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Health informatics — Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated information on substances

Informatique de santé — Identification des produits médicaux — Eléments de données et structures pour l'identification unique et l'échange d'informations réglementées sur les substances

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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 should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2. www.iso.org/directives

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received. www.iso.org/patents

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation on 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 WTO principles in the Technical Barriers to Trade (TBT) see the following URL: Foreword - Supplementary information.

This document was prepared by ISO/TC 215, *Health informatics*.

This second edition cancels and replaces the first edition ISO 11238:2012[2], which has been technically revised.

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Introduction

This document was developed in response to a worldwide demand for internationally harmonized specifications for medicinal products. It is one of a group of five standards and four technical specifications which together provide the basis for the unique identification of medicinal products. The group of standards and technical specifications comprises:

ISO 11615[3], *Health informatics — Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated medicinal product information*

ISO 11616[4], *Health informatics — Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated pharmaceutical product information*

ISO 11238, *Health informatics — Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated information on substances*

ISO 11239[5], *Health informatics — Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated information on pharmaceutical dose forms, units of presentation, routes of administration and packaging*

ISO 11240[6], *Health informatics — Identification of medicinal products — Data elements and structures for the unique identification and exchange of units of measurement*

ISO/TS 19844, *Health informatics — Identification of medicinal products — Implementation guidelines for data elements and structures for the unique identification and exchange of regulated information on substances*

ISO/TS 20440[7], *Health informatics — Identification of Medicinal Products — Implementation guide for ISO 11239 data elements and structures for the unique identification and exchange of regulated information on pharmaceutical dose forms, units of presentation, routes of administration and packaging*

ISO/TS 20443[8], *Health informatics — Identification of Medicinal Products — Implementation guide for ISO 11615 data elements and structures for the unique identification and exchange of regulated Medicinal Product information*

ISO/TS 20451[9], *Health informatics — Identification of Medicinal Products — Implementation guide for ISO 11616 data elements and structures for the unique identification and exchange of regulated pharmaceutical product information*

These standards for the identification of medicinal products (IDMP) support the activities of medicines regulatory agencies worldwide by jurisdiction. These include a variety of regulatory activities related to development, registration and life cycle management of medicinal products, as well as pharmacovigilance and risk management.

To meet the primary objectives of the regulation of medicines and pharmacovigilance, it is necessary to reliably exchange medicinal product information in a robust and reliable manner. The IDMP standards therefore support the following interactions:

— between one medicine regulatory agency and another, e.g. European Medicines Agency to the US Food and Drug Administration (FDA), or vice versa; and between the European Medicines Agency and the National Competent Authorities in the EU, vice versa;

— between pharmaceutical companies and medicine regulatory agencies, e.g. "Pharma Company A" to Health Canada;

— between the sponsor of a clinical trial to a medicine regulatory agency, e.g. "University X" to the Austrian Agency for Health and Food Safety (AGES);

— between a medicine regulatory agency and other stakeholders, e.g. UK Medicines and Health Care Products Regulatory Agency (MHRA) to the National Health Service (NHS);

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— between medicine regulatory agencies and worldwide-maintained data sources, e.g. the Pharmaceutical and Medical Device Agency (PMDA) and the organization responsible for assigning substance identifiers.

Unique identifiers produced in conformance with the IDMP standards will support applications for which it is necessary to reliably identify and trace the use of medicinal products and the ingredients within medicinal products.

This document provides a structure that enables the assignment and maintenance of unique identifiers for all substances in medicinal products. This document sets out the general rules for defining and distinguishing substances, and provides a high-level model for substances and specified substances to support the organization and capturing of data.

It is anticipated that implementation will use the ISO/TS 19844 and HL7 messaging (see 5.8) to deliver a strong, non-semantic unique identifier for every substance present in a medicinal product. It is anticipated that a single maintenance organization will be responsible for the generation of global identifiers for every substance and that such an organization would retain the defining elements upon which the substance identifier was based. At the specified substance level, a more regional approach may be necessary because of the proprietary nature of much of the information.

The use of the identifier is essential for the description of substances in medicinal products on a global scale. This document does not involve developing nomenclature for substances or specified substances, but common and official substance names in current use can be mapped to each identifier.

Ingredients used in medicinal products range from simple chemicals to gene-modified cells to animal tissues. To unambiguously define these substances is particularly challenging. This document defines substances based on their scientific identity (i.e. what they are) rather than on their use or method of production. Molecular structure or other immutable properties, such as taxonomic, anatomical and/or fractionation information, are used to define substances. This document contains five single substance types and a mixture substance class that are sufficient to define all substances. Although it is certainly possible to define or classify substances in other ways, this document uses a minimalistic structured scientific concept approach focusing on the critical elements necessary to distinguish two substances from one another. There are frequently interactions between substances when they are mixed together, but this document has intentionally not included these supramolecular interactions at the substance level because of the variable nature and strength of such interactions. This document also allows for the capture of multiple terms which refer to a given substance and a variety of reference information that could be used to classify substances or relate one substance to another.

In addition to the substance level, this document also provides elements for the capture of further information on substances that make up the defining characteristics of specified substances, such as grade, manufacturer, manufacturing information and specifications, and also to capture information on substances that are frequently combined together in commerce but are not strictly a medicinal product. At the specified substance level, four groups of elements provide information essential to the tracking and description of substances in medicinal products.

The basic concepts in the regulatory and pharmaceutical standards development domain use a wide variety of terms in various contexts. The information models presented in this document depict elements and the relationship between elements that are necessary to define substances. The terms and definitions described in this document are to be applied for the concepts that are required to uniquely identify, characterize and exchange information on substances in regulated medicinal products.

The terms and definitions adopted in this document are intended to facilitate the interpretation and application of legal and regulatory requirements, but they are without prejudice to any legally binding document. In case of doubt or potential conflict, the terms and definitions contained in legally binding documents prevail.

In this document, "% (V/V)" is used in place of "% volume fraction".

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Health informatics — Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated information on substances

CAUTION — This document uses colour. This should be taken into consideration when printing.

1 Scope

This document provides an information model to define and identify substances within medicinal products or substances used for medicinal purposes, including dietary supplements, foods and cosmetics. The information model can be used in the human and veterinary domain since the principles are transferrable. Other standards and external terminological resources are referenced that are applicable to this document.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO/TS 19844:2018, *Health informatics — Identification of medicinal products (IDMP) — Implementation guidelines for ISO 11238 for data elements and structures for the unique identification and exchange of regulated information on substances*

3 Terms and definitions

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

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

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

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

3.1
adjuvant
component that potentiates the immune response to an antigen and/or modulates it towards the desired immune response

3.2
active marker
constituent or groups of constituents of a (herbal) Substance (fresh), Herbal Drug, Herbal preparation or herbal medicinal product which are of interest for control purposes and are generally accepted to contribute to therapeutic activity

Note 1 to entry: Active markers are not equivalent to analytical or signature markers that serve solely for identification or control purposes.

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3.3
allergen
material of concern used as ingredient or in a device capable of stimulating a type-I hypersensitivity or allergic reaction in atopic individuals

Note 1 to entry: In this document the definition is specified to a molecule (substance) capable of inducing an immunoglobulin E (IgE) response and/or a Type I allergenic reaction.

3.4
allergoids
allergen extracts chemically modified (e.g. by formaldehyde or glutaraldehyde) in order to reduce allergenicity while maintaining immunogenicity

Note 1 to entry: Formaldehyde and glutaraldehyde react with primary amino groups in the polypeptide chain of the allergen leading to intramolecular and intermolecular cross-linked high-molecular-weight allergen polymers; in this way conformational IgE epitopes should be destroyed while the linear T-cell epitopes remain unaffected.

3.5
analytical data
set of elements to describe and capture methods and reference material used to determine purity, potency or identity in a specified substance

3.6
analytical marker
constituent or groups of constituents that serve for analytical purposes

Note 1 to entry: Active markers are not equivalent to analytical or signature markers that serve solely for identification or control purposes.

3.7
ATC Code
Anatomical Therapeutic Chemical Classification code
substance classification code
code used for the classification of drugs

Note 1 to entry: It is controlled by the WHO Collaborating Centre for Drug Statistics Methodology (WHOCC)[1)].

Note 2 to entry: This pharmaceutical coding system divides drugs into different groups according to the organ or system on which they act and/or their therapeutic, pharmacological and chemical properties. Each bottom-level ATC code stands for a pharmaceutically used substance or a combination of substances in a single indication (or use). This means that one drug can have more than one code: Acetylsalicylic acid, for example, has A01AD05 as a drug for local oral treatment, B01AC06 as a platelet inhibitor, and N02BA01 as an analgesic and antipyretic. On the other hand, several different brands share the same code if they have the same active substance and indications.

3.8
CAS Index name
Chemical Abstracts Service Index name
CAS Registry name
identifier that usually identifies a single substance

Note 1 to entry: For further explanations see subclause A.1.2.

3.9
CAS Registry Number
CAS number[2)]
unique numerical identifier of a substance in the CAS Registry system

Note 1 to entry: For further explanations see subclause A.1.2.

1) https://www.whocc.no/atc/structure_and_principles/

2) https://www.cas.org/content/chemical-substances/faqs

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3.10
chemical bond
condition that occurs when forces acting between two atoms or groups of atoms lead to the formation of a stable discrete molecular entity

3.11
chemical substance
type of substance that can be described as a stoichiometric or non-stoichiometric single molecular entity and is not a protein, nucleic acid or polymer substance

Note 1 to entry: Chemical substances are generally considered "small" molecules which have associated salts, solvates or ions and may be described using a single definitive or representative structure.

3.12
chiral substance
substance whose molecular structure is not superimposable on its mirror image

3.13
co-crystals
homogenous (single phase) crystalline structures made up of two or more components in a definite stoichiometric ratio where the arrangement in the crystal lattice is not based on ionic bonds

3.14
component
substance which is part of a mixture and that defines a multi-substance material at the Specified Substance Group 1 level

EXAMPLE Dimethicone and silicon dioxide are components of simethicone. Human insulin and protamine are the components in human insulin isophane.

Note 1 to entry: Components are used to describe a multi-substance material.

3.15
composition stoichiometry
quantitative relationships between the chemical elements or moieties that make up a substance

EXAMPLE Disodium hydrogen phosphate heptahydrate and disodium hydrogen phosphate dihydrate are defined as different substances because they differ in composition stoichiometry.

3.16
configuration
method for indicating the three-dimensional arrangement of atoms at a stereogenic carbon, phosphorous, sulfur centre or stereocenter

3.17
constituent
substance present within a Specified Substance or a parent substance

Note 1 to entry: Constituents can be impurities, degradants, extraction solvents, vehicles, active markers or signature substances, parent substances or single substances mixed together to form a multi-substance material.

Note 2 to entry: Constituents shall have an associated role and amount at the Specified Substance Group 1 information model. Constituent specifications shall be used to describe components as well as limits on impurities or related substances for a given material.

EXAMPLE The substance, triamcinolone acetonide is the parent (constituent) substance of the Specified Substance Group 1 substance, triamcinolone acetonide, micronized.

Note 3 to entry: Constituent component is part of a mixture belonging to a homologous group of individual components, described as parent substances for the manufacture of an allergenic extract.

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3.18
controlled vocabulary
finite set of values that represent the only allowed values for a data item

Note 1 to entry: The allowed values can be codes, text or numeric.

[SOURCE: CDISC Clinical Research Glossary V10.0, 2016, modified][16]

3.19
copolymer
polymer with more than one type of structural repeat unit linked through covalent bonds

Note 1 to entry: Copolymers are obtained by copolymerization or sequential polymerization of two or more different monomers. Copolymers can be random, statistical, alternating, periodic, block, cross, graft or mixed.

3.20
critical process parameter
process parameter whose variability has an impact on a critical quality attribute and therefore should be monitored or controlled to ensure the process produces the desired quality

Note 1 to entry: A manufacturing parameter is considered "critical" and necessary for production of Substance or Specified Substance e.g. inclusion of chromatographic step for removal or reduction of impurities, viruses.

Note 2 to entry: The critical process is tied to the Production Method type.

3.21
cytokine
small protein released by cells that has a specific effect on the interactions between cells, on communications between cells or on the behaviour of cells

3.22
degree of polymerization
average number of monomers or repeat units in a polymeric block or chain

Note 1 to entry: Applies to both homopolymers and block copolymers where it refers to the degree of polymerization within a block.

3.23
diverse origin
substances that are not isolated together or the result of the same process

3.24
drug extract ratio
ratio of the quantity of the (herbal) substance (fresh), or herbal drug to the quantity of the resulting herbal preparation

3.25
enhancer
cis-acting sequence of DNA that increases the utilization of some eukaryotic promoters and which can function in either orientation and in any location (upstream or downstream) relative to the promoter

3.26
extract ratio for allergens
extraction ratio indicating the relative proportions (m/V) of allergenic source materials and solvents

Note 1 to entry: This ratio is a minimal requirement for allergens for which there are not enough patients to determine the total allergenic activity *in vivo* or *in vitro*.

3.27
extraction solvents
solvents which are used for the extraction process

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3.28
fraction
distinct portion of material derived from a complex matrix, the composition of which differs from antecedent material

Note 1 to entry: This concept is used to describe source material and is recursive in that a subsequent fraction can be derived from an antecedent fraction.

EXAMPLE Serum immunoglobulins to polyclonal IgG is an example of recursive fractionation.

3.29
gene
basic unit of hereditary information composed of chains of nucleotide base pairs in specific sequences that encodes a protein or protein subunit

3.30
gene element
individual element within a gene such as a promoter, enhancer, silencer or coding sequence

3.31
glycosylation
enzymatic process that links saccharides or oligosaccharides to substances

3.32
glycosylation type
significant differences in glycosylation between different types of organisms

Note 1 to entry: This distinguishes the pattern of glycosylation across organism types, e.g. human, mammalian and avian. The glycosylation type is a defining element when a glycosylated protein exists as a substance.

3.33
grade
set of specifications indicating the quality of a substance or specified substance

3.34
harvesting
process of collecting a (herbal) substance (fresh) or parts of botanical material from the field or process of collecting viral or bacterial material from its production/manufacturing site

3.35
homeopathic stocks
substances, products of preparations used as starting materials for the production of homeopathic preparations.

Note 1 to entry: A stock is usually one of the following: a mother tincture or a glycerol macerate, for raw materials of botanical, zoological or human origin, or the substance itself, for raw materials of chemical or mineral origin.

3.36
homopolymer
polymer containing a single structural repeat unit

3.37
isotope
variants of a chemical element that differ by atomic mass, having the same number of protons and differing in the number of neutrons in the nucleus

Note 1 to entry: Radionuclides or nuclides with a non-natural isotopic ratio are shown in the structural representation with the nuclide number displayed. Natural abundance isotopes are represented by an elemental symbol without a nuclide number.

EXAMPLE ^{13}C refers to a carbon atom that has an atomic mass of 13.

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3.38
manufactured item
qualitative and quantitative composition of a product as contained in the packaging of the Medicinal Product

Note 1 to entry: A Medicinal Product may contain one or more manufactured items. In many instances the manufactured item is equal to the pharmaceutical product. However, there are instances where the manufactured item(s) undergo a transformation before being administered to the patient (as the pharmaceutical product) and the two are not equal.

3.39
manufacturer
organization that holds the authorization for the manufacturing process

Note 1 to entry: In this document the definition refers to a company responsible for the manufacturing of the substance

3.40
manufacturing
process of production for a substance or medicinal product from the acquisition of all materials through all processing stages

Note 1 to entry: The critical process, critical process steps, starting and processing materials and critical production parameters are included.

3.41
material
entity that has mass, occupies space and consists of one or more substances

3.42
medicinal product
pharmaceutical product or combination of pharmaceutical products that can be administered to human beings (or animals) for treating or preventing disease, with the aim/purpose of making a medical diagnosis or to restore, correct or modify physiological functions

Note 1 to entry: A Medicinal Product may contain in the packaging one or more manufactured items and one or more pharmaceutical products. In certain regions, a Medicinal Product may also be defined as any substance or combination of substances which may be used to make a medical diagnosis.

3.43
microheterogeneity
substances isolated together that contain minor differences in structure between essentially identical substances that are isolated/source material (e.g. sequence heterogeneity) and/or post-translational modification such as glycosylation

Note 1 to entry: Microheterogeneity is not a defining characteristic of substances but can be a defining one at the specified substance group 1 information level, e.g. differences in glycans.

Note 2 to entry: Microheterogeneity consists of variability in the type of glycosylation (biantennary, triantennary), extent of glycosylation at a given site (site occupancy), sequence heterogeneity due to polymorphism in source material, translation errors or variable proteolytic processing or other.

3.44
mixture
type of polydisperse substance that is a combination of single substances isolated together or produced in the same synthetic process

Note 1 to entry: Single substances of diverse origin that are brought together and do not undergo a chemical transformation as a result of that combination are defined as multi-substance materials (Specified Substance Group 1) and not as mixture.

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EXAMPLE 1 Gentamicin is defined as a mixture substance of Gentamicin C1, Gentamicin C1A, Gentamicin C2, Gentamicin C2A and Gentamicin C2B. Glyceryl monoesters are defined as mixture substances of two single substances which differ in the position of esterification. Simethicone, which consists of dimethicone and silicon dioxide, is not defined as a mixture substance since these are diverse materials brought together to form a multi-substance material.

EXAMPLE 2 Glyceryl monoesters could be defined as a mixture of two single substances which differ in the position of esterification.

Note 2 to entry: Mixture could be used for a homologous group of structurally diverse single substances used as starting materials in order to prepare an allergen extract. The extract is further described by using the class 'Source Material', element group 'Fraction Description' (allergen preparation) obtained from the structurally diverse single substances (starting materials) as parent substances. This substance (allergen extract) is the result of the same (synthetic) process and hence the extract is considered as a mixture substance.

3.45
moiety
entity within a substance that has a complete and continuous molecular structure

EXAMPLE The strength of a medicinal product is often based on what is referred to as the active moiety of the molecule, responsible for the physiological or pharmacological action of the drug substance. To avoid ambiguity, the free acid and/or free base should be used as the moiety upon which strength is based.

Note 1 to entry: The active moiety of a stoichiometric or non-stoichiometrical substance molecule is considered that part of the molecule that is the base, free acid or ion molecular part of a salt, solvate, chelate, clathrate, molecular complex or ester.

3.46
molecular formula
chemical formula that shows the total number and kind of atoms in a molecule indicating atomic proportional ratios (the numerical proportions of atoms of one type to those of other types) which is a way of expressing information about the proportions of atoms that constitute a particular chemical compound, using a single line of chemical element symbols, numbers, and sometimes other symbols

Note 1 to entry: The molecular formula could contain other symbols, such as parentheses, dashes, brackets, and plus (+) and minus (–) signs. These are limited to a single typographic line of symbols, which may include subscripts and superscripts. A chemical formula contains no words (e.g. Glucose is represented as $C_6H_{12}O_6$).

Note 2 to entry: Molecular formulas are written in accordance with the Hill system/ Hill notation such that the number of carbon atoms in a molecule is indicated first, the number of hydrogen atoms next, and then the number of all other chemical elements subsequently, in alphabetic order. When the formula contains no carbon, all the elements, including hydrogen, are listed alphabetically.

Note 3 to entry: Inorganic acids and metal salts are shown without charges or bonds: $HClO_4$ and $KMnO_4$ respectively. If metal salts of inorganic acids include several metals, the symbols for the metals are shown in alphabetic order, e.g. K_2NaPO_4.

3.47
molecular formula by moiety
way of describing of the molecular formula of a stoichiometric or non-stoichiometric substance existing of two or more moieties, the molecular formula of each moiety shall be described separated by a dot

Note 1 to entry: The molecular formula of the chemical salt Amlodipine besilate is described as $C_{20}H_{25}ClN_2O_5 . C_6H_6O_3S$.

Note 2 to entry: In non-cyclic linear structures like sodium nitroprusside: $Na_2[Fe(CN)_5(NO)].2H_2O$, a non-cyclic structure is constructed in the following order:

a) symbol of the central atom placed on the left;

b) ionic ligands with cations first then anions;

c) neutral ligands.

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3.48
molecular fragment
portion of a molecule that has one or more sites of attachment to other fragments or moieties

Note 1 to entry: Molecular fragments are used in the description of polymers to represent substituents and in structural modifications to a substance.

3.49
molecular structure
unambiguous representation of the arrangement of atoms

Note 1 to entry: For the purposes of defining substances, the three-dimensional conformations are not captured. Individual conformations or conformers of substances would only be captured in either a general sense for proteins (i.e. denatured) or when a given rotation about a single bond is restricted in such a way that the two different conformers are isolatable from each other and do not interconvert at room temperature (e.g. substituted biphenyls).

Note 2 to entry: This representation should be generally translatable into a graphical representation.

3.50
molecular weight
mass of one molecule of a homogenous substance or the average mass of molecules that comprise a heterogeneous substance, which is derived from the molecular structure or the molecular formula

Note 1 to entry: It is calculated as the sum of the mass of each constituent atom multiplied by the number of atoms of that element in the molecular formula. The unified atomic mass unit is the unit of molecular weight and includes the type of molecular weight (g/mol).

Note 2 to entry: For stoichiometric chemicals, the molecular weight is calculated from the molecular formula using standard masses for each of the elements. The molecular mass refers to the complete structure or a moiety or a fragment.

Note 3 to entry: The unified atomic mass unit or Dalton is the unit of molecular weight. The type of molecular weight should always be captured.

Note 4 to entry: For polymers, there are several different types of molecular weight (weight average, number average, etc.).

Note 5 to entry: For a substance not described in a Pharmacopoeia a mass spectrum may be provided to substantiate the calculated molecular weight.

3.51
monodisperse substance
single substance that is homogeneous in molecular weight, that is, it does not have a distribution of different molecular weight chains within the total mass

3.52
multi-substance material
single substances or specified substances of diverse origin that are brought together and do not undergo a chemical transformation

EXAMPLE Materials such as human insulin isophane, simethicone, aluminium lakes, nicotine polacrilex, and phosphate buffered saline are all multi-substance ingredients.

Note 1 to entry: Each substance part of the multi-substance material is a parent substance of the multi-substance material and should be registered first. The multi-substance material is captured at the Specified Substance Group 1 information level.

3.53
multi-substance starting material
mixture of multi-substances of which another substance will be prepared

EXAMPLE Aqueous extract of a mixture of homologous group of allergenic source material.

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3.54
nucleic acid substance
type of substance that can be defined by a linear sequence of nucleosides typically linked through phosphate or phosphate-like diester bonds

Note 1 to entry: The type of nucleic acid substance, e.g. ribonucleic acid (RNA) and deoxyribonucleic acid (DNA), is also identified. Oligonucleotides and gene elements, e.g. promoters, enhancers, coding sequences and silencers, are defined as nucleic acid substances.

3.55
official name
name given by an official registration authority/organization

3.56
organism
individual living entity anatomical origin that can react to stimuli reproduce, grow, and maintain homeostasis

3.57
part
entity of anatomical origin and location of source material within an organism

Note 1 to entry: Entity is a thing with distinct and independent existence.

3.58
pharmaceutical product
qualitative and quantitative composition of a Medicinal Product in the dose form approved for administration in line with the regulated product information

Note 1 to entry: In many instances, the pharmaceutical product is equal to the manufactured item. However, there are instances where the manufactured item shall undergo a transformation before being administered to the patient (as the pharmaceutical product) and the two are not equal.

3.59
physical form
physical state, either gas, liquid or solid, and the type of organization for solid matter

Note 1 to entry: Solids can be either crystalline or amorphous and can show polymorphism. Amorphous material is characterized by the absence of distinct reflections in the X-ray powder diffraction (XRPD) pattern. Polymorphism which is ability of crystalline materials to exist in more than one form, can also be captured.

3.60
polydisperse substance
single substance containing multiple related entities

Note 1 to entry: Polydisperse substances include polymers, mixture and structurally diverse material isolated from a single source. Chemical substances, proteins and nucleic acids with defined sequences are not described as polydisperse substances.

3.61
polydispersity
measure of the range of molecular masses in a polymer substance

Note 1 to entry: The dispersity of polymers is typically calculated by the ratio of weight average molecular weight to number average molecular weight

3.62
polymer connectivity
copolymer sequence type (Polymer connectivity) can either be random, statistical, alternating, periodic, block, graft or mixed

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3.63
polymer substance
type of polydisperse substance that contains structural repeat units linked by covalent bonds

Note 1 to entry: Monodisperse proteins and nucleic acids with defined sequences shall not be defined using the polymer substance elements.

3.64
post-translational modification
modification of a protein that typically occurs *in vivo* during or after translation

Note 1 to entry: Post-translational modification is described within the structural representation and not as a modification of a protein.

3.65
potentization
process by which dilutions and triturations are obtained from homeopathic stocks in accordance with a homeopathic manufacturing procedure: this means successive dilutions and successions, or successive appropriate triturations, or a combination of the two processes

Note 1 to entry: The number of potentization steps defines the degree of dilution; for example, “D3”, “3DH” or “3X” means three decimal potentization steps (diluted 1:1 000), and “C3” or “3CH” means three centesimal potentization steps (diluted 1:1 000 000).

3.66
processing material
type of material essential to the manufacturing process that is not incorporated into the resultant material but can be present in the resultant material as constituent

3.67
protein sequence
order and identity of amino acids within a protein or peptide

Note 1 to entry: Protein sequences will be represented by single letter Dayhoff codes and listed from the N-terminal to the C-terminal.

3.68
protein substance
type of substance with a defined sequence of alpha-amino acids connected through peptide bonds

Note 1 to entry: A protein consists of one or more chains with a length of more than 40 amino acids. A peptide is defined as a linear sequence consisting of 2 to 40 amino acid residues.

Note 2 to entry: Synthetic peptides and proteins with defined sequences, recombinant proteins and highly purified proteins extracted from biological matrices are described as protein substances. Sites of glycosylation, disulphide linkages and glycosylation type (e.g. fungal, plant, anthropoid, avian mammalian, human) are defining elements of protein substances, when known. A graphical molecular structure is also included in the definition of all peptides of 40 amino acid residues or less.

Note 3 to entry: The absolute configuration at the a-carbon atom of the a-amino acids is designated by the prefixed small capital letter D or L to indicate a formal relationship to D- or L-serine and thus to D- or L-glyceraldehyde. The prefix ξ (Greek xi) indicates unknown configuration[17].

3.69
protein sub-unit
linear sequence of amino acid residues connected through peptide bonds

Note 1 to entry: Protein sub-units usually adopt specific structural motives (e.g. β-sheets, α-helical structures) and have specific functions/roles within the protein (e.g. catalytic centre, substrate binding). Sub-units are linked to each other to make up the fully functional protein.

Note 2 to entry: Repeated sub-units in proteins are captured.

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EXAMPLE Monoclonal antibodies typically consist of four sub-units.

3.70
resultant material
material that is the result of a manufacturing process

Note 1 to entry: Resultant material may be the starting material of the next process step or the final material or actual specified substance.

3.71
salt
ionic substances formed from the neutralization reaction of an acid and a base

Note 1 to entry: Salts are ionic compounds composed of cations (positive ions) and anions (negative ions).

3.72
signature substance
substance used to be able to follow the quality of the production or extraction process

Note 1 to entry: Signature substance is not necessarily the intended active substance or resultant material. It is a substance used for analytical purpose which is representative for the quality of the manufacturing or extraction process.

3.73
silencer
DNA sequence that suppresses transcription

3.74
single substance
substance that can be described by a single representation or set of descriptive elements

Note 1 to entry: A single substance can be described using one or more of five types of elements: chemical, protein, nucleic acid, polymer or structurally diverse substances.

Note 2 to entry: Racemates and substances with unknown, epimeric or mixed chirality can be defined as single substances because a single structural representation may be generated and the stereochemistry indicated as descriptive text.

3.75
solvate
substance formed through association of a solvent molecule (e.g. water, alcohol) with another moiety

Note 1 to entry: Solvates can be either stoichiometric or non-stoichiometric and are predominately present in the solid form of substances.

Note 2 to entry: Solvates formed with water as solvent are referred to as hydrates.

3.76
source material
material from which a substance is derived, which is defined based on taxonomic and anatomical origins

Note 1 to entry: Source material is used to define structurally diverse, chemical, mixture, polymer and protein substances isolated from biological matrices.

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3.77
specification
list of tests, references to analytical procedures, and appropriate acceptance criteria, which are numerical limits, ranges, or other criteria for the tests described. It establishes the set of criteria to which a drug substance should conform to be considered acceptable for its intended use

Note 1 to entry: "Conformance to specifications" means that the drug substance, when tested according to the listed analytical procedures, will meet the listed acceptance criteria. Specifications are critical quality standards that are proposed and justified by the manufacturer and approved by regulatory authorities as conditions of approval.

3.78
specified substance
substance defined by groups of elements that describes multi-substance materials or specifies further information on substances relevant to the description of Medicinal Products

Note 1 to entry: This could include grade, units of measure, physical form, constituents, manufacturer, critical manufacturing processes (e.g. extraction, synthetic or recombinant processes), specification and the analytical methods used to determine whether a substance is in compliance with a specification. There are four different groups of elements that can be used to define a given specified substance and specific relationships between each group of elements.

3.79
starting material
material from which the manufacturing process of the substance starts. This material is a building block which will be (partly) incorporated in the structure of the resultant product

3.80
stereochemistry
relative spatial arrangement of atoms within molecules

3.81
stoichiometric substance
substance that contains moieties in simple integral ratios

Note 1 to entry: Defined composition stoichiometry shall be represented in the structural representation of a given substance. Moieties shall be represented using the lowest common factors such that a fractional representation is avoided. Substances will either be defined as stoichiometric or non-stoichiometric.

Note 2 to entry: Chemicals have defined composition stoichiometry when the ratio of all moieties (ion, counter ion and solvate) can be represented as simple integral ratios.

3.82
structural repeat unit
fundamental descriptor of a polymer typically derived from a monomer that is used to synthesize the polymer

3.83
structurally diverse substance
type of polydisperse substance isolated from a single source that is a complex combination which cannot be described as a mixture of a limited number of single substances

Note 1 to entry: Structurally diverse substances are defined based on immutable properties of a given material. Modifications that irreversibly alter the structure of the material, distinctive physical properties or components subsumed into the material, e.g. a gene in gene therapy substances, are defining elements for structurally diverse substances. Fractions derived from source material (oils/juices and extracts) are also captured in the definition. Protein mixtures containing a large number of diverse sequences such as polyclonal immunoglobulins are defined as structurally diverse substances.

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3.84
substance
matter of defined composition that has discrete existence, whose origin may be biological, mineral or chemical

Note 1 to entry: A substance can be a moiety. A moiety is an entity within a substance that has a complete and continuous molecular structure. The strength of a pharmaceutical product is often based on what is referred to as the active moiety of the molecule, responsible for the physiological or pharmacological action of the drug substance. Chemically, the active moiety of a stoichiometric or non-stoichoimetrical substance molecule is considered that part of the molecule that is the base, free acid or ion molecular part of a salt, solvate, chelate, clathrate, molecular complex or ester.

Note 2 to entry: In this document substances are further described as single substances, mixture substances or one of a group of specified substances. Single substances are defined using a minimally sufficient set of data elements divided into five types: chemical, protein, nucleic acid, polymer and structurally diverse. Substances may be salts, solvates, free acids, free bases or mixtures of related compounds that are either isolated or synthesized together. Pharmacopoeial terminology and defining characteristics will be used when available and appropriate. Defining elements are dependent on the type of substance.

Note 3 to entry: Discrete existence refers to the ability of a substance to exist independently of any other substance. Substances can either be well-defined entities containing definite chemical structures, synthetic (e.g. isomeric mixtures) or naturally-occurring (e.g. conjugated oestrogens) mixtures of chemicals containing definite molecular structures, or materials derived from plants, animals, microorganisms or inorganic matrices for which the chemical structure may be unknown or difficult to define

3.85
substituent
molecular fragment attached to a structural repeat unit of a polymer that typically replaces a hydrogen atom

Note 1 to entry: This information is captured as part of the structural repeat unit when the position of substitution is fully occupied. When occupancy of a site is incomplete, the amount of a substituent is specified as either a fragment or moiety structural modification.

3.86
succession
process of agitating a liquid preparation in the manufacturing of homeopathic medicinal products.

Note 1 to entry: As intermediate step in the process of serial dilution, it is part of the potentization process.

3.87
tautomer
molecular structure capable of interconversion with an isomeric molecular structure that typically involves facile migration of a hydrogen atom between two adjacent atoms

Note 1 to entry: It is anticipated that a single tautomeric form will be associated with each substance and detailed rules will be developed within the implementation guide to indicate the tautomeric form associated with each chemical substance. If individual isomers may be isolated under normal conditions and are known to have distinct molecular properties, they are defined as separate substances [see ISO/TS 19844 (liquid dextrose)].

3.88
taxonomy
scientific organism classification system needed to describe the origin of source material in substances isolated from biological matrices

Note 1 to entry: Taxonomic information is captured to the species level for all polydisperse substances isolated from biological matrices, if such information is available and the source material is consistently derived from the species. Taxonomic family, genus and species along with the taxon author are necessary to identify the source organism. Kingdom, phylum, class and order are also captured when available. Intraspecific information (e.g. subspecies, strain or variety) is captured when the forms exhibit consistent differences in either material content or function.

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3.89
unitage
specifications of the amount constituting a unit

3.90
vehicle
excipient used for the preparation of certain homeopathic stocks or for the potentization process

Note 1 to entry: They may include, for example, purified water, ethanol of a suitable concentration, glycerol 85 per cent and lactose monohydrate.

Note 2 to entry: Vehicle description is in reference to homeopathy formulations and not in relation to other vehicles which are carriers or inert media used as solvents (diluents) in medicinally active agent formulations and/or their administration.

4 Symbols and abbreviated terms

NOTE Only general abbreviations are listed. They are used either within ISO 11238 or ISO/TS 19844 since the two documents are regarded as inseparable.

4.1

ACS

American Chemical Society[3)]

4.2

ASK Number

ID of a substance in German “Arzneistoffkatalog” (Pharmaceutical Substance Dictionary)

4.3

BAN

British Approved Name[4)]

4.4

DCF

Dénominations Communes Françaises (French approved drug name)[5)]

4.5

EVcode

EudraVigilance Code (Unique Identifier) used for a substance in the Extended EudraVigilance Medicinal Product Dictionary (XEVMPD)[6)]

4.6

HAB

3) https://www.acs.org/content/acs/en.html

4) https://www.tsoshop.co.uk/Medicine/Pharmacopoeia/&Action=Book&ProductID=9780113230334

5) http://ansm.sante.fr/Mediatheque/Publications/Pharmacopee-francaise-Denominations-communes-et-scientifiques-de-medicaments

6) http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000596.jsp

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