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Health informatics — Clinical particulars — Core principles for the harmonization of therapeutic indications terms and identifiers

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Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular, the different approval criteria needed for the different types of ISO ~~documents~~document should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

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For an explanation of the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT), see ~~www.iso.org/iso/foreword.html~~www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 215, *Health* ~~Informatics.~~*informatics*, in collaboration with the European Committee for Standardization (CEN) Technical Committee CEN/TC 251, *Health informatics*, in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

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Introduction

The need for improved communication between health agencies, hospitals, pharmacies, pharmaceutical companies and the general public about drug safety and efficacy information requires migration from manual text entry and unstructured data that cannot be coded, to a structured data model that is interoperable across the health care ecosystem ~~[1].~~ [1] The clinical particulars conceptual class of the ISO 11615 Identification of Medicinal Products (IDMP) ~~11615~~ data model captures information about a medicinal product's indication(s), contraindication(s), undesirable effect(s) and interactions. ~~-~~Within this conceptual class, the Therapeutic Indication subclass captures information about the therapeutic indication for the target disease or condition for which a medicinal product is ~~authorised~~authorized, under investigation, or utilized in clinical practice. Therapeutic indications can be described using free text as presented in approved product labelling documents, and as terms and codes from standard terminologies. ~~–~~Consistent and accurate coding of therapeutic indication terms is needed to support a variety of processes and is found in various terminological resources and official documents, which include epidemiological and real-world databases, electronic health records and health authority reporting processes. Therefore, a key principle for terminology mapping is that maps are based on specific use cases, and stakeholders who can provide feedback on the form, content and scope of the mapping should be engaged from the beginning of and throughout the mapping exercise.

A universally accepted terminology for coding therapeutic indications does not yet exist and is not feasible due to differing international medicinal product and healthcare regulations and reporting requirements. There is a difference between the therapeutic indication of a specific medicinal product and the diseases, conditions or problems listed in an electronic health record (EHR). While most EHRs will manage a problem list and/or a list of findings and diagnoses and a medication list, it is less frequent that the indication (or indications) for each specific medication is specified for a particular patient.

In medicinal product labels, a range of authorized indications is listed, often with qualifiers (diagnostic, preventive, curative, disease-modifying) or specified patient target groups. Sometimes, diseases or conditions are explicitly listed as not being indications for a specific drug. For example, "drug x" is not indicated in von Willebrand disease, or "drug y" is contraindicated with Haemophilia A. Use of medicinal products outside the authorized indications is considered ~~"off-label". Off-label is the~~ off-label ~~prescribing of a medicinal product for an unapproved/unauthorized indication when a health care provider determines that it is medically appropriate for their patient.~~

The indication wording, and thus the related coding, is based on a highly complex process over the years-long development of a pharmaceutical product. The relationship between a medicinal product and an indication is based on evidence from clinical trials, which are often comparative in nature (e.g. placebo versus active substance, or active substance A versus active substance B). Evidence synthesis in systematic reviews is often constrained by a Patient/intervention/comparator/outcome (PICO) statement, which results in a clinical recommendation to prefer or not to prefer the use of a particular medicinal product over another intervention for a particular patient (with a specific disease or condition), aiming at a specific outcome. In a regulatory document, this information is often reduced to a statement that "this medicinal product is indicated for ….".

In regulatory documents, the relationship is specified between a particular medicinal product (with specific substance(s), dose form(s), strength(s) and pack sizes), on the one hand and the indication(s), which are often specified in a detailed form. The formulation of this detailed indication often results from strong and intricate debate between the medical department of a pharmaceutical company, medical experts and regulators. ~~-~~The finesse of such formulation is often difficult to catch by any of the existing terminologies.~~-~~ For example, the therapeutic indications for a preparation that is licensed for over-the-counter (OTC) use can be more restrictive than the indications for the same preparation when prescribed by a clinician. For example, treatment of candidiasis in pregnancy using a clotrimazole must be under the direction of a physician; an OTC preparation is not ~~authorised~~authorized for this indication.

In handbooks of pharmacology and in drug classifications, indications might be formulated at a higher level of aggregation, and substances can be aggregated to drug classes. Hence, relationships between high level indications and drug classes (rather than individual substances) can be described.

Terminologies describing drug classes (e.g. the Anatomical Therapeutic Chemical (ATC) codes, SNOMED CT®[1], Standard Drug Groups from WHO Drug, etc.) are built using different principles and dimensions (chemical class, anatomical target, therapeutic intent, mechanism of action, molecular target site), and exhibit variable levels of granularity. The same is true for terminologies describing diseases, conditions and signs and symptoms as proxies for indications. Therefore, using different terminologies (and maps between these terminologies) to establish relationships between medicinal products/drug classes and specific indications/high level indications can be bewilderingly complex. Hence, ~~harmonisation~~harmonization of terminologies for therapeutic indications should account for both the specific level of regulatory listing of authorized indications for specific medicinal products, as well as the relationship between high level aggregations of indications and substances.

The most common standard terminological resources used to describe and code medicinal product indication terms are the Medical Dictionary for Regulatory Activities (MedDRA®[2]), SNOMED CT, the International Statistical Classification of Diseases and Related Health Problems (ICD™[3]) and Medical Subject Headings (MeSH). Mappings between these terminological resources are necessary for documentation and reporting purposes; however, the different hierarchy levels and variation in the number of terms for each resource introduce significant complexity in the creation and maintenance of terminology maps. Map usage is often restricted by the limited availability of centrally provided and approved map sets and contributes to inefficiencies and redundant manual curation by individual stakeholders for specific use cases. Creation and maintenance of comprehensive maps between clinical terminologies to support coding of indication terms will thus liberate workforce effort and enable more efficient processes, responses and comprehensive reporting.

There are safety and maintenance implications when creating and applying maps that directly impact clinical care and decision-making. Therefore, a key principle is the requirement to identify the use case for any map before creating or using mappings. For example, there is an allowable semantic shift during mapping such as for statistics and billing because of aggregation to a group level, whereas in use cases to support clinical care at the individual (patient) level, no semantic shift can be tolerated because of potential safety issues. Thus, mappings between e.g. SNOMED CT and MedDRA are semantic maps of total meaning focused on adverse events. However, additional maps between these two terminologies with use cases focused on therapeutic indications are possibly needed, so a use case will need to be developed and tested against existing maps before deciding on next steps.

This document describes use cases and principles that are applicable for creation, assessment and selection of maps specific to Therapeutic Indications. This document thus refers to and builds on the following ~~ISO~~ documents regarding terminologies and mapping:

- ISO/TR 14872 ~~Core~~on core principles for maintenance of identifiers and terms
  - ~~Propose a new annex to this document (specific to Clinical Particulars)~~

[1] SNOMED CT® is the registered trademark of a product supplied by the International Health Terminology Standards ~~Organisation~~Organization (IHTSDO). This information is given for the convenience of users of this document and does not constitute an endorsement by ISO of the product named. ~~Equivalent products may be used if they can be shown to lead to the same results.~~

[2] MedDRA is the registered trademark of a product supplied by the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) on behalf of the International Council for ~~Harmonisation~~Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH). This information is given for the convenience of users of this document and does not constitute an endorsement by ISO of the product named. ~~Equivalent products may be used if they can be shown to lead to the same results.~~

[3] ICD™ (International Classification of Diseases) maintained by the World Health Organization is an example of a suitable product available commercially. This information is given for the convenience of users of this document and does not constitute an endorsement by ISO of this product.

213 — ISO/TR 12300 ~~Principles~~on principles of mapping between terminological systems

214 — ISO/TS 21564 ~~Terminology~~on terminology resource map quality measures (MapQual)

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Health informatics — Clinical ~~Particulars —~~particulars — Core ~~Principles~~principles for the ~~Harmonisation~~harmonization of ~~Therapeutic Indications Terms~~therapeutic indications terms and ~~Identifiers~~ identifiers

1 Scope

The objective of this document is to establish common principles for the creation, assessment, selection and maintenance of maps between terminological resources used to describe and code IDMP therapeutic indications for investigational and medicinal products, medical devices, combination products, biologics and companion diagnostics. ~~-~~Core maintenance principles, such as reliability, reproducibility and quality assurance of the maps for future indication terminology use, are also discussed. The intended audience for this document includes:

~~a.~~a) Global regulators, pharmaceutical/biopharmaceutical companies, Clinical Research Organizations (CROs) and universities/scientific institutes involved in the development, authorization and marketing of medicinal products

~~b.~~b) Implementers of IDMP seeking more information about coding of Therapeutic Indications

~~c.~~c) Healthcare providers

~~d.~~d) Standards Organizations

~~e.~~e) Implementers and software vendors developing and implementing terminology map sets

~~f.~~f) Patients

2 Normative references

There are no normative references in this document.

3 Terms, definitions and abbreviated terms

3.1 ~~3.1~~ Terms and definitions

For the purposes of this document, the following terms and definitions apply.

ISO and IEC maintain ~~terminological~~terminology databases for use in standardization at the following addresses:

— ~~—~~ISO Online browsing platform: available at ~~https://www.iso.org/obp~~https://www.iso.org/obp

— ~~—~~IEC Electropedia: available at ~~http://www.electropedia.org/~~https://www.electropedia.org/

~~3.1.1~~
~~**clinical trial authorisation**~~
~~approval given by a Medicines Regulatory Agency to conduct a clinical trial in a region~~

~~[SOURCE: ISO 11615:2017, 3.1.12]~~

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3.1.1
~~3.1.2~~
comorbidity

concurrent condition or co-infection described as part of the indication

~~3.1.3~~
3.1.2
electronic health record

EHR

repository of information regarding the health status of a subject of care, in computer processable form

[SOURCE: ISO/TR 20514:2005, 2.11, modified]

3.1.3
~~3.1.4~~
electronic health record system

EHR system

system for recording, retrieving and manipulating information in electronic health record

~~[SOURCE: ISO 18308:2011, 3.20]~~

~~3.1.5~~
3.1.4
individual map

map

cross map

index from one term to another, sometimes using rules that allow translation from one representation to another indicating degree of equivalence

Note 1 to entry: Entry in a map which indicates how to translate from an individual source concept to a target concept. The term map is often used to indicate a table of individual map entries. It is for this reason that the individual and map tables are being differentiated.

Note 2 to entry: The use of this term is often used in ways which are confusing. It is essential to always make it clear whether you are referring to an individual map or a map table (or set).

Note 3 to entry: In SNOMED CT, each individual map is represented as a row or group of rows in a map Reference Set. It links a single map source concept code (e.g. SNOMED CT Concept ID) to one or more codes in a map target (e.g. ICD Code).

Note 4 to entry: A map is often computable and is the outcome of the mapping process.

[SOURCE: ISO/TR 12300:2014, 2.1.9]

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