INTERNATIONAL STANDARD

ISO 11238

First edition
2012-11-01

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 médicaments — Éléments de données et structures pour l'identification unique et l'échange d'informations réglementées concernant les substances

Reference number
ISO 11238:2012(E)

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Published in Switzerland

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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.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

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.

ISO 11238 was prepared by Technical Committee ISO/TC 215, *Health informatics*.

Introduction

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

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

ISO 11616, *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, *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, *Health informatics — Identification of medicinal products — Data elements and structures for the unique identification and exchange of units of measurement*.

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;

— 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 Medicines Agency;

— 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);

— 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.

The necessary messaging specifications are included as an integral part of the IDMP standards to secure the interactions listed above.

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 materials within medicinal products.

This International Standard provides a structure that enables the assignment and maintenance of unique identifiers for all substances in medicinal products or in packaging materials in which medicinal products are contained. This International Standard sets out the general rules for defining and distinguishing substances, and provides a high-level model that structures substances and specified substances for the organization and capturing of data.

This International Standard has been developed using HL7’s Common Product Model, and detailed modelling of substances and specified substances has been undertaken in that domain. It is anticipated that implementation will use the HL7 substances implementation guide and messaging to deliver a strong, non-semantic unique identifier for every substance present in a medicinal product. It is anticipated that a single organization will be

responsible for the generation of 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 International Standard 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.

Materials used in medicinal products range from simple chemicals to gene-modified cells to animal tissues. To unambiguously define these substances is particularly challenging. This International Standard 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 International Standard contains five groups of elements that are sufficient to define all substances. Although it is certainly possible to define or classify substances in other ways, this International Standard uses a minimalist 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 International Standard has intentionally not included these supramolecular interactions at the substance level because of the variable nature and strength of such interactions. This International Standard 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 International Standard also provides elements for the capture of further information on substances, such as grade, manufacturer, manufacturing 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 International Standard depict elements and the relationship between elements that are necessary to define substances. The terms and definitions described in this International Standard 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 International Standard 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.

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

1 Scope

This International Standard provides an information model to define and identify substances within medicinal products or substances used for medicinal purposes, including dietary supplements, foods and cosmetics. Other standards and external terminological resources are referenced that are applicable to this International Standard.

2 Terms, definitions, symbols and abbreviated terms

2.1 Terms and definitions

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

2.1.1
active marker
constituent, or groups of constituents, of an herbal substance, herbal preparation or herbal medicinal product which are of interest for control purposes and are generally accepted to contribute to therapeutic activity

NOTE Active markers are not equivalent to analytical or signature markers that serve solely for identification or control purposes.

2.1.2
analytical data
set of elements to describe and capture methods and reference material used to determine purity, potency or identity in a specified substance

2.1.3
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

2.1.4
chemical substance
type of substance that can be described as a stoichiometric or non-stoichiometric single molecular entity and is not a protein or nucleic acid substance

NOTE 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.

2.1.5
chiral substance
substance whose molecular structure is not superimposable on its mirror image

2.1.6
component
intended constituent of a specified substance

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

NOTE Components are used to describe the substances and specified substances that form a multi-substance material.

2.1.7
composition stoichiometry
quantitative relationships between the chemical elements or moieties that make up a substance

EXAMPLE Sodium phosphate dibasic heptahydrate and sodium phosphate dibasic dihydrate are defined as different substances.

2.1.8
constituent
substance present within a specified substance

NOTE Constituents can be impurities, degradants, active markers or signature substances, or single substances mixed together to form a product. Constituents shall have an associated role and amount. Constituent specifications shall be used to describe components as well as limits on impurities or related substances for a given material.

2.1.9
controlled vocabulary
finite set of values that represent the only allowed values for a data item

NOTE 1 The allowed values can be codes, text or numeric.

NOTE 2 Adapted from CDISC Clinical Research Glossary V8.0, 2009.

2.1.10
copolymer
polymer with more than one type of structural repeating unit linked through covalent bonds

NOTE Copolymers are obtained by copolymerization or sequential polymerization of two or more monomers. Copolymers can be random, alternating, block or graft.

2.1.11
critical process step
manufacturing step necessary for production of a specified substance

2.1.12
degree of polymerization
number of structural repeating units in a polymeric block or chain

NOTE Applies to both homopolymers and block copolymers where it refers to the degree of polymerization within a block.

2.1.13
diverse origin
substances that are not isolated together or the result of the same chemical synthetic process

NOTE Material containing multiple substances is defined either as a mixture substance or a multi-substance (group 1) specified substance based on origin. Two substances brought together that do not undergo a chemical reaction resulting in the formation or breakage of specific chemical bonds would be defined as separate substances, even if there are non-bonding interactions between the substances.

2.1.14
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

2.1.15
fraction
distinct portion of material derived from a complex matrix, the composition of which differs from antecedent material

NOTE This concept is used to describe source material and is recursive in that a subsequent fraction can be derived from an antecedent fraction, which is implied in the order of listing.

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

2.1.16
gene
basic unit of hereditary material that encodes and controls the expression of a protein or protein subunit

2.1.17
gene element
individual element within a gene such as a promoter, enhancer, silencer or coding sequence

2.1.18
glycosylation
enzymatic process that links saccharides or oligosaccharides to proteins, lipids or other organic molecules

2.1.19
glycosylation type
significant differences in glycosylation between different types of organisms

NOTE This distinguishes the pattern of glycosylation across organism types, e.g. human, mammalian and avian. The glycosylation type is a defining element when polydisperse organism-based glycosylation exists in a substance.

2.1.20
grade
set of specifications indicating the quality of a specified substance

2.1.21
homopolymer
polymer containing a single structural repeating unit

2.1.22
isotope
variants of a chemical element that differ by molecular mass

NOTE 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.

2.1.23
manufacturing
process of production for a substance or medicinal product from the acquisition of all materials through all processing stages

NOTE The critical process, starting and processing materials, and critical production parameters are included.

2.1.24
material
any entity that has mass, occupies space and consists of one or more substances

2.1.25
medicinal product
any substance or combination of substances which may be administered to human beings or animals for treating or preventing disease, with the view to making a medical diagnosis or to restore, correct or modify physiological functions

NOTE 1 A medicinal product may contain one or more manufactured items and one or more pharmaceutical products.

NOTE 2 In certain jurisdictions, a medicinal product may also be defined as any substance or combination of substances which may be used to make a medical diagnosis.

2.1.26
microheterogeneity
substances isolated together that contain minor differences in glycosylation, or post-translational modification such as glycosylation or sequence heterogeneity

NOTE 1 Microheterogeneity is not a defining characteristic of either substances or specified substances.

NOTE 2 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, variable proteolytic processing or other.

2.1.27
mixture substance
type of polydisperse substance that is a combination of single substances isolated together or produced in the same synthetic process

NOTE 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 (Group 1 specified substances) and not as mixture substances.

EXAMPLE Gentamicin is defined as a mixture substance of Gentamicin C1A, Gentamicin C1 and Gentamicin C2. 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 product.

2.1.28
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 and should be defined in a consistent manner across all products. To avoid ambiguity, the free acid and/or free base should be used as the moiety upon which strength is based.

NOTE In this International Standard, moiety shall be used in the context of non-stoichiometric chemical substances and in modification of nucleic acid, proteins, polymers and structurally diverse substances. Moieties shall be single substances, ions or solvate molecules.

2.1.29
molecular fragment
portion of a molecule that has one or more sites of attachment to other fragments or moieties

NOTE Molecular fragments are used in the description of polymers to represent substituents and in structural modifications to a substance.

2.1.30
molecular structure
unambiguous representation of the arrangement of atoms

NOTE 1 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 This representation should be generally translatable into a graphical representation.

2.1.31
molecular weight
mass of one molecule of a homogenous substance or the average mass of molecules that comprise a heterogeneous substance

NOTE 1 The unified atomic mass unit is the unit of molecular weight. The type of molecular weight should always be captured.

NOTE 2 For polymers, there are several different types of molecular weight (weight average, number average, etc.).

2.1.32
multi-substance material
multiple substances and/or specified substances of diverse origin used as a component in the formulation of a medicinal product

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

NOTE Multi-substance materials are Group 1 specified substances. Any medicinal product used to formulate another medicinal product could also be considered a multi-substance material.

2.1.33
nucleic acid substance
type of substance that can be defined by a linear sequence of nucleosides typically linked through phosphate esters

NOTE The type of nucleic acid substance (RNA, DNA) is also identified. Oligonucleotides and gene elements (i.e. promoters, enhancers, coding sequences and silencers) are defined as nucleic acid substances.

2.1.34
official name
name given by an official registration authority

2.1.35
parent organism
organism from which biological source material is derived

2.1.36
part
anatomical origin and location of source material within an organism

2.1.37
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 A medicinal product may contain one or more pharmaceutical products.

NOTE 2 In many instances, the pharmaceutical product is equal to the manufactured item. However, there are instances where the manufactured item must undergo a transformation before being administered to the patient (as the pharmaceutical product) and the two are not equal.

2.1.38
physical form
physical state, either gas, liquid or solid, and the type of organization for solid matter

NOTE Solids can be either crystalline or amorphous. Polymorphism can also be captured.

2.1.39
polydisperse substance
substance containing multiple related molecular components

NOTE Polydisperse substances include polymers and structurally diverse material isolated from a single source. Chemical substances, proteins and nucleic acids with defined sequences are not described as polydisperse substances.

2.1.40
polydispersity
measure of the range of molecular masses in a polymer substance

NOTE The polydispersity index of polymers is typically calculated by the ratio of weight average molecular weight to number average molecular weight.

2.1.41
polymer substance
type of polydisperse substance that contains structural repeating units linked by covalent bonds

NOTE Monodisperse proteins and nucleic acids with defined sequences shall not be defined using the polymer substance elements.

2.1.42
post-translational modification
modification of a protein that typically occurs in vivo during or after translation

NOTE Post-translational modification is described within the structural representation and not as a modification of a protein.

2.1.43
processing material
type of material essential to the manufacturing process that is not incorporated into the resultant material

2.1.44
protein substance
type of substance with a defined sequence of alpha-amino-acids connected through peptide bonds

NOTE 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, disulfide linkages and glycosylation type (e.g. fungal, plant, arthropod, 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 15 amino acid residues or less.

2.1.45
protein sequence
order and identity of amino acids within a protein sub-unit

NOTE Protein sequences will be represented by single letter Dayhoff codes and listed from the *N*-terminus to the *C*-terminus.

2.1.46
protein sub-unit
linear sequence of amino acid residues connected through peptide bonds

NOTE Repeated sub-units in proteins are captured.

EXAMPLE Monoclonal antibodies typically consist of four sub-units.

2.1.47
resultant material
material that is the result of a critical process

NOTE Resultant material may be the starting material of the next process or the final material or actual specified substance.

2.1.48
salt
ionic substances formed from the neutralization reaction of an acid and base

NOTE Salts are ionic compounds composed of cations (positive ions) and anions (negative ions).

2.1.49
silencer
DNA sequence that suppresses transcription

2.1.50
single substance
substance that can be described by a single representation or set of descriptive elements

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

NOTE 2 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.

2.1.51
solvate
substance formed through association of a solvent molecule (e.g. water, alcohol) with another moiety.

NOTE Solvates can be either stoichiometric or non-stoichiometric and are predominately present when substances exist in a solid form.

2.1.52
source material
material from which a substance is derived, which is defined based on taxonomic and anatomical origins

NOTE This class is used to define structurally diverse and polymer substances isolated from biological matrices.

2.1.53
specified substance
group of elements which describe multi-substance materials and specify further information on substances and multi-substance materials relevant to the description of medicinal products

EXAMPLE This could include grade, units of measure, physical form, constituents, manufacturer, critical manufacturing processes (i.e. extraction, synthetic, recombinant processes), specification and the analytical methods used to determine that a substance is in compliance with a specification.

NOTE 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.

2.1.54
starting material
type of material that is modified through a manufacturing process

2.1.55
stoichiometric
substances that contain moieties in simple integral ratios

NOTE 1 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 Chemicals have defined composition stoichiometry when the ratio of all moieties (ion, counter ion and solvate) can be represented as simple integral ratios.

2.1.56
stereochemistry
relative spatial arrangement of atoms within molecules

2.1.57
structurally diverse substance
type of polydisperse substance isolated from a single source that is a complex mixture which cannot be described as a mixture of a limited number of single substances

NOTE 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 and juices) 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.