ICH Consensus Guideline
Released for Consultation on 10 May 2005, at *Step 2* of the ICH Process

Data Elements and Standards for Drug Dictionaries
M5

Recommended for Adoption at Step 2 of the ICH Process on 10 May 2005 by the ICH Steering Committee

This guideline has been developed by the appropriate ICH Expert Working Group and is subject to consultation in accordance with the ICH process.

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Data Elements and Standards for Drug Dictionaries

1. INTRODUCTION

1.1 Objectives of the Guideline

It is desirable for regulators and pharmaceutical industry to engage in an intensive information exchange during the drug development phase, the drug evaluation and approval phase and the post-authorization phase. The standardization of medicinal product information is regarded as one of the key elements of this information flow.

However, regulators in the ICH regions and observer countries have established their own procedures and applications with standards that differ in data format, content, language and applied terminology (e.g. terminology used for active ingredients, routes of administration, pharmaceutical dose forms).

Due to the lack of a common and harmonized approach, both regulators and pharmaceutical industry are confronted with the following issues:

- No possibility to exchange medicinal product information between regulators and industry in a structured and efficient way;
- Difficulties in ensuring data consistency and in evaluating and comparing medicinal product-related information across the ICH regions due to the lack of harmonized definitions of terminologies and data sets. This currently impairs pharmacovigilance activities in particular;
- For the pharmaceutical industry, major administrative burdens and duplication of efforts requiring substantial human and financial resources to comply with and handle different regional requirements.
- Lack of consistency in the use of terminology in the health care community.

The objectives of this guideline are to address the issues outlined above by developing harmonized standards that build on the processes currently established in the three ICH regions and the observer countries and to support the population of existing systems/applications with fully reliable regulatory medicinal product information. More specifically, the objectives focus on the development of:

- '***Unique identifiers'*** at the level of
  - Medicinal products: Medicinal Product Identifiers (MedIDs)
  - Pharmaceutical products: Pharmaceutical Product Identifiers (PhPIDs)
  - The controlled vocabulary: Terminology Identifiers (TermIDs)

- ***'Controlled vocabulary'*** as a standard for the electronic transmission of core sets of medicinal product information related to the following terminologies:

    - Active ingredients
    - Pharmaceutical dose forms
    - Routes of administration
    - Units and measurements
- '***Data elements'*** for the electronic transmission of core sets of medicinal product information based on the following data set:
    - Proprietary medicinal product name
    - Active ingredient(s)
    - Pharmaceutical dose form(s)
    - Strength of the active ingredient(s)
    - Route(s) of administration
    - Marketing authorization holder
    - Marketing authorization number
    - Country of authorization

    The *'Data elements'* have been developed for the electronic transmission of MedIDs and the related core medicinal product information.

This guideline does not cover the establishment and maintenance of a drug dictionary.

1.2 Background

The lack of internationally harmonized standards related to core sets of medicinal product information and medicinal product terminology is hindering the scientific evaluation and comparison of product data as well as healthcare. This applies in particular to the area of pharmacovigilance, where the exchange and management of medicinal product information in expedited and periodic adverse reaction reports at the international level is a key aspect of ensuring drug safety.

This document provides guidance on the harmonized standards that are being proposed by the ICH M5 EWG to facilitate the exchange and practical use of medicinal product data by regulators and pharmaceutical industry.

1.3 Scope of the Guideline

This guideline refers to approved medicinal products. Homeopathic medicinal products and investigational medicinal products are excluded from this guideline.

2. GUIDELINE

2.1 Medicinal Product and Term Identifiers

2.1.1 Medicinal Product Identifier (MedID)

Definition:

An identifier assigned to a medicinal product by the regulator of the country/territory of authorization.

General Conventions:

The regulators in the regions and observer countries have various processes established to identify individual medicinal products. Because medicinal product information is exchanged internationally, worldwide unique medicinal product identifiers (MedIDs) are desirable.

Regulators intend to assign MedIDs as follows:

- At the ***'medicinal product level'***, which means that a specific medicinal product has only one identifier for different pack sizes.
  For example, the medicinal product 'TRADENAME X' has the same MedID related to two different presentations; a pack size of 50 tablets and a pack size of 100 tablets.

or

- At ***'medicinal product package level'***, which means that for each package presentation of the medicinal product a different MedID is assigned.
  For example, the medicinal product 'TRADENAME Y' has two different MedIDs for each of the two different presentations available: a MedID for the pack size of 50 tablets and a MedID for the pack size of 100 tablets.

Methodology:

The world-wide unique MedID is constructed as follows:

- Prefix of the country code of that region followed by
- The regionally-assigned identifier followed by
- An error detection code

The regionally-assigned identifier refers to the medicinal product level or to the medicinal product package level. As a general rule, the MedID should accompany the exchange of the medicinal product information.

Examples:

EU-EU/1/2342323/001-K
FR-123456-X
JP-123456789-Y
US-0123456789-Z
CA-2323232-V

2.1.2 Pharmaceutical Product Identifier (PhPID)

Definition:

An identifier assigned at the level of the pharmaceutical product based on the active ingredient(s), the strength(s) of the ingredient(s) and the pharmaceutical dose form.

Methodology:

PhPIDs represent the pharmaceutical product at four levels as defined as follows:

- PhPID4 = Ingredient(s) - Strength(s) - Strength unit(s) - Pharmaceutical Dose Form
- PhPID3 = Ingredient(s) - Pharmaceutical Dose Form
- PhPID2 = Ingredient(s) - Strength(s) - Strength unit(s)
- PhPID1 = Ingredient(s)

Each PhPID is a unique, non-semantic, alphanumeric code and is derived from the ICH M5 data elements, but is not part of these data elements.

Examples:

Medicinal products with the same active ingredients, strengths and pharmaceutical dose form share a common PhPID4.
Medicinal products with the same active ingredients and pharmaceutical dose form share a common PhPID3.
Medicinal products with the same active ingredients and strengths share a common PhPID2.
Medicinal products with the same active ingredients share a common PhPID1.

2.1.3 Controlled Vocabulary Term Identifier (TermID)

Definition:

An identifier assigned at the level of each term of the controlled vocabulary (active ingredients, pharmaceutical dose forms, routes of administrations and units and measurements).

Methodology:

The TermID is a unique, non-semantic, alphanumeric code assigned for each term of the controlled vocabulary.

2.2 Controlled Vocabulary

2.2.1 Background

Different regulatory standard terminologies are in place in the ICH regions and observer countries, which makes it difficult to exchange this information at the international level. These terminology differences complicate specifically activities in the area of pharmacovigilance and healthcare and the management of medicinal product information.

To address the identified terminology differences, the ICH M5 EWG is developing controlled vocabularies for active ingredient(s), pharmaceutical dose form(s), route(s) of administrations and unit(s) and measurement(s) using the following methodology:

- Preparing an inventory of the different regulatory standard terminologies including those defined in the ICH E2B(M) guideline (version 4.4.1 includes the Post Step 4 corrections agreed by the Steering Committee on 5 February 2001);
- Analyzing definitions for the different regulatory standard terminologies;
- Developing a controlled vocabulary that supports good terminological practice;
- Defining mapping procedures to determine unique terms and related synonym terms on the basis of the regional definitions in place;
- Mapping the individual terms;
- Assigning unique TermIDs.

The Active Ingredients Controlled Vocabulary, the Pharmaceutical Dose Forms Controlled Vocabulary, the Routes of Administration Controlled Vocabulary and the Units and Measurements Controlled Vocabulary will be made available on the ICH website.

2.2.2 Active Ingredients Controlled Vocabulary

Scope:

The Active Ingredients Controlled Vocabulary includes active ingredient terms related to approved medicinal products. Excluded are active ingredients related to homeopathic medicinal products and investigational medicinal products.

Definitions:

An ***active ingredient*** is defined as a substance that alone or in combination with one or more other ingredients produces the intended activity of a medicinal product.

A ***substance*** is any matter and can be of human, animal, vegetable or chemical (natural, semi-synthetic or synthetic) origin.

An ***active moiety*** is the portion of the active ingredient that is responsible for the effect.

Methodology:

A comprehensive list of active ingredient terms has been collected based on the standard terminologies currently used by the EMEA, FDA, MHLW and Health Canada.

The active ingredient terms are limited to English language terms, with the exception of herbal active ingredients, for which the Latin language terms and/or Japanese language terms are also included.

Within the list, the indication of the provenance of the term (i.e. its source) is also included.

An active ingredient TermID will be assigned to each unique term.

The following approach will be used for the mapping:

- Chemical Abstract Service Number (CAS Number)
- Reference Source for each active ingredient name (e.g. USAN, INN, JAN) that is linked to the chemical structure by the organizations
- Chemical name (e.g. following the IUPAC nomenclature)

Mapping of synonyms will be performed on the level of both the active moiety and the active ingredient where applicable.

Herbal substances will be mapped on the following principles:

- Botanical scientific name according to the Latin binomial system (genus + species)
- The author (e.g., Linnaeus, abbreviated L.) if known,
- The plant parts (if known) and
- The process (when applicable, and if known)

Herbal preparations will be mapped on the basis of the standardized treatments (for instance extraction, distillation, expression, fractionation, purification, concentration or fermentation) as described in the official Pharmacopoeias of the three regions. For extractions, the solvent will also be specified.

For vaccine antigens the mapping of active substances will be based on the following principles:

- Conformity with the pharmacopoeia monograph terminology for vaccine antigens in the regions;
- For non-pharmacopoeia active substances, according to the formal Latin/Greek name and/or the disease being protected against.

For bacteria and viruses, the strain serotype or other appropriate sub-species the designation will also be mapped with the name of each antigen, if relevant.

In addition, the nature of any cellular system(s) used for production, and if relevant the use of recombinant DNA technology (including the use of the expression 'produced in XXX cells <by recombinant DNA technology>) will be mapped, following the pattern set by the following examples:

- 'produced in human diploid (MRC-5) cells'
- 'produced in Escherichia coli cells by recombinant DNA technology'
- 'produced in chick-embryo cells'

The inclusion of a mention of the production process in vaccine active substance names will be mapped at the level of the following terms:

- 'live, attenuated' (in the case of vaccines containing living micro-organisms)
- 'inactivated' (in the case of vaccines containing killed micro-organisms).

2.2.3 Pharmaceutical Dose Form Controlled Vocabulary

Scope:

The Pharmaceutical Dose Form Controlled Vocabulary includes pharmaceutical dose form terms of standard terminologies in use by the regulators in the ICH regions and observer countries.

Definitions:

A ***Dose Form*** is defined as the physical manifestation ["entity"] that contains the active and/or inactive ingredients that deliver a dose of the medicinal product. The key defining characteristics of the Dose Form can be the state of matter, delivery method, release characteristics, and the administration site or route for which the product is formulated.

A ***Pharmaceutical Dose Form*** is the form in which a pharmaceutical product is presented in the medicinal product package as supplied by the marketing authorization holder/manufacturer/distributor.

Methodology:

A comprehensive list of Dose Form terms has been collected, which includes:

- European Pharmacopoeia Standard terms
- United States Pharmacopeia (USP) terms
- Japanese Pharmacopoeia terms
- MHLW terms
- Health Canada terms

Within the list, the indication of the provenance of the term (i.e. its source) will also be included.

Tasks to be undertaken include:

- A term identifier will be allocated to each term (entry) in the list, enabling linkage with original dose form lists.
- Each term will initially be identified as a "dose form concept", pending identification of synonymy.
- Synonymous terms will be identified and "annotated" e.g. "otic drops" and "ear drops".
- Terms that do not fit (for example, device terms) will be identified and annotated, as will be all terms that do not fit within the agreed definition (for example, dose forms that describe aspects of medication such as strength or shape or indication).
- Each of the "dose form concepts" will be analyzed against the agreed defining characteristics to create a logical description pattern. This pattern will assist in the identification of unrecognized synonymy and hence will ensure that the resulting

Dose Form concepts are unique and unambiguous. A description logic will enable concepts to be defined by the pattern or "graph" of their relationships with other concepts.

- Having analyzed all the "dose form concepts", any concepts found to be sharing an identical "set" of characteristics will again be reviewed; additional "distinguishing" characteristics will be added as appropriate.

The dose form description applies to only one concept at a time. Therefore, items that are marketed as packs containing more than one medicinal product will not themselves have a "combination dose form", but each medicinal product within them will have a dose form description. This will avoid terms such as "pessary + cream" or "powder + solvent".

2.2.4 Routes of Administration Controlled Vocabulary

Scope:

The Routes of Administration Controlled Vocabulary includes routes of administration terms of standard terminologies in use by the regulators in the ICH regions and observer countries and defined in the ICH E2B(M) guideline (version 4.4.1 includes the Post Step 4 corrections agreed by the Steering Committee on 5 February 2001).

Definitions:

The ***Route of Administration*** indicates the part of the body through or into which, or the way in which, the medicinal product is intended to be introduced.

In some cases a medicinal product can be intended for more than one route and/or method of administration.

Methodology:

A comprehensive list of Route of Administration terms has been collected and includes:

- European Pharmacopoeia Standard terms;
- United States Pharmacopeia (USP) terms;
- Health Canada terms;
- MHLW terms;
- ICH E2B(M) Routes of Administration List

Each term is given an identifier, a description and relationships to other terms within the terminology.

Tasks undertaken include:

- A term identifier is allocated to each term (entry) in the list, enabling linkage with the original route of administration term lists.
- Within the list there is an indication of the provenance of the term (i.e. its source). A formal definition from the source vocabulary is included, where necessary.

Synonymous terms are identified and "annotated" e.g. ocular use and ophthalmic use.

- The route of administration terms are mapped on the basis of the same or the equivalent meaning for route of administration

purposes e.g. ocular, ophthalmic. In specific cases the regional definitions were crosschecked to clarify the meaning.

- An adjective is used to describe the route of administration where a suitable adjective is available, e.g. inhalational not inhalation.
- The descriptor 'use' is generally not supported unless it adds a specific meaning e.g. ‘oral’ was used instead of ‘oral use’.
- Where a prefix and a main word in the terms are concatenated, the concatenated word is hyphenated only if the ending of the prefix and the beginning of the next word were both vowels (a, e, i, o, u).
- Where a suitable ICH E2B(M) route of administration term exists, this is used as the basis for the official ICH M5 Route of Administration Controlled Vocabulary term. Where a suitable ICH E2B(M) route of administration term is not available to represent the route concept, a new term is added to the vocabulary. In either case, the above procedures are applied.
- The Routes of Administration Controlled Vocabulary presents the corresponding terms (translations) applicable in the different regions and in the E2B(M) list as follows:
    - MedID: e.g. 001
    - ICH M5 Route of Administration Term e.g. Auricular (OTIC)
    - Regional Standard Terms:
        - EU e.g. Auricular Use
        - FDA e.g. Auricular (OTIC)
        - MHLW e.g. Otological Agent
        - Health Canada e.g. OTIC
        - E2B(M) e.g. Auricular (OTIC)
- Where, within one region, two or more terms (e.g. a current term and a historic non-current term) refer to the same route of administration, these terms were specified in sequence and separated by the symbol "/". The preferred or current term is specified as the first term, e.g. ocular use/ophthalmic use for EU or unknown/unassigned for the US.
- A draft translation for the ICH M5 Routes of Administration Controlled Vocabulary in Japanese has been included.

2.2.5 Units and Measurements Controlled Vocabulary

Scope:

The Units and Measurements Controlled Vocabulary includes units and measurements in use by the regulators in the ICH regions and observer countries and defined in the ICH E2B(M) guideline (version 4.4.1 includes the Post Step 4 corrections agreed by the Steering Committee on 5 February 2001).

General Conventions:

The International System of Units (SI) and the Units and Measurements as described in the E2B(M) guideline, (version 4.4.1 includes the Post Step 4 corrections agreed by the Steering Committee on 5 February 2001) are followed in the ICH regions and observer countries. Additional, region specific units are in use specifically regarding biological and microbiological units.

Methodology:

A comprehensive list of Units and Measurements has been collected and includes:

- International System of Units (SI)
- Units and Measurements as described in the E2B(M) guideline[1]
- Region specific units and measurements (CA, EU, JP, US)

Each unit and measurement is given an identifier, a description, a symbol and relationships to other terms within the terminology.

Tasks undertaken include:

- A term identifier is allocated to each unit and measurement (entry) in the list, enabling linkage with the original unit and measurement entries in the lists.
- Within the list there is an indication of the provenance of the term (i.e. its source) and a formal definition from the source vocabulary is included, where appropriate.
- Synonymous entries are identified and "annotated" e.g. %(v/v) and (v/v)%.
- The mapping of Units and Measurements is based on the International System of Units (SI) and its abbreviations and definitions. The definitions of the SI base units refer to the NIST Special Publication 330 (SP 330).
- Lower case has been used for the term description.
- Exponents of symbols are not expressed in superscript format; e.g. the symbol 'm2' has been used for square meters.
- Some important and widely used units outside the International System have been added with regard to biological and microbiological units. Descriptions of these units and their abbreviations were added as appropriate.

2.3 Data Elements

This chapter describes the data elements for the electronic transmission of a core set of medicinal product information.

The data elements as presented in this guideline refer to the consolidated core data sets of medicinal products as defined in the scope of this guideline, chapter 1.3.

These data elements are based on the regional standards already established by these regulators to support the local data collection process and do not replace or supersede the regional standards or legal requirements for data collection between the regulators and pharmaceutical companies.

As a result, a medicinal product is characterized in the frame of this guideline as follows:

- A Medicinal Product has:
  - One and only one MedID
  - One and only one Medicinal Product Name

[1] Version 4.4.1 includes the Post Step 4 corrections agreed by the Steering Committee on 5 February 2001

- One and only one Marketing Authorization Holder
- One and only one Marketing Authorization (number)
- One or more Pharmaceutical Products

- A Pharmaceutical Product has
  - One or more Active Ingredients with a specific strength (the same active ingredient with a different strength is considered a different pharmaceutical product)
  - One and only one Pharmaceutical Dose Form
  - One or more possible Routes of Administration

In order to facilitate the understanding of the relationship of the data elements described in this chapter, a conceptual model is included as follows:

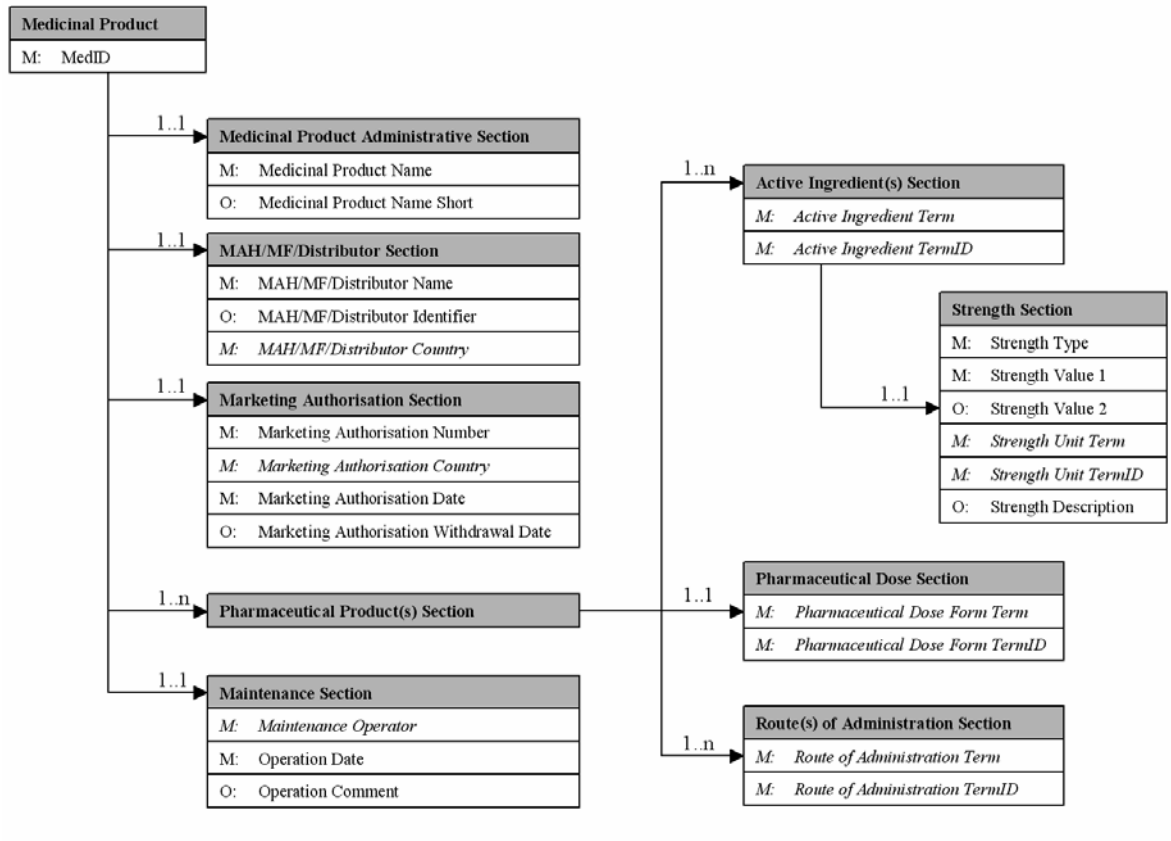

Figure 1 - Conceptual Model of the ICH M5 MedID and Data Element Set

This conceptual model does not define the actual message specifications for the exchange format of MedIDs and the related ICH M5 data elements.

The figure provides the relationship between the ICH M5 data elements and the MedID.

- All data elements are grouped as elements or attributes within a section.
- A section defines a concept which is further described by its data elements or attributes.
- The data elements are flagged as Mandatory[2] (M:) or Optional (O:).

[2] The use of 'Mandatory' in the remainder of this document refers to technical and not legal requirements.

- The data elements for which the entry is strictly controlled by a list of values (e.g. ISO Country Code 3166) or by the ICH M5 Controlled Vocabulary are in *italics*.

There are relationships between entities, with a specific cardinality.

- The relationship with cardinality **1..1** means that, for example, a Pharmaceutical Product has precisely one pharmaceutical dose form.
- The relationship with cardinality **1..n** means that, for example, a Pharmaceutical Product has one or more Active Ingredients.

Each section and each element of the ICH M5 data element set is described in the following paragraphs.

As a general principle, it should be noted that depending on regional laws and regulations a formal marketing authorization might not be required for certain categories of medicinal products (e.g. certain OTC drugs, 'grandfather' drugs). For these medicinal products the same principles apply as for 'authorised' medicinal products.

2.3.1 Medicinal Product Identifier

2.3.1.1 Medicinal Product Identifier (MedID)

User Guidance:

The MedID as defined in chapter 2.1.1 of the medicinal product and as presented in the ICH M5 data element set should be provided in this field.

As a general rule, the MedID should be maintained in any re-

Type:

Mandatory

Example:

FR-123456-X
EU-EU/1/2342323/001-K
JP-123456789-Y
US-0123456789-Z
CA-2323232-V

2.3.2 Medicinal Product Administrative Section

2.3.2.1 Medicinal Product Name

Definition:

The name assigned to a medicinal product as approved by the regulator of the country of authorization.

User Guidance:

The naming of a medicinal product differs in the ICH regions and observer countries.

The full and complete medicinal product name as approved by the regulator of the country or territory of authorization and as

appearing on the package of the medicinal product, the container or the package insert should be provided in this field.

For medicinal products which do not require prior marketing authorization under regional law, the full and complete medicinal product name as appearing on the package of the medicinal product, the container or the package insert should be provided in this field.

Synonyms:

Proprietary Medicinal Product Name (ICH E2B(M))
Name of the Medicinal Product
Product Name

Type:

Mandatory

Examples:

Lithium Carbonate liq. Paediatric Company D
ABC Tabs 500 Company B
Vinblastine Sulphate Injection Solution 10mg/ml
Tri-Product C Forte
Product X Oral Gel
BRANDX 100 U/ml Concentrate for solution for infusion-Intravenous use Vial (glass) 5 ml (100 U/ml) 1 vial

2.3.2.2 Medicinal Product Short Name

Definition:

The medicinal product name without the trademark or the name of the marketing authorization holder or any other descriptor (e.g. strength, dosage form, user group, route of administration).

User Guidance:

The name assigned to a medicinal product as approved by the regulator of the country or territory of authorization, without the trademark or the name of the marketing authorization holder or any other descriptor should be provided in this field.

For medicinal products which do not require prior marketing authorization under regional law, the medicinal product name without the trademark or the name of the manufacturer/distributor or any other descriptor should be provided in this field.

Synonyms:

Trade Name
Brand Name
Scientific Name
Common Name
Invented Name

Type:

Optional

Example:

Lithium Carbonate
ABC
Vinblastine Sulphate
Tri-Product C
Product X

BRANDX

2.3.3 Marketing Authorization Holder/Manufacturer/Distributor Section

Definitions:

Marketing Authorization Holder (MAH)
Natural or legal person in possession of the marketing authorization or license for a medicinal product within a given country/territory.

Manufacturer (MF)
Natural or legal person in possession of a license for manufacturing a medicinal product within a given country/territory.

Distributor
Natural or legal person in possession of a license covering the procuring, holding, supplying or exporting of medicinal products, apart from supplying medicinal products to the public.
Such activities are carried out with manufacturers or their depositories, importers, other wholesale distributors or with pharmacists and persons authorized or entitled to supply medicinal products to the public within a given country/territory.

2.3.3.1 Name of the Marketing Authorization Holder or Manufacturer or Distributor

User Guidance:

The full and complete name of the marketing authorization holder of an authorized medicinal product as appearing on the package of a medicinal product, the container or the package insert should be provided in this field.

For medicinal products which do not require prior marketing authorization under regional law, the full and complete name of the manufacturer/distributor, as appearing on the package, the container or the package insert, should be provided in this field.

Type:

Mandatory

2.3.3.2 Marketing Authorization Holder or Manufacturer or Distributor Identifier

User Guidance:

The identifier assigned by a regulator of a region or observer country to a marketing authorization holder for authorized medicinal products, or to the manufacturer/distributor for medicinal products that do not require prior marketing authorization, should be provided in this field.

Type:

Optional

2.3.3.3 Country of the Marketing Authorization Holder or Manufacturer or Distributor

User Guidance:

The two letter ISO 3166 country code of the country in which the marketing authorization holder is located should be provided in this field.

For medicinal products that do not require prior marketing authorization under regional law, the two letter ISO 3166 country code of the country in which the manufacturer/distributor is located should

Type:

Mandatory

2.3.4 Marketing Authorization Section

Definitions:

The marketing authorization information of the medicinal product as granted by the regulator in the respective territory/country should be provided.

For medicinal products that do not require prior marketing authorization under regional law, the section should be completed as specified.

2.3.4.1 Marketing Authorization Number

Definition:

The marketing authorization number of the medicinal product as granted by the regulator in the respective territory/country.

User Guidance:

The marketing authorization number of the medicinal product as granted by the regulator in the respective territory/country should be provided.

For medicinal products that do not require prior marketing authorization under regional law, a unique identifier should be

Synonyms:

Authorization Number
License Number
Identifier

Type:

Mandatory

2.3.4.2 Marketing Authorization Country

Definition:

The marketing authorization country refers to the country/territory in which the marketing authorization was granted by the regulator of

this country/territory.

User Guidance:

The medicinal product authorization country for the medicinal product should be provided as a two letter country code (ISO 3166).

For medicinal products in the United States and Japan the country code will be set as default to US or JP. For centrally authorized medicinal products in the European Union, the country code will be set to EU.

For medicinal products that do not require prior marketing authorization under regional law, the country of marketing should be specified in this field.

Synonyms:

Authorization Country
License Country

Type:

Mandatory

2.3.4.3 Marketing Authorization Date

Definition:

The date on which the marketing authorization was granted by the regulator of the respective country/territory.

User Guidance:

The date on which the authorization for the medicinal product was granted by the regulator should be provided in this field. A complete date consisting of day, month and year should be specified.

For medicinal products that do not require prior marketing authorization under regional law, a default date will be provided by the regulator of the region in this field.

Synonyms:

Authorization Date
License Date

Type:

Mandatory

2.3.4.4 Marketing Authorization Withdrawal Date

Definition:

The date on which the authorization for the medicinal product was withdrawn/revoked by the regulator of the country/territory or by the marketing authorization holder/manufacturer/distributor, depending on the regulatory requirements in the region or observer countries.

User Guidance:

The date on which the authorization for the medicinal product was withdrawn/revoked by the regulator of the respective country/territory or by the marketing authorization holder/manufacturer/distributor should be provided in this field. A complete date consisting of day, month and year should be specified.

For medicinal products that do not require prior marketing authorization under regional law, this field is not applicable.

This information should be provided if applicable.

Synonyms:

Withdrawal Date
License Withdrawal Date
Revocation Date

Type:

Optional

2.3.5 Pharmaceutical Product Section

Definition:

The pharmaceutical product section reflects the active ingredient(s), strength(s), pharmaceutical/dosage form(s) and routes of administration(s) that constitute a medicinal product.
A medicinal product can consist of one or several pharmaceutical products, given to (or taken by) a patient with a therapeutic or

User Guidance:

The Pharmaceutical Product Section is repeatable to allow for the entry of each pharmaceutical product that constitutes the medicinal product.

The exact composition at the level of the active ingredient(s), the strength of the ingredient(s), the pharmaceutical dose form and the route(s) of administration should be provided for each pharmaceutical product.
The majority of medicinal products contain only one pharmaceutical

Examples:

Product A
consists of one pharmaceutical product as follows:

Pharmaceutical Product:
Active Ingredient: Acetaminophen
Strength of the Active Ingredient: 500 mg
Pharmaceutical/Dosage Form: Tablet
Route of Administration: Oral Use

Product Z ®
consists of two tablets with different composition as follows:

White tablet with Estradiol 2mg
Pink tablet with Estradiol 2mg and Levonorgestrel 0.075mg

Pharmaceutical Product 1:
Active Ingredient: Estradiol
Strength of the Active Ingredient: 2 mg
Pharmaceutical/Dosage Form: Tablet
Route of Administration: Oral Use

Pharmaceutical Product 2:
Active Ingredient: Estradiol
Strength of the Active Ingredient: 2 mg
Active Ingredient: Levonorgestrel
Strength of the Active Ingredient: 0.075mg
Pharmaceutical/Dosage Form: Tablet
Route of Administration: Oral Use

Product Combi ®[3]
consists of two pharmaceutical products as follows:

Pharmaceutical Product 1:
Active Ingredient: Clotrimazole
Strength of the Active Ingredient: 500 mg
Pharmaceutical/Dosage Form: Pessary
Route of Administration: Vaginal Use

Pharmaceutical Product 2:
Active Ingredient: Clotrimazole
Strength of the Active Ingredient: 2% w/w
Pharmaceutical/Dosage Form: Cream
Route of Administration: Cutaneous Use

2.3.6 Active Ingredient(s) Section

User Guidance:

The active ingredient section is a repeatable section.

If a pharmaceutical product contains more than one active ingredient, the section should be repeated for each active ingredient.

Type:

Mandatory

2.3.6.1 Active Ingredient Term

User Guidance:

The active ingredient as reflected in the medicinal product labeling should be provided as a standard term in line with the ICH M5 Active

[3] This type of medicinal product is not available in Japan.

Ingredients Controlled Vocabulary in this field.

Type:

Mandatory

2.3.6.2 Active Ingredient TermID

User Guidance:

The ICH M5 Active Ingredients Controlled Vocabulary TermID for the active ingredient term should be provided in this field.

Type:

Mandatory

2.3.6.3 Strength Section

Definition:

The content of the active ingredient expressed quantitatively per dosage unit, per unit of volume or per unit of weight, according to the pharmaceutical dose form.

User Guidance:

This section includes the strength of the active ingredient.

Synonyms:

Concentration, Unit dose

Type:

Mandatory

Example:

Solid forms:

the strength is defined as the amount of active ingredient per unit dose;

Liquid ready-to-use preparations:

the strength is identical to the concentration;

Powder for reconstitution, powder for oral solution, etc.:

as a general principle, the strength is identical to the concentration after reconstitution to the volume recommended.

2.3.6.3.1 Strength Type

Definition:

Descriptor that specifies the strength type of the active ingredient of a medicinal product.

User Guidance:

For some medicinal products, the exact dose strength cannot be indicated and is therefore expressed as a concentration range or as 'not greater than' or as 'not less than' a particular value.

The following four descriptors are available to express the strength of an active ingredient:

Equal:

The dose strength is indicated as a unique value in the 'Strength Value 1' field.

Range:

If the strength is expressed as a range, the minimum value and the maximum value of the dose strength are indicated in the 'Strength Value 1' field and in the 'Strength Value 2' field.

Not greater than:

If the dose strength is expressed as "not greater than", the maximum dose strength is indicated in the 'Strength Value 1' field.

Not less than:

If the dose strength is expressed as "not less than", the minimum dose strength is indicated in the 'Strength Value 1' field.

If the dose strength is expressed as a range where both an upper and lower value are designated, and only one value can be provided, the strength value should be specified in the field 'Strength Value 1'.

Type:

Mandatory

2.3.6.3.2 Strength Value 1

User Guidance:

The numeric value of the dose strength of the active ingredient as specified in the medicinal product labeling should be indicated in this field. For numeric values with decimal fractions, a full stop should be used.

If the strength is expressed as a range, the minimum value of the dose strength should be specified in the field 'Strength Value 1'.

If the dose strength is expressed as a range where both an upper and lower value is designated, and only one value can be provided, the

Type:

Mandatory

2.3.6.3.3 Strength Value 2

User Guidance:

The numeric value of the dose strength of the active ingredient as specified in the medicinal product labeling should be indicated in this field. For numerical values with decimal fractions, a full stop should be used.

If the strength is expressed as a range, the maximum value of the dose

Type:

Optional

2.3.6.3.4 Strength Unit Term

User Guidance:

The strength unit symbol should be specified as the corresponding descriptor of the ICH M5 Units and Measurements Controlled Vocabulary.

Type:

Mandatory

2.3.6.3.5 Strength Unit TermID

User Guidance:

The Unit and Measurement Controlled Vocabulary TermID of the corresponding unit and measurement term should be provided in this

Type:

Mandatory

2.3.6.3.6 Strength Description

User Guidance:

This free text field can be used to describe a concentration range for some medicinal products where the exact dose strength cannot be structured in the Strength Section.

Type:

Optional

2.3.7 Pharmaceutical Dose Form Section

User Guidance:

This section refers to the pharmaceutical dose form. Each pharmaceutical product can have only one pharmaceutical dose form. Therefore, this section is not repeatable.

2.3.7.1 Pharmaceutical Dose Form Term

User Guidance:

The pharmaceutical dose form as reflected in the medicinal product labeling should be provided as standard term in line with the ICH M5 Pharmaceutical Dose Form Controlled Vocabulary in this field.

Synonyms:

Pharmaceutical Form E2B(M)
Dosage Form E2B(M)

Type:

Mandatory

2.3.7.2 Pharmaceutical Dose Form TermID

User Guidance:

The ICH M5 Pharmaceutical Dose Form Controlled Vocabulary TermID of the corresponding pharmaceutical dose form term should be provided in this field.

Type:

Mandatory

2.3.8 Route of Administration Section

User Guidance:

This section refers to the route(s) of administration of the pharmaceutical product. The route of administration section is a repeatable section.

2.3.8.1 Route(s) of Administration Term

User Guidance:

The route of administration as reflected in the medicinal product labeling should be provided as standard term in line with the ICH M5 Route of Administrations Controlled Vocabulary in this field.

Type:

Mandatory

2.3.8.2 Route of Administration TermID

User Guidance:

The ICH M5 Routes of Administration Controlled Vocabulary TermID of the corresponding pharmaceutical dose form term should be provided in this field.

Type:

Mandatory

2.3.9 Maintenance Section

User Guidance:

This section contains information related to the maintenance of MedIDs and the medicinal product information as specified in the ICH M5 data element set.

2.3.9.1 Maintenance Operator

Definition:

The maintenance operator:

- Refers to the ICH M5 data element set for a specific medicinal product and to the MedID assigned by the regulator for that product
- Specifies the operation type regarding the ICH M5 data element set and the MedID for a specific medicinal product.

Three types of maintenance operators are available:

- **New**

  This operator applies for the initial transmission of the MedID and the related ICH M5 data elements for a specific medicinal product.

- **Update**

  This operator applies for the transmission of the MedID and the related ICH M5 data elements for a specific medicinal product, when previously transmitted information needs to be updated.

- **Nullify**

This operator applies for the transmission of the MedID and the related ICH M5 data elements for a specific medicinal product, when previously transmitted information needs to be nullified.

User Guidance:

- As a general principle, the complete information available for a medicinal product in line with the ICH M5 data element set should be provided for any maintenance operator i.e. New, Update and Nullify.

- The maintenance operator 'New' should be used in line with the assignment of the MedID. Every time a new MedID is assigned by a regulator in a country/territory the full information of the medicinal product with the corresponding MedID and the complete ICH M5 data element set should be transmitted with the maintenance operator set to New.
  In this case the status of the MedID and the complete ICH M5 data element set is 'Current'.

- The maintenance operator 'Update' should be used any time any information related to the ICH M5 data element set needs to be updated for an existing MedID.
  In this case the status of the most recently transmitted ICH M5 data element set for the MedID is 'Current'.
  The status of the previous ICH M5 data element set(s) is 'Replaced'.

- The maintenance operator 'Nullify' should be used if an existing MedID and any of the related ICH M5 data elements are void or erroneous and need to be deleted.
  In particular the maintenance operator 'Nullify' should be used if a MedID previously reported is wrong.
  The status of the MedID and the ICH M5 data element set is 'Nullified'.

Type:

Mandatory

2.3.9.2 Operation Date

Definition:

The date at which the maintenance operation is effective.

User Guidance:

The operation date should be specified for any transmission of a MedID and the related ICH M5 data element set including the applicable maintenance operator.
Based on the maintenance operator and the operation date, the status of each MedID and the related ICH M5 data element set can be maintained i.e. entries can be flagged as 'Current', 'Replaced' or

Type:

Mandatory

2.3.9.3 Operation Comments

User Guidance:

Comments on the maintenance operator can be provided, e.g. the reason for an update or a nullification of a MedID and the ICH M5 data element set.

Type:

Optional

3. GLOSSARY

This glossary defines the way in which certain terms are used for the purpose of the guideline and for which no specific definition has been provided within the guideline itself.

In addition this glossary provides an overview of acronyms used throughout the document.

Glossary of Terms

Medicinal Product Package

Definition:

Delivery unit of a medicinal product in an outer container.

Synonyms:

Package presentation

Country or Territory

Definition:

A country or territory is defined as geographical, political or economic area.

Acronyms

CA
: Canada

CAS
: Chemical Abstract Service Number

EMEA
: European Medicines Agency, EU

EU
: European Union

FDA
: Food and Drug Administration, US

HL7
: Health Level 7

ICH
: International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use

ICH M5 EWG
: International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use M5 Data Elements and Standards for Drug Dictionaries Expert Working Group

ICH E2B (M)
: International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use E2B(M): Clinical Data Management: Data Elements for Transmission of Individual Case Safety Reports

INN
: International Non-proprietary Name

ISO
: International Organization for Standardization

IUPAC
: International Union of Pure and Applied Chemistry

JAN
: Japanese Accepted Name

JP
: Japan

MAH
: Marketing Authorization Holder

MedID
: Medicinal Product Identifier

MF
: Manufacturer

MHLW
: Ministry of Health, Labour and Welfare, Japan

NDC
: National Drug Code

NIST
: National Institute of Standards and Technology

OTC
: Over the Counter

PhPID
: Pharmaceutical Product Identifier

SI
: International System of Units

TermID
: Terminology Identifier of the ICH M5 controlled Vocabulary

US
: United States

USAN
: United States Adopted Name

USP
: United States Pharmacopoeia

4. REFERENCES

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:
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