriate to select “Gallbladder cancer” or “Metastasis” or both “Gallbladder cancer” and “Metastasis”

Sometimes more than one choice of term selection is provided within the document. If only one term is selected, specificity might be lost, whereas the selection of two terms might lead to redundant counts. Organizations are encouraged to document their established procedures.

2.5 Do not subtract or add information

2.5.1 Do not omit reported information

Terms should be selected for every ADR/AE reported, regardless of perceived relationship to the drug product. No reported medical concept should be excluded from the term selection process.

Terms should be selected for each reported indication, investigation, medical history and social history concept, as appropriate.

2.5.2 Do not add information

No new medical concepts should be added. Neither a diagnosis nor a mechanism of action should be derived or inferred from reported signs or symptoms.

Example: If “abdominal pain, increased serum amylase, and increased serum lipase” are reported, it is considered inappropriate to assign a diagnosis of “pancreatitis”

2.5.3 Diagnosis reported with signs and symptoms

If both a diagnosis and its characteristic signs and symptoms are provided by the reporter, one can select terms for both, but it is considered sufficient to select a term for the diagnosis and not for the signs and symptoms. However, terms should also be selected for signs or symptoms that are not generally recognized as part of that diagnosis.

Example: If “anaphylactic reaction” is reported with rash, dyspnea, hypotension, and laryngospasm, selecting “anaphylactic reaction” alone is considered appropriate

Example: If “myocardial infarction” is reported with “chest pain, dyspnea, diaphoresis, ECG changes, and jaundice”, it would be considered appropriate to select terms for both “myocardial infarction” and “jaundice”

2.6 Quality Assurance

Tools such as auto-encoders can be helpful, but human intervention is necessary to assure the end result fully reflects the original information and makes medical sense.

To promote consistent term selection, organizations are encouraged to document their term selection strategies, methods, and quality assurance procedures in coding guidelines, which should be consistent with the *Points to Consider* document.

The MedDRA terminology is multi-axial and more complex than common terminologies previously used. Therefore, term selection should be reviewed by a qualified individual, a person with medical background and/or training who is also trained in the use of MedDRA.

MedDRA is a standardized terminology. It is considered essential that *ad hoc* structural changes in MedDRA not occur. The assignment of terms across SOC's is pre-determined within the terminology and should not be altered by users. If MedDRA users believe that term(s) are inappropriately placed in the hierarchy, they should inform the MSSO by the change request process.

Example: In a previous version of MedDRA it was found that the primary SOC for the term "Factor VIII deficiency" was "Blood and lymphatic system disorders". It was corrected by making "Congenital, familial and genetic disorders" the primary SOC and "Blood and lymphatic system disorders" the secondary SOC.

3.0 TERM SELECTION POINTS

3.1 Provisional diagnoses

3.1.1 If only a single provisional diagnosis, e.g., "suspicion of", "probable", "presumed", "likely", "questionable", is provided, in the absence of additional clinical information, it should be managed as if a confirmed diagnosis.

Example: If "possible myocardial infarction" is the only information reported, "Myocardial infarction" can be selected

3.1.2 If both a provisional diagnosis and its characteristic signs and symptoms are provided by the reporter, one can select terms for both, but it is considered sufficient to select a term for only the provisional diagnosis and not for the signs and symptoms. However, terms should also be selected for signs or symptoms that are not generally recognized as part of that provisional diagnosis.

Example: If "chest pain, dyspnea, diaphoresis, and jaundice (possible myocardial infarction)" is reported, "Myocardial infarction" and "Jaundice" can be selected

Alternatively it is considered sufficient to select terms for only the signs and symptoms.

Example: If “chest pain, dyspnea, diaphoresis, and jaundice (possible myocardial infarction)” is reported “Chest pain”, “Dyspnea”, “Diaphoresis”, “Jaundice” can be selected

- 3.1.3 If there are multiple provisional diagnoses without signs and symptoms, terms for each provisional diagnosis can be selected.

Example: If a differential diagnosis that includes “pulmonary embolism, myocardial infarction, and congestive heart failure” is reported, “Pulmonary embolism”, “Myocardial infarction”, “Congestive heart failure” can be selected

- 3.1.4 If multiple provisional diagnoses are reported together with signs and symptoms, it is considered sufficient to select terms for only the signs and symptoms. It is also acceptable to select terms for each provisional diagnosis in addition to the signs and symptoms.

Example: If a differential diagnosis that includes “pulmonary embolism, myocardial infarction, and congestive heart failure” is reported along with “chest pain, cyanosis, shortness of breath, and blood pressure decreased”, then “Chest pain”, “Cyanosis”, “Shortness of breath”, and “Blood pressure decreased” can be selected

3.2 Death and Other Patient Outcomes

When an ADR/AE is reported in association with an outcome, a term for the ADR/AE should be selected and the outcome should be captured in the appropriate field.

3.2.1 Death

- 3.2.1.1 Death is an outcome and is not usually considered to be an ADR/AE.

Example: If “death due to myocardial infarction” is reported, “Myocardial infarction” can be selected and death should be captured as the outcome

- 3.2.1.2 If multiple ADR/AEs are reported in association with a fatal outcome, MedDRA terms for each reported event should be selected.

Example: If “constipation, ruptured bowel, peritonitis, sepsis, and patient died” are reported, “Constipation”, “Perforated bowel”, “Peritonitis”, and “Sepsis” can be selected, and death should be captured as the outcome

3.2.1.3 If the only information reported is death, then the most specific death term available should be selected.

Example: If a reporter states only that “a patient was found dead”, “Found dead” can be selected

3.2.2 Other Patient Outcomes

Patient outcomes such as hospitalization and disability are not generally considered to be ADR/AEs.

Example: If “hospitalisation due to congestive heart failure” is reported, “Congestive heart failure” can be selected and hospitalisation should be captured as the outcome

3.2.2.1. If the only information reported is the outcome term, then the most specific term available should be selected.

Example: If a reporter states only that “a patient was hospitalised”, “hospitalisation” can be selected

3.3 Conflicting/ambiguous/vague information

When conflicting, ambiguous, or vague information is provided, it can be difficult to select a term that will lead to appropriate data retrieval. In such circumstances, attempts should be made to obtain more specific information. (See *General Principles: Quality of source data*).

If clarification attempts have failed, the examples below might be helpful:

3.3.1 **Conflicting information:**

Example: If only “hyperkalemia with a serum potassium of 1.6 mEq/L” is reported, “Serum potassium abnormal” can be selected because this single term conveys both medical concepts

3.3.2 **Ambiguous information:**

Example: If “GU pain” is reported, “GU” could refer to either “genito-urinary” or “gastric ulcer”. However, since pain was reported, “Pain” can be selected

3.3.3 **Vague information:**

Example: If the only information reported is “patient experienced every listed adverse event”, and attempts to obtain more specific information are unsuccessful, “Unevaluable event” can be selected

3.4 Combination terms

When combination terms are reported, medical judgment should be applied and the following points should be considered:

3.4.1 If one of the terms is a diagnosis and the other is a characteristic sign and/or symptom, the diagnosis term can be selected (See Section 2.5.3).

3.4.2 If one term is more specific than the other, then the most specific term should be selected.

Example: If “arrhythmia due to atrial fibrillation” is reported, “Atrial fibrillation” can be selected

Example: If “hepatic function disorder (acute hepatitis)” is reported, “Hepatitis acute” can be selected

3.4.3 If a term exists that describes the combination, it should be used.

Example: If “retinopathy due to diabetes” is reported, “Diabetic retinopathy” can be selected

Example: If “rash with itching” is reported, “Itchy rash” can be selected

3.4.4 If splitting provides more clinical information, it is considered appropriate to select more than one term.

Example: If “diarrhea and vomiting” is reported, “Diarrhea” and “Vomiting” can be selected

Example: If “DIC due to sepsis” is reported, “DIC” and “Sepsis” can be selected

Example: If “wrist fracture due to fall” is reported, “Wrist fracture” and “Fall” can be selected

3.4.5 If the reported term is a combination of an event and a pre-existing condition that has not changed (see Section 3.7) and the combination term does not exist in MedDRA, it is considered sufficient to select a term for the event.

Example: If “pain due to cancer” is reported in a patient with cancer, “Cancer pain” can be selected

Example: If “shortness of breath due to cancer” is reported in a patient with cancer, “Shortness of breath” can be selected

3.5 Body site vs. Event specificity

3.5.1 Some MedDRA terms describe both the body site location and the event. If available, the term with both the specific body site and the event should be selected.

Example: If “skin rash on face” is reported, “Rash on face” can be selected

- 3.5.2 Not all MedDRA terms describe body sites. If the suitable MedDRA term with the specific site description is not available, the relevant medical event should have priority.

Example: If “skin rash on chest” is reported, “Skin rash” can be selected

- 3.5.3 If a term contains multiple body sites, and all link to the same PT, the relevant medical event should have priority.

Example: If “skin rash on face and neck” is reported, “Skin rash” can be selected

3.6 Location vs. Infectious agent

- 3.6.1 Some MedDRA terms have both the location and the specific organism/infection. If available, the term with both the specific location and the organism should be selected.

Example: If “pneumococcal pneumonia” is reported, “Pneumococcal pneumonia” can be selected

- 3.6.2 Not all infection terms in MedDRA describe location. If the suitable MedDRA term with the organism description is not available, the infective agent should generally have priority. It is also considered acceptable to select the infection site term alone or to select terms for both concepts.

Example: If “respiratory chlamydial infection” is reported, “Chlamydial infection” can be selected

Example: If “respiratory chlamydial infection” is reported, “Respiratory infection” can be selected

Example: If “respiratory chlamydial infection” is reported, “Chlamydial infection” and “Respiratory infection” can be selected

3.7 Pre-existing medical conditions

Pre-existing medical conditions that have not changed should generally be classified as medical and/or social history (See Section 3.18). Pre-existing medical conditions that have changed can be classified as ADR/AEs.

- 3.7.1 It is important to capture the concept that a pre-existing condition was modified, such as aggravated, exacerbated, worsened, intermittent, recurrent, progressive, or improved. If a pre-existing medical

condition is modified, the specific MedDRA term should be selected, provided that it exists.

Example: If “exacerbation of myasthenia gravis” is reported, “Myasthenia gravis aggravated” can be selected

3.7.2 In the absence of such a term, the following options are considered appropriate:

3.7.2.1 A term for the condition should be selected and the modification should be captured in a consistent, documented way. The non-specific modifier term alone should not be selected.

Example: If “halitosis worsened” is reported, “Halitosis” only can be selected

3.7.2.2 A term for the condition and an additional term to describe the modification of the condition should be selected, e.g., “Condition aggravated”, “Disease progression”

Example: If “progression of Alzheimer’s disease” is reported, “Alzheimer’s disease” and “Disease progression” can be selected.

Example: If “aggravation of jaundice” is reported, “Jaundice” and “Condition aggravated” can be selected

3.7.2.3 A new term can be requested from the MSSO. In general, the MSSO will add such terms if medical significance has been demonstrated (Introductory Guide, MedDRA Version 7.1).

3.8 Congenital terms

The definition of “congenital” for MedDRA is “any condition present at birth, whether genetically inherited or occurring in utero” (Introductory Guide, MedDRA Version 7.1).

3.8.1 Terms from the SOC *Congenital, familial and genetic disorders* should be used when the condition is described as congenital by the reporter or when medical judgment establishes that the condition was present in the child at the time of birth.

Example: If either “congenital heart disease” or “child born with heart disease” is reported, “Heart disease congenital” can be selected

3.8.2 If the condition is not specified as congenital and not stated to be present at birth, the non-specific term should be selected or in its absence, the acquired term should be selected

Example: If “night blindness” is reported, the term “Night blindness” can be selected which links to the PT “Acquired night blindness”

Example: If “cholangiectasis” is reported, the term “Cholangiectasis acquired” can be selected

Note that a non-specific term is not always linked to the acquired term at a higher level.

Example: “color blindness” is reported, the term “Color blindness” can be selected which links to the HLT “Ocular disorders congenital NEC” through the PT “Colour blindness”

3.9 Medical/Surgical Procedures

The use of the SOC *Surgical and medical procedures* is generally not appropriate for ADR/AEs. The terms in the SOC *Surgical and medical procedures* are not multi-axial in MedDRA. Users should be aware of the impact that use of these terms will have on data retrieval, data analysis, and reporting. When selecting terms for procedures, the following points might be helpful.

- 3.9.1 If the procedure represents the only information provided, a term should be selected for the procedure.

Example: If “patient had gallbladder surgery” is the only information reported, “Gallbladder operation” can be selected

Example: If “patient had tonsillectomy in childhood” is reported, “Tonsillectomy” can be selected

- 3.9.2 If a procedure is reported in combination with a diagnosis, it is considered sufficient to select a term for the diagnosis alone. It is also considered acceptable to select a term for the procedure in addition to a term for the diagnosis.

Example: If “liver transplantation due to liver failure” is reported, either “Liver failure” alone or both “Liver failure” and “Liver transplant” can be selected.

Example: If “surgery for bleeding gastric ulcer” is reported, either “Bleeding gastric ulcer” alone or both “Bleeding gastric ulcer” and “Gastric ulcer surgery” can be selected

3.10 Investigations

SOC *Investigations* includes test names alone and test names with qualifiers (e.g., increased, decreased, abnormal, normal). Corresponding medical conditions, such as “hyper” and “hypo” terms, are represented in other “disorder” SOC. By design, the terms in SOC *Investigations* are not

multi-axial. Therefore, for data retrieval, SOC *Investigations* should always be considered, in addition to the specific “disorder” SOC(s).

3.10.1 Investigation terms without qualifiers

Terms in SOC *Investigations* without qualifiers can be used to capture test names.

Example: If “bilirubin” test is performed, then “Bilirubin” can be selected

Example: If “cardiac output” is measured, then “Cardiac output” can be selected

3.10.2 The results of investigations might represent ADR/AEs. When selecting terms for results of investigations, the following points might be helpful.

3.10.2.1 Medical conditions vs. laboratory results.

Example: If “hypoglycemia” is reported, “Hypoglycemia” can be selected

(Note: “Hypoglycemia” links to SOC *Metabolism and nutrition disorders*)

Example: If “decreased glucose” is reported, “Glucose decreased” can be selected

(Note: “Glucose decreased” links to SOC *Investigations*)

3.10.2.2 Unambiguous laboratory results

Example: If a value is reported that is clearly below the reference range, e.g., glucose 40 mg/dL, “Glucose low” can be selected

3.10.2.3 Ambiguous laboratory results

Example: If “his glucose was 40” is reported without units, and additional clarification cannot be obtained, “Glucose abnormal” can be selected

3.10.3 It is not considered necessary to select terms for each diagnostic result that is consistent with the clinical diagnosis provided by the reporter. (See Section 2.5.3)

Example: If “elevated potassium, K 7.0 mmol/L and hyperkalemia” are reported, “Hyperkalemia” can be selected

- 3.10.4 It is considered necessary to select terms for each diagnostic result that is not consistent with the clinical diagnosis provided by the reporter.

Example: If “alopecia, rash, and elevated potassium 7.0 mmol/L” are reported as adverse events, then “Alopecia”, “Rash”, and “Potassium increased” can be selected

- 3.10.5 Non-specific investigation terms should only be used when more specific result terms are not available.

Example: If “abnormal liver function tests” is reported, “Abnormal liver function tests” can be selected

Example: If “increased alkaline phosphatase, increased SGPT, increased SGOT, and elevated LDH ” is reported, four individual terms should be selected. A single term such as “Liver function tests abnormal” should not be selected

3.11 Medication/administration errors and accidental exposures

- 3.11.1 If a medication error results in clinical consequences, term(s) for the clinical consequences should be selected. A term can also be selected for the medication error.

Example: If “hives due to medication error” is reported, “Hives” can be selected. “Medication error” can also be selected

- 3.11.2 Medication errors in the absence of clinical consequences are not ADR/AEs; however, it is important to capture the occurrence of a medication error. The closest term available should be selected, e.g., “Drug maladministration” or “Medication error”.

Example: If “medication was given intravenously instead of intramuscularly” is reported, “Wrong route of administration” can be selected

- 3.11.3 The same principle applies to accidental exposures.

Example: If “nurse splashed an injectable drug in her eye” is reported, “Inadvertent exposure to drug” can be selected

Example: If “child exposed to drug during breast feeding” is reported, “Drug exposure via breast milk” can be selected

- 3.11.4 It is considered acceptable to select the additional term “No adverse effect”, if specifically so reported. (See Section 3.14)

Example: If “medication was given intravenously instead of intramuscularly without sequelae” is reported, “Wrong route of administration” and “No adverse effect” can be selected

3.12 Overdose/Toxicity/Poisonings

- 3.12.1 Overdose, toxicity, and poisoning terms exist within MedDRA. Toxicity and poisoning terms are grouped under the HLT *Poisoning and toxicity* (for more information please refer to the Introductory Guide, MedDRA Version 7.1). If overdose, toxicity, or poisoning, is explicitly reported, the appropriate term should be selected.

Example: If “overdose of pills” is reported, “Overdose” can be selected

- 3.12.2 Terms for signs and/or symptoms reported in association with an overdose should be selected.

Example: If “stomach upset from study drug overdose” is reported, “Stomach upset” and “Overdose” can be selected

- 3.12.3 If an overdose is reported and it was specifically stated that there were no adverse effects, it is considered acceptable to select “Overdose” and the additional term “No adverse effect”. (See Section 3.14)

3.13 Drug interactions

This term includes drug/drug³, drug/food, drug/device, and drug/alcohol interactions. With respect to interactions, MedDRA does not include specific product names.

- 3.13.1 When the reporter specifically states that an interaction occurred, an appropriate interaction term should be selected in addition to term(s) for any medical event(s) described.

Example: If “torsade de pointes with suspected drug interaction” is reported, “Torsade de pointes” and “Drug interaction” can be selected

- 3.13.2 If two products are used together and the reporter does not specifically state there is an interaction but does report a medical event, only an event term should be selected.

Example: If “patient was started on an anti-seizure medication and a heart medication and developed syncope” is reported, “Syncope” can be selected

³ In this document, the term “drug” includes biological products

Example: If “patient was already on an anti-seizure medication and was started on a heart medication and anti-seizure medication levels increased” is reported, “Anticonvulsant drug level increased” can be selected

3.14 No adverse effect

Some organizations might wish to use this term to maintain records for administrative purposes, e.g., for pregnancy registries, overdoses, and medication errors.

The term “No adverse effect” could be used when it is specifically reported that no ADR/AE occurred, despite exposure to a product. (See Section 3.11.4 and 3.12.3)

Terms describing normal states and outcomes exist in MedDRA, such as “Normal baby”, “Normal electrocardiogram”, and “Sinus rhythm”, which can be used as needed.

3.15 Unexpected therapeutic effect

Some organizations might wish to use the term “Unexpected therapeutic effect” although such effects are not usually considered ADR/AEs. Reports occasionally describe a beneficial effect of a drug aside from the use for which it had been given.

Example: If “a bald patient was pleased that he grew hair while on an antihypertensive” is reported, the term “Unexpected therapeutic effect” can be selected. In addition, “Hair growth increased” can be selected

3.16 Modification of effect

Modifications of effect are not always considered ADR/AEs; however, it is important to capture this information, and in certain situations, lack of effect is a reportable event. MedDRA contains many terms that describe modifications of effect. The closest term(s) available to capture the reported medical concept(s) should be selected, unless this information is captured by other means.

- 3.16.1 It is considered appropriate to use lack of effect terms when the reporter specifically states that the drug was ineffective (or did not work, or similar wording)

Example: If “antibiotic didn’t work” is reported, “Lack of drug effect” can be selected

Example: If “patient took drug, her headache didn’t go away, drug is ineffective” is reported, “Drug ineffective” can be selected

- 3.16.2 It is considered appropriate to use lack of effect terms when the information reported clearly communicates that the expected effect was not obtained.

Example: If “an epileptic patient took an anti-convulsant, but the seizures continued unchanged” is reported, “Lack of drug effect” can be selected

3.16.3 It is not considered appropriate to infer lack of effect.

Example: If “AIDS patient taking anti-HIV drug died” is reported, “Lack of drug effect” should not be assumed. A term for death should be selected, as described in Section 3.2 of this document

3.16.4 Increased, Decreased, and Prolonged effects

It is considered appropriate to use this group of terms when the reporter specifically identifies a modification of effect.

Example: If “patient had increased effect from drug A” is reported, “Increased drug effect” can be selected

Example: If “patient had decreased effect from drug A” is reported, “Drug effect decreased” can be selected

Example: If “patient had prolonged effect from drug A” is reported, “Drug effect prolonged” can be selected

3.17 Social Circumstances

The terms in this SOC describe social factors and might be suitable for social and medical history data term selection. Use of the SOC *Social circumstances* is generally not considered appropriate for ADR/AEs. However, some terms currently contained within this SOC are the only option for capturing certain ADR/AEs.

Example: If “patient was abusing an analgesic” is reported, “Analgesic abuse” can be selected

The terms in SOC *Social circumstances* are not multi-axial in MedDRA. This SOC contains terms that are similar to terms in the disorder SOCs. Users should be aware of the impact that use of these terms will have on data retrieval, data analysis, and reporting. The following examples are illustrative:

SOC Social Circumstances	“Disorder” SOC
Alcoholic	Alcoholism
Drug addict	Drug addiction

3.18 Medical and/or social history

The examples below illustrate how MedDRA can be used to capture medical and/or social history.

Example: If “history of gastrointestinal bleed and hysterectomy” is reported, “Gastrointestinal bleed” and “Hysterectomy” can be selected

Example: If “patient is a cigarette smoker with coronary artery disease” is reported, “Cigarette smoker” and “Coronary artery disease” can be selected

3.19 Indication for product use

These principles can be applied to product indications collected either pre-market or post-market. Specific regulatory requirements are not addressed in this document.

Historically, indication data have not been collected in a complete or consistent way, nor has a controlled terminology been widely used for the entry of these data. Consideration should be given to the importance of accurate data collection, the use of auto-encoders and the impact on data retrieval.

Reported indications can include: medical conditions, prophylaxis of such conditions, diagnostic tests, replacement therapies, procedures such as anesthesia induction and terms such as “anti-hypertension”.

It might be unclear in the reporting of indication data whether a medical condition or a desired outcome is being reported.

Example: If the indication reported is “weight loss”, “Weight loss” can be selected, as it is unknown if the reporter is expressing that the drug was taken to induce weight loss (overweight patient) or to treat weight loss (underweight patient)

Example: If the indication reported is “immunosuppression”, “Immunosuppression” can be selected, as it is unknown if the reporter is expressing that the drug was taken to induce immunosuppression or to treat the condition of immunosuppression

3.19.1 Medical Conditions

3.19.1.1 Where the indication is a medical condition, a term that expresses the medical condition should be selected.

Example: If the reported indication is “hypertension”, “Hypertension” can be selected

Example: If the reported indication is “anti-hypertensive”, “Hypertension” can be selected

Example: If the reported indication is “chemotherapy for breast cancer”, “Breast cancer” can be selected

Example: If “medication for gastrointestinal problem” is reported as an indication, “Gastrointestinal disorder” can be selected

- 3.19.1.2 If the only information reported is a type of therapy, then the most specific term available should be selected.

Example: If a reporter states only that “a patient had received chemotherapy”, “Chemotherapy” can be selected

3.19.2 **Prevention and Prophylaxis**

- 3.19.2.1 When the concept of prevention or prophylaxis is expressed, the specific MedDRA term should be selected, provided that it exists. The terms prevention and prophylaxis can be used interchangeably.

Example: If “arrhythmia prophylaxis” is reported, “Arrhythmia prophylaxis” can be selected

Example: If “prevention of migraine” is reported, “Migraine prophylaxis” can be selected

- 3.19.2.2 In the absence of a specific prophylaxis term, the following options are considered appropriate.

- 3.19.2.2.1 A term for the condition can be selected.

Example: If “prevention of miscarriage” is reported, “Miscarriage” can be selected

- 3.19.2.2.2 Or the closest prophylaxis or prevention term can be selected.

Example: If “prevention of miscarriage” is reported, “Prevention” can be selected

- 3.19.2.2.3 Or the closest terms for both concepts can be selected.

Example: If “prevention of miscarriage” is reported, the terms “Prevention” and “Miscarriage” can be selected

3.19.3 **Diagnostic Testing**

If the product is being used to perform a diagnostic test, a term for the test should be selected.

Example: If “contrast agent for angiogram” is reported, “Angiogram” can be selected

Example: If “contrast agent for Coronary angiogram” is reported, “Coronary angiogram” can be selected

3.19.4 **Procedures**

If the product is being used to perform a procedure, a term for the procedure should be selected.

Example: If “induction of anesthesia” is reported, “Induction of anesthesia” can be selected

3.19.5 **Supplementation and Replacement Therapies**

Supplement and replacement therapies can be found in SOC *Surgical and medical procedures*. (See Section 3.9)

If the product indication specifies or describes supplementation or replacement, the closest term should be selected.

Example: If “testosterone replacement therapy” is reported, “Androgen replacement therapy” can be selected

Example: If “thyroid replacement therapy” is reported, “Thyroxine therapy” can be selected

Example: If “prenatal vitamin” is reported, “Vitamin supplementation” can be selected

3.19.6 **Indication not reported**

If the indication is not known and no clarification is available, then the term “Drug use for unknown indication” can be selected.

Example: If “aspirin was taken for an unknown indication” is reported, “Drug use for unknown indication” can be selected

4.0 Appendices:

4.1 Current members of the ICH *Points to Consider* working group:

Rapporteur:

Reinhard Fescharek

Japan:

Ministry of Health, Labour and Welfare:

Tatsuo Kishi

Kenichi Tamiya

Manabu Yamamoto

Japan Pharmaceutical Manufacturers Association

Takayoshi Ichikawa

Yo Tanaka

Japanese Maintenance Organization

Reiji Tezuka

Yasuo Sakurai

Akemi Ishikawa

European Union:

Commission of the European Communities

Dolores Montero

Carmen Kreft-Jais

European Federation of Pharmaceutical Industries Associations

Reinhard Fescharek

Christina Winter

Canada:

Health Canada

Bill Wilson

United States:

US Food and Drug Administration

John (Jake) Kelsey

Toni Piazza-Hepp

Pharmaceutical Research and Manufacturers of America

Susan M. Lorenski

JoAnn Medbery

MedDRA MSSO

Patricia Mozzicato

4.2 Past members/affiliations of the ICH *Points to Consider* working group:

Japan:

Ministry of Health, Labour and Welfare

Tamaki Fushimi

Kazuhiro Kemmotsu

Chie Kojima

Emiko Kondo

Kenji Kuramochi

Kaori Nomura

Takashi Yasukawa

Japan Pharmaceutical Manufacturers Association

Akemi Ishikawa

Satoru Mori

Yasuo Sakurai

Kunikazu Yokoi

Japanese Maintenance Organization

Yuki Tada

Canada:

Health Canada

Heather Morrison

European Union:

European Federation of Pharmaceutical Industries Associations

Barry Hammond – past ***Rapporteur***

United States:

US Food and Drug Administration

Miles Braun

Brad Leissa

Andrea Feight

Pharmaceutical Research and Manufacturers of America

David Goldsmith

Sidney Kahn

Margaret M. Westland – past ***Rapporteur***

MedDRA MSSO:

JoAnn Medbery