EUROPEAN MEDICINES AGENCY
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Information Management

Product Management Service (PMS) - Implementation of International Organization for Standardization (ISO) standards for the identification of medicinal products (IDMP) in Europe

Chapter 8 – Practical examples

Version 2.1.1.

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Summary of changes

Following the publication of version 2.1 of this document in July 2022, the content of the below listed sections was amended as follows:

- Section 2. Full model examples were updated to reflect new data elements added to PMS model based on the updated version of EU IG Chapter 2:
  - 1.18.6. URL value,
  - 1.18.7. (Attached document) Status,
  - 4.3 Manufacturer,
  - 4.4.1. Quantity operator,
  - 4.8.5.1. Quantity operator,
  - 4.8.6.1. Identifier value,
  - 4.8.6.2. Identifier system,
  - 4.10.5.1. Quantity operator,
  - 4.10.6. Medical device description,
  - 4.10.6.1. Language,
  - 4.10.7. Medical device description of intended purpose,
  - 4.10.7.1. Language,
  - 4.10.8. Medical device classification,
  - 4.10.9. Medical device manufacturer,
  - 4.11.2.1. Quantity operator,
  - 4.7. Marketing authorisation (Package level);
- general editorial and minor updates were introduced across the document;
- graphs were updated to reflect new data elements added to PMS model and includes minor updates;
- content of the table in section *3.3. Expression of strength* (patterns table) was updated;
- examples were added in section *3.3.13. Multidose vial*;
- section *3.4. Medicinal Product with multiple pharmaceutical products* medicinal product composed of two pharmaceutical products with two different administrable dose forms and manufactured dose; medicinal product composed of one package item, several manufactured items and pharmaceutical products with the same active substances, but with a different manufactured/administrable dose form;
  - Section *3.7. Shelf Life and Storage Conditions*,
  - *5. Examples of submission of attached document*;
- updated contents of the table in section *3.5. Alignment of Manufactured Item Quantity, Unit of Presentation and Pack Size* (column Manufactured Item (MI) - Quantity);

- updated section *4. Relationship between PMS ID, MPIDs and PCIDs.*

1. Introduction

1.1. Context

The International Organisation for Standardisation (ISO), identification of medicinal products (IDMP) standards specify the use of standardised definitions for the identification and description of medicinal products for human use. The purpose of these standards is to facilitate the reliable exchange of medicinal product information in a robust and consistent manner, by providing a common product 'language' for stakeholders to use in their interactions.

The specific application of the IDMP standards for human medicinal products at the European Union and European Economic Area are described in ***EU IG Chapter 2 – Data elements for the electronic submission of information on medicinal products for human use***. This includes information on what medicinal product information (data fields) are applicable and the associated business rules, data types and conformance governing the submission of the product information. Therefore, EU IG Chapter 2 should be considered as the main reference document while preparing a medicinal product submission of products that fall under the scope of Article 57(2) of Regulation (EC) No 726/2004, as amended by Regulation (EU) 1235/2010 and Regulation (EU) 1027/2012.

While ***EU IG Chapter 2 – Data elements for the electronic submission of information on medicinal products for human use*** provides general examples for each specific data type relevant to the implementation of the Product Management Service (PMS), the European Medicines Agency (EMA), upon consultation with different stakeholders (representatives of marketing authorisation holders and sponsors, national competent authorities, industry associations, international public organisations and software vendors) through the SPOR Task Force (SPOR TF), has identified the need to set up a specific document describing examples in more detail and tackling the interpretation of IDMP standards for a diverse range of medicinal products.

1.2. Scope of this guidance

This document provides detailed guidance on the interpretation of IDMP standards in the European regulatory framework with the provision of practical examples aiming to complement the understanding and narrative of ***EU IG Chapter 2 – Data elements for the electronic submission of information on medicinal products for human use:***

- real medicinal product examples of different nature are described with graphical representations in order to include the full data-model foreseen for implementation of PMS;
- focus examples on specific domains of the PMS data model for which the interpretation of IDMP and business rules described in ***EU IG*** **Chapter 2 -** ***Data elements for the electronic submission of information on medicinal products for human use*** may be challenging due to the different nature of medicinal products types are also included.

This chapter on practical examples is expected to be a living document with additional examples or corrections being included as the experience of the European Medicines Regulatory network and marketing authorisation holders with IDMP standards increases.

1.3. Principles

In addition, the following principles must be taken into consideration before using this guidance:

- The real examples included in this guidance contain information available in the public domain through different regulatory documents [e.g., SmPCs, European Public Assessment Reports (EPAR), national competent authority databases] which is not considered to be of confidential nature. The data provided within this chapter may not be up-to-date and is provided for illustration purposes only.
- For confidentiality reasons, the data provided in these examples derive from the publicly available SmPCs as authorised. However, to submit a new product entity in PMS, data should be collected based on the principles stated in sections *Submission of medicinal product data using FHIR*, *4. Packaged medicinal product* and *6. Pharmaceutical product* of **EU IG Chapter 2 - Data elements for the electronic submission of information on medicinal products for human use** and as illustrated in section *1.3.1.* of this chapter, when applicable.
- Some data elements included in EU IG Chapter 2 qualify as restricted data not available in the public domain (e.g., certain manufacturing operations). In these cases, "dummy" data has been included to ensure practical examples serve the educational purpose and are complete. Dummy data is highlighted using red text.
- Graphical examples include data elements with values including text for informative purposes and for codable data types, the RMS/OMS/SMS code which is the key information in the FHIR message generation needed for submission.
- A colour classification is used across all graphical representations categorising data elements in seven main groups in line with ISO IDMP standards (Yellow – Medicinal Product, Grey – Manufacturer / Organisations, Green – Marketing Authorisation, Orange – Ingredient, Violet – Clinical Particulars, Pink – Pharmaceutical Product, Blue - Packaged Medicinal Product).
- The development of PMS is in progress and is linked to the new creation or update of controlled vocabularies in SPOR Referentials Management Service (RMS). Therefore, this guidance marks missing data with a red cross "X" e.g., in case where the value might be dependent upon a new RMS vocabulary which has not yet been created. This is expected to be corrected in future versions of this guidance.
- Practical examples include product information available at the time of drafting of this document. Implicitly product information contained in this guidance will be outdated as time passes and may be outdated at the time of publication. The product information included in this guide shall not be used for any other purpose than for educational purposes regarding the EU implementation of PMS and IDMP.

1.3.1. **Public Documents (e.g., SmPC) and Module 3 information**

This section illustrates, in accordance with sections *4. Packaged medicinal product* and *6. Pharmaceutical product* of **Chapter 2 - Data elements for the electronic submission of information on medicinal products for human use**, the harmonization of legacy product data resulting from the data load from XEVMPD to PMS and the different level of detail reported in various authorised SmPCs across EU countries, and/or between SmPC and module 3, for the "same" authorised medicinal product.

Topic	Topic description
Description of the challenge	How to express/align product data in PMS in case of misalignment across the SmPC and Relevant sections in Module 3 – Quality. Applicable to any medicinal product entry already available in PMS, following the data load from XEVMPD to PMS database (legacy product data).
Chapter 2 References	Submission of medicinal product data using FHIR 4. Packaged medicinal product 6. Pharmaceutical product
Out of scope	Not applicable to any new medicinal product entity created in PMS and referring to authorised medicinal products via FHIR message (i.e., following completion of the MAA).
Additional reference(s)	n/a

As stated in the above-mentioned sections of Chapter 2, the contents of each document [i.e., Module 1.2 – Electronic Application form (eAF), Relevant sections in Module 3 – Quality, Summary of Product Characteristics (SmPC)] supporting the regulatory process must be aligned, where applicable, to ensure the discrepancies between the documents are minimized. The content should enhance the quality of the product data reported in PMS.

This principle is applicable to any new authorised medicinal product.

However, for medicinal products authorised prior to the implementation of PMS, hence subject of the data load from XEVMPD to PMS database (legacy product data), the following instances may occur:

- different levels of details, for the same medicinal product, across SmPC(s);
- different expressions of the basis of strengths;
- lack of uniformity in the excipients list in different SmPC(s) and/or in the relevant sections of Module 3;
- different phrasing or way of presenting the information (i.e., due to national requirements).

Each of the scenarios listed above may lead to uncertainty on how to adequately populate the PMS data elements and align the product data despite the differences in the relevant product documentation.

The two examples below provide further clarifications on how legacy medicinal product information should be aligned and reported in PMS.

1.3.1.1. Example 1: Different level of completeness in the national SmPCs

Contents of the current SmPC(s):

This example compares the content of two SmPC(s) from two different member states for the same authorised medicinal product

SmPC 1:

Powder for reconstitution <<Vaccine ABC >> is supplied as a white pellet in a vial (Type I neutral glass) with stoppers (bromobutyl rubber) and overcaps with flip-off tops (aluminium), containing one dose. Solvent for reconstitution: the diluent (Sterile Saline Solution (0.9%)), when provided, is a clear and colourless liquid in a glass ampoule or pre-filled syringe. The pre-filled syringe (Type I glass) contains 0.5 ml, with a plunger stopper (rubber butyl). The green, 38mm, 21-gauge needle has been provided for reconstitution of the ABC vaccine. The blue, 25mm, 23-gauge needle has been provided for administration of the ABC vaccine. This vaccine needs to be injected to the appropriate depth in order for it to be effective. Choose the most appropriate needle for your patient to ensure the vaccine reaches the correct tissue as specified in section 4.2 (Posology and Method of Administration). If the needle supplied for administration is not appropriate for your patient, a different needle can be used.

SmPC 2:

The lyophilised ABC vaccine is presented as a white powder in a type I glass vial. The solvent is a clear and colourless liquid in a glass ampoule or syringe. Pack sizes of 1 with or without needles

Expected Result:

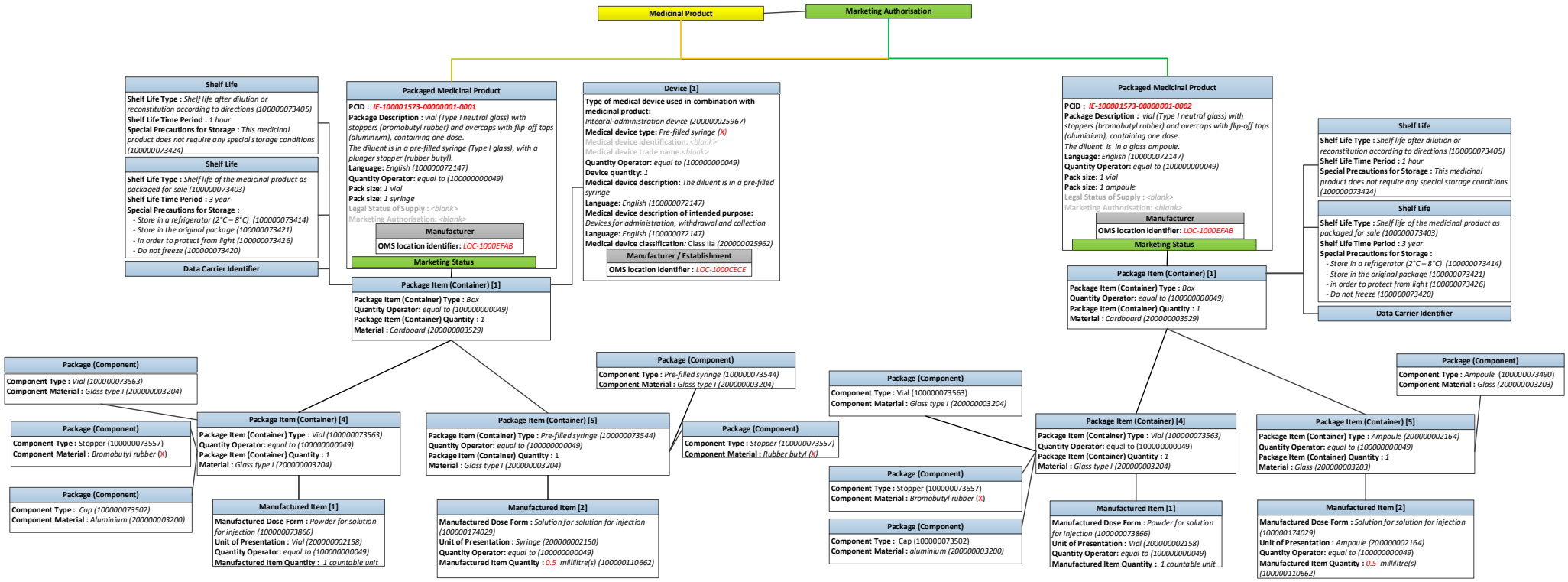
The medicinal product structured data should be the same based on the most granular level of details included in the SmPC.

The product data are expected to be populated by including the aligned information in PMS based on the data fields described in EU IG Chapter 2.

To manage this case, the alignment is based on the content of the Dossier. It is expected to refer to the information present in the SmPC(s) and align the data with the values available in Module 3, without adding complexity and ensuring confidentiality. The information contained in the first SmPC is aligned with Module 3 information, consequently, in this case data have been aligned on the first SmPC.

Of note:

- the confidential information has been anonymized (invented data are used);
- data fields which are not part of the PMS implementation are not displayed in the result here below, even if defined in ISO. Only the data elements defined in **EU IG Chapter 2 - Data elements for the electronic submission of information on medicinal products for human use** are available and must be populated with the related value(s).

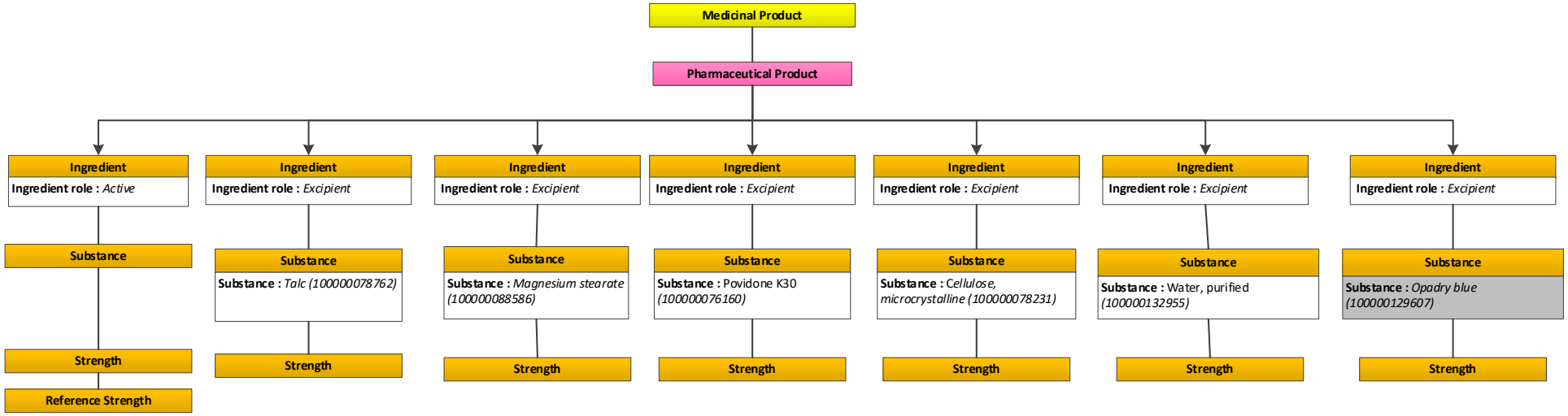

Medicinal Product
Marketing Authorisation
Shelf Life
Shelf Life Type : Shelf life after dilution or reconstitution according to directions (100000073405)
Shelf Life Time Period : 1 hour
Special Precautions for Storage : This medicinal product does not require any special storage conditions (100000073424)
Shelf Life
Shelf Life Type : Shelf life of the medicinal product as packaged for sale (100000073403)
Shelf Life Time Period : 3 year
Special Precautions for Storage :
- Store in a refrigerator (2°C – 8°C) (100000073414)
- Store in the original package (100000073421)
- in order to protect from light (100000073426)
- Do not freeze (100000073420)
Data Carrier Identifier
Packaged Medicinal Product
PCID : IE-100001573-00000001-0001
Package Description : vial (Type I neutral glass) with stoppers (bromobutyl rubber) and overcaps with flip-off tops (aluminium), containing one dose.
The diluent is in a pre-filled syringe (Type I glass), with a plunger stopper (rubber butyl).
Language: English (100000072147)
Quantity Operator: equal to (100000000049)
Pack size: 1 vial
Pack size: 1 syringe
Legal Status of Supply : <blank>
Marketing Authorisation: <blank>
Manufacturer
OMS location identifier: LOC-1000EFAB
Marketing Status
Package Item (Container) [1]
Package Item (Container) Type : Box
Quantity Operator: equal to (100000000049)
Package Item (Container) Quantity : 1
Material : Cardboard (200000003529)
Device [1]
Type of medical device used in combination with medicinal product:
Integral-administration device (200000025967)
Medical device type: Pre-filled syringe (X)
Medical device identification: <blank>
Medical device trade name:<blank>
Quantity Operator: equal to (100000000049)
Device quantity: 1
Medical device description: The diluent is in a pre-filled syringe
Language: English (100000072147)
Medical device description of intended purpose:
Devices for administration, withdrawal and collection
Language: English (100000072147)
Medical device classification: Class IIa (200000025962)
Manufacturer / Establishment
OMS location identifier : LOC-1000CECE
Packaged Medicinal Product
PCID : IE-100001573-00000001-0002
Package Description : vial (Type I neutral glass) with stoppers (bromobutyl rubber) and overcaps with flip-off tops (aluminium), containing one dose.
The diluent is in a glass ampoule.
Language: English (100000072147)
Quantity Operator: equal to (100000000049)
Pack size: 1 vial
Pack size: 1 ampoule
Legal Status of Supply : <blank>
Marketing Authorisation: <blank>
Manufacturer
OMS location identifier: LOC-1000EFAB
Marketing Status
Package Item (Container) [1]
Package Item (Container) Type : Box
Quantity Operator: equal to (100000000049)
Package Item (Container) Quantity : 1
Material : Cardboard (200000003529)
Shelf Life
Shelf Life Type : Shelf life after dilution or reconstitution according to directions (100000073405)
Shelf Life Time Period : 1 hour
Special Precautions for Storage : This medicinal product does not require any special storage conditions (100000073424)
Shelf Life
Shelf Life Type : Shelf life of the medicinal product as packaged for sale (100000073403)
Shelf Life Time Period : 3 year
Special Precautions for Storage :
- Store in a refrigerator (2°C – 8°C) (100000073414)
- Store in the original package (100000073421)
- in order to protect from light (100000073426)
- Do not freeze (100000073420)
Data Carrier Identifier
Package (Component)
Component Type : Vial (100000073563)
Component Material : Glass type I (200000003204)
Package (Component)
Component Type : Stopper (100000073557)
Component Material : Bromobutyl rubber (X)
Package (Component)
Component Type : Cap (100000073502)
Component Material : Aluminium (200000003200)
Package Item (Container) [4]
Package Item (Container) Type : Vial (100000073563)
Quantity Operator: equal to (100000000049)
Package Item (Container) Quantity : 1
Material : Glass type I (200000003204)
Manufactured Item [1]
Manufactured Dose Form : Powder for solution for injection (100000073866)
Unit of Presentation : Vial (200000002158)
Quantity Operator: equal to (100000000049)
Manufactured Item Quantity : 1 countable unit
Package Item (Container) [5]
Package Item (Container) Type : Pre-filled syringe (100000073544)
Quantity Operator: equal to (100000000049)
Package Item (Container) Quantity : 1
Material : Glass type I (200000003204)
Manufactured Item [2]
Manufactured Dose Form : Solution for solution for injection (10000014029)
Unit of Presentation : Syringe (200000002150)
Quantity Operator: equal to (100000000049)
Manufactured Item Quantity : 0.5 millilitre(s) (100000110662)
Package (Component)
Component Type : Pre-filled syringe (100000073544)
Component Material : Glass type I (200000003204)
Package (Component)
Component Type : Stopper (100000073557)
Component Material : Rubber butyl (X)
Package (Component)
Component Type : Vial (100000073563)
Component Material : Glass type I (200000003204)
Package (Component)
Component Type : Stopper (100000073557)
Component Material : Bromobutyl rubber (X)
Package (Component)
Component Type : Cap (100000073502)
Component Material : aluminium (200000003200)
Package Item (Container) [4]
Package Item (Container) Type : Vial (100000073563)
Quantity Operator: equal to (100000000049)
Package Item (Container) Quantity : 1
Material : Glass type I (200000003204)
Manufactured Item [1]
Manufactured Dose Form : Powder for solution for injection (100000073866)
Unit of Presentation : Vial (200000002158)
Quantity Operator: equal to (100000000049)
Manufactured Item Quantity : 1 countable unit
Package (Component)
Component Type : Ampoule (200000002164)
Component Material : Glass (200000003203)
Package Item (Container) [5]
Package Item (Container) Type : Ampoule (200000002164)
Quantity Operator: equal to (100000000049)
Package Item (Container) Quantity : 1
Material : Glass (200000003203)
Manufactured Item [2]
Manufactured Dose Form : Solution for solution for injection (100000174029)
Unit of Presentation : Ampoule (200000002164)
Quantity Operator: equal to (100000000049)
Manufactured Item Quantity : 0.5 millilitre(s) (100000110662)

1.3.1.2. Example 2: Different granularity of information across national SmPC

SmPC AT	SmPC BE+LU	SmPC FR	SmPC DE	SmPC IT
Active substance	*Active substance*	*Active substance*	*Active substance*	*Active substance*
Talc	Talc	Talc	Talc	Talc
Magnesium stearate	Magnesium stearate	Magnesium stearate	Magnesium stearate (Ph.Eur.)	Magnesium stearate
Povidone K30	Povidone/Polyvidone	Povidone K30	Povidone K30	Povidone K30
Microcrystalline cellulose	Microcrystalline cellulose	Microcrystalline cellulose	Microcrystalline cellulose	Microcrystalline cellulose
	Purified water		Purified water	
Colouring agents (E132, E171)	Opadry blue (E132)	Opadry YS-1-4215		Opadry YS-1-4215
		Hypromellose	Hypromellose	
		Titanium dioxide (E171)	Titanium dioxide (E171)	
		Macrogol 8000	Macrogol 8000	
		Aluminium lacquer of indigotine	Indigocarmin Aluminium Salt (E132)	

Of note:

- information is expected to be aligned based on the dossier content;
- for this example, we focus only on the qualitative composition which is not described in the same way across the different SmPC. For reason of confidentiality, Module 3 data is not included;
- the Substance Management Service (SMS) ID of the relevant substance ingredient as registered in SMS should be selected in PMS. This SMS ID references the substance name registered as the preferred term (PT) and can be associated to one or more synonyms in SMS. If a SPOR user performs a search using a registered synonym for a PT, the relevant PT will always appear in PMS. This principle applies to any substance.



2. Full model examples

This section describes how medicinal product information is completed in accordance with IDMP standards for two real examples of medicinal products in the European Union at the time of drafting of this guidance.

These examples aim to show, with a graphical representation, how medicinal product information is completed based on the intrinsic nature of these products by following the business rules, data elements and conformance as laid down in ***EU IG* Chapter 2 – *Data elements for the electronic submission of information on medicinal products for human use***. Therefore, users must follow **EU IG Chapter 2** as the main reference to complete their submission and should follow the practical example in this guide to assist them.

The selected examples are the following:

- Losec Control 20 mg gastro-resistant tablets – SmPC;
- Hiberix. Haemophilus Type b (Hib) vaccines. Powder and Solvent for Solution for Injection – SmPC

For each product example, the SmPC is the main source of the medicinal product data. A link to the SmPC is provided to add clarity. Sections of the SmPC content are highlighted in different colours corresponding with the colours assigned to the seven main groups (Yellow – Medicinal Product, Grey – Manufacturer / Organisations, Green – Marketing Authorisation, Orange – Ingredient, Violet – Clinical Particulars, Pink – Pharmaceutical Product, Blue - Packaged Medicinal Product) in line with ISO IDMP standards.

Since the product information is extensive, two graphical representations are included for each selected medicinal product example to help the user understand how to complete medicinal product data in PMS.

The user must consider the principles listed in section *1.3 – Principles when using these examples*. In addition, the following aspects must be considered when using the examples in this section:

- neither the simplified models nor the full model examples include all manufacturing operations and ingredients. However, they provide sufficient graphical information for users to understand relationships between attributes;
- ingredients of the medicinal products are completed separately and subsequently linked as applicable to the 'Pharmaceutical Product' and 'Manufactured item';
- SmPCs included in this guidance may be outdated and must not be used for any other purpose than for educational purposes regarding the EU implementation of PMS and IDMP.

2.1. Simplified representation

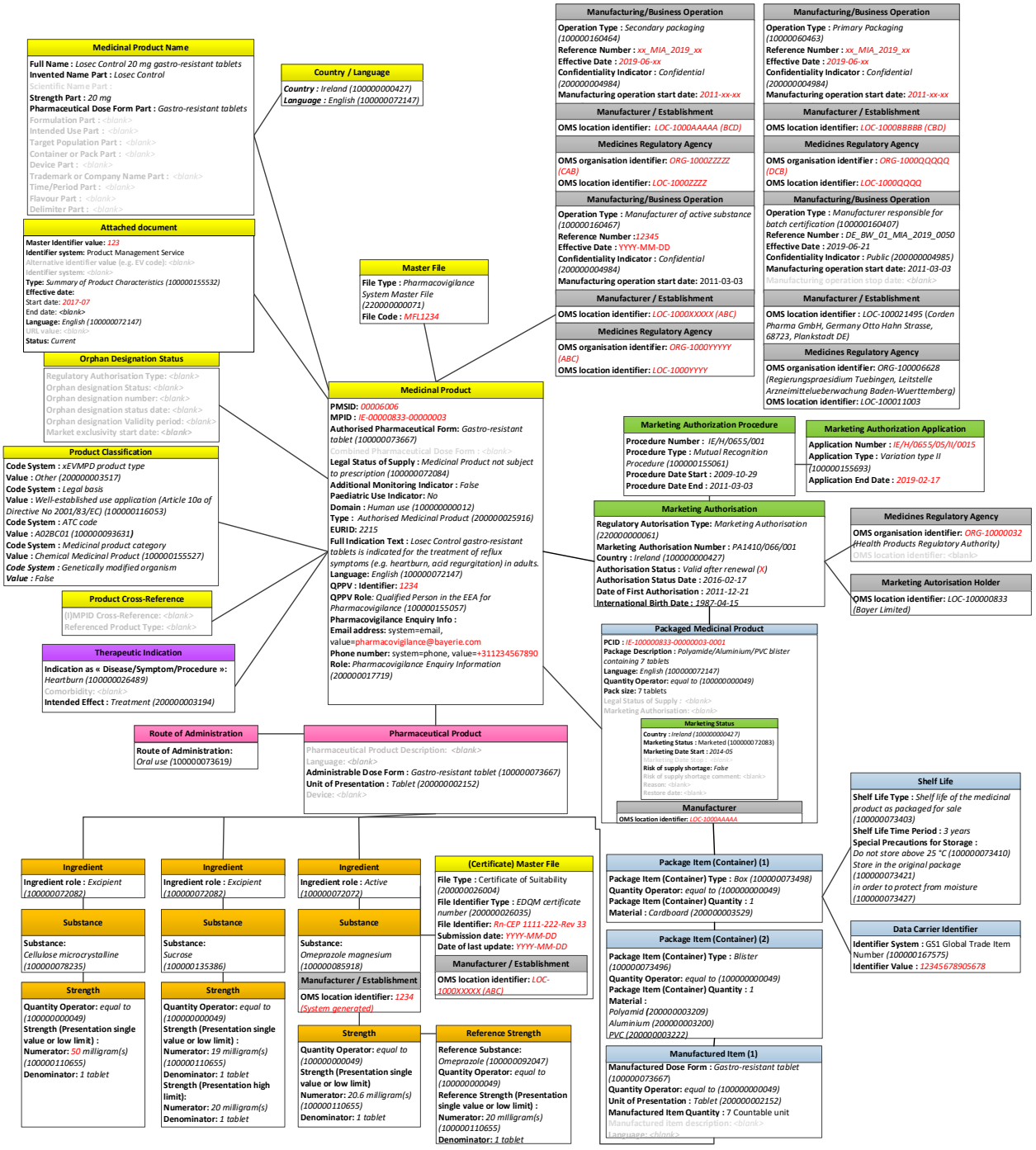
Due to the size of the full data model certain diagrams show simplified representations to render them legible for the purposes of this document. Complete representations are included as annex to this document.

Simplified representation diagrams include only a **subset** of data fields from the full data model as reflected in *Figure 1: Iteration 1 ISO IDMP information model for authorised medicinal products with PMS extensions* ***EU IG* Chapter 2 – *Data elements for the electronic submission of information on medicinal products for human use.***

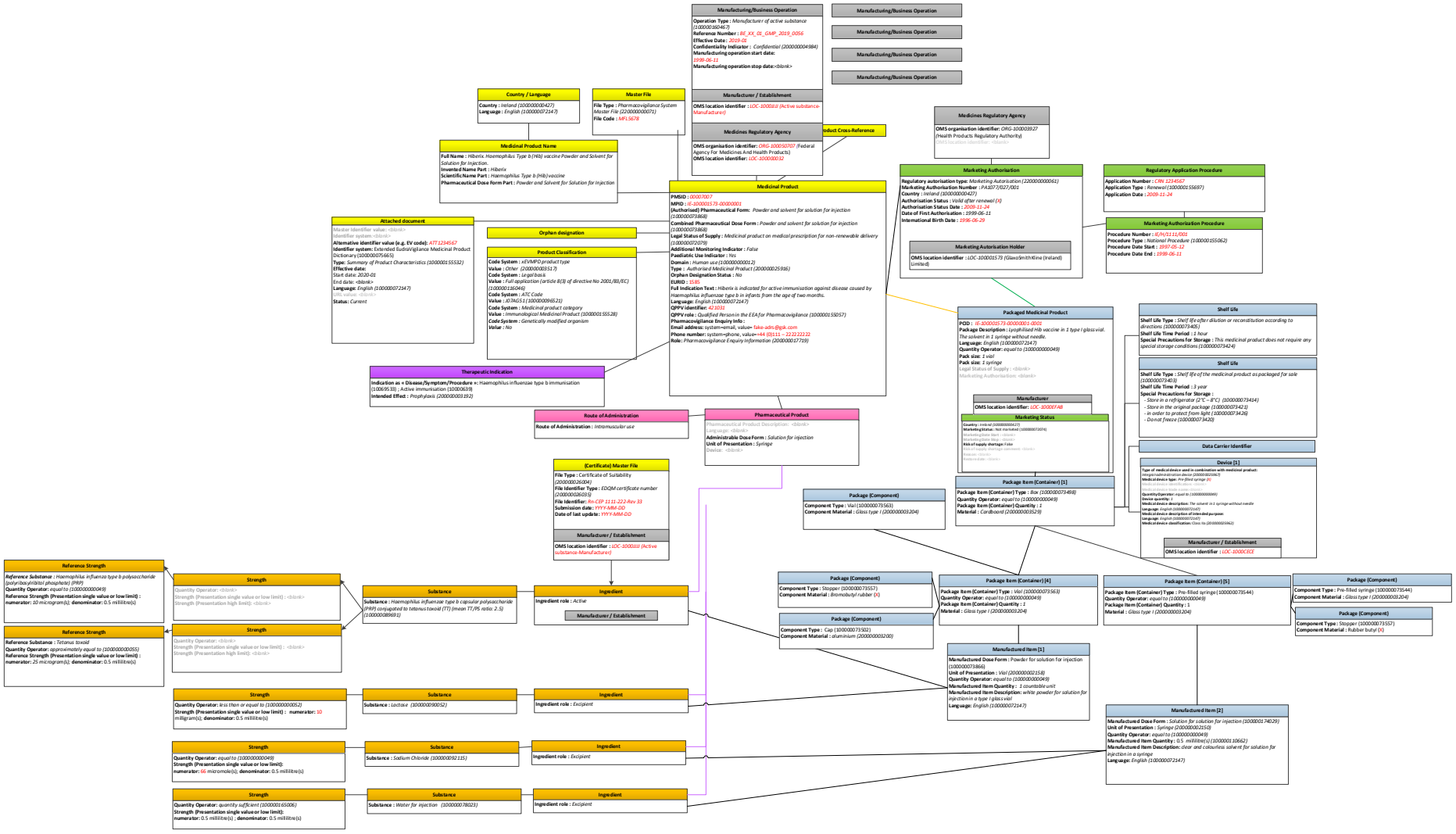
Simplified representations are designed to provide a visual snapshot of the key medicinal product data and data relationship among data groups.

Note that, simplified presentations do not include all packaged medicinal products due to size constraints. 'Packaged medicinal product' section must be repeated for each package approved in the product.

Example 1 - Losec Control 20mg gastro-resistant tablets



Example 2 - Hiberix. Haemophilus Type b (Hib) vaccines. Powder and Solvent for Solution for Injection



2.2. Complete representation

Complete representation diagrams include all data fields included in the full data model implemented in PMS and as reflected in *Figure 1: Iteration 1 ISO IDMP information model for authorised medicinal products with PMS extensions* ***EU IG*** **Chapter 2 -** ***Data elements for the electronic submission of information on medicinal products for human use*****.**

Complete representations are being published separately as annex I to this document.

- Losec Control 20mg gastro-resistant tablets
- Hiberix. Haemophilus Type b (Hib) vaccines. Powder and Solvent for Solution for Injection

As a reminder, the user must consider the principles stated in section 1.3 before interpreting or using these examples.

3. Section-specific examples

This section describes how medicinal product information is completed in accordance with IDMP standards with focus on specific sections of ***EU IG* Chapter 2 – *Data elements for the electronic submission of information on medicinal products for human use*.** This section aims to:

- provide practical examples on specific sections of EU IG Chapter 2, where the data submission of medicinal product information and the interpretation of IDMP standards is complex and stakeholders can benefit from additional clarification and practical examples;
- provide practical examples on specific sections of EU IG Chapter 2, where the data submission of certain medicinal product types is different and more complex (e.g., products with non-frequent dose forms, products with multiple pharmaceutical forms) rendering the data structure more complex as per IDMP standard.

The SPOR TF identified the following product information areas as requiring additional examples:

Section in EU IG Chapter 2	Description
1.7.	Legal status of supply
1.19.	Product Cross-reference
5.5., 5.5.2.	Expression of strength
4.11., 6	Medicinal products with multiple manufactured items and pharmaceutical products
4.11.2., 4.11.1., 4.4.	Alignment of Manufactured Item Quantity, Unit of Presentation and Pack Size
4.10, 4.8.	Medical device which is immediate Package item container
4.12.	Shelf Life/Storage conditions

Users must consider the principles listed in Section *1.3 – Principles* when using these examples. In addition, the following aspects must be considered:

- additional reading materials and references are suggested for each of the topics covered in this section. However, these references are not exhaustive and other/additional regulatory guidelines may apply. Users must complete medicinal product data as per submitted/approved or official regulatory documents [SmPC, electronic application form (eAF), dossier modules];
- EU IG Chapter 8 – Practical examples is expected to be a living document with additional examples being included over time. Current examples may be modified as the European Regulatory Network obtains additional experience on the practical implementation of IDMP with a broad range of medicinal products.

3.1. Legal Status of Supply

This section illustrates the rules for expressing the legal status of supply when completing medicinal product information in accordance with sections *1.7 – Legal status of supply* (medicinal product level) and *4.5 – Legal status of supply* (packaged medicinal product level) of ***EU IG* Chapter 2 – *Data elements for the electronic submission of information on medicinal products for human use***. Particularly, this section highlights differentiation when legal status of supply is defined at medicinal product level or at package level.

Topic	Topic description
Description of the challenge	The presence of the field 'Legal status of supply' at medicinal product level and packaged medicinal product level requires clarification to users. The rules on when to use the correct field 'Legal status of supply' with practical representation are included: • How to enter values for the 'Legal status of supply' of a product with a single legal status of supply. • How is the legal status of supply represented when different legal statuses apply in the same medicinal product depending on the pack size. E.g., over-the-counter (OTC) pack, and pack size only valid on prescription.
Chapter 2 References	1.7 – Legal Status of Supply 4.5 – Legal Status of Supply
Additional reference(s)	https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guideline-legal-status-supply-patient-centrally-authorised-medicinal-products_en.pdf RMS list: Legal Status for the Supply *Note: The information contained in these references is non-exhaustive. Companies should refer to all relevant European Union legislation and guidelines when drawing up applications and use the information in the SmPC and regulatory documents (e.g., eAF) to complete medicinal product data.*

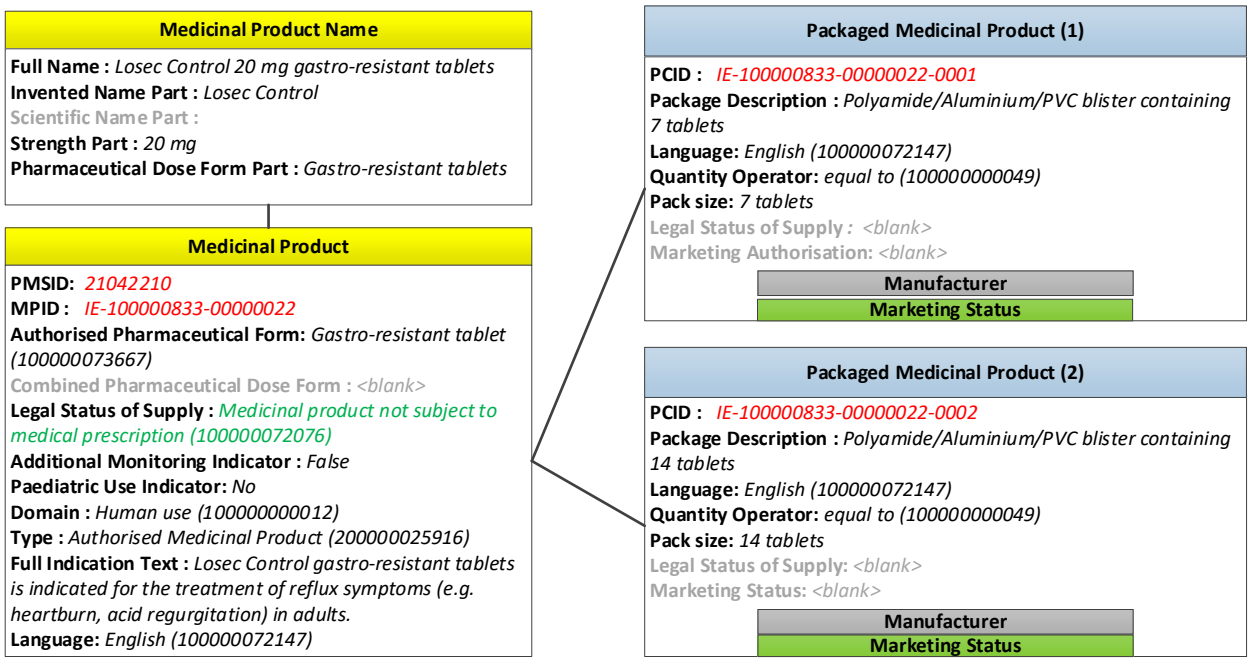
Legal status of supply of the medicinal product as authorised by the relevant competent authority must be provided as part of the medicinal product submission.

When the legal status of supply differs at package level (different legal status for different package sizes of the same medicinal product), this information at medicinal product level is to be completed with the term "Medicinal product subject to medical prescription exempt for some pack sizes" "". For those cases, the legal status of supply must be filled in as applicable at package level (see section *4.5 - Legal Status of Supply* at Package Medicinal Product Level).

- For **centrally authorised products (CAPs)**, the information on the applicable legal status can be retrieved from Annex II.B - CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE and from section 4.2 – Posology of the Product information.
- For **nationally authorised products (NAPs)**, this information can be retrieved from different sources; these include the Summary of Product Characteristics (SmPC), Package Leaflet (PL) or other annexes, the National Register of Medicinal Products etc.

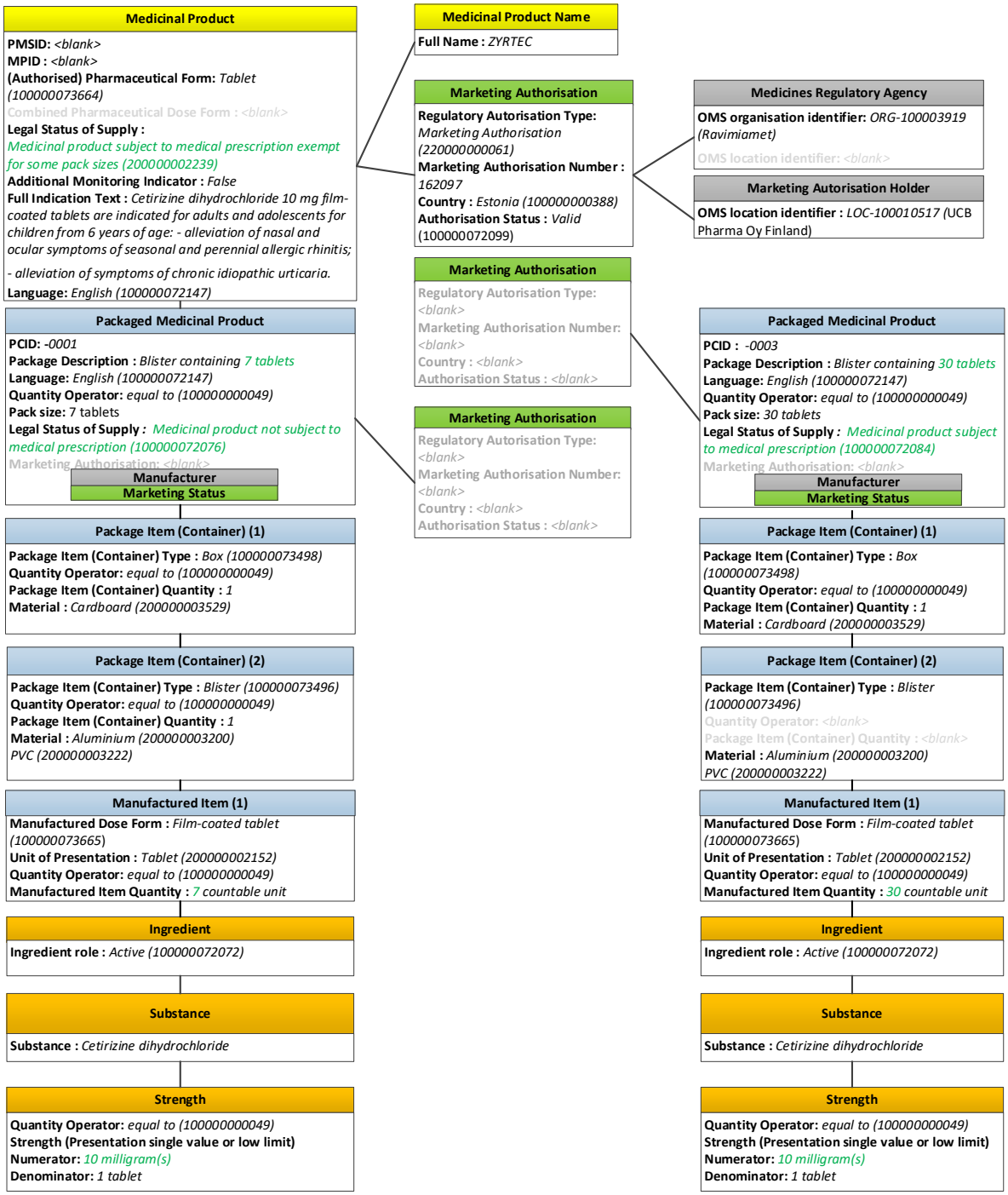
These differences are shown in the example below.***1. How to capture the legal status of supply of a product with a single legal status of supply***

Medicinal Product example: Losec control (Ireland) where the legal status of supply is the same for all pack sizes (OTC). Since the legal status of supply is the same across all packages, the same legal status of supply applies at medicinal product level (Losec Control 20 mg gastro-resistant tablets).



2. How is the legal status of supply represented when different legal statuses apply in the same medicinal product depending on the pack size? E.g., over-the-counter (OTC) pack, and pack size only valid on prescription.

Medicinal Product example: Zyrtec (Estonia), with pack sizes of 7 tablets over-the-counter (OTC) and 30 tablets available on prescription only. In this example, the legal status of supply differs across packaged medicinal products. Therefore, information on legal status of supply must be filled in as applicable in each packaged medicinal product. Legal status of supply at medicinal product level must be completed with the term "Medicinal product subject to medical prescription exempt for some pack sizes" "".


Medicinal Product
PMSID: <blank>
MPID : <blank>
(Authorised) Pharmaceutical Form: Tablet (100000073664)
Combined Pharmaceutical Dose Form : <blank>
Legal Status of Supply :
Medicinal product subject to medical prescription exempt for some pack sizes (200000002239)
Additional Monitoring Indicator : False
Full Indication Text : Cetirizine dihydrochloride 10 mg film-coated tablets are indicated for adults and adolescents for children from 6 years of age: - alleviation of nasal and ocular symptoms of seasonal and perennial allergic rhinitis; - alleviation of symptoms of chronic idiopathic urticaria.
Language: English (100000072147)
Medicinal Product Name
Full Name : ZYRTEC
Marketing Authorisation
Regulatory Autorisation Type: Marketing Authorisation (220000000061)
Marketing Authorisation Number : 162097
Country : Estonia (100000000388)
Authorisation Status : Valid (100000072099)
Medicines Regulatory Agency
OMS organisation identifier: ORG-100003919 (Ravimiamet)
OMS location identifier: <blank>
Marketing Autorisation Holder
OMS location identifier : LOC-100010517 (UCB Pharma Oy Finland)
Marketing Authorisation
Regulatory Autorisation Type: <blank>
Marketing Authorisation Number: <blank>
Country : <blank>
Authorisation Status : <blank>
Marketing Authorisation
Regulatory Autorisation Type: <blank>
Marketing Authorisation Number: <blank>
Country : <blank>
Authorisation Status : <blank>
Packaged Medicinal Product
PCID: -0001
Package Description : Blister containing 7 tablets
Language: English (100000072147)
Quantity Operator: equal to (100000000049)
Pack size: 7 tablets
Legal Status of Supply : Medicinal product not subject to medical prescription (100000072076)
Marketing Authorisation: <blank>
Manufacturer
Marketing Status
Packaged Medicinal Product
PCID : -0003
Package Description : Blister containing 30 tablets
Language: English (100000072147)
Quantity Operator: equal to (100000000049)
Pack size: 30 tablets
Legal Status of Supply : Medicinal product subject to medical prescription (100000072084)
Marketing Authorisation: <blank>
Manufacturer
Marketing Status
Package Item (Container) (1)
Package Item (Container) Type : Box (100000073498)
Quantity Operator: equal to (100000000049)
Package Item (Container) Quantity : 1
Material : Cardboard (200000003529)
Package Item (Container) (1)
Package Item (Container) Type : Box (100000073498)
Quantity Operator: equal to (100000000049)
Package Item (Container) Quantity : 1
Material : Cardboard (200000003529)
Package Item (Container) (2)
Package Item (Container) Type : Blister (100000073496)
Quantity Operator: equal to (100000000049)
Package Item (Container) Quantity : 1
Material : Aluminium (200000003200)
PVC (200000003222)
Package Item (Container) (2)
Package Item (Container) Type : Blister (100000073496)
Quantity Operator: <blank>
Package Item (Container) Quantity : <blank>
Material : Aluminium (200000003200)
PVC (200000003222)
Manufactured Item (1)
Manufactured Dose Form : Film-coated tablet (100000073665)
Unit of Presentation : Tablet (200000002152)
Quantity Operator: equal to (100000000049)
Manufactured Item Quantity : 7 countable unit
Manufactured Item (1)
Manufactured Dose Form : Film-coated tablet (100000073665)
Unit of Presentation : Tablet (200000002152)
Quantity Operator: equal to (100000000049)
Manufactured Item Quantity : 30 countable unit
Ingredient
Ingredient role : Active (100000072072)
Ingredient
Ingredient role : Active (100000072072)
Substance
Substance : Cetirizine dihydrochloride
Substance
Substance : Cetirizine dihydrochloride
Strength
Quantity Operator: equal to (100000000049)
Strength (Presentation single value or low limit)
Numerator: 10 milligram(s)
Denominator: 1 tablet
Strength
Quantity Operator: equal to (100000000049)
Strength (Presentation single value or low limit)
Numerator: 10 milligram(s)
Denominator: 1 tablet

3.2. Product Cross-Reference

EU IG* Chapter 2 – *Data elements for the electronic submission of information on medicinal products for human use requires the submission of 'Product Cross-Reference' information on a conditional basis. This section provides practical examples that demonstrate how cross-reference information for a medicinal product should be provided.

Topic	Topic description
Description of the challenges	• When is a cross-reference applicable? • Which PMS ID should be provided? • Should the PMS ID of the originator still be referred to if it has been withdrawn from the market?
Chapter 2 References	1.19. Product cross-reference 1.19.1 Product cross-reference type 1.19.2 Product Cross-Reference resource identifier
Out of scope	Medicinal product Parallel Distributed Investigational Medicinal Product Identifiers for iteration 1
Additional reference(s)	RMS list: Product Cross Reference Type *Note: The information contained in these references is non-exhaustive. Companies should refer to all relevant European Union legislation and guidelines when drawing up applications and use the information in the SmPC and regulatory documents (e.g., eAF) to complete medicinal product data.*

Product cross-reference triggered by the legal basis:

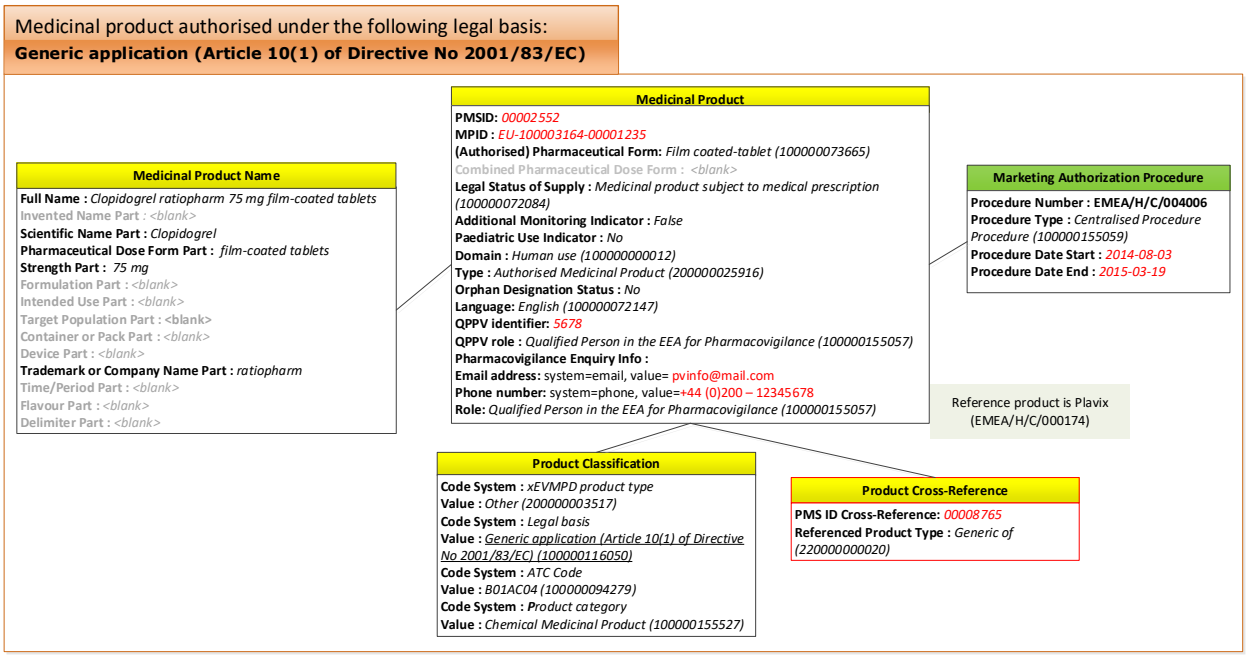
A product cross-reference may be necessary depending on the legal basis. The legal bases shown below trigger the need for cross-referencing, along with practical examples for each scenario. List of examples in this section:

1. Legal basis is generic application (Article 10(1) of Directive No 2001/83/EC)
    a. Clopidogrel ratiopharm
    b. Terlipressin acetate SUN
2. Legal basis is hybrid application (Article 10(3) of Directive No 2001/83/EC)
    a. Xromi
3. Legal basis is similar biological application (Article 10(4) of Directive No 2001/83/EC)
    a. Semglee
4. Legal basis is informed consent application (Article 10(c) of Directive No 2001/83/EC)
    a. Roteas
    b. Adjupanrix
5. Duplicate applications of any legal basis submitted under Article 82(1) of Regulation (EC) No 726/2004
    a. Iblias
6. Imported medicinal product (Article 76(3) of Directive No 2001/83/EC)
    a. Imurel/Imuran

The RMS list "Product Cross-Reference Type" contains the possible values to be used. In the examples below, (X) indicates terms not yet available in RMS. Products must be referenced even when the originator product is no longer on the market. However, for older products, particularly those approved decades ago, it is possible that the reference product is no longer on the market nor present in PMS for it to be used as a reference. In this scenario, the attributes 1.19 - Product cross-reference must be left blank.

3.2.1. **Legal basis is generic application (Article 10(1) of Directive No 2001/83/EC)**

For generic applications the reference product PMS ID is indicated in the product cross reference and the RMS term "Generic of" (220000000020) selected as the Referenced Product Type. **Clopidogrel ratiopharm**

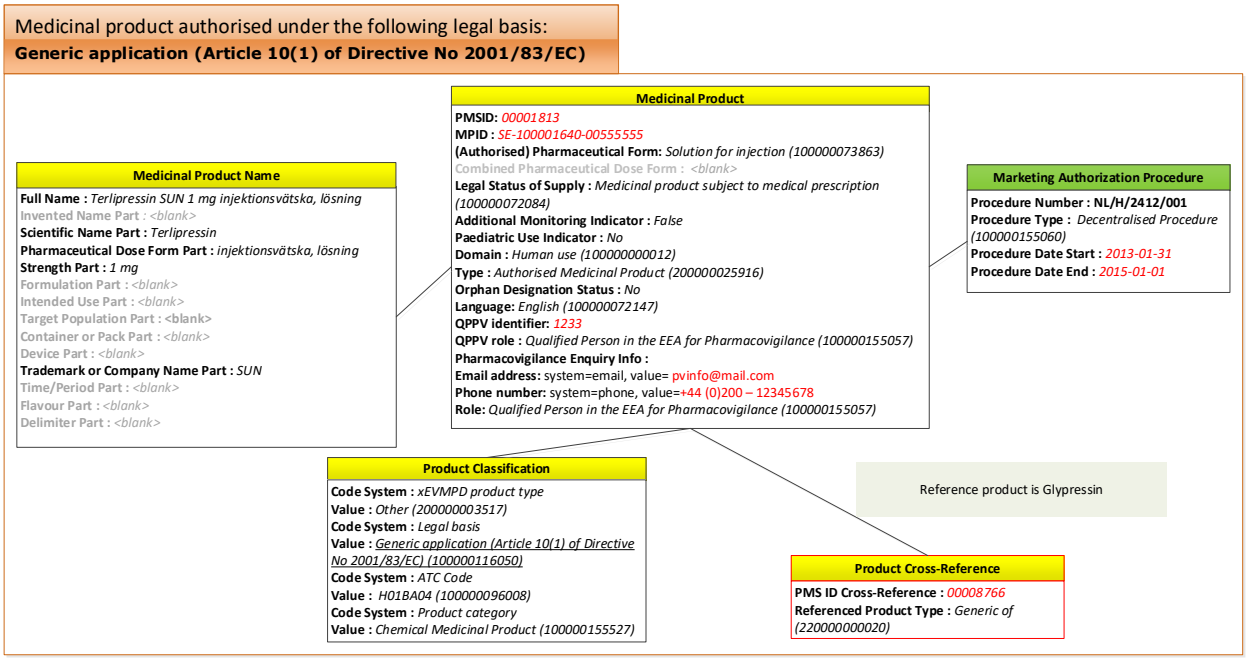


https://www.ema.europa.eu/en/medicines/human/EPAR/clopidogrel-ratiopharm

In this example, Plavix is the reference product and Clopidogrel ratiopharm is the generic.

Terlipressin acetate SUN

In this example, Glypressin is the reference product and Terlipressin acetate SUN is the generic.

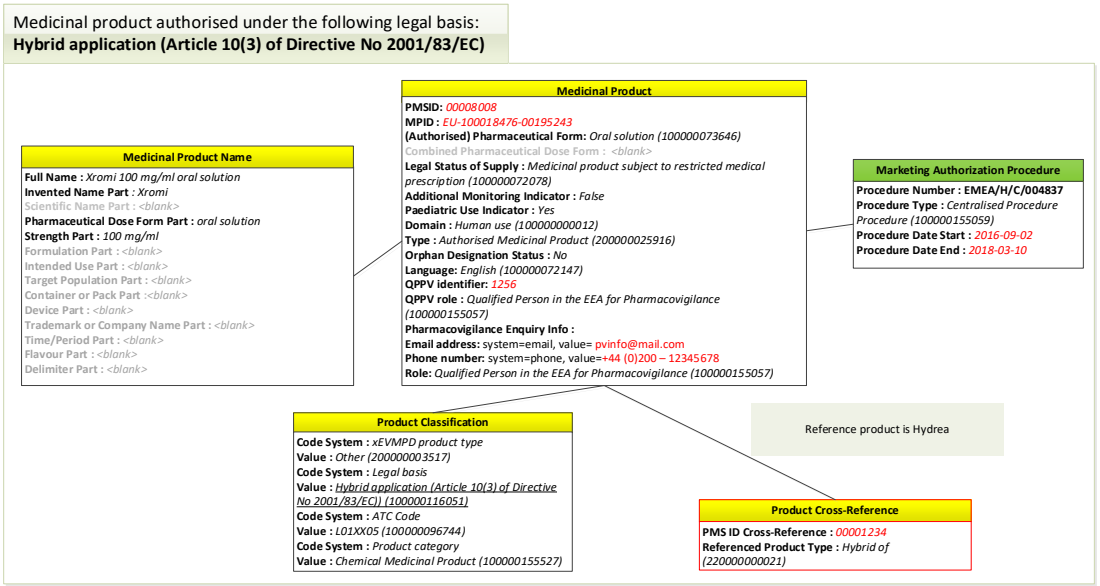


https://www.geneesmiddeleninformatiebank.nl/Pars/h110384.pdf

https://docetp.mpa.se/LMF/Terlipressin%20SUN%20solution%20for%20injection%20SmPC_09001bee807a73ff.pdf

3.2.2. **Legal basis is hybrid application (Article 10(3) of Directive No 2001/83/EC)**

For hybrid applications, the reference product PMS ID is indicated in the product cross reference and the RMS term "Hybrid of" (220000000021) selected as the Referenced Product Type. **Xromi**



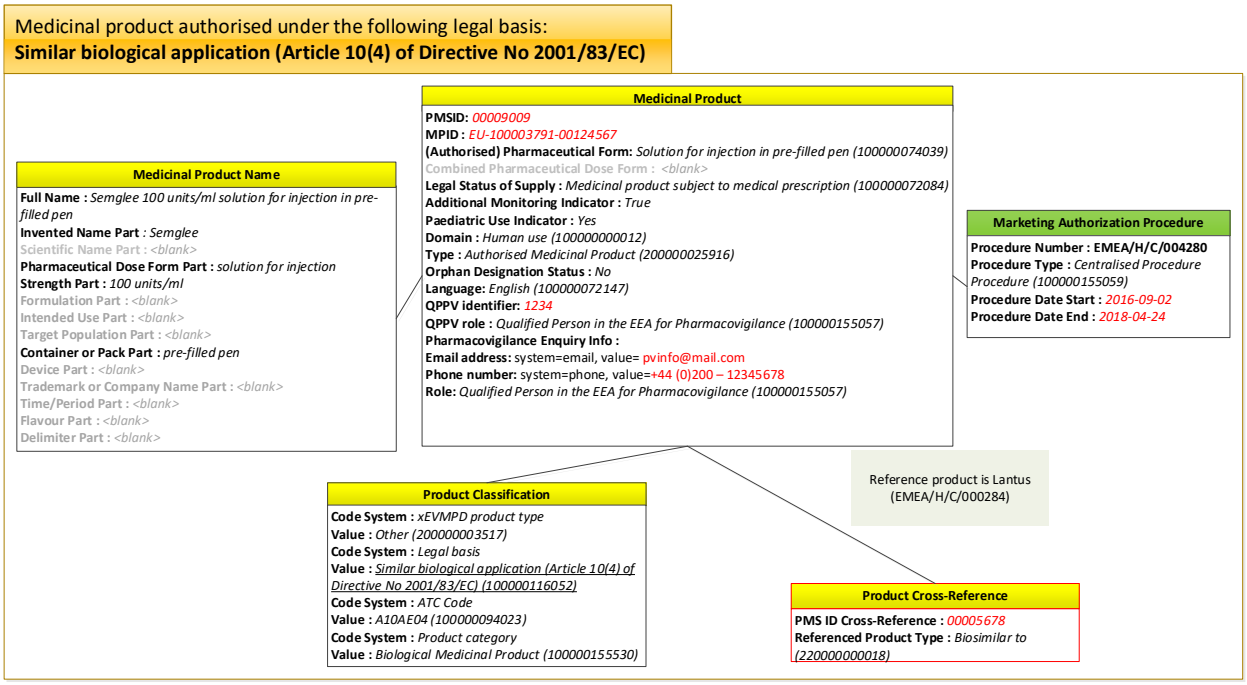
https://www.ema.europa.eu/en/medicines/human/EPAR/xromi

In this example, Hydrea is the reference product and Xromi is the hybrid.

3.2.3. **Legal basis is similar biological application (Article 10(4) of Directive No 2001/83/EC)**

For similar biological applications, the reference product PMS ID is indicated in the product cross reference and the RMS term "Biosimilar to" (220000000018) selected as the Referenced Product Type. **Semglee**

In this example, Lantus is the reference product and Semglee is the biosimilar.

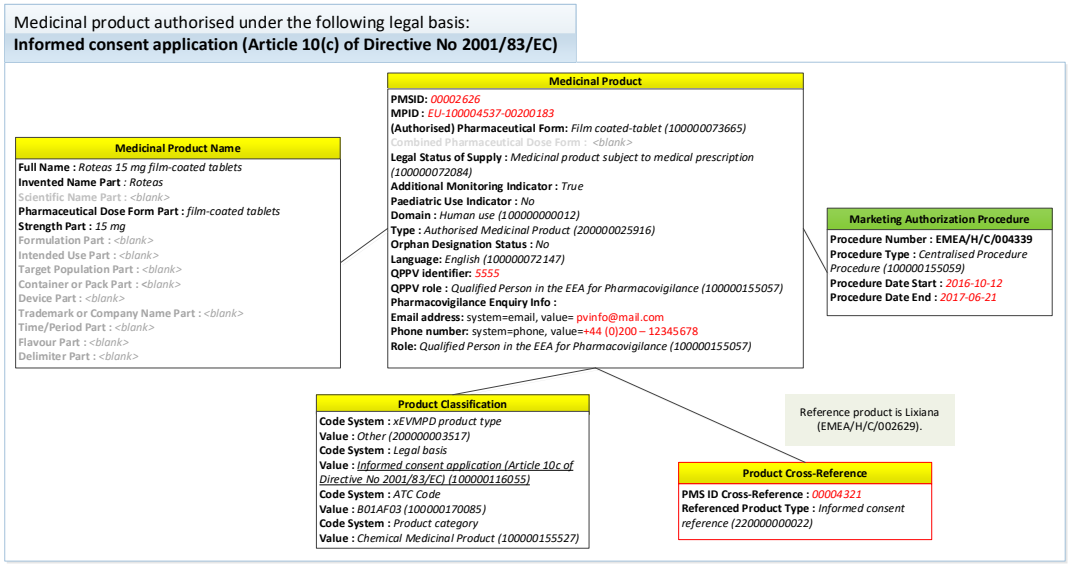


https://www.ema.europa.eu/en/medicines/human/EPAR/semglee

3.2.4. **Legal basis is informed consent application (Article 10(c) of Directive No 2001/83/EC)**

For informed consent applications, the reference product PMS ID is indicated in the product cross reference and the RMS term "Informed Consent reference" (220000000022) selected as the Referenced Product Type". **Roteas**

In this example, Lixiana is the reference product and Roteas is the product authorised under informed consent application.



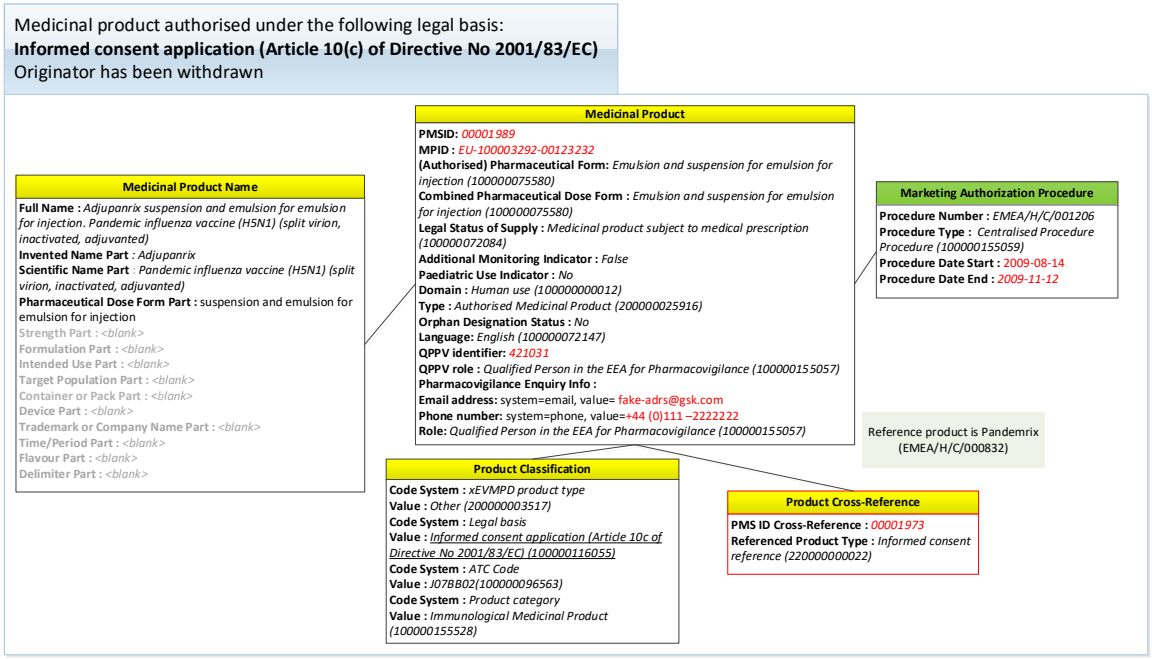
https://www.ema.europa.eu/en/medicines/human/EPAR/roteas

https://www.ema.europa.eu/en/documents/smop-initial/chmp-summary-positive-opinion-roteas_en.pdf

Adjupanrix

Product cross-reference should be included even when the originator product has been withdrawn from the market.

In the informed consent application example below for Adjupanrix, the originator product, Pandemrix has been withdrawn.

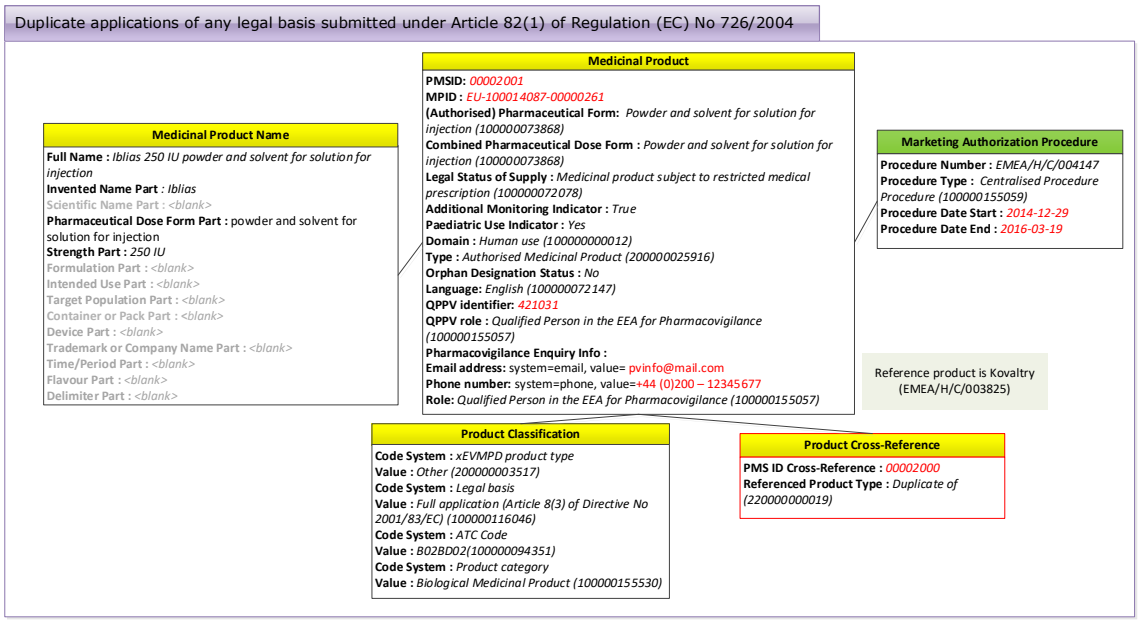


https://www.ema.europa.eu/en/documents/product-information/adjupanrix-previously-pandemic-influenza-vaccine-h5n1-split-virion-inactivated-adjuvanted_en.pdf

3.2.5. **Duplicate applications of any legal basis submitted under Article 82(1) of Regulation (EC) No 726/2004**

For duplicate applications, the reference product PMS ID is indicated in the product cross reference and the RMS term "Duplicate of" (220000000019) selected as the Referenced Product Type. **Iblias**

In this example, Kovaltry is the reference product and Iblias is the duplicate.



https://www.ema.europa.eu/en/medicines/human/EPAR/iblias

https://www.ema.europa.eu/en/medicines/human/EPAR/kovaltry

Product cross-reference triggered by an Imported Medicinal Product:

3.2.6. **Imported medicinal product (Article 76(3) of Directive No 2001/83/EC)**

A cross-reference to one or more medicinal products is to be made a part of the submission of a Parallel Imported Medicinal Product. If such scenario applies, two product cross-references must be included to complete the medicinal product information:

- Source Medicinal Product of Parallel Import: medicinal product authorised in a different country acting as source of the imported medicinal product in the destination country;
- Reference Medicinal Product of Parallel Import: medicinal product already authorised in the destination country and which serves as a reference for the parallel imported product intended to be imported into the destination country.

Source Medicinal Product of Parallel Import and Reference Medicinal Product of Parallel Import are products with marketing authorization which have been previously approved, and they are present in PMS database with their respective PMS ID.

A practical example of imported medicinal Product (**Imurel**) is described below:

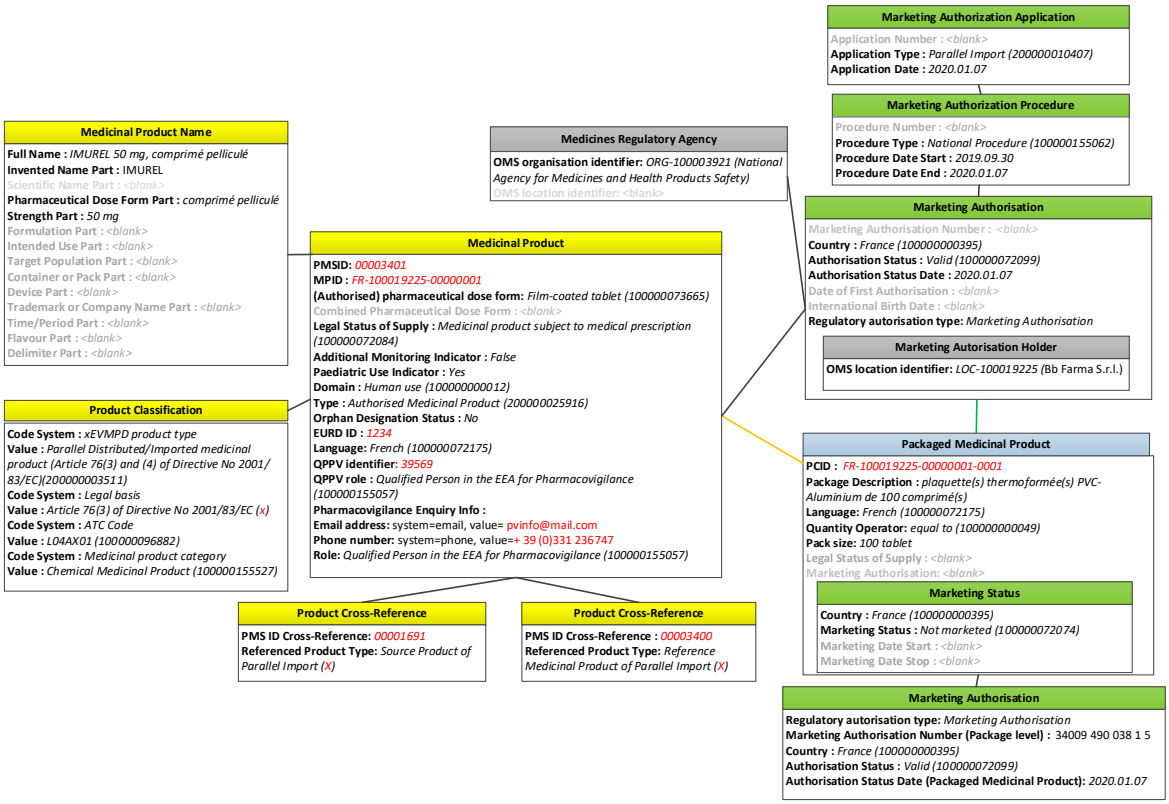
- ***Imuran Film-coated Tablets 50 mg*** (PMS ID: 00001691; MA n°: PA1691/003/003; MAH: Aspen Pharma Trading Limited) is a medicinal product authorized in **Ireland.** The product is packed by PVC/aluminium foil blister packs containing 100 film-coated tablets;

- ***IMUREL 50 mg, comprimé pelliculé*** (PMS ID: 00003400; MA n°: 34009 364 146 1 7, 34009 364 147 8 5, 34009 364 148 4 6; 34009 364 149 0 7; MAH: Aspen Pharma Trading Limited) is authorized in France with 4 marketing authorization numbers, including the MA n°34009 364 149 0 7 referring to the package containing 100 tablets in blister (PVC/Aluminium);
- ANSM has authorized the pharmaceutical company BB Farma S. r. l. based in Italy to the parallel import of the medicinal product *Imuran Film-coated Tablets 50 mg* from Ireland to France with the new French MA n° 34009 490 038 1 5;
- The imported product marketed in France by the MAH BB Farma S. r. l. is named *IMUREL 50 mg, comprimé pelliculé* (MA n° 34009 490 038 1 5; PMS ID: 00003401; MPID: FR-100019225-00000001) and corresponds to 100 tablets in blister (PVC/Aluminium).

Based on the above scenario, the Parallel Imported Medicinal Product *IMUREL 50 mg, comprimé pelliculé* (MA n° 34009 490 038 1 5/ Parallel Imported Notification Number; MPID: FR-100019225-00000001) is to be cross-referenced as follow:

- ***Imuran Film-coated Tablets 50 mg*** *(*PMS ID Cross-Reference*: 00001691)* corresponding to the **Source Medicinal Product** of Parallel Import;
- ***IMUREL 50 mg, comprimé pelliculé*** (PMS ID Cross-Reference: *00003400*) corresponding to the **Reference Medicinal Product** of Parallel Import.

It might be possible that the Member State authorizing the parallel import does not provide with a MA N° for this Medicinal product. Instead, a Parallel Imported Notification Number would be issued. In this case, this number should be reported in the relevant data field.



3.3. Expression of strength

This section provides guidance on how to record information on strength, and reference strength of active ingredients present in pharmaceutical products and manufactured items of medicinal products as per ***EU IG Chapter 2 – Data elements for the electronic submission of information on medicinal products for human use*.**

Currently there are different practices across the EU when it comes to expressing the strength in the labelling of medicinal products, especially for parenteral preparations, products with a multidose presentation and older products if both types to express the strength are included in the SmPC. These split views are well acknowledged by all the stakeholders and must be considered when completing this information.

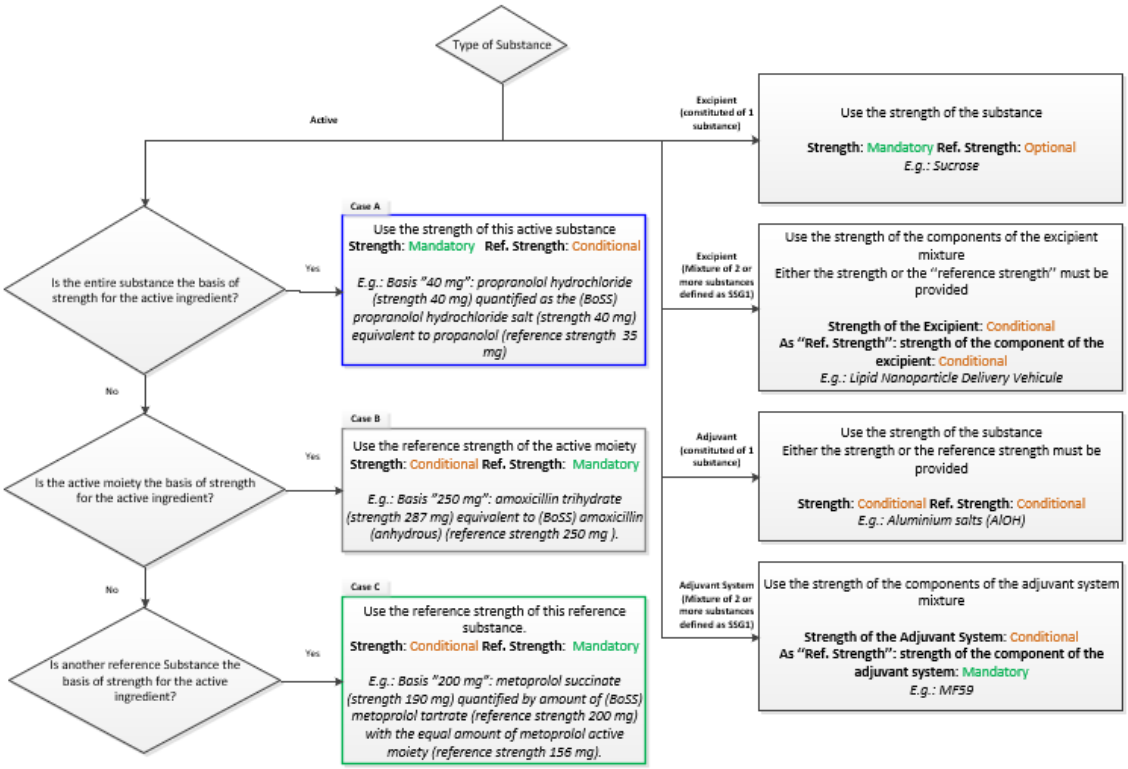
Overall, the purpose of this section is to provide examples of the most common ways to express the strength for different types of products and must not substitute or trigger a change on how strength is represented as a result of regulatory decisions taken on a case-by-case basis. In all cases, the information of strength as presented in the approved SmPC of the applicable medicinal product must be taken as a reference and should prevail over the examples presented below in case of differences.

Topic	Topic description
Description of the challenges	• How to express the ingredients' strengths in the 'Manufactured Item' and 'Pharmaceutical Product' entities. • Based on the product context, which type(s) of strength must be used? • Should the overfill be included in the manufactured item expression? • Can the same ingredients be re-used for both 'Manufactured item' and the 'Pharmaceutical Product'?
Chapter 2 References	5.5.2. Strength (quantitative composition) 5.5.3. Reference strength
Out of scope	Overview of the QRD guidance
Additional reference(s)	QRD recommendations on the expression of strength in the name of centrally authorised human medicinal products (as stated in section 1 of SPC, and in the name section of Labelling and PL) ISO 11615, Health informatics — Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated medicinal product information ISO/TS 20443, 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 *Note: The information contained in these references is non-exhaustive. Companies should refer to all relevant European Union legislation and **guidelines** when drawing up applications and used the information in the SmPC and regulatory documents (e.g., eAF) to complete medicinal product data.*

When expressing the strength of active ingredients, applicants and marketing authorisation holders should abide by the following principles:

- the SmPC and Module 3should be used as a main reference for expressing the strength in ingredients to be linked both to the manufactured item and pharmaceutical product;
-

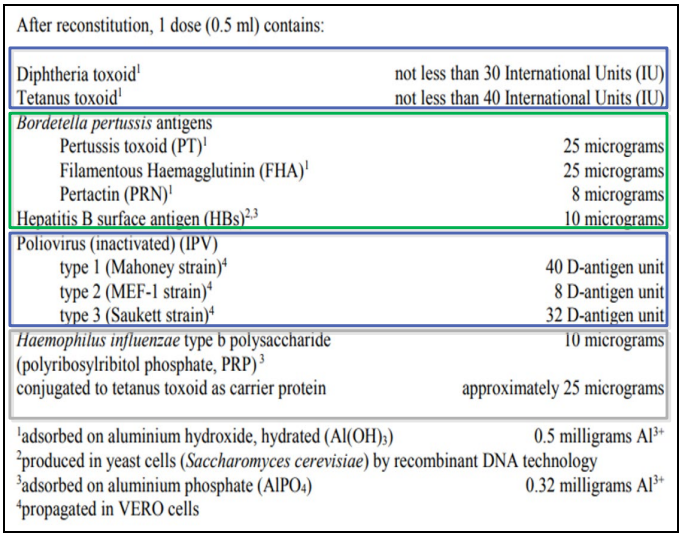
- The quantitative composition of the active ingredient should be expressed by means of Presentation strength and depending on cases Concentration strength. If the presentation strength is clearly stated in the relevant SmPC and/or Module 3, it shall be populated in addition to the concentration strength if both ways to express the strength are included in the SmPC/Module 3. the expression of the strength in the SmPC has been approved by a regulatory scientific assessment and therefore should be used in all cases as the main reference to express the strength. In case of differences between the strength expressed for a specific medicinal product in the SmPC and the guidance provided in Chapter 8 – Practical examples and QRD guidance on expression of strength, the information on the SmPC prevails;
- where the active ingredient is an ester or pro-drug, the quantitative composition must follow how the substance is expressed in the SmPC. SmPC guidance says that the substance should be stated in terms of the quantity of that ester or pro-drug. If the active moiety is an active substance in an already approved medicinal product, the reference substance should be given in terms of this active moiety (as per the SmPC guidelines, e.g., 75 mg of fosphenytoin is equivalent to 50 mg of phenytoin). If the active moiety has not been approved separately, then the reference substance should be the ester or pro-drug and not any presumed active moiety (refer to chapter 2, section *5.5.3 Reference strength*);
- It can happen that not all information about the substance strength and the reference substance strength is available in the document. A guideline along with examples for vaccines and medicines (Infanrix Hexa and Losec respectively) provides additional help in such cases, as well as what information should be provided for excipients and adjuvants using MF59C.1 as an example.



On the diagram above, conditional shall be understood as follows: the related information must be provided when it is present in the document. For adjuvant (one substance) and excipients (mixture of 2 or more substances), conditional depends on the availability of the strength or the reference strength. Either one or the other must be provided.

The Basis of Strength Substance (BoSS) is the active ingredient or active moiety in a drug product that is measured to provide the product strength.[1]

Infanrix hexa



After reconstitution, 1 dose (0.5 ml) contains:

Diphtheria toxoid[1]	not less than 30 International Units (IU)
Tetanus toxoid[1]	not less than 40 International Units (IU)
Bordetella pertussis antigens	
Pertussis toxoid (PT)[1]	25 micrograms
Filamentous Haemagglutinin (FHA)[1]	25 micrograms
Pertactin (PRN)[1]	8 micrograms
Hepatitis B surface antigen (HBs)[2,3]	10 micrograms
Poliovirus (inactivated) (IPV)	
type 1 (Mahoney strain)[4]	40 D-antigen unit
type 2 (MEF-1 strain)[4]	8 D-antigen unit
type 3 (Saukett strain)[4]	32 D-antigen unit
Haemophilus influenzae type b polysaccharide (polyribosylribitol phosphate, PRP)[3]	10 micrograms
conjugated to tetanus toxoid as carrier protein	approximately 25 micrograms

[1]adsorbed on aluminium hydroxide, hydrated ($Al(OH)_3$) 0.5 milligrams Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisiae*) by recombinant DNA technology
[3]adsorbed on aluminium phosphate ($AlPO_4$) 0.32 milligrams Al^{3+}
[4]propagated in VERO cells

#	Substance	Strength (Presentation)	Reference Substance	Reference Strength (Presentation)
1	Diphtheria toxoid, Adsorbed on aluminium hydroxide hydrated	Mandatory *≥ 30 IU/ 0.5 ml*	Not applicable	Empty
2	Tetanus toxoid, Adsorbed on aluminium hydroxide hydrated	Mandatory *≥ 40 IU/ 0.5 ml*	Not applicable	Empty
3	Pertussis toxoid, Adsorbed on aluminium hydroxide hydrated	Empty	Pertussis toxoid	Mandatory 25 µg/ 0.5 ml
4	Pertussis filamentous haemagglutinin antigen, Adsorbed on aluminium hydroxide hydrated	Empty	Pertussis filamentous haemagglutinin antigen	Mandatory 25 µg/ 0.5 ml
5	Pertactin, Adsorbed on aluminium hydroxide hydrated	Empty	Pertactin	Mandatory 8 µg/ 0.5 ml
6	Hepatitis B surface antigen, Adsorbed on aluminium phosphate	Empty	Hepatitis B surface antigen	Mandatory 10 µg/ 0.5 ml
7	Poliomyelitis virus, serotype 1, strain Mahoney, inactivated	Mandatory *40 D-Antigen Units/ 0.5 ml*	Not applicable	Empty
8	Poliomyelitis virus, serotype 2, strain MEF-1, inactivated	Mandatory *8 D-Antigen Units/ 0.5 ml*	Not applicable	Empty
9	Poliomyelitis virus, serotype 3, strain Saukett, inactivated	Mandatory *32 D-Antigen Units/ 0.5 ml*	Not applicable	Empty
10	Haemophilus influenza type B polysaccharide tetanus toxoid conjugated antigen	Empty	Haemophilus influenza type B polysaccharide Tetanus toxoid carrier protein	Mandatory 10 µg/ 0.5 ml 25 µg/ 0.5 ml
11a 11b	Aluminium hydroxide Aluminium phosphate	Empty	Aluminium ion Aluminium ion	Mandatory 0.5 mg/ 0.5 ml 0.32 mg/ 0.5 ml

Ingredients on rows 1,2 7,8 & 9, this is the entire substance (according to the pharmacopoeia) which is the basis of the strength.

Ingredients on row 10, the active moieties of Haemophilus influenza type B polysaccharide tetanus toxoid conjugated antigen are the basis for the strength. Indeed the document does not contain any information as regards the strength. Instead we have the reference substance strength of the 2 moieties.

Ingredients from row 3 to 6, this is another reference substance which is the basis of the strength. The document only provides information on the antigen (reference substance): therefore, the reference strength must be captured for this reference substance.

[1] Source of definition: https://www.nlm.nih.gov/research/umls/rxnorm/docs/appendix4.html

Ingredient on row 11, No strength information exists in the document for either Aluminium hydroxide or aluminium phosphate.; however, information exists for reference substance aluminium ion (Al+3). Therefore, the reference strength 0.5 mg/0.5 ml and 0.32 mg/0.5 ml of Aluminium cation must be provided as the reference strength of aluminium hydroxide and aluminium phosphate respectively.

The information is taken from the Infanrix Hexa SmPC.

Losec

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gastro-resistant tablet contains 20.6 mg omeprazole magnesium equivalent to 20 mg omeprazole.
Excipients: Each gastro-resistant tablet contains 19–20 mg sucrose.
For a full list of excipients, see section 6.1.

#	Substance	Strength (Presentation)	Reference Substance	Reference Strength (Presentation)
1	Omeprazole magnesium	20.6 mg/tablet	Omeprazole	20 mg/tablet
2	Sucrose	19-20 mg/tablet	Not applicable	Empty

In the Losec example, both substance strength and substance reference strength can be found in the document for the active ingredient and must be reported. The strength must be reported for the excipient (sucrose).

MF59C.1 – Adjuvant system being a combination of substances (SSG1)

MF59C.1 Adjuvant System - patent EP 0 399 843 B1

Substance	Strength	Reference substance	Reference Strength
MF59C.1	Empty	Squalene	9.75 mg/0.5 ml
		Polysorbate 80	1.175 mg/0.5ml
		Sorbitan Trioleate	1.175 mg/0.5 ml

For an adjuvant system (mixture), as the adjuvant strength is unknown, the immunostimulant substances must be reported as "reference substances" along with their "(reference) strength".

Excipient asa combination of substances (SSG1)

Note: For excipients which are a combination of 2 or more substances, e.g., lipid nanoparticle delivery vehicle, the excipient components will also be considered as "reference substances" if detailed in the document and their strength will be recorded as "reference strengths" of the excipient. Overall, expression of strength varies significantly depending on the pharmaceutical form, route of administration and type of medicinal product. In order to capture these differences, the following examples are presented in this section:

1. **Medicinal Product with a solid, countable dosage form** – Tablet – Gastro-resistant tablet (**Losec**)
2. **Product transformed before administration** – Effervescent Tablet – Oral solution (**Berocca**)
3. **Radiopharmaceutical product** – Vial – Solution for Injection
4. **Continuous Presentation where dosing is individual/not accurate** – Tube – Cream (**Daktarin**)

5. **Liquid presentation with volume delivery device** – Bottle – Liquid (**COSOPT**)
6. **Vaccine** – Prefilled-Syringe – Suspension for injection (**Havrix Junior & Havrix Adult**)
7. **Inhalation powder and dry powder inhaler (DPI)** – Combination product (**Relvar Ellipta**)
8. **Inhalation solution and pressurises metered-dose inhaler (pMDI)** - Combination product – Inhalator (**Trimbow**)
9. **Liquid presentation where concentration of content is clinically relevant** - Anaesthesia – Bottle – Inhalation vapour, liquid
10. **Patch -** Transdermal patch - (**Estalis Sequi**)
11. **Solid dose forms in "Container"** – Sachet – Oral Solution (**Voltfast**)
12. **Quantity Operator in Ingredients**
13. **Multidose vial (Spikevax)**

To give structure to these examples, a set of patterns has been developed. The patterns show how the Manufactured Item (MI) and the Pharmaceutical Product (PhP) should be expressed for a particular type of product. Products can then be matched to the appropriate pattern which then shows how the MI and PhP should look, for which the strength is mandatory. The following reference table provides the necessary guidance to select between Presentation strength, and Concentration Strength. This reference table has been built and refined based on an IDMP pilot carried out by the SPOR Task Force.

Note 1: The guidance presented in this section does not substitute scientific assessment performed by the relevant competent authority where a different decision may be taken on how to express the strength on a case-by-case basis. Therefore, information of strength as presented in the approved Summary of Product Characteristics (SmPC) of the applicable medicinal product must be taken as reference and should prevail over the patterns presented above in case of difference.

Pattern	Type of product	Examples	Manufac. Item Unit of Present.	Pharm. Prod. unit of Present	Strength by Presentation	Strength by Concentration
1a	Solid, countable	Tablets, capsules, suppositories	Basic dose form related to the pharmaceutical form of the MI (tablet, capsule, etc.)	Basic dose form related to the pharmaceutical form of the Pharm Prod (tablet, capsule etc.)	Mandatory	Empty
1b	Solid dose forms in "container"	Powder or granules in sachet, ampoules, vials, Spincap, Rotocap – the whole content of the capsule is delivered to the patient via one or more actuations	Container (vial, sachet, etc.)	Container (vial, sachet, etc…) – not always informative depending on the dosing instructions	Mandatory	Empty
1c	Metered dose delivered by a metered actuation - dose cannot be adjusted	Dry-powder inhalers (DPI) pressurised metered-dose inhalers (pMDI), nasal sprays	Actuation (inhaler)	Actuation (inhaler, etc.)	Mandatory	Empty
2a	Products enclosed in a "presentation", where the total amount per presentation is clinically relevant	Unit dose solutions, parenteral liquid, unit dose nebuliser solutions NOT partial use preparations	Container (vial, etc.)	Container (vial, etc.)	Mandatory Expressed per total volume of the presentation (not per unit of presentation). This makes calculations easier	Mandatory (QRD)

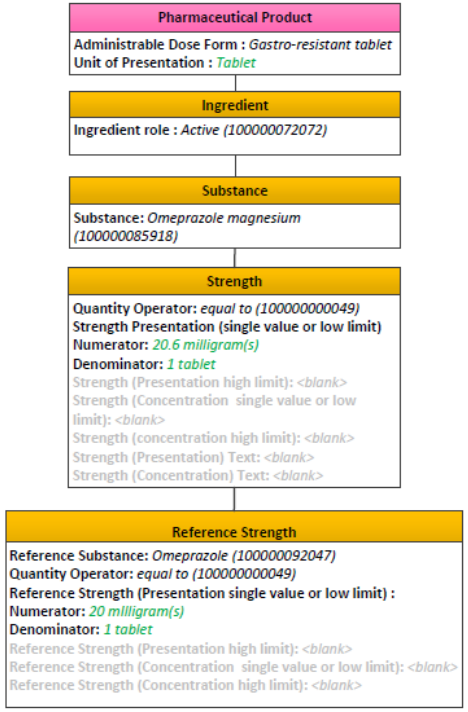
Pattern	Type of product	Examples	Manufac. Item Unit of Present.	Pharm. Prod. unit of Present	Strength by Presentation	Strength by Concentration
2b	Products enclosed in a "presentation", where the concentration is clinically relevant rather than the total amount in the presentation	Multi-dose syringe, Partial dose syringe, infusion bags, Multidose vial	Container (bottle, etc.)	N/A since it is the concentration that is relevant	Conditional	Mandatory
3a	Continuous presentation (dosing is individual/not accurate and the total volume in the container is of less importance for dosing purposes)	Bulk powders/granules, semi-solids "bulk" liquids (e.g., eye drops)	Not useful clinically	N/A since it is the concentration that is relevant	– Conditional	Mandatory
3b	Products enclosed in a "presentation", where the dose has a delivery rate	Transdermal patches	Patch	N/A since it is the concentration that is relevant	Conditional	Mandatory – as a delivery rate over time

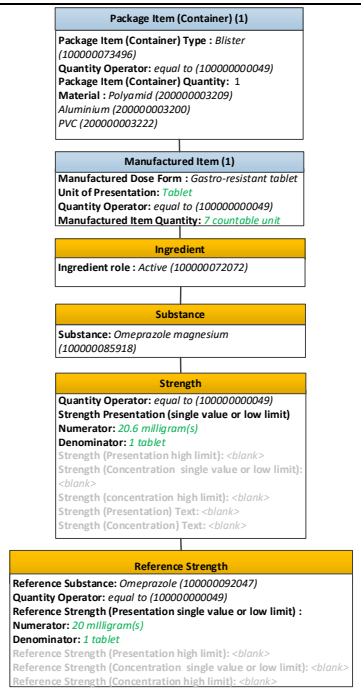
3.3.1. **Medicinal Product with a solid, countable dosage form – Tablet – Gastro-resistant tablet**

<table>
<tr>
<td>2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gastro-resistant tablet contains 20.6 mg omeprazole magnesium equivalent to 20 mg omeprazole.
Excipients: Each gastro-resistant tablet contains 19–20 mg sucrose.
For a full list of excipients, see section 6.1.</td>
<td>Losec</td>
<td>6.5 Nature and contents of container

Polyamide/Aluminium/PVC blister containing 7 or 14 tablets.

Not all pack sizes may be marketed.</td>
</tr>
<tr>
<td> 
</td>
<td>Points of attention for this example:

• This example fits with the Pattern 1a (Solid, countable). In this case, only the Presentation Strength is required for both manufactured Item and Pharmaceutical Products.
• The strength(s) of all the ingredients are always expressed using the Numerator and Denominator. For this example, the Presentation Strength is expressed in [milligram(s)] per [tablet].
• If there is no reference substance that differs from the ingredient actually in the product, active substance and its strength must be repeated in the data object « Reference Strength »
• On the graphical representation some entities and links are missing, and other boxes have been replicated for human readability purposes.
• Manufactured Item quantity – please refer to the section Alignment of Manufactured Item Quantity, Unit of Presentation and Pack Size for more guidance.</td>
<td> 
</td>
</tr>
</table>

3.3.2. **Product transformed before administration – Effervescent Tablet – Oral solution**

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

This product is a multivitamin preparation with high dosed B-complex vitamins and vitamin C as well as calcium, magnesium and zinc. This product is a multivitamin and mineral preparation, containing 9 vitamins and 3 minerals.

One effervescent tablet contains:

Ascorbic acid 500 mg

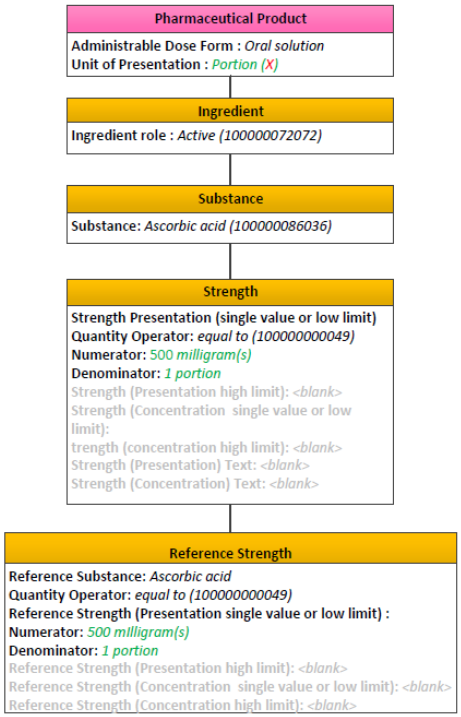
Berocca

6.5 Nature and contents of container

Packages: 10, 15, 2x10, 2x15, 3x15, 4x15 (the effervescent tablets are wrapped in aluminium foil before packing into PP plastic tablet containers and aluminium tablet containers, LDPE plastic caps containing a desiccant.

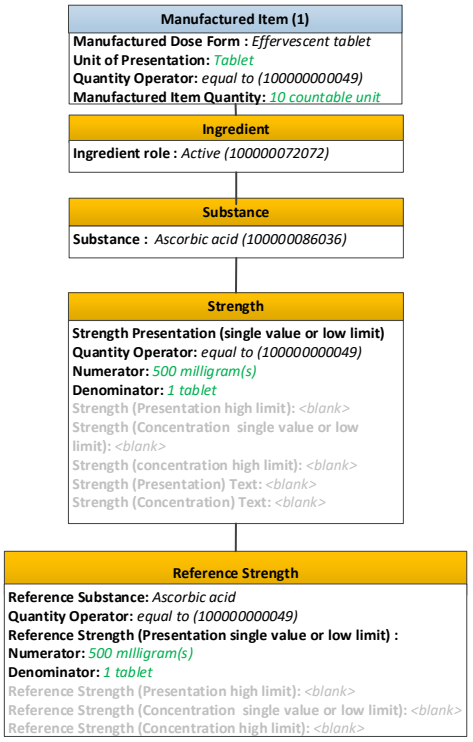
Desiccator capsule:
Pure silica gel (white gel) with a molecular sieve.

Aluminium foil strip packs of 1 tablet (with desiccant).



Points of attention for this example:

- This example fits with the Pattern 1a (Solid dose form in container) – Only the Presentation Strength is required. The concentration strength of the Pharmaceutical Product is outside the scope of EU IG Chapter 2 requirements.
- PhP – Unit of Presentation: Portion – To reflect the ISO/TS 20451:2017 (section 8.1.2.2), the use of portion is mandated when "final volume and concentration of the ingredients are not known". Such as in the case where the Pharmaceutical Product represents the "portion of solution resulting from dissolving one tablet".
- This example also applies for liquid products that undergo product transformation prior to administration and therefore the "final volume and concentration of the ingredients are not known". In these cases, the Pharmaceutical Product represents the "portion of solution resulting from dilution of a liquid".
- MI – Unit of Presentation: Tablet – Attention, in this case the correct value is "Tablet", and not portion as mentioned under Pharmaceutical product. Manufactured Item reflecting what is produced. Pharmaceutical Product reflects what is taken by the patient after transformation.
- If there is no reference substance that differs from the ingredient actually in the product, active substance and its strength must be repeated in the data object « Reference Strength»
- Manufactured Item quantity – please refer to the Chapter 2 section 4.11.2. and Chapter 8 section 3.5. for more guidance.



3.3.3. **Radiopharmaceutical product – Vial – Solution for Injection**

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL of solution contains 1100 kBq radium Ra 223 dichloride (radium-223 dichloride), corresponding to 0.58 ng radium-223 at the reference date. Radium is present in the solution as a free ion.

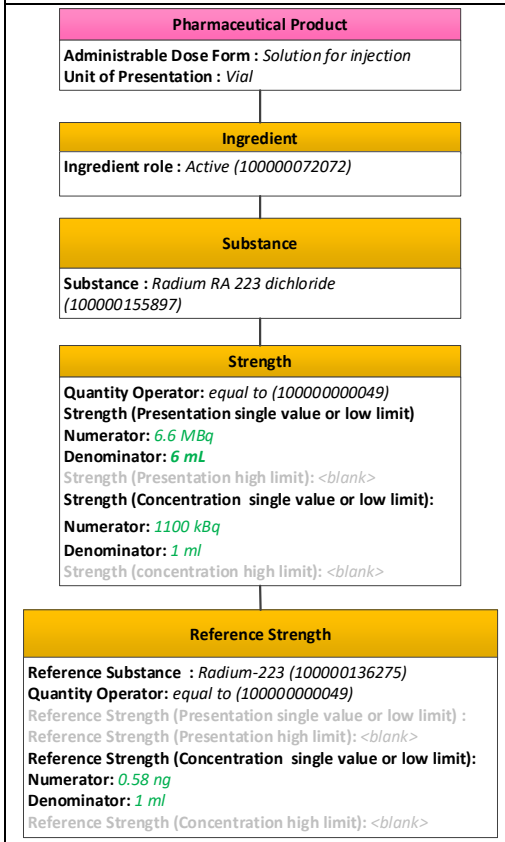
Each vial contains 6 mL of solution (6.6 MBq radium-223 dichloride at the reference date).

Radium-223 is an alpha particle-emitter with a half-life of 11.4 days. The specific activity of radium-223 is 1.9 MBq/ng.

Xofigo

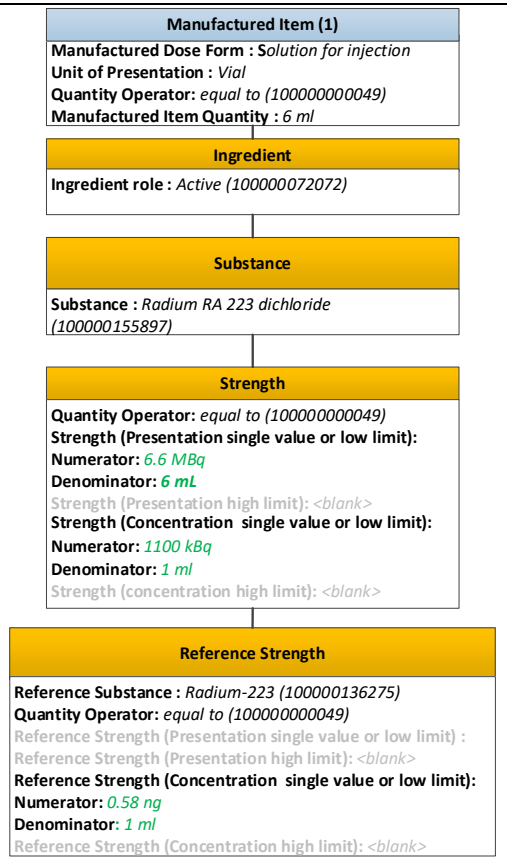
6.5 Nature and contents of container

Colourless Type I glass vial closed with a grey bromobutyl rubber stopper either with or without foil-clad made of Ethylene tetrafluoroethylene (ETFE), both capped with aluminium seal, containing 6 mL of solution for injection.



Points of attention for this example:

- This example fits with the Pattern 3a (Product enclosed in a "presentation", where the concentration of the content is clinically relevant). In this case, the Concentration Strength is mandatory; and the Presentation Strength is conditional ,which means that if
- the presentation strength is provided in the SmPC, it has to be provided. In this example the presentation strength is provided in the SmPC and must be reported. As mentioned in the section 2 of the SmPC of this product, the reference strength is measured in reference to a specific reference substance.
- Manufactured Item quantity – please refer to the section Alignment of Manufactured Item Quantity, Unit of Presentation and Pack Size for more guidance.



12. INSTRUCTION FOR PREPARATION OF RADIOPHARMACEUTICALS

The volume to be administered to a given patient should be calculated using the:

- Patient's body weight (kg)
- Dosage level (55 kBq/kg body weight)
- Radioactivity concentration of the product (1100 kBq/mL) at reference date. The reference date is stated on the vial and lead pot label.
- Decay correction (DK) factor to correct for physical decay of radium-223. A table of DK factors is provided with each vial as part of the booklet (preceding the package leaflet).

The amount of radioactivity in the dispensed volume shall be confirmed by measurement in a properly calibrated activimeter.

The total volume to be administered to a patient is calculated as follows:

$$\textbf{Volume to be administered (mL)} = \frac{\textbf{Body weight (kg)} \times \textbf{activity (55 kBq/kg body weight)}}{\textbf{DK factor} \times \textbf{1100 kBq/mL}}$$

3.3.4. **Continuous Presentation where dosing is individual/not accurate – Tube – Cream**

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Miconazole nitrate 2% w/w.

(Each gram of cream contains 20mg of miconazole nitrate)

Excipients with known effect:
Benzoic acid 2 mg/g
Butylated hydroxyanisole 0.052 mg/g

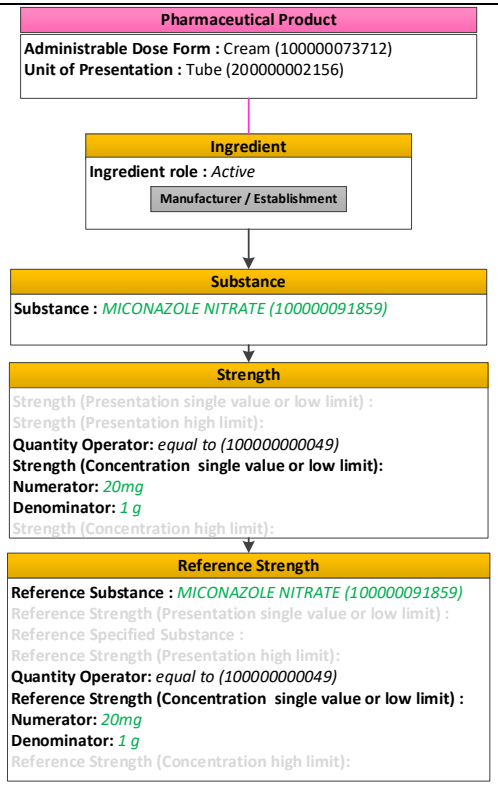
For the full list of excipients, see Section 6.1

Daktarin

6.5 Nature and contents of container

Aluminium tube inner lined with heat polymerised epoxy-phenol resin with a white polypropylene cap containing 15 g, 30 g or 70 g of cream, or aluminium tube inner lined with heat polymerised epoxy-phenol resin with a high density polyethylene cap containing 5 g of cream.

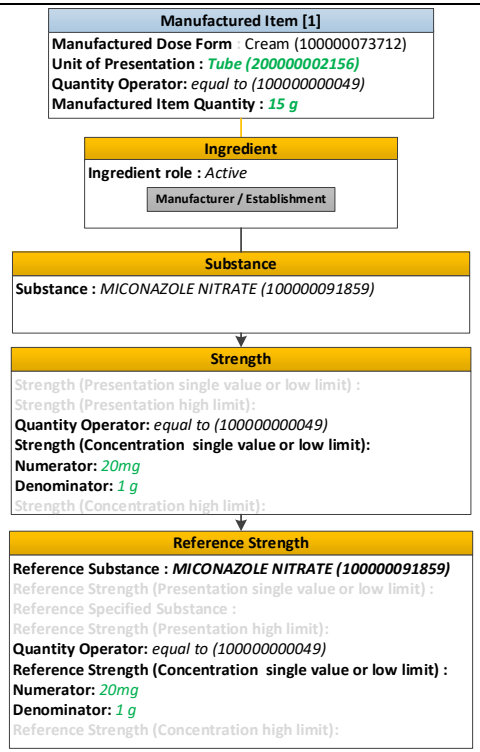
*Not all pack sizes may be marketed.



Points of attention for this example:

- This example fits with the Pattern 3a (Continuous Presentation):
  - Concentration Strength is mandatory.
  - MI – Presentation Strength is Conditional.
- PhP – Presentation Strength is not in SmPC but if provided in module 3 it must be reportedStrength(s) must be expressed as per SmPC.
  - If **two expressions of the concentration are available** ("2% w/w" and "20mg/gram"), the "mg per gram" should be prioritized.
  - –
- If there is no reference substance that differs from the ingredient actually in the product, active substance and its strength must be repeated in the data object « Reference Strength »

Manufactured Item quantity – please refer to the section 4.11.2 for more guidance.



3.3.5. **Liquid presentation with volume delivery device – Bottle – Liquid**

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains 22.26 mg of dorzolamide hydrochloride corresponding to 20 mg dorzolamide and 6.83 mg of timolol maleate corresponding to 5 mg timolol.
Excipients: Benzalkonium chloride 0.075 mg/ml

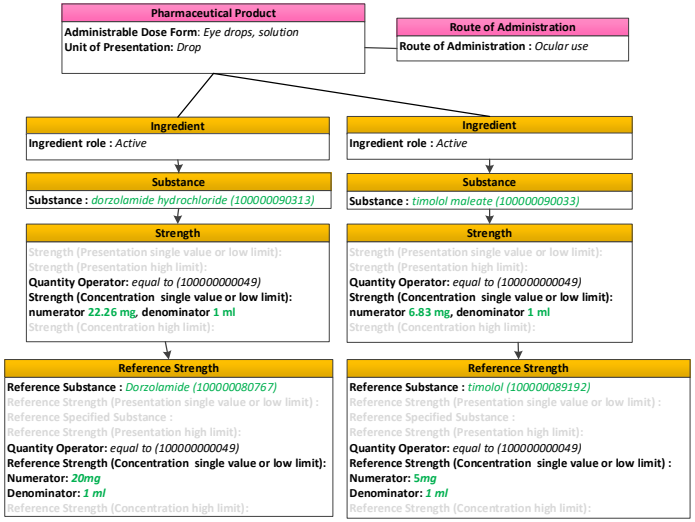
For the full list of excipients, see section 6.1.

COSOPT

6.5 Nature and contents of container

The COSOPT container contains 5 ml of solution. Two alternate containers may be marketed.

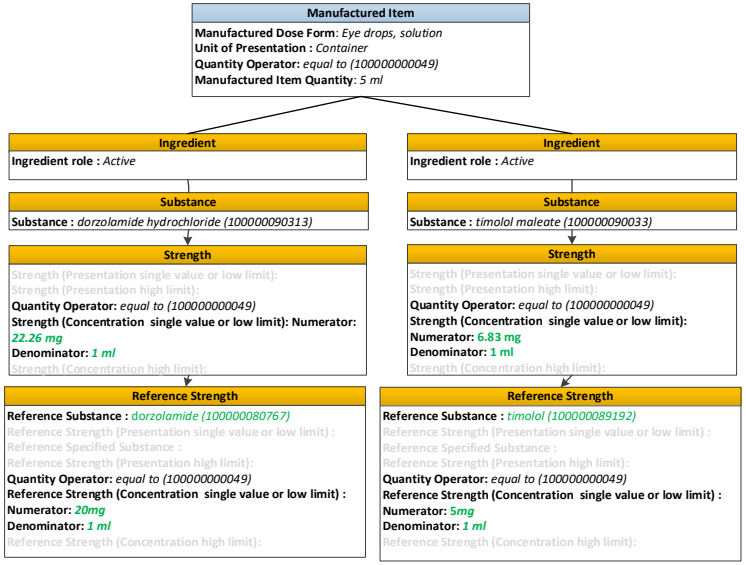
White translucent low-density polyethylene container, a transparent dropper and a white cap
or
The OCUMETER Plus Ophthalmic Dispenser consisting of a translucent, high-density polyethylene container with a sealed dropper tip, a flexible fluted side area which is depressed to dispense the drops, and a 2-piece cap assembly. The 2-piece cap mechanism punctures the sealed dropper tip upon initial use, then locks together to provide a single cap during the usage period.



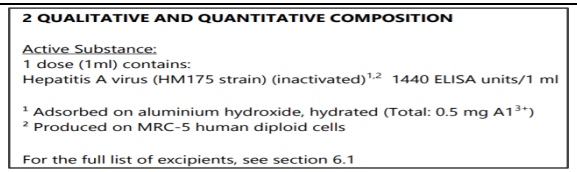
Points of attention for this example:

- This example fits with the Pattern 2b (Volume delivery Device where the concentration is clinically relevant):
  - Concentration Strength is mandatory.
  - MI – Presentation Strength is Conditional (if the presentation strength is clearly stated it shall be reported)
- If there is no reference substance, active substance and its strength must be repeated in the data object « Reference Strength ».

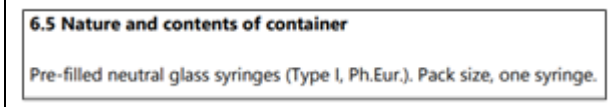
Manufactured Item quantity – please refer to the section 4.11.2 for more guidance.

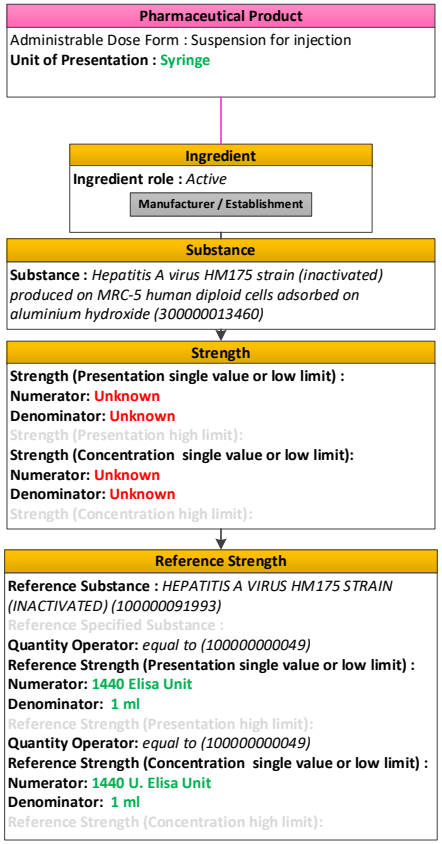


3.3.6. **Vaccine – Prefilled-Syringe – Suspension for injection**



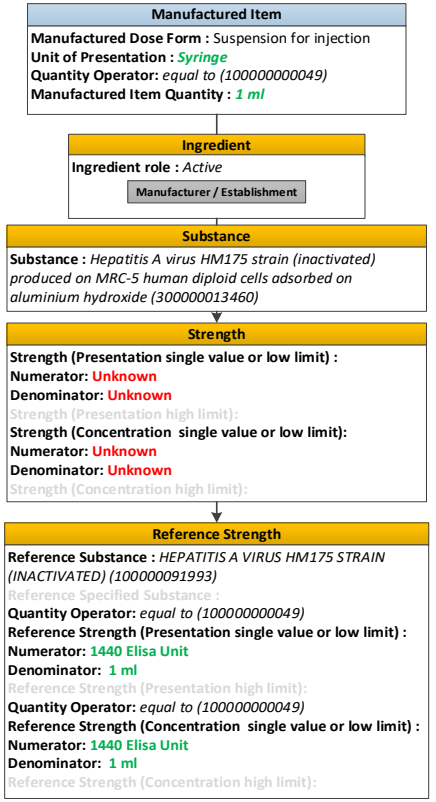
Havrix Adult





Points of attention for this example:

- This example fits with the Pattern: 2a (Presentation enclosed in a "presentation" where the total amount per presentation is clinically relevant):
  - Presentation Strength is Mandatory
  - Concentration Strength is mandatory
- When only the reference substance strength is provided in the SmPC, the substance must be provided, and its strength must remain empty
- The Manufactured Item quantity for 'liquid' product, is the one mentioned in the SmPC. (Understood as excluding the ~0,1 ml overfills in this example)
- The **strength** must be expressed as in the section 2 of the SmPC or as in module 3.



2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (0.5 ml) contains:
Hepatitis A virus (inactivated)[1,2] 720 ELISA Units

[1] Produced on human diploid (MRC-5) cells
[2] Adsorbed on aluminium hydroxide, hydrated Total: 0.25 milligrams Al^{3+}

Havrix Junior Monodose vaccine may contain traces of neomycin B sulfate, which is used during the manufacturing process (see section 4.3).

For the full list of excipients, see section 6.1.

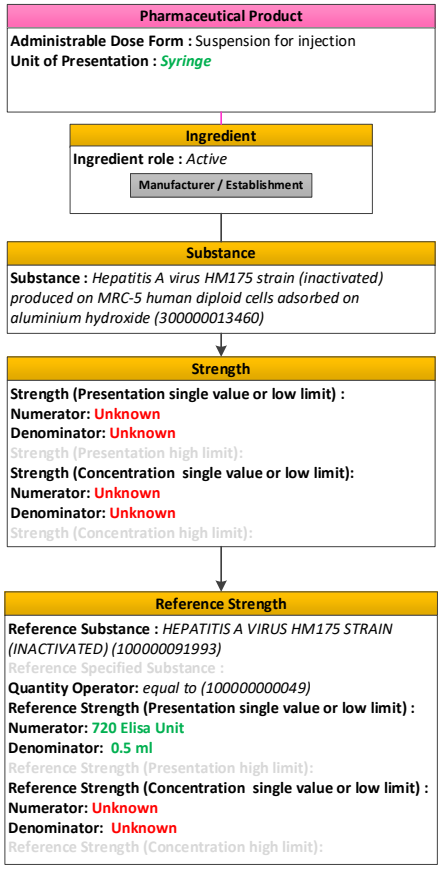
Havrix Junior

6.5 Nature and contents of container

Neutral glass vials (type 1, PhEur) with grey butyl rubber stoppers and aluminium overcaps fitted with flip-off tops.

0.5 ml of suspension in prefilled syringe or vial (type I glass) with a plunger stopper (rubber butyl) with or without needles - pack size of 1 or 10.

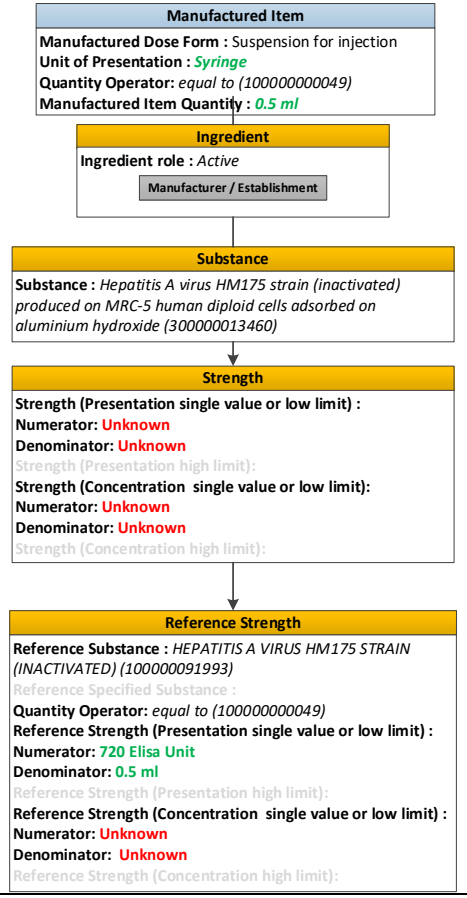
Not all pack sizes may be marketed.



- This second example for Havrix, illustrates why the presentation strength is important to have in addition to the concentration strength (standardized strength).

  Standardized to 1 ml, the adult and Junior versions of this vaccine share the same concentration (1440 Elisa Unit / 1ml). Only the presentation strength enables to differentiate them.

- In such example, when available, the concentration strength must be reported.



3.3.7. **Inhalation powder and dry powder inhaler (DPI) – Combination product**

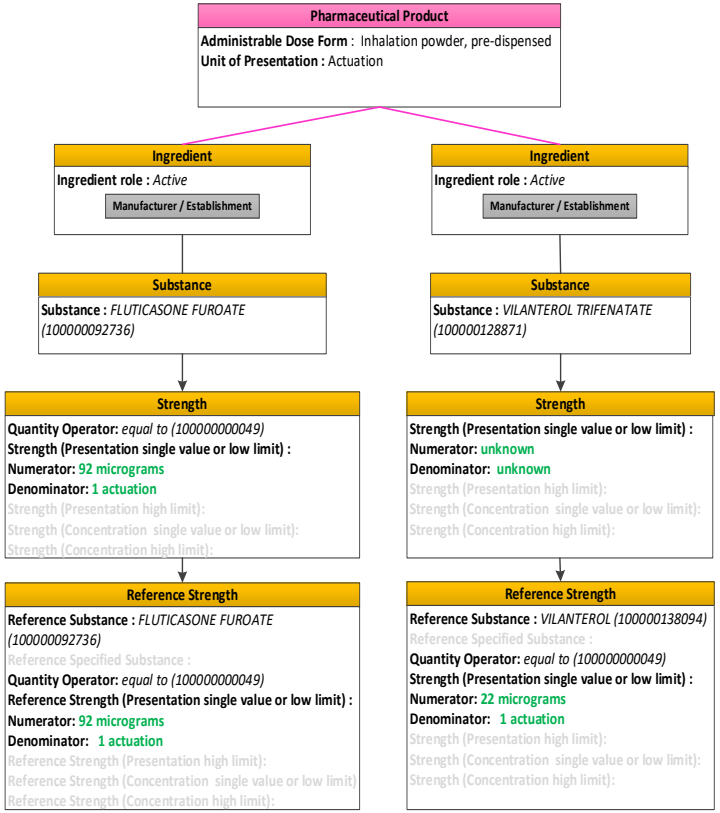
2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each single inhalation provides a delivered dose (the dose leaving the mouthpiece) of 92 micrograms of fluticasone furoate and 22 micrograms of vilanterol (as trifenatate). This corresponds to a pre-dispensed dose of 100 micrograms of fluticasone furoate and 25 micrograms vilanterol (as trifenatate).

Relvar Ellipta

6.5 Nature and contents of container

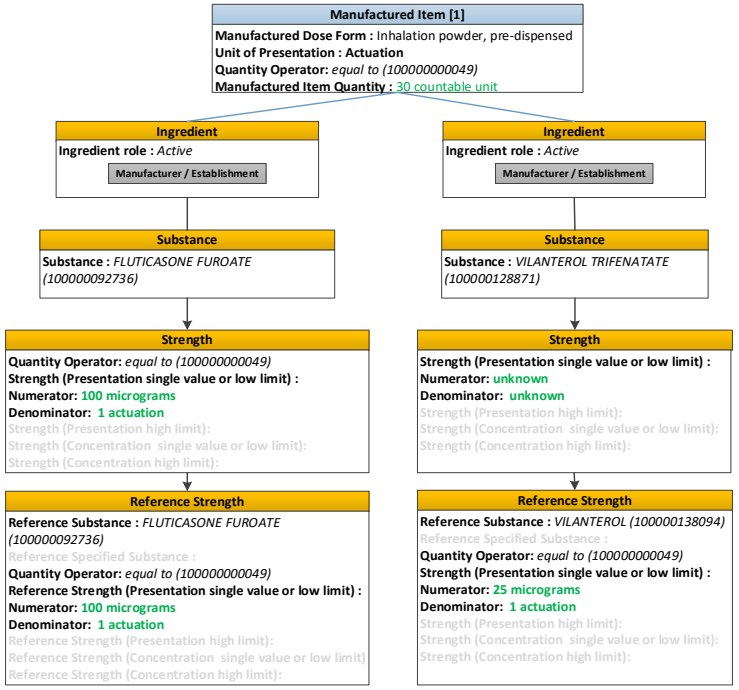
The inhaler consists of a light grey body, a yellow mouthpiece cover and a dose counter, packed into a foil laminate tray containing a silica gel desiccant sachet. The tray is sealed with a peelable foil lid.
The inhaler is a multi-component device composed of polypropylene, high density polyethylene, polyoxymethylene, polybutylene terephthalate, acrylonitrile butadiene styrene, polycarbonate and stainless steel.
The inhaler contains two aluminium foil laminate strips of 14 or 30 doses.
Pack sizes of 14 or 30 dose Inhalers. Multipack of 3 x 30 dose Inhalers.



Points of attention for this example:

- This example matches the Pattern: 1c [Dose (actuation), dose cannot be adjustable] – Presentation strength is mandatory; Concentration is optional.
- The Delivered Dose must be used for the Pharmaceutical Product strength, and Metered Dose for the Manufactured Item
- Denominator : use "actuation" for the pharmaceutical product, and for the manufactured Item.

If there is no reference substance that differs from the ingredient actually in the product, active substance and its strength must be repeated in the data object « Reference Strength »



3.3.8. **Inhalation solution and pressurises metered-dose inhaler (pMDI) - Combination product – Inhalator**

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each delivered dose (the dose leaving the mouthpiece) contains 87 micrograms of beclometasone dipropionate, 5 micrograms of formoterol fumarate dihydrate and 9 micrograms of glycopyrronium (as 11 micrograms glycopyrronium bromide).

Each metered dose (the dose leaving the valve) contains 100 micrograms of beclometasone dipropionate, 6 micrograms of formoterol fumarate dihydrate and 10 micrograms of glycopyrronium (as 12.5 micrograms glycopyrronium bromide).

For the full list of excipients, see section 6.1.

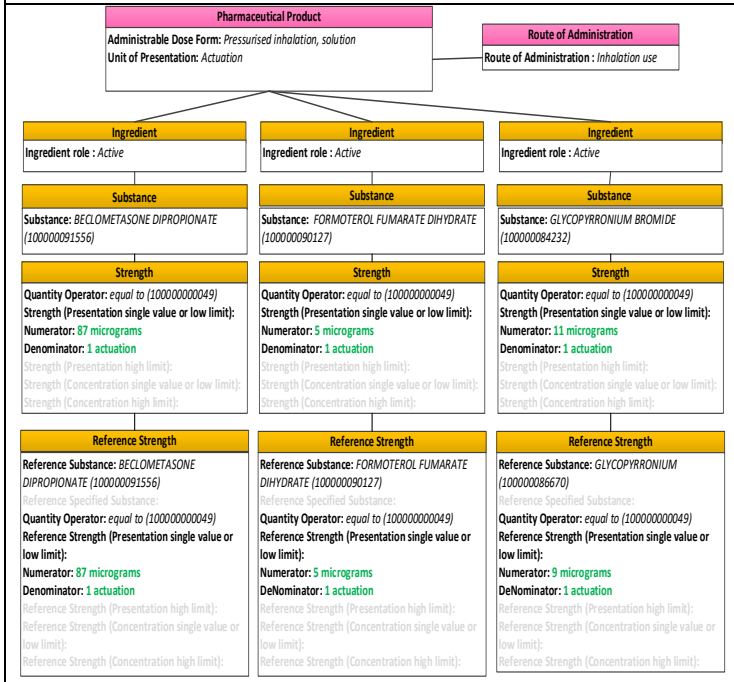
Trimbow

6.5 Nature and contents of container

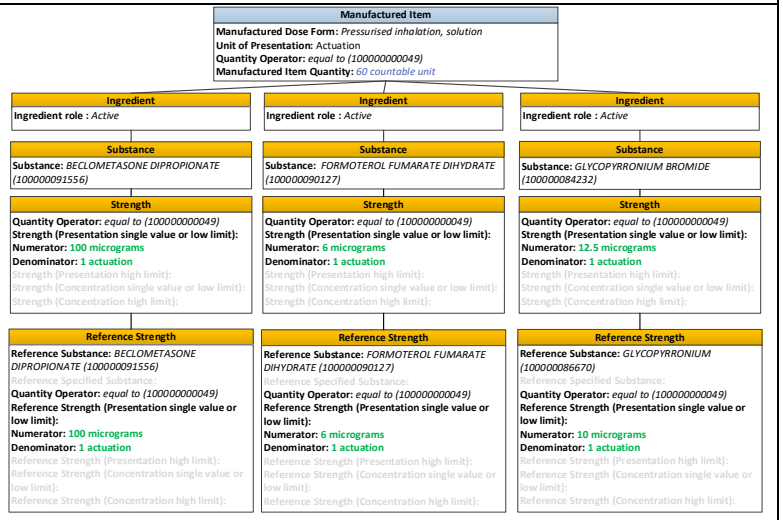
Pressurised container (coated aluminium), with a metering valve. The pressurised container is inserted in a polypropylene inhaler which incorporates a mouthpiece and a dose counter (60 actuations or 120 actuations per pressurised container) or dose indicator (180 actuations per pressurised container) and is provided with a polypropylene mouthpiece cap.

Pack sizes of 1 container of 60, 120 or 180 actuations and multipacks of 2 or 3 containers of 120 actuations each.

Not all pack sizes may be marketed.



- **Pattern: 1c** [Dose (actuation), the dose cannot be adjustable] – The **presentation strength is mandatory**; Concentration is optional.
- The **Delivered Dose** must be used for the Pharmaceutical Product strength, and **Metered Dose** for the Manufactured Item.
- **Denominator** : use "actuation" for the pharmaceutical product, and for the manufactured Item.
- If there is no reference substance that differs from the ingredient in the product (e.g., beclomethasone dipropionate), active substance and its strength must be repeated in the data object « Reference Strength »



3.3.9. **Liquid presentation where concentration of content is clinically relevant - Anaesthesia – Bottle – Inhalation vapour, liquid**

QUALITATIVE AND QUANTITATIVE COMPOSITION

Sevoflurane 100%.

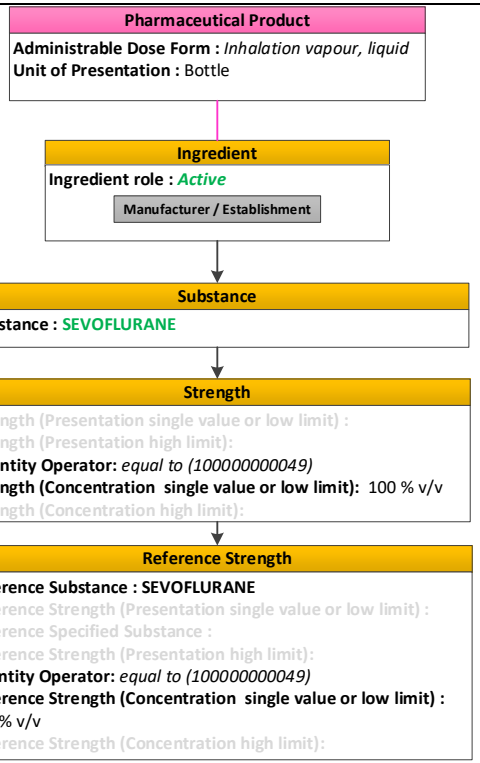
Excipient with known effect:

None

The finished product is comprised only of the active ingredient, see section 6.1

Sevoflurane

Nature and contents of container
Type III, 250 ml amber glass bottles (with or without an external PVC coating) with two component screw cap made up of outer black phenolic cover and inner translucent low density polyethylene cone. The pack is provided with an LDPE yellow-coloured collar.
OR
Type III, 250 ml amber glass bottle (without an external PVC coating) with an integrated adaptor multi- component closure (HDPE, EPDM rubber, stainless steel) attached to the bottle with an aluminium crimp ring. This container is specifically designed to work with a Dräger-Vapor2000 vaporizer with a Dräger Fill or Piramal Fill port



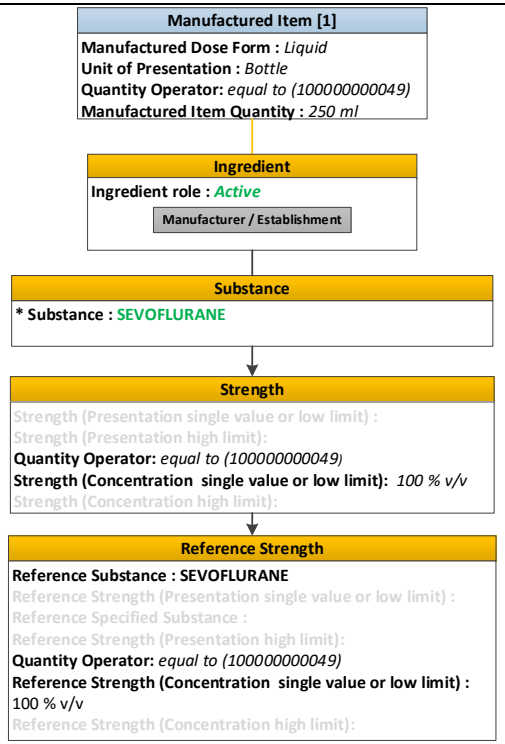
Points of attention for this example:

- This example fits the Pattern: 3a [Products enclosed in a "presentation", where the concentration of content is clinically relevant]
  - Concentration Strength is Mandatory
  - Presentation Strength is Conditional (if the presentation strength is clearly stated it shall be reported)
- Do not include dosing information in accordance to posology in this section in Pharmaceutical product.

Table 1. MAC Values for Adults and Paediatric Patients According to Age

AGE OF PATIENT (YEARS)	SEVOFLURANE IN OXYGEN	SEVOFLURANE IN 65% N20/35%02
0 – 1 months*	3.3%	
1 - < 6 months	3.0%	
6 months - < 3 years	2.8%	2.0%@
3 - 12	2.5%	
25	2.6%	1.4%
40	2.1%	1.1%
60	1.7%	0.9%
80	1.4%	0.7%

- If there is no reference substance (e.g., Sevoflurane), active substance and its strength must be repeated in the data object « Reference Strength ».



3.3.10. **Patch - Transdermal patch**

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Phase I
Each patch contains estradiol hemihydrate equivalent to 0.78 mg estradiol in a patch of 5 cm^2, releasing nominal 50 micrograms estradiol per 24 hours.

Phase II
Each patch contains estradiol hemihydrate equivalent to 0.51 mg estradiol and 4.80 mg norethisterone acetate in a patch of 16 cm^2, releasing 50 micrograms estradiol and 250 micrograms norethisterone acetate per 24 hours.

For the full list of excipients, see section 6.1.

Estalis Sequi

6.5 Nature and contents of container

The transdermal patches are individually packed in heat-sealed paper/polyethylene pouches. Pouches are provided in cartons of 8 patches (4 Phase I and 4 Phase II patches) or 24 patches (12 Phase I and 12 Phase II patches).

Not all pack sizes may be marketed.

Phase I

Pharmaceutical Product
Administrable Dose Form: *Transdermal patch (100000073741)*
Unit of Presentation: *Patch (200000002134)*

Ingredient
Ingredient role : *Active (100000072072)*

Substance
Substance: *ESTRADIOL HEMIHYDRATE (100000089218)*

Strength
Strength (Presentation single value or low limit):
Numerator: <blank>
Denominator: <blank>
Strength (Presentation high limit): <blank>
Strength (Concentration single value or low limit):
Numerator: <blank>
Denominator: <blank>
Strength (Concentration high limit): <blank>
Strength (Presentation) Text: <blank>

Reference Strength
Reference Substance : *ESTRADIOL* (100000091739)
Reference Strength (Presentation single value or low limit):
Numerator: <blank>
Denominator: <blank>
Strength (Presentation high limit): <blank>
Reference Strength (Concentration single value or low limit):
Numerator: *50 micrograms*
Denominator: *24 hour (100000110804)*
Strength (Concentration high limit): <blank>
Strength (Presentation) Text: <blank>

Points of attention for this example:

- This example fits the Pattern: 3b (Products in a presentation with a dose delivery rate) Products enclosed in a "presentation", where the concentration of content is clinically relevant.
  - Concentration Strength is Mandatory
  - Presentation Strength is Conditional (if the presentation strength is clearly stated it shall be reported.)
- As shown in the Patch phase II, **if there is no reference substance,** active substance and its strength must be repeated in the data object « Reference Strength ».
- The strength must be expressed as in the Summary of Product Characteristics: do not change the unit even if it is equivalent: 24 hours should be expressed in hours and not with the unit 'day'.

Phase I

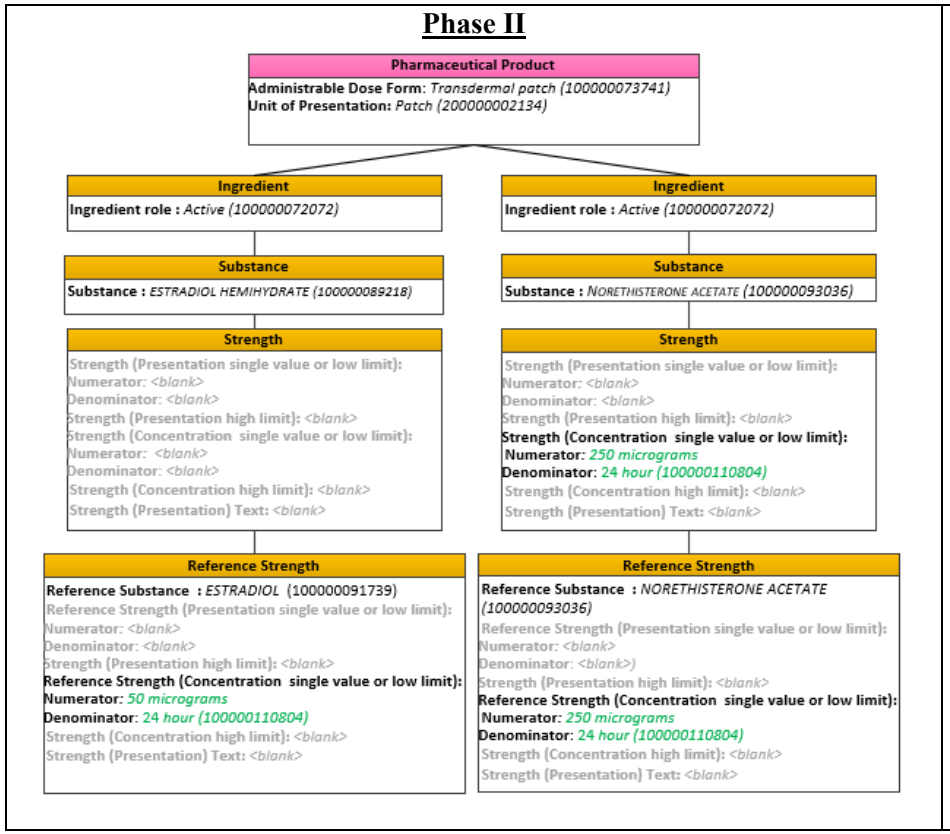
Manufactured Item
Manufactured Dose Form: *Transdermal patch (100000073741)*
Unit of Presentation : *Patch (200000002134)*
Quantity Operator: *equal to (100000000049)*
Manufactured Item Quantity: *4 countable unit*

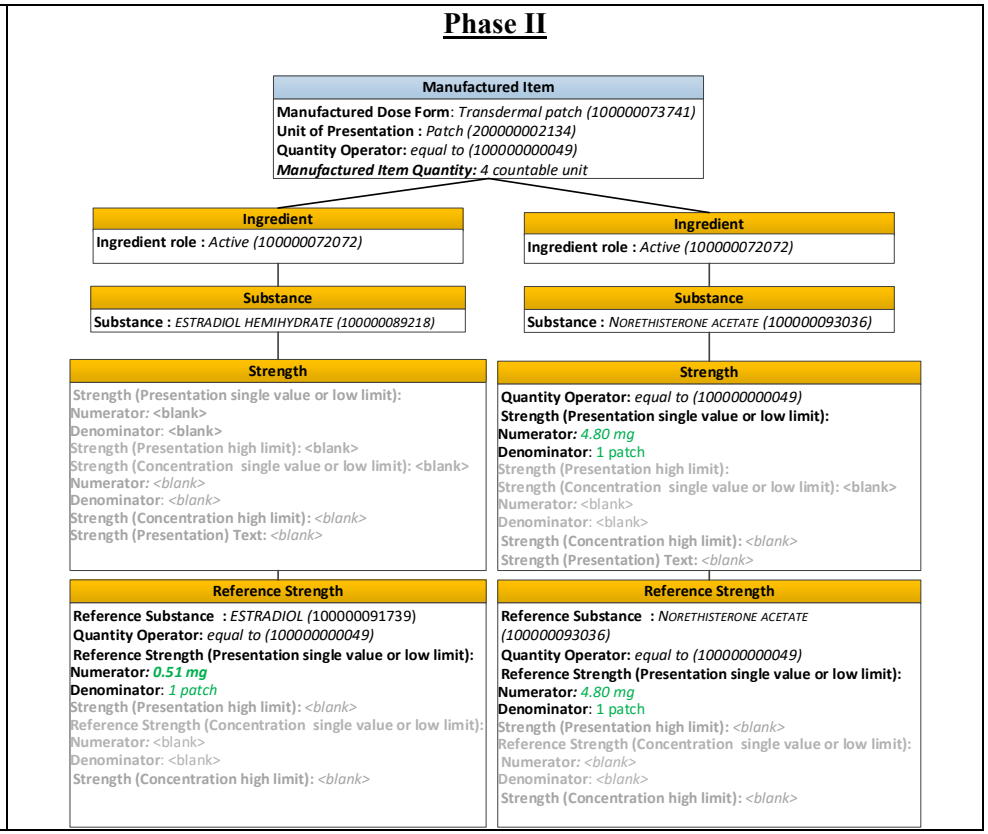
Ingredient
Ingredient role : *Active (100000072072)*

Substance
Substance: *ESTRADIOL HEMIHYDRATE (100000089218)*

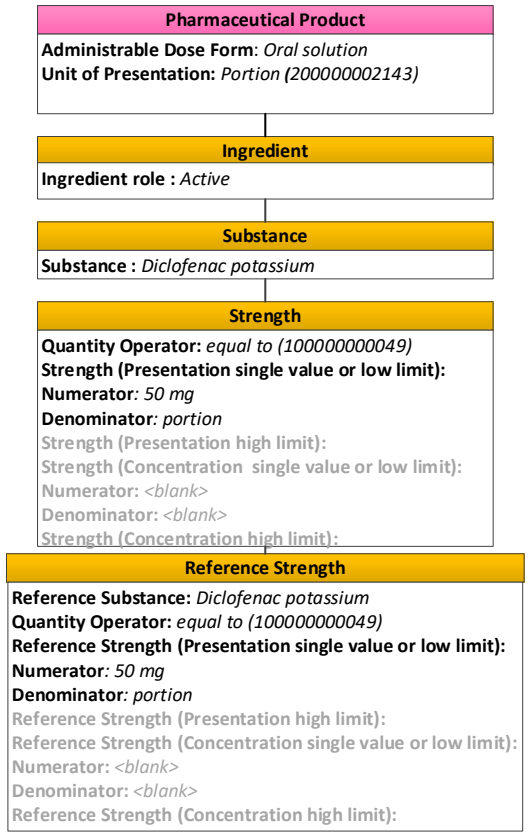
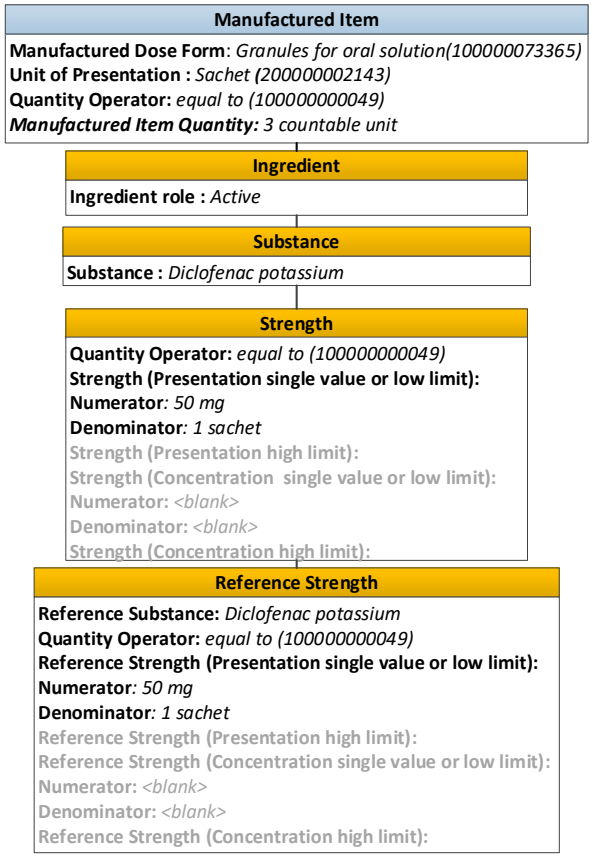
Strength
Strength (Presentation single value or low limit):
Numerator: <blank>
Denominator: <blank>
Strength (Presentation high limit): <blank>
Strength (Concentration single value or low limit):
Numerator: <blank>
Denominator: <blank>
Strength (Concentration high limit): <blank>

Reference Strength
Reference Substance : *ESTRADIOL* (100000091739)
Quantity Operator: *equal to (100000000049)*
Reference Strength (Presentation single value or low limit):
Numerator: *0.78 mg*
Denominator: 1 patch *(...)*
Strength (Presentation high limit): <blank>
Reference Strength (Concentration single value or low limit):
Numerator: <blank>
Denominator: <blank>
Strength (Concentration high limit): <blank>


Phase II
Pharmaceutical Product
Administrable Dose Form: Transdermal patch (100000073741)
Unit of Presentation: Patch (200000002134)
Ingredient
Ingredient role : Active (100000072072)
Substance
Substance : ESTRADIOL HEMIHYDRATE (100000089218)
Strength
Strength (Presentation single value or low limit):
Numerator: <blank>
Denominator: <blank>
Strength (Presentation high limit): <blank>
Strength (Concentration single value or low limit):
Numerator: <blank>
Denominator: <blank>
Strength (Concentration high limit): <blank>
Strength (Presentation) Text: <blank>
Reference Strength
Reference Substance : ESTRADIOL (100000091739)
Reference Strength (Presentation single value or low limit):
Numerator: <blank>
Denominator: <blank>
Strength (Presentation high limit): <blank>
Reference Strength (Concentration single value or low limit):
Numerator: 50 micrograms
Denominator: 24 hour (100000110804)
Strength (Concentration high limit): <blank>
Strength (Presentation) Text: <blank>
Ingredient
Ingredient role : Active (100000072072)
Substance
Substance : NORETHISTERONE ACETATE (100000093036)
Strength
Strength (Presentation single value or low limit):
Numerator: <blank>
Denominator: <blank>
Strength (Presentation high limit): <blank>
Strength (Concentration single value or low limit):
Numerator: 250 micrograms
Denominator: 24 hour (100000110804)
Strength (Concentration high limit): <blank>
Strength (Presentation) Text: <blank>
Reference Strength
Reference Substance : NORETHISTERONE ACETATE (100000093036)
Reference Strength (Presentation single value or low limit):
Numerator: <blank>
Denominator: <blank>)
Strength (Presentation high limit): <blank>
Reference Strength (Concentration single value or low limit):
Numerator: 250 micrograms
Denominator: 24 hour (100000110804)
Strength (Concentration high limit): <blank>
Strength (Presentation) Text: <blank>


Phase II
Manufactured Item
Manufactured Dose Form: Transdermal patch (100000073741)
Unit of Presentation : Patch (200000002134)
Quantity Operator: equal to (100000000049)
Manufactured Item Quantity: 4 countable unit
Ingredient
Ingredient role : Active (100000072072)
Substance
Substance : ESTRADIOL HEMIHYDRATE (100000089218)
Strength
Strength (Presentation single value or low limit):
Numerator: <blank>
Denominator: <blank>
Strength (Presentation high limit): <blank>
Strength (Concentration single value or low limit): <blank>
Numerator: <blank>
Denominator: <blank>
Strength (Concentration high limit): <blank>
Strength (Presentation) Text: <blank>
Reference Strength
Reference Substance : ESTRADIOL (100000091739)
Quantity Operator: equal to (100000000049)
Reference Strength (Presentation single value or low limit):
Numerator: 0.51 mg
Denominator: 1 patch
Strength (Presentation high limit): <blank>
Reference Strength (Concentration single value or low limit):
Numerator: <blank>
Denominator: <blank>
Strength (Concentration high limit): <blank>
Ingredient
Ingredient role : Active (100000072072)
Substance
Substance : NORETHISTERONE ACETATE (100000093036)
Strength
Quantity Operator: equal to (100000000049)
Strength (Presentation single value or low limit):
Numerator: 4.80 mg
Denominator: 1 patch
Strength (Presentation high limit):
Strength (Concentration single value or low limit): <blank>
Numerator: <blank>
Denominator: <blank>
Strength (Concentration high limit): <blank>
Strength (Presentation) Text: <blank>
Reference Strength
Reference Substance : NORETHISTERONE ACETATE (100000093036)
Quantity Operator: equal to (100000000049)
Reference Strength (Presentation single value or low limit):
Numerator: 4.80 mg
Denominator: 1 patch
Strength (Presentation high limit): <blank>
Reference Strength (Concentration single value or low limit):
Numerator: <blank>
Denominator: <blank>
Strength (Concentration high limit): <blank>

3.3.11. **Solid dose forms in "Container" – Sachet – Oral Solution**

2 QUALITATIVE AND QUANTITATIVE COMPOSITION The active ingredient is potassium [o-[(2,6-dichlorophenyl)-amino]-phenyl-acetate (diclofenac potassium). One sachet contains 50 mg of diclofenac potassium. One sachet also contains 50mg aspartame (E951). For a full list of excipients, see section 6.1.	**Voltfast**	**6.5 Nature and contents of container** Sachet consisting of coupled paper/aluminium/polyethylene, hermetically sealed in four directions. Three sachets are packaged in one carton.
	Points of attention for this example: • This example fits the Pattern: 1b [Solid dose forms in "container"] – Presentation Strength is Mandatory – Concentration Strength must be Empty. • PhP – Unit of Presentation: Portion – To reflect the ISO/TS 20451:2017 (section 8.1.2.2), the use of portion is mandated when "final volume and concentration of the ingredients are not known". Such as in the case where the Pharmaceutical Product represents the "portion of solution resulting from dissolving one tablet".	

3.3.12. **Quantity operator in Ingredients**

In many cases, the exact amount of an ingredient is not known precisely. This is the case when the amount of the ingredient (more commonly an excipient than an active substance) is expressed as "not more than", or "circa" or "quantity sufficient (quantum satis)" etc. This information should be in a quantity operator for ingredient strength.

1 LÄKEMEDLETS NAMN

Alutard SQ Björk, 100 000 SQ-E/ml, injektionsvätska, suspension
Alutard SQ Björk, styrkeserie (100 SQ-E/ml, 1 000 SQ-E/ml, 10 000 SQ-E/ml och 100 000 SQ-E/ml), injektionsvätska, suspension
Alutard SQ 3-Träd, 100 000 SQ-E/ml injektionsvätska, suspension
Alutard SQ 3-Träd, styrkeserie (100 SQ-E/ml, 1 000 SQ-E/ml, 10 000 SQ-E/ml och 100 000 SQ-E/ml), injektionsvätska, suspension

2 KVALITATIV OCH KVANTITATIV SAMMANSÄTTNING

Alutard SQ är ett depotpreparat innehållande standardiserade allergen adsorberade till aluminiumhydroxid.

Alutard SQ Björk: *Betula verrucosa* (björk)
Alutard SQ 3-Träd: 1/3 *Alnus glutinosa* (klibbal), 1/3 *Betula verrucosa* (björk), 1/3 *Corylus avellana* (hassel)

Alutard SQ 3-Trees

6.5 Förpackningstyp och innehåll

Alutard SQ levereras i glasflaskor (typ I) försedda med en klorbutylkork och förseglade
färgat aluminiumlock med avrivningspunkt. Flaskornas nummer är färgkodade så att de
kan skiljas åt.

Alutard SQ finns i två olika förpackningar, en upptrappningsförpackning (styrkeserie) oc
underhållsförpackning (100 000 SQ-E/ml).
Eventuellt kommer inte alla förpackningsstorlekar att marknadsföras.

Tabell 9: Upptrappningsförpackning (styrkeserie) 4 × 5 ml

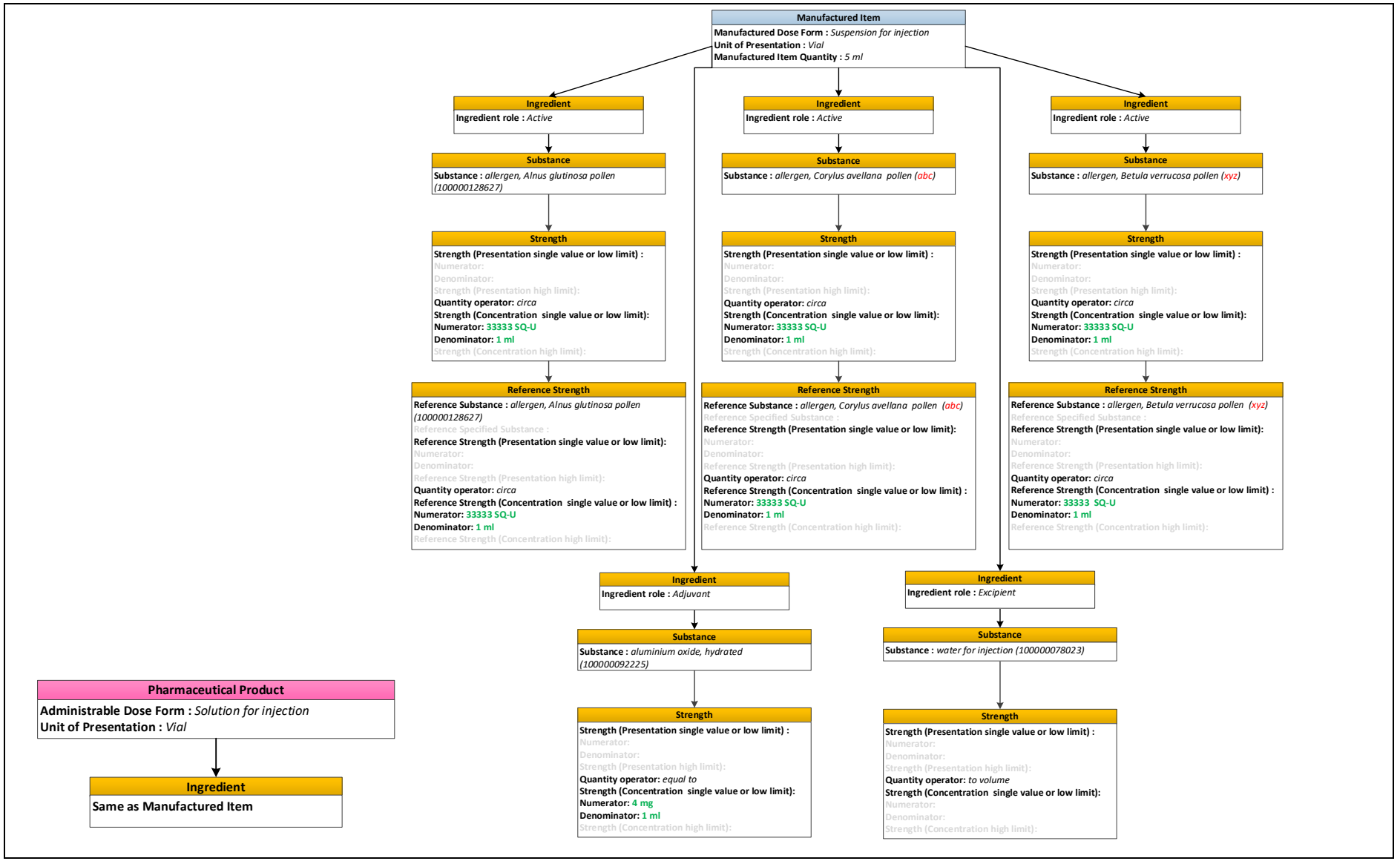
Flaska nr.	Styrka (SQ-E/ml)	Färgkod
1	100	grå
2	1 000	grön
3	10 000	orange
4	100 000	röd

Tabell 10: Underhållsförpackning 5 ml

Flaska nr.	Styrka (SQ-E/ml)	Färgkod
4	100 000	röd

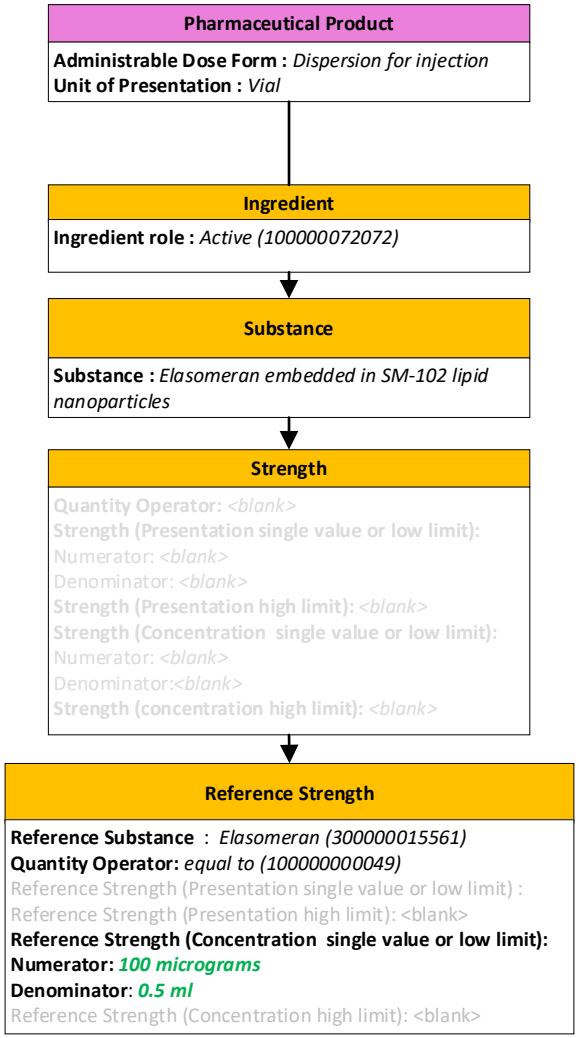
Points of attention for this example:

- Quantity operator for the active allergens is “circa”
- Quantity operator for the adjuvant is “equal to”
- Quantity operator for the excipient “Water for injection” is “to volume”
- This example fits the Pattern: 3a [Products enclosed in a "presentation", where the concentration of content is clinically relevant]
  - Concentration Strength is Mandatory
  - Presentation Strength is Conditional (if the presentation strength is clearly stated it shall be reported).


Manufactured Item
Manufactured Dose Form : Suspension for injection
Unit of Presentation : Vial
Manufactured Item Quantity : 5 ml
Ingredient
Ingredient role : Active
Substance
Substance : allergen, Alnus glutinosa pollen (100000128627)
Strength
Strength (Presentation single value or low limit) :
Numerator:
Denominator:
Strength (Presentation high limit):
Quantity operator: circa
Strength (Concentration single value or low limit):
Numerator: 33333 SQ-U
Denominator: 1 ml
Strength (Concentration high limit):
Reference Strength
Reference Substance : allergen, Alnus glutinosa pollen (100000128627)
Reference Specified Substance :
Reference Strength (Presentation single value or low limit):
Numerator:
Denominator:
Reference Strength (Presentation high limit):
Quantity operator: circa
Reference Strength (Concentration single value or low limit) :
Numerator: 33333 SQ-U
Denominator: 1 ml
Reference Strength (Concentration high limit):
Ingredient
Ingredient role : Active
Substance
Substance : allergen, Corylus avellana pollen (abc)
Strength
Strength (Presentation single value or low limit) :
Numerator:
Denominator:
Strength (Presentation high limit):
Quantity operator: circa
Strength (Concentration single value or low limit):
Numerator: 33333 SQ-U
Denominator: 1 ml
Strength (Concentration high limit):
Reference Strength
Reference Substance : allergen, Corylus avellana pollen (abc)
Reference Specified Substance :
Reference Strength (Presentation single value or low limit):
Numerator:
Denominator:
Reference Strength (Presentation high limit):
Quantity operator: circa
Reference Strength (Concentration single value or low limit) :
Numerator: 33333 SQ-U
Denominator: 1 ml
Reference Strength (Concentration high limit):
Ingredient
Ingredient role : Active
Substance
Substance : allergen, Betula verrucosa pollen (xyz)
Strength
Strength (Presentation single value or low limit) :
Numerator:
Denominator:
Strength (Presentation high limit):
Quantity operator: circa
Strength (Concentration single value or low limit):
Numerator: 33333 SQ-U
Denominator: 1 ml
Strength (Concentration high limit):
Reference Strength
Reference Substance : allergen, Betula verrucosa pollen (xyz)
Reference Specified Substance :
Reference Strength (Presentation single value or low limit):
Numerator:
Denominator:
Reference Strength (Presentation high limit):
Quantity operator: circa
Reference Strength (Concentration single value or low limit) :
Numerator: 33333 SQ-U
Denominator: 1 ml
Reference Strength (Concentration high limit):
Ingredient
Ingredient role : Adjuvant
Substance
Substance : aluminium oxide, hydrated (100000092225)
Strength
Strength (Presentation single value or low limit) :
Numerator:
Denominator:
Strength (Presentation high limit):
Quantity operator: equal to
Strength (Concentration single value or low limit):
Numerator: 4 mg
Denominator: 1 ml
Strength (Concentration high limit):
Ingredient
Ingredient role : Excipient
Substance
Substance : water for injection (100000078023)
Strength
Strength (Presentation single value or low limit) :
Numerator:
Denominator:
Strength (Presentation high limit):
Quantity operator: to volume
Strength (Concentration single value or low limit):
Numerator:
Denominator:
Strength (Concentration high limit):
Pharmaceutical Product
Administrable Dose Form : Solution for injection
Unit of Presentation : Vial
Ingredient
Same as Manufactured Item

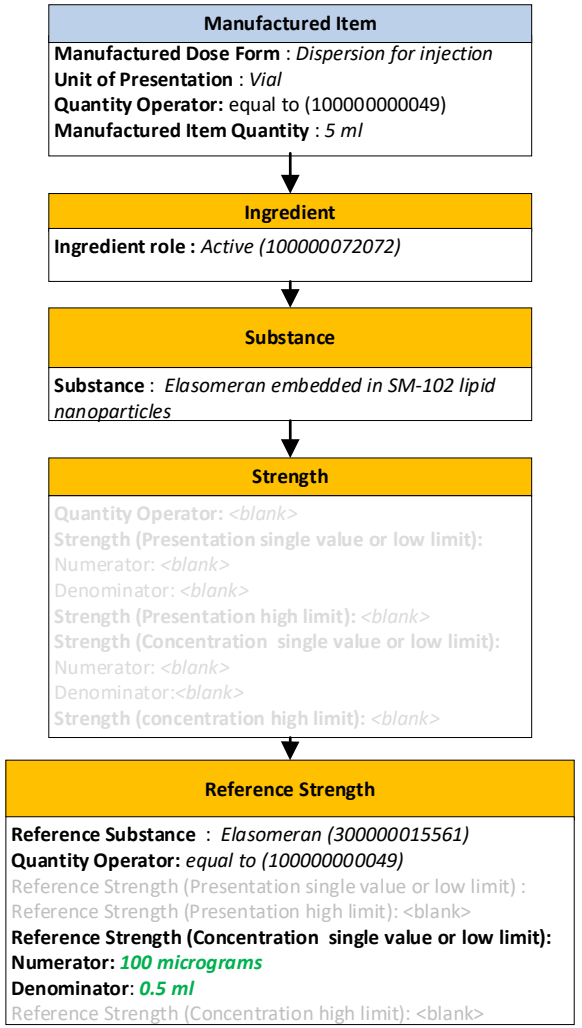
3.3.13. **Multidose vial**

2. QUALITATIVE AND QUANTITATIVE COMPOSITION This is a multidose vial that contains 10 doses of 0.5 mL each or a maximum of 20 doses of 0.25 mL each. One dose (0.5 mL) contains 100 micrograms of elasomeran, a COVID-19 mRNA Vaccine (embedded in SM-102 lipid nanoparticles). One dose (0.25 mL) contains 50 micrograms of elasomeran, a COVID-19 mRNA Vaccine (embedded in SM-102 lipid nanoparticles). Elasomeran is a single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free *in vitro* transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2.	**Spikevax**	**6.5 Nature and contents of container** 5 ml dispersion in a vial (type 1 or type 1 equivalent glass) with a stopper (chlorobutyl rubber) and a flip-off plastic cap with seal (aluminium seal). Each vial contains 10 doses of 0.5 mL. Pack size: 10 multidose vials



Points of attention for this example:

- This example fits the Pattern: 2b [Products enclosed in a "presentation", where the concentration is clinically relevant rather than the total amount in the presentation
  - Presentation Strength is conditional (if the presentation strength is clearly stated it shall be reported.)
  - Concentration Strength is mandatory.
- Strength(s) must be expressed as per SmPC.
  - If **the presentation strength and the concentration strength are both expressed in the SmPC, both must be reported.**



	• In the case of multidose containers, where the strength is expressed per dose (different from actuation), with a quantity of active substance contained in a defined administered volume, the concentration strength is expressed according to the volume of the corresponding dose. This is in accordance with the **no computation rule**- if the presentation strength is not mentioned as-is in the SmPC, it shouldn't be provided even if it can be computed based on the quantity & concentration. In this example the normalised concentration is not reported in the SmPC, that's why the strength to be reported is the concentration strength per 0.5ml as in the SmPC.	

3.4. Medicinal Product with multiple pharmaceutical products

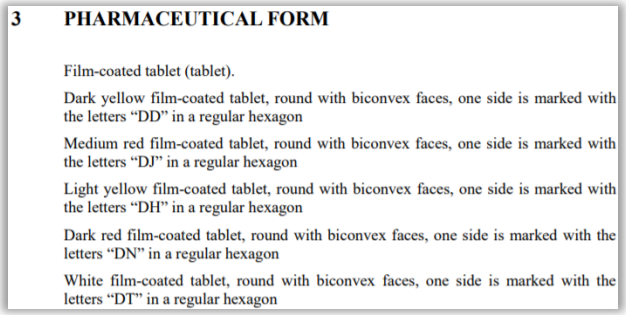
This section provides guidance on how to structure the information for medicinal products submission as per ***EU IG* Chapter 2 – *Data elements for the electronic submission of information on medicinal products for human use*** focussing on medicinal products containing multiple pharmaceutical products.

Topic	Topic description
Description of the challenges	How to represent a medicinal product with multiple pharmaceutical products, when they must all be taken by the patient as part of that product and have the same administrable dose form? How to represent a placebo which is a part of a Medicinal Product? How to handle several different manufactured items and pharmaceutical products contained in a Medicinal Product? How to represent a medicinal product with multiple pharmaceutical products with the same active substances but with a different administrable dose form?
Chapter 2 References	1.5 (Authorised) pharmaceutical form 1.6 Combined pharmaceutical dose forms 6. Pharmaceutical product 5.5.1. Substance 4.11. Manufactured Item
Out of scope	Medicinal product with several manufactured dose forms that are intended to be combined to create a single administrable dose form. Medical devices
Additional reference(s)	ISO 11616 - Health informatics — Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated medicinal product information. *Note: The information contained in these references is non-exhaustive. Companies should refer to all relevant European Union legislation and* ***guidelines*** *when drawing up applications and use the information in the SmPC and regulatory documents (e.g., eAF) to complete medicinal product data.*

A pharmaceutical product can be defined as the qualitative and quantitative composition of a medicinal product in the authorised dose form approved for administration. There are several instances where medicinal products may contain multiple pharmaceutical products characterised by different strengths, pharmaceutical forms or substances.

To illustrate this concept, the example of contraceptive medicinal product *Qlaira* is used. This medicinal product is composed of several different manufactured items which are not transformed, giving several different pharmaceutical products, including a placebo. These pharmaceutical products all have the same administrable dose form and units of presentation, which are the same for the manufactured items and the pharmaceutical products.

The following information is included in the SmPC of this example:



3 PHARMACEUTICAL FORM

Film-coated tablet (tablet).

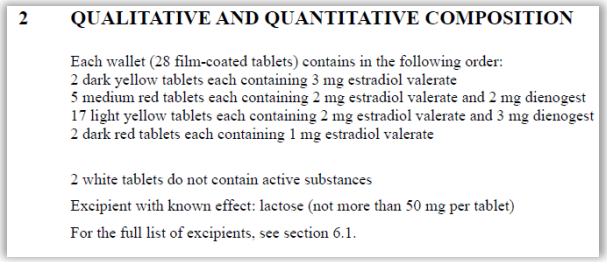
Dark yellow film-coated tablet, round with biconvex faces, one side is marked with the letters "DD" in a regular hexagon

Medium red film-coated tablet, round with biconvex faces, one side is marked with the letters "DJ" in a regular hexagon

Light yellow film-coated tablet, round with biconvex faces, one side is marked with the letters "DH" in a regular hexagon

Dark red film-coated tablet, round with biconvex faces, one side is marked with the letters "DN" in a regular hexagon

White film-coated tablet, round with biconvex faces, one side is marked with the letters "DT" in a regular hexagon



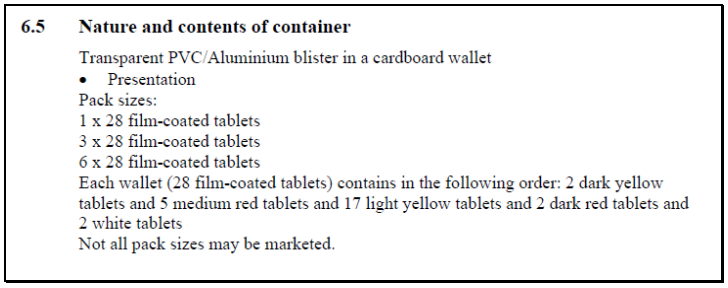
2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each wallet (28 film-coated tablets) contains in the following order:
2 dark yellow tablets each containing 3 mg estradiol valerate
5 medium red tablets each containing 2 mg estradiol valerate and 2 mg dienogest
17 light yellow tablets each containing 2 mg estradiol valerate and 3 mg dienogest
2 dark red tablets each containing 1 mg estradiol valerate

2 white tablets do not contain active substances

Excipient with known effect: lactose (not more than 50 mg per tablet)

For the full list of excipients, see section 6.1.



6.5 Nature and contents of container

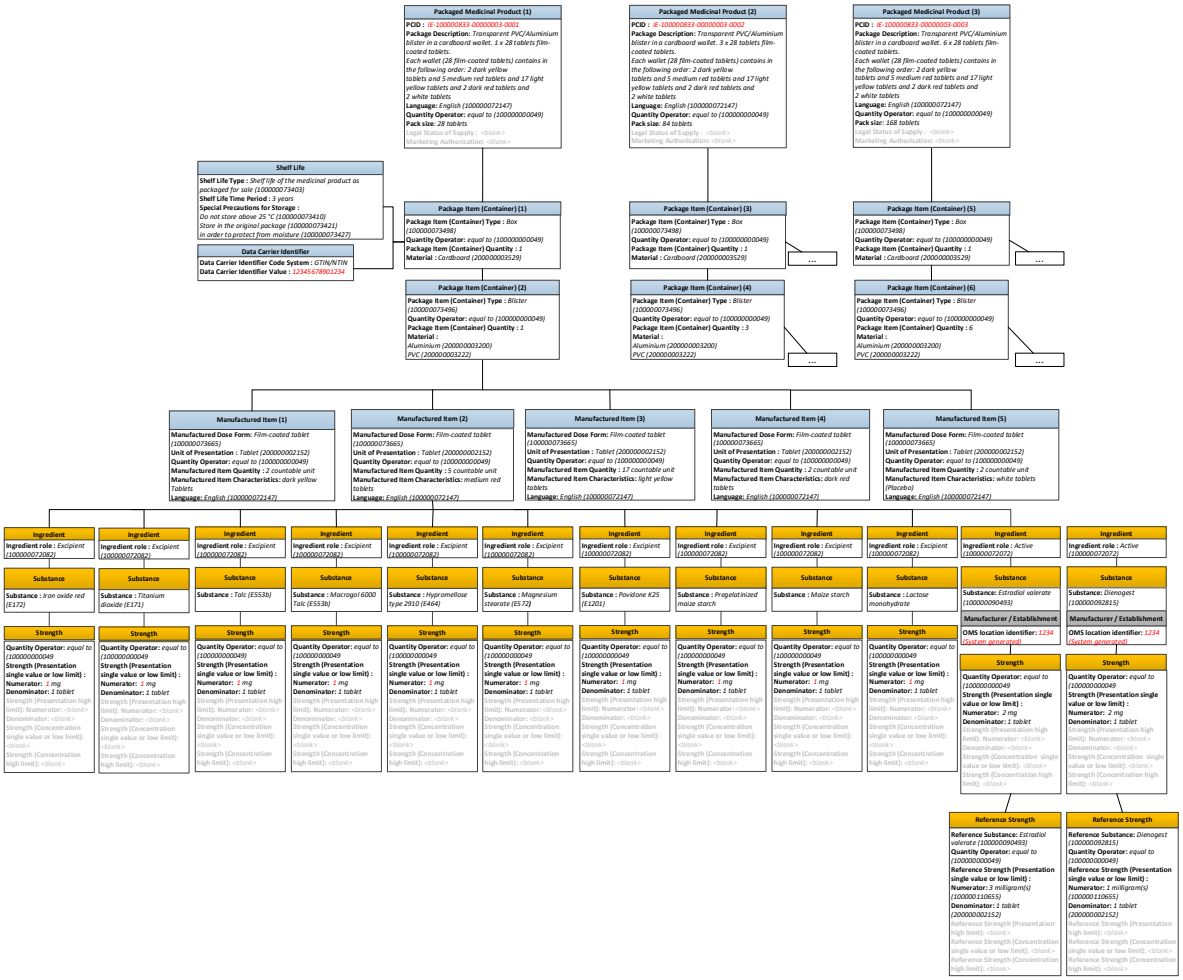
Transparent PVC/Aluminium blister in a cardboard wallet
- Presentation

Pack sizes:
1 x 28 film-coated tablets
3 x 28 film-coated tablets
6 x 28 film-coated tablets
Each wallet (28 film-coated tablets) contains in the following order: 2 dark yellow tablets and 5 medium red tablets and 17 light yellow tablets and 2 dark red tablets and 2 white tablets
Not all pack sizes may be marketed.

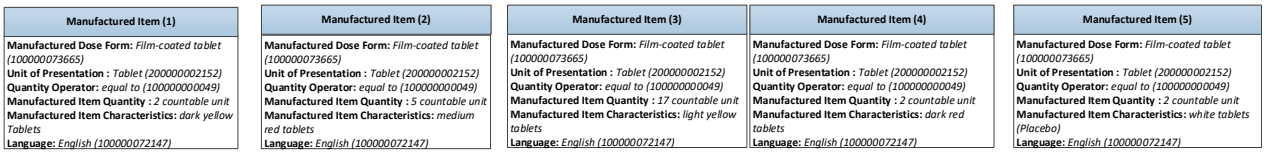
Representation of Manufactured Items

When a product contains multiple pharmaceutical products, the manufactured items are usually identical to the pharmaceutical products unless the pharmaceutical product is made by combining manufactured items prior to administration. Therefore, ingredient information used for the manufactured item may also be used for pharmaceutical product.

The ingredients of each manufactured item of a medicinal product must be described and submitted. For reasons of legibility, ingredients details for only one of the manufactured items are shown below.

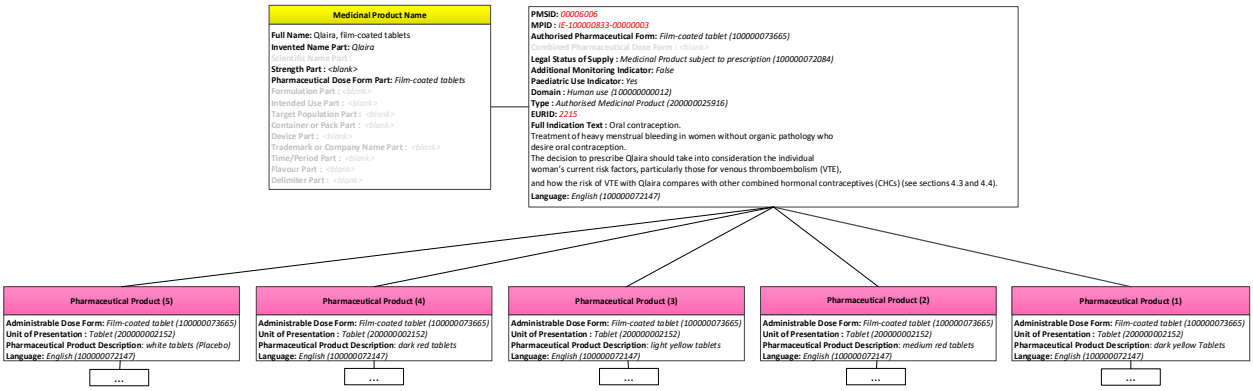


A manufactured Item description text can be used to differentiate between manufactured items when necessary. In this example (contraceptive), this includes the colour of each manufactured item.



Representation of Pharmaceutical Products

In situations where the medicinal product contains several pharmaceutical products which do not require reconstitution (combining) prior to administration (e.g., powder and solvent), the field "combined pharmaceutical dose form" is not relevant and should be left blank.



In this example of contraceptive, a pharmaceutical product section is to be completed for each "pharmaceutical product" present in the medicinal product, including one for the placebo, as the pharmaceutical products contained in Qlaira do not undergo any transformation before administration. The pharmaceutical section is "repeated".

For each pharmaceutical product section, the administrable dose form, the unit of presentation, the route of administration and the ingredients present in each of the pharmaceutical product must be completed. Note: for reasons of simplicity, not all items are shown in this example.

Pharmaceutical Product (1)

Administrable Dose Form: *Film-coated tablet (100000073665)*
Unit of Presentation : *Tablet (200000002152)*
Pharmaceutical Product Description: *dark yellow Tablets*
Language: *English (100000072147)*

Route of Administration

Route of Administration : *Oral use (*100000073619*)*

Note: the Pharmaceutical Product Description field can be used to add any additional elements to further describe and differentiate pharmaceutical products.

Pharmaceutical Product (2)

Administrable Dose Form: *Film-coated tablet (100000073665)*
Unit of Presentation : *Tablet (200000002152)*
Pharmaceutical Product Description: *medium red tablets*
Language: *English (100000072147)*

Pharmaceutical Product (3)

Administrable Dose Form: *Film-coated tablet (100000073665)*
Unit of Presentation : *Tablet (200000002152)*
Pharmaceutical Product Description: *light yellow tablets*
Language: *English (100000072147)*

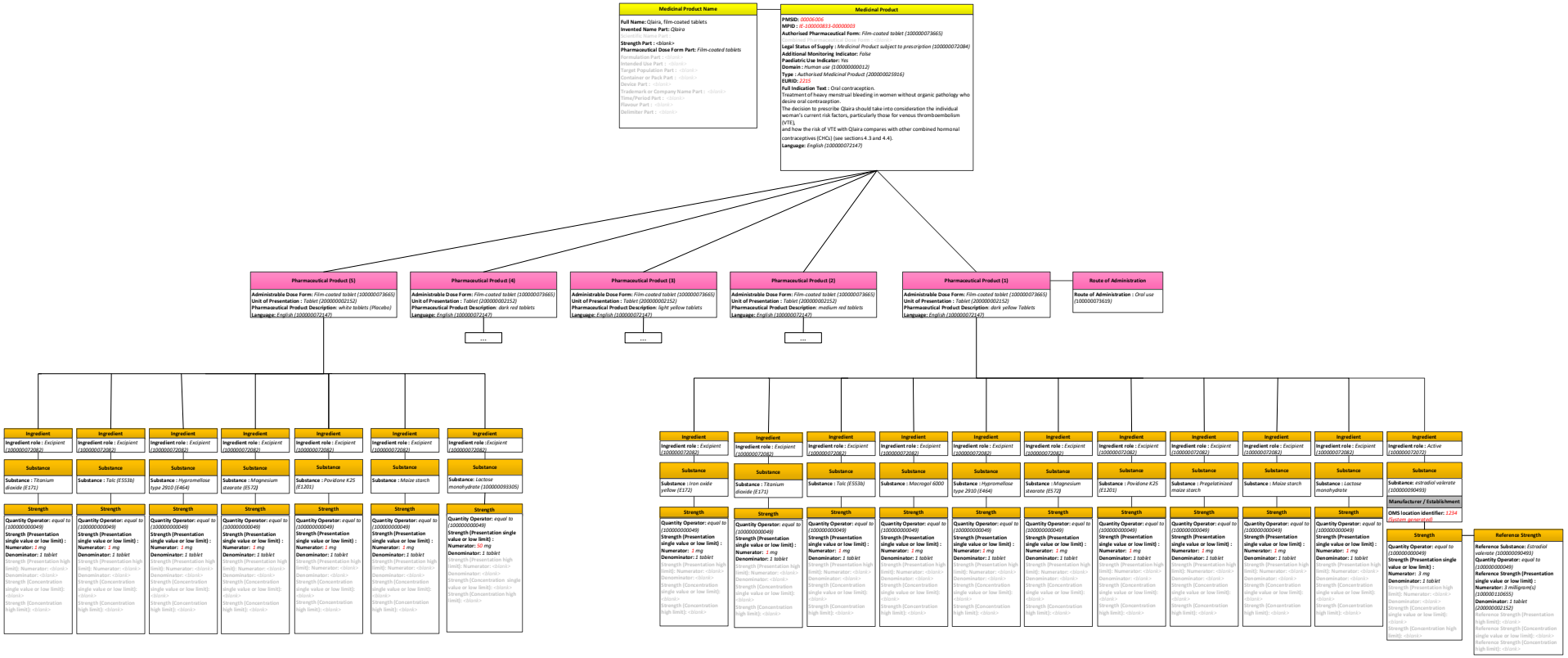
Pharmaceutical Product (4)

Administrable Dose Form: *Film-coated tablet (100000073665)*
Unit of Presentation : *Tablet (200000002152)*
Pharmaceutical Product Description: *dark red tablets*
Language: *English (100000072147)*

Pharmaceutical Product (5)

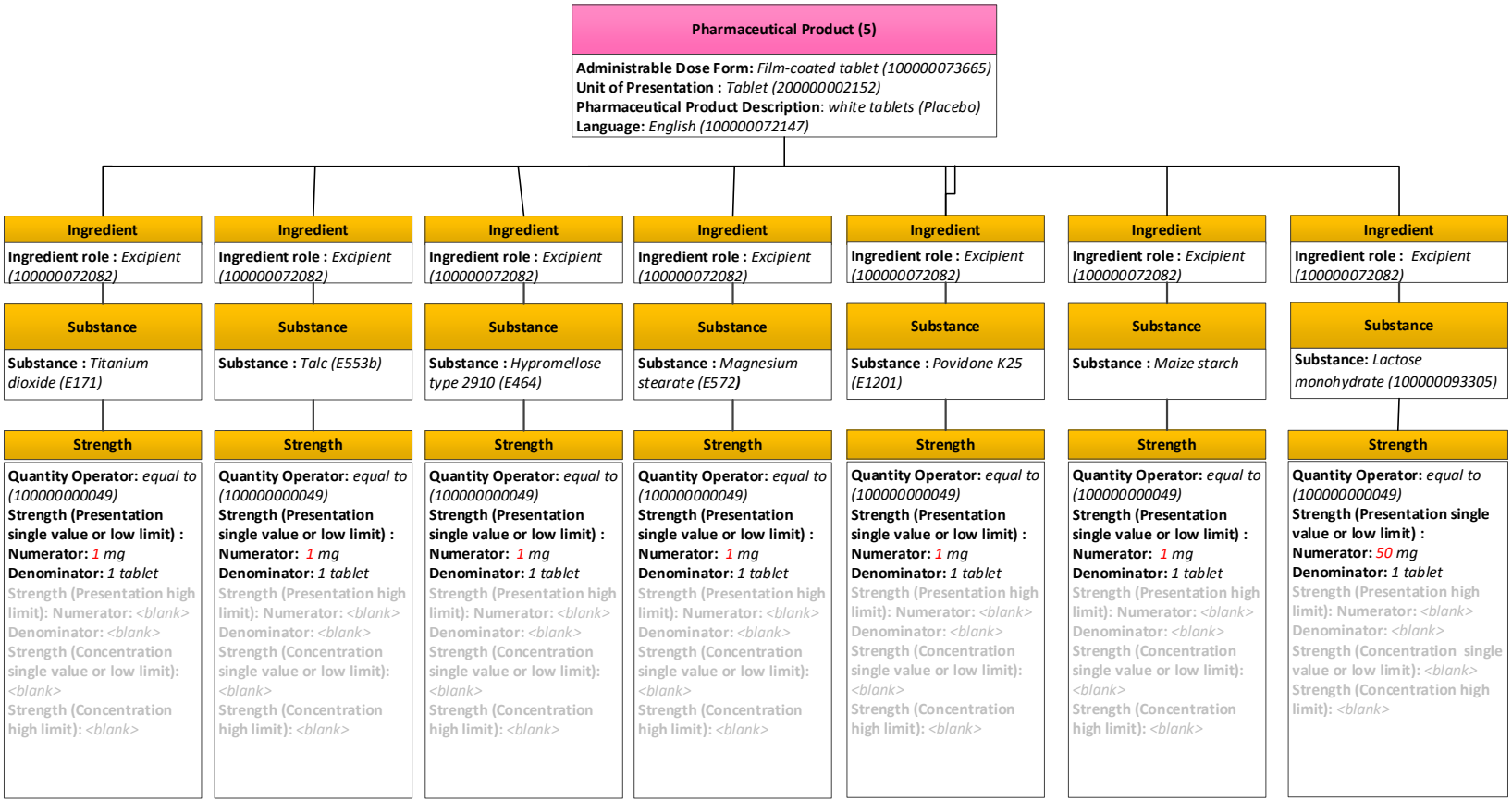
Administrable Dose Form: *Film-coated tablet (100000073665)*
Unit of Presentation : *Tablet (200000002152)*
Pharmaceutical Product Description: *white tablets (Placebo)*
Language: *English (100000072147)*

Pharmaceutical Product Ingredients Each pharmaceutical product must contain the ingredient details. For reasons of legibility, ingredient details for only two of the pharmaceutical products are shown below: the placebo and dark yellow tablets.



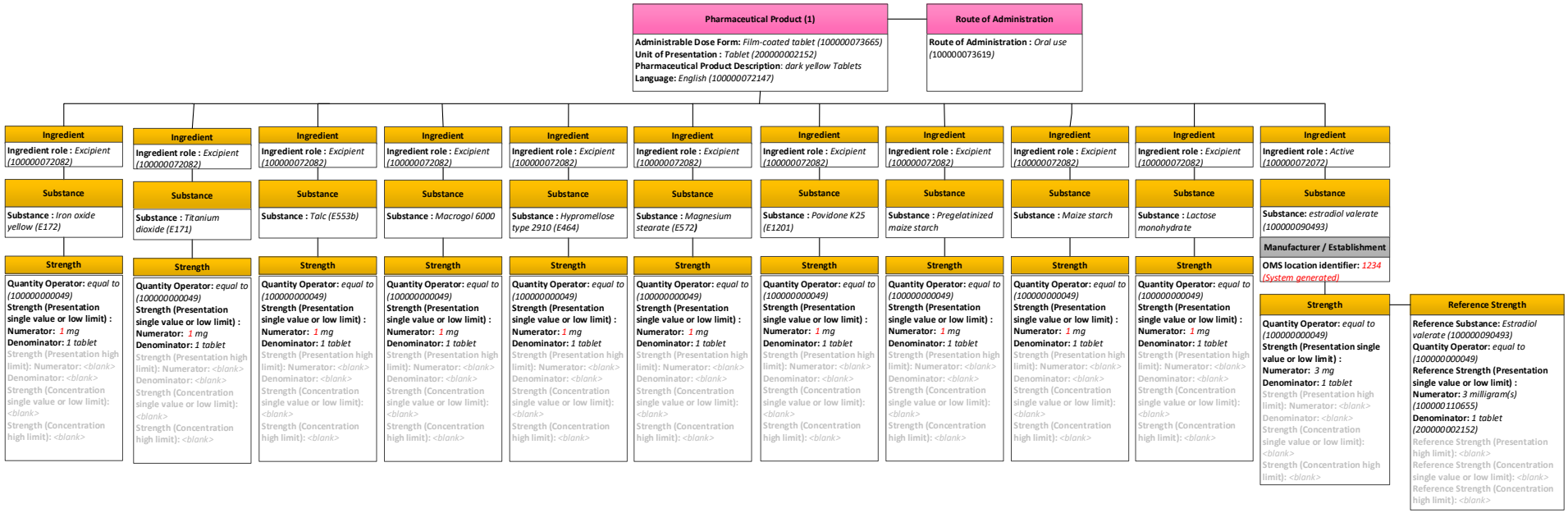
Placebo as pharmaceutical product

The EudraVigilance system requires that every pharmaceutical product must have at least one active ingredient. There is no such requirement in PMS if a pharmaceutical product contains no active ingredient (for instance placebo in a contraceptive), none of the excipients must be labelled as the active ingredient (refer to information in **EU IG – Chapter 2**).



Detailed example of one of the pharmaceutical products

This pharmaceutical product contains the active ingredient estradiol valerate and the other ingredients have the role of excipient.



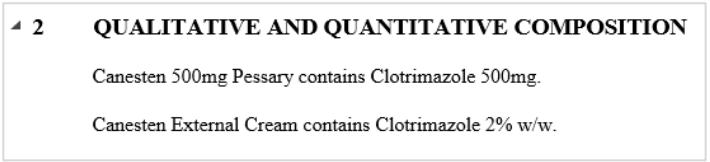
Examples with a different pharmaceutical form and unit of presentation (e.g., cream + tablet)

To strengthen the concept of medicinal products which may contain multiple pharmaceutical products characterised by different strengths, pharmaceutical forms or substances, additional examples are provided:

Canesten Combi Pessary & External Cream 500mg / 2% w/w pessary & cream.

This medicinal product is composed of two pharmaceutical products that correspond with two different administrable dose forms and manufactured dose forms (e.g., pessary and cream). As consequence, this medicinal product contains two different unit of presentations for the pharmaceutical product and manufactured item. However, the two pharmaceutical products have the same route of administration (e.g., vaginal use).

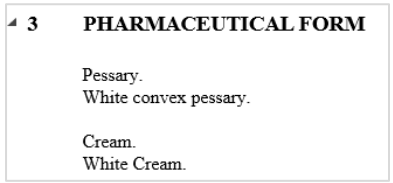
The following information are included in the SmPC:



2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Canesten 500mg Pessary contains Clotrimazole 500mg.

Canesten External Cream contains Clotrimazole 2% w/w.



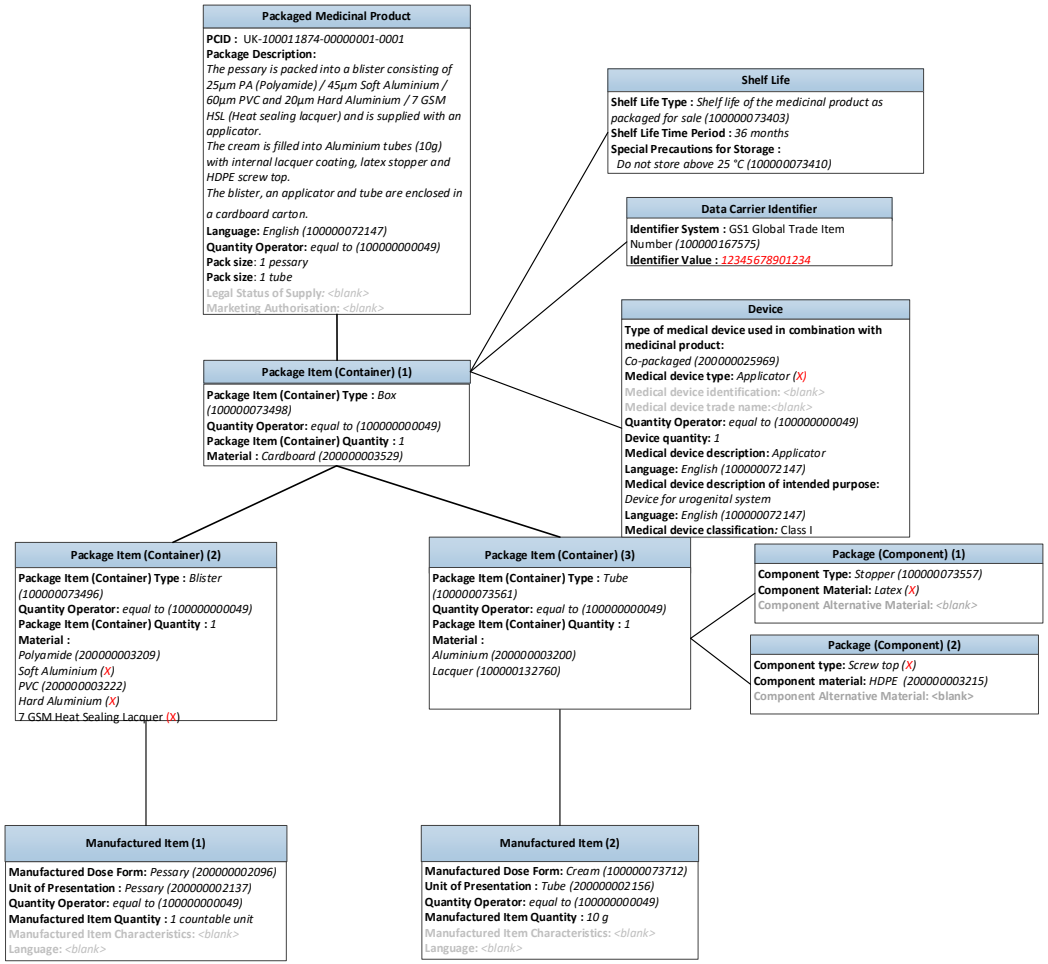
3 PHARMACEUTICAL FORM

Pessary.
White convex pessary.

Cream.
White Cream.

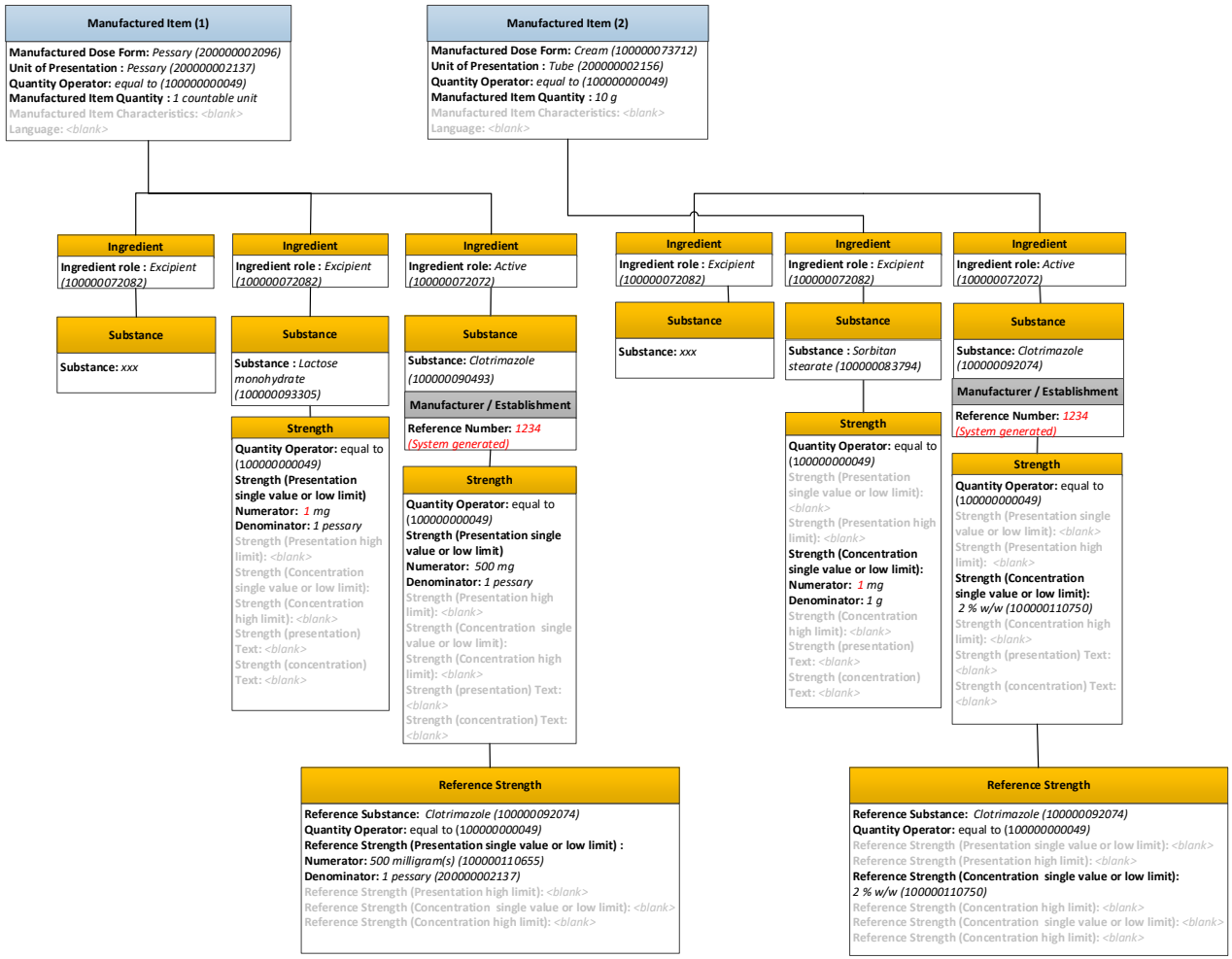
In this situation, where medicinal products consist of two pharmaceutical products that correspond with two different administrable dose forms, the Authorized Pharmaceutical Dose Form to report is: cream + pessary. The field "combined pharmaceutical dose form" should be left blank as it is not applicable to the case (the manufactured item does not need to be combined before administration to the patient).

Therefore, in this case, there are two different manufactured items that should be reported as follows:



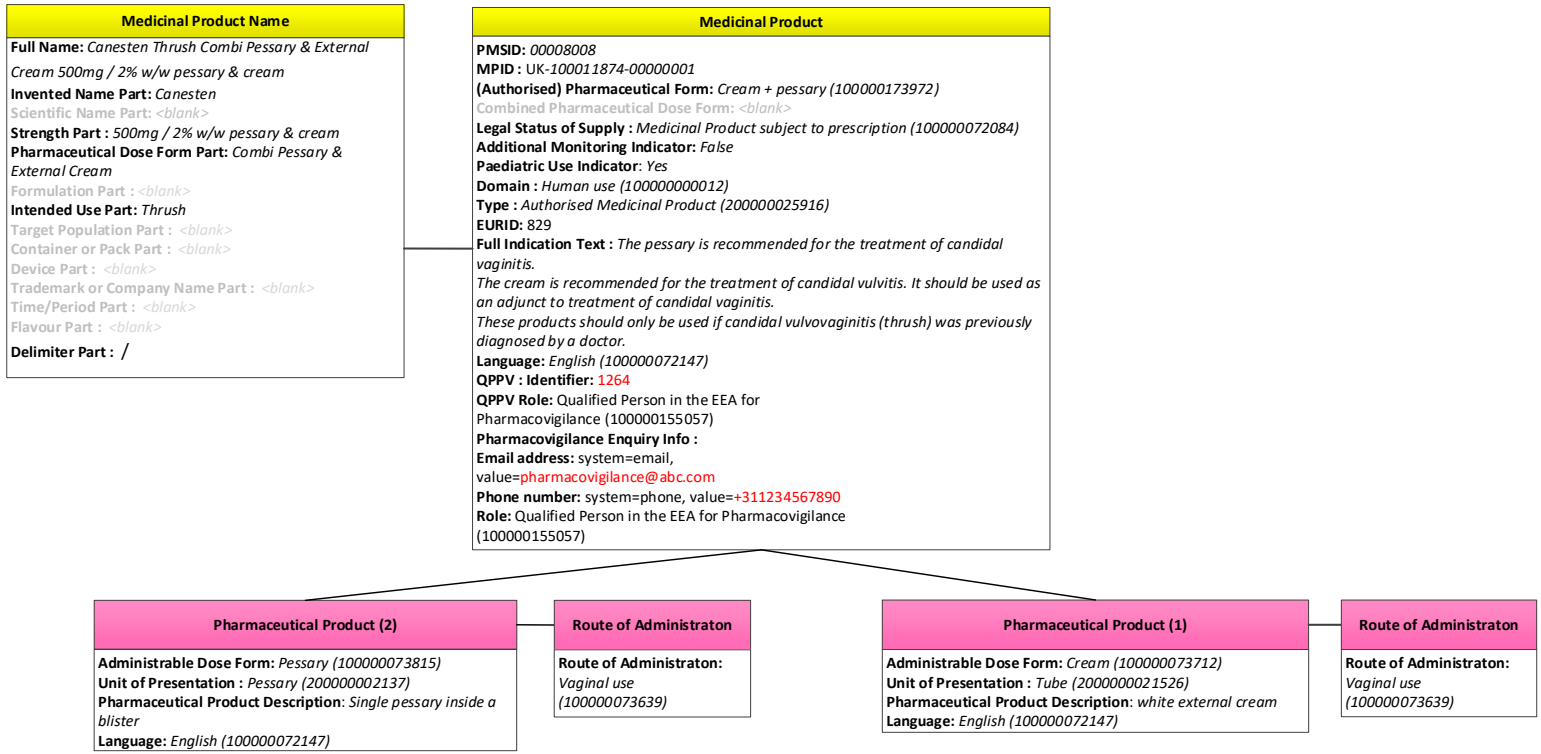
Considering that the medicinal product contains more than one pharmaceutical product, manufactured item description text is reported as per information provided in the SmPC.

The unit of presentation and the ingredients present in each of the manufactured item must be detailed as below, according to the information reported in the SmPC. For a better readability, a limited number of excipients have been reported.

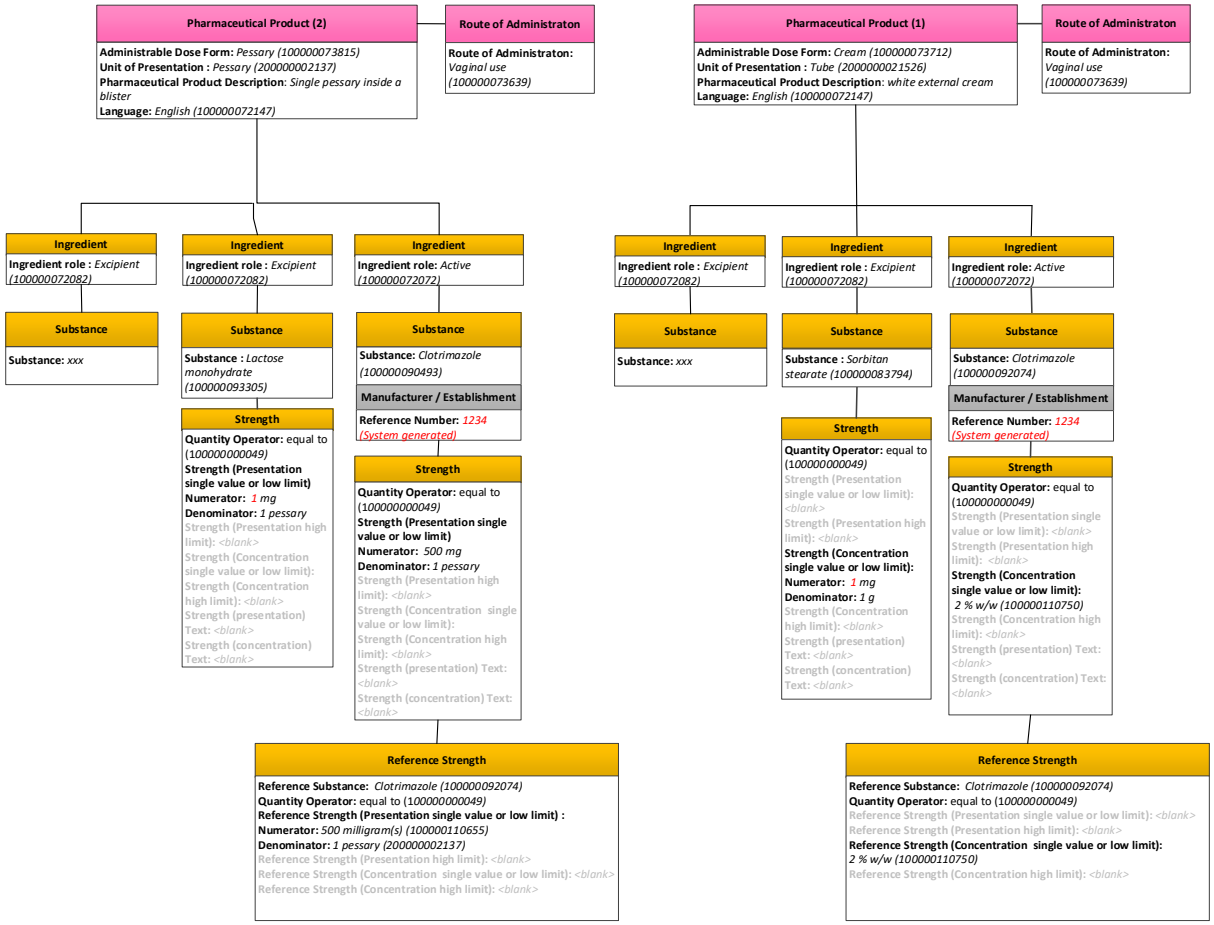


Note: Considering that in this case, the SmPC does not contain the specific quantitative composition of the excipients (confidential information), dummy data 1 mg is reported to all excipients in each manufactured item of the medicinal product Canesten Combi Pessary & External Cream for illustrative process only.

As per previous Qlaira example, a pharmaceutical product section is to be completed with the relevant information and repeated for each "pharmaceutical product" present in the medicinal product.



In this case, the same route of administration applies to both pharmaceutical products while the administrable dose forms are “pessary” and “cream” respectively. Similarly, to the previous provided example, the pharmaceutical products are identical to manufactured items. Therefore, the same ingredients information completed for manufactured items are also used for pharmaceutical product description.



Note: Considering that in this case, the SmPC does not contain the specific quantitative composition of the excipients (confidential information), dummy data 1 mg is reported to all excipients in each pharmaceutical product of the medicinal product Canesten Combi Pessary & External Cream for illustrative process only.

Arilin® Combination Pack Metronidazole 250 mg per film-coated tablet 100 mg metronidazole per vaginal suppository for female adults.

This medicinal product is composed of two pharmaceutical products with two different administrable dose forms and manufactured dose forms (e.g.,, film-coated tablet and pessary). As consequence, this medicinal product contains two different unit of presentations for the pharmaceutical product and manufactured item. These two pharmaceutical products have different routes of administration.

The following information are included in the SmPC:

SmPC	Translation
2. QUALITATIVE UND QUANTITATIVE ZUSAMMENSETZUNG 1 Vaginalzäpfchen enthält 100 mg Metronidazol. 1 Filmtablette enthält 250 mg Metronidazol. Filmtabletten Sonstige(r) Bestandteil(e) mit bekannter Wirkung: Lactose-Monohydrat. Vollständige Auflistung der sonstigen Bestandteile siehe Abschnitt 6.1.	1 vaginal suppository contains 100 mg metronidazole. 1 film-coated tablet contains 250 mg metronidazole. Film-coated tablets Excipient(s) with known effect: lactose monohydrate. For a full list of excipients, see section 6.1
3. DARREICHUNGSFORM Filmtablette Runde, weiße Filmtabletten ohne Bruchkerbe. Vaginalzäpfchen Weißlich-gelbliches Vaginalzäpfchen.	Film-coated tablet: Round, white, film-coated tablets with no score Vaginal suppositories: Whitish-yellowish vaginal cone

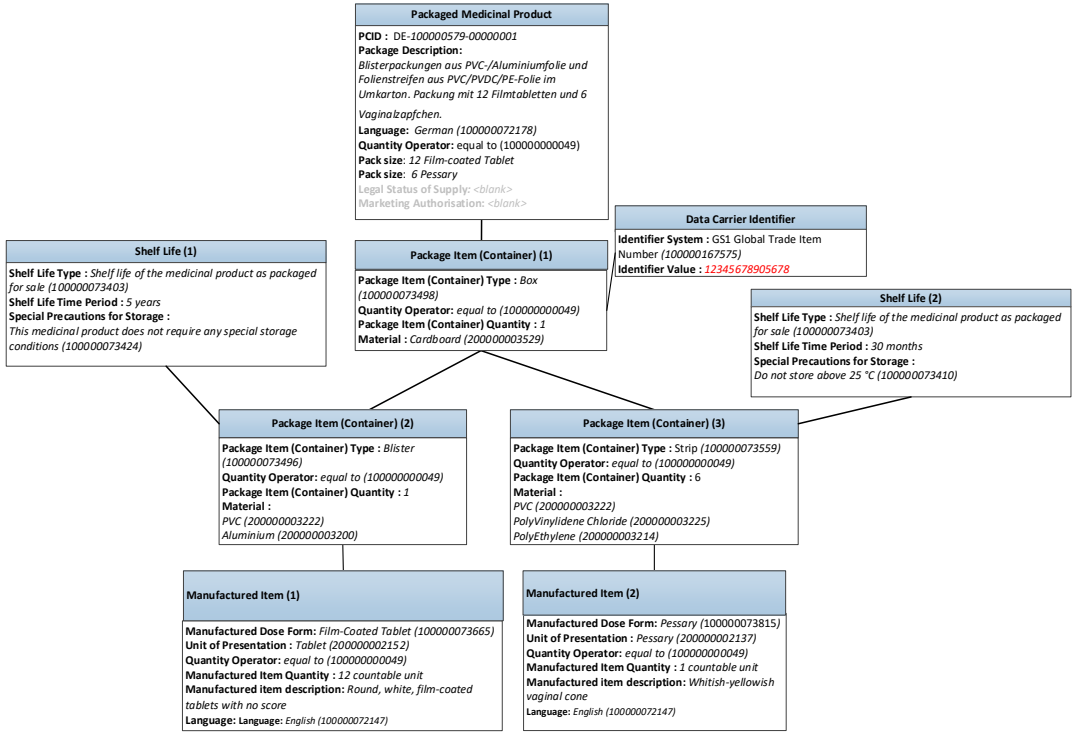
The Authorized Pharmaceutical Dose Form to report is: Film-coated Tablet + pessary. The field "combined pharmaceutical dose form" should be left blank as it is not applicable to the case (the manufactured item does not need to be combined before administration to the patient).

The SmPC provides two different storage conditions– one for the tablet and one for the pessary.

SmPC	Translation
6.4 Besondere Vorsichtsmaßnahmen für die Aufbewahrung Filmtabletten Für dieses Arzneimittel sind keine besonderen Lagerungsbedingungen erforderlich.	This medicinal product does not require special storage conditions
Vaginalzäpfchen Nicht über 25 °C lagern.	Do not store above 25 °C

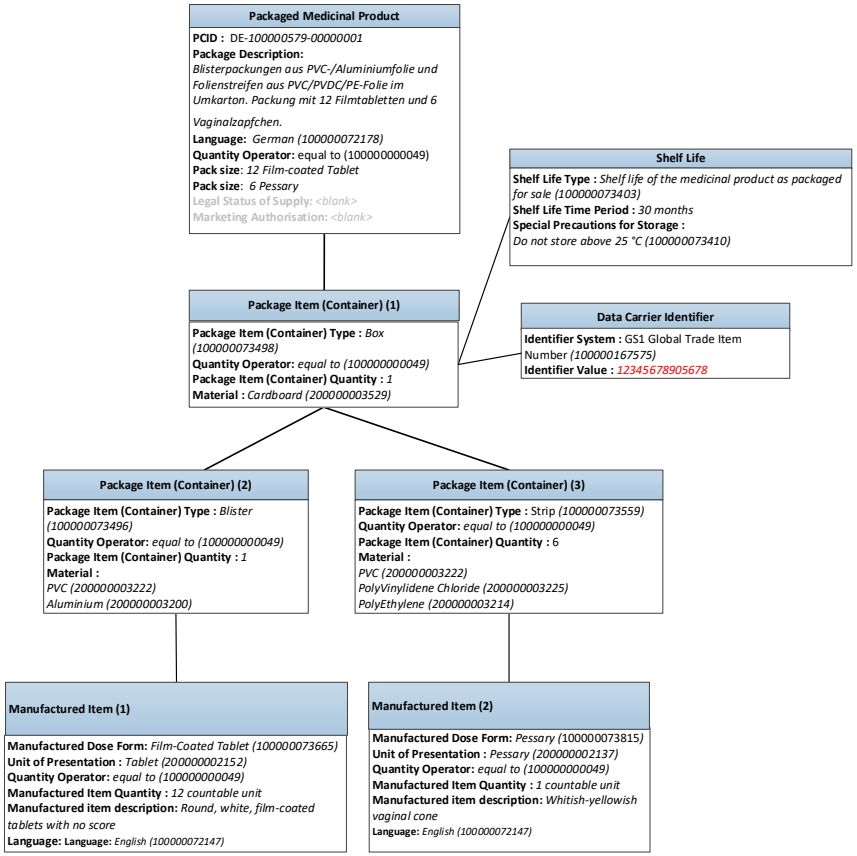
Therefore, the shelf life can be reported in either of the following methods:

1. Report shelf life at the level of the primary packaging



In this case, the Shelf Life has been repeated for each manufactured item and is reported at the level of the primary packaging. For more information refer to section 4.12 in *EU IG* Chapter 2 – *Data elements for the electronic submission of information on medicinal products for human use".*

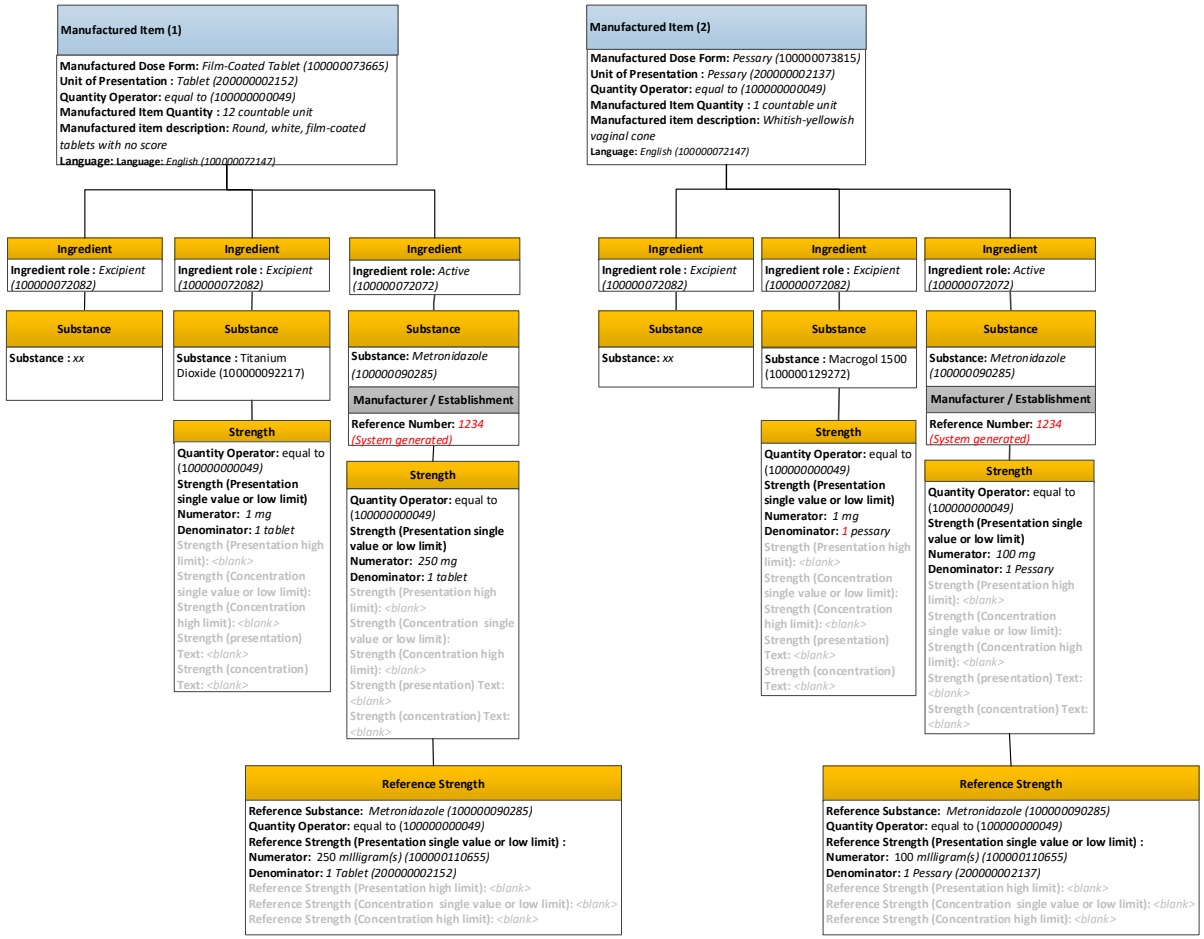
2. Report shelf life at the level of the outer packaging



In this case, only the most critical Shelf Life has been reported at the level of the outer packaging. For more information refer to section 4.12 in *EU IG* Chapter 2 – *Data elements for the electronic submission of information on medicinal products for human use".*

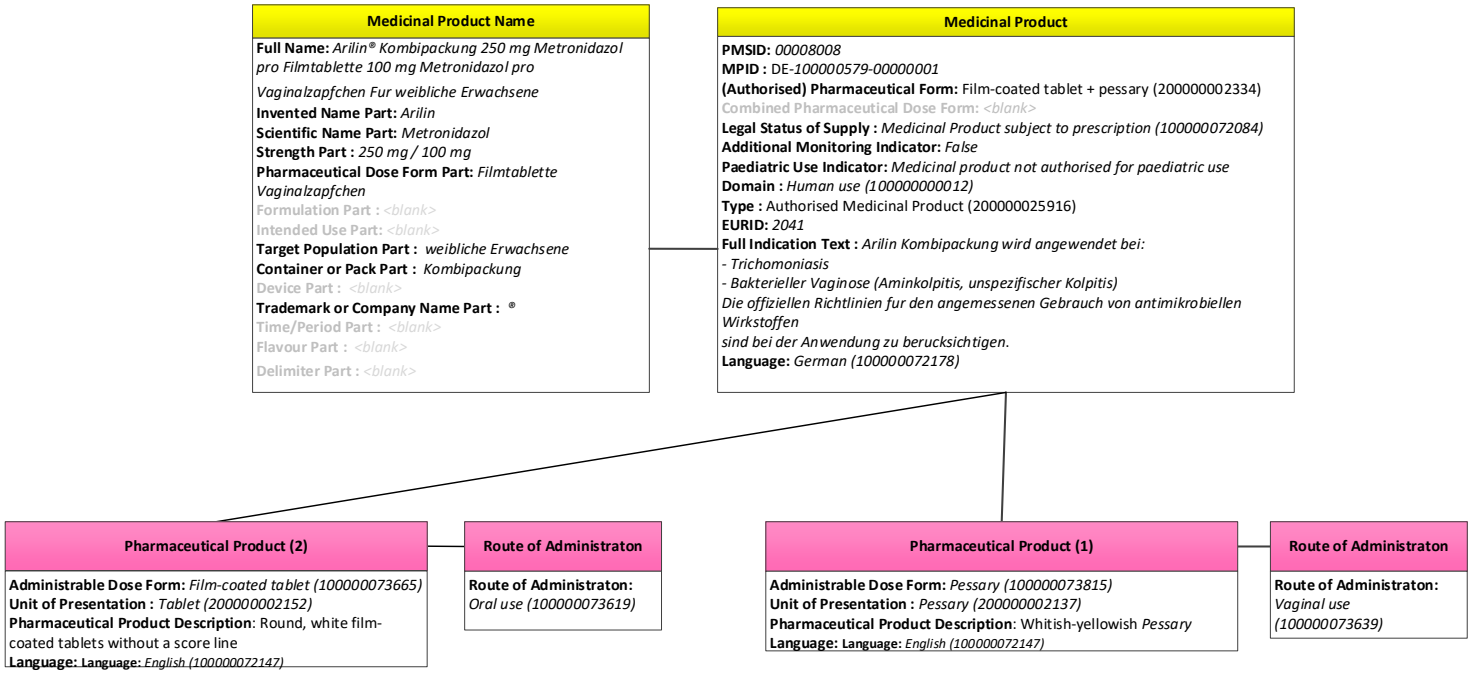
Considering that the medicinal product contains more than one pharmaceutical product, manufactured item description text is reported as per information provided in the SmPC.

The unit of presentation and the ingredients present in each of the manufactured item must be detailed as below, according to the information reported in the SmPC. For a better readability, a limited number of excipients have been reported.

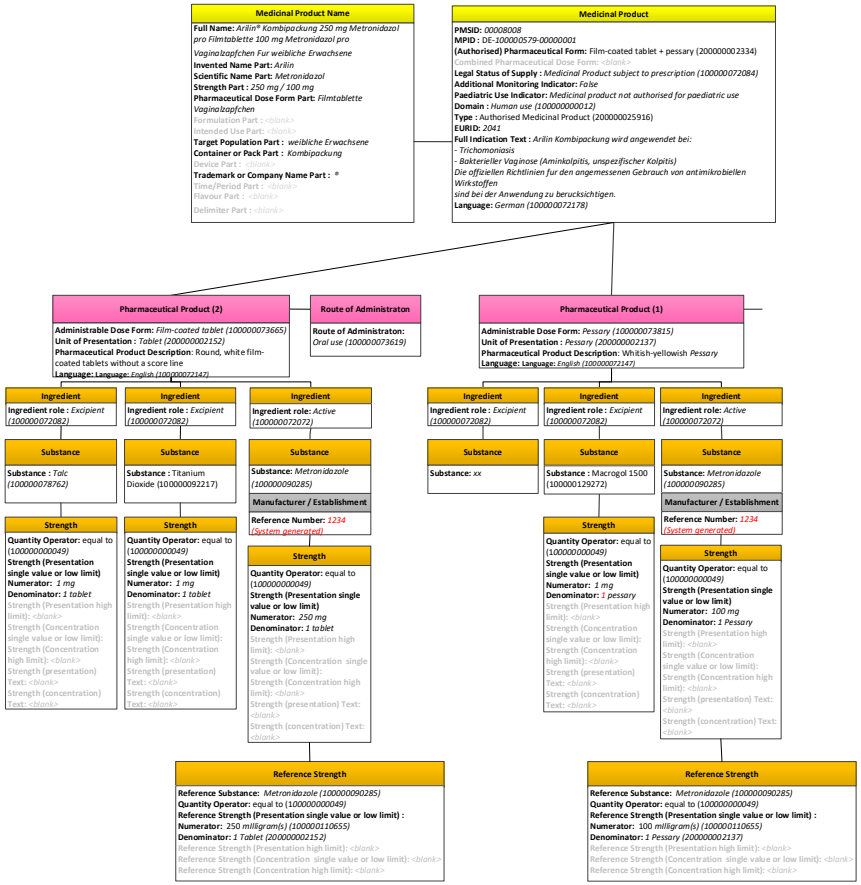


Note: Considering that in this case, the SmPC does not contain the specific quantitative composition of the excipients (confidential information), dummy data 1 mg is reported to all excipients in each manufactured item of the medicinal product Arilin Combination Pack Film-Coated Tablet & Pessary for illustrative process only.

As per previous Qlaira example, a pharmaceutical product section is to be completed with the relevant information and repeated for each "pharmaceutical product" present in the medicinal product.



Unlike the Canesten example, the route of administration of the pharmaceutical products is different. Similarly, to the previous provided example, the pharmaceutical products are identical to manufactured items. Therefore, the same ingredients information completed for manufactured items are also used for pharmaceutical product description.



Note: Considering that in this case, the SmPC does not contain the specific quantitative composition of the excipients (confidential information), dummy data 1 mg is reported to all excipients in each pharmaceutical product of the medicinal product Arilin Combination Pack Film-Coated Tablet & Pessary for illustrative process only.

Aromatol: **concentrate for the preparation of a solution for rinsing the mouth and throat, oral solution, for use on the skin and for steam inhalation**:

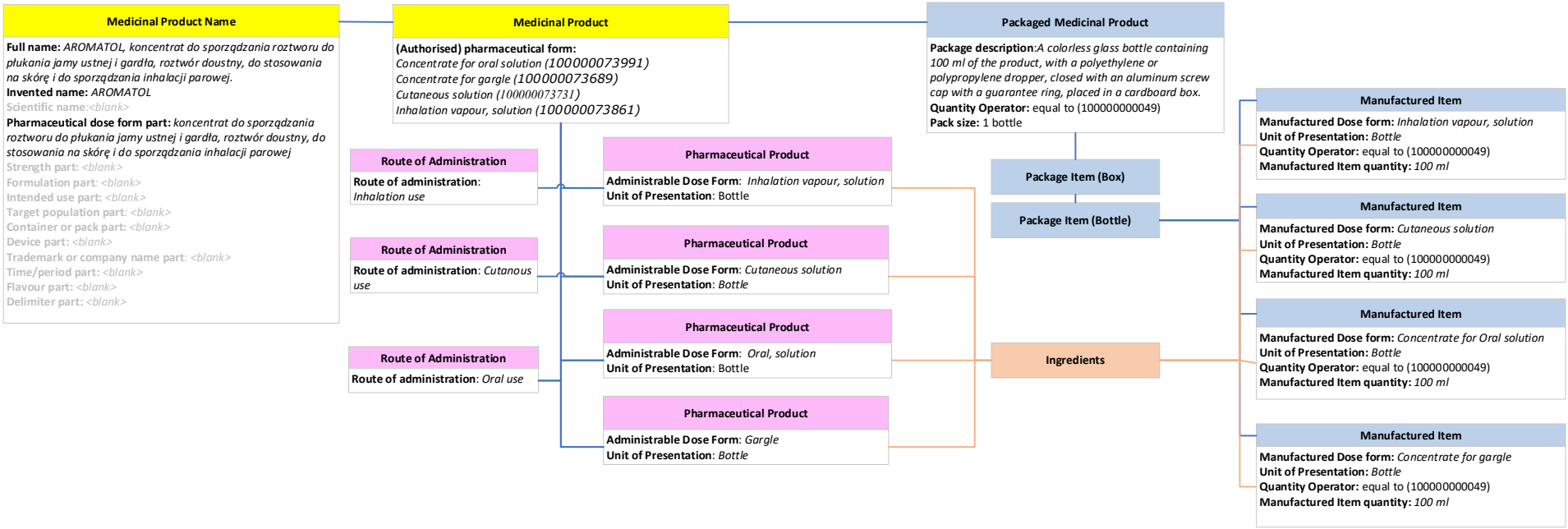
This medicinal product is composed of one package item (1 bottle), corresponding to 4 manufactured items, 4 pharmaceutical products with the same active substances, each with a different administrable dose form depending on if mixing the content of the bottle with water and on different routes of administration.

The following information are included in the SmPC:

SmPC	Translation
CHARAKTERYSTYKA PRODUKTU LECZNICZEGO **1. NAZWA PRODUKTU LECZNICZEGO** AROMATOL, koncentrat do sporządzania roztworu do płukania jamy ustnej i gardła, roztwór doustny, do stosowania na skórę i do sporządzania inhalacji parowej. **2. SKŁAD JAKOŚCIOWY I ILOŚCIOWY** 100 g roztworu zawiera: *Levomentholum* (Lewomentol) 1,72 g *Limonis aetheroleum* (olejek cytrynowy) 0,57 g *Cinnamomi zeylanici corticis aetheroleum* (olejek z kory cynamonowca cejlońskiego) 0,24 g *Menthae arvensis aetheroleum partim mentholi privum* olejek mięty polnej (z obniżoną zawartością mentolu) 0,24 g *Lavandulae aetheroleum* (olejek lawendowy) 0,24 g *Citronellae aetheroleum* (olejek cytronelowy) 0,1 g *Caryophylli floris aetheroleum* (olejek goździkowy) 0,1 g Substancja pomocnicza o znanym działaniu: etanol Produkt zawiera 63% – 72 % (V/V) etanolu. Pełny wykaz substancji pomocniczych, patrz punkt 6.1.	AROMATOL, concentrate for the preparation of a solution for rinsing the mouth and throat, oral solution, for use on the skin and for steam inhalation. 100 g of the solution contains: Levomentholum (Levomenthol) 1.72 g Limonis aetheroleum (Lemon oil) 0.57 g Cinnamomi zeylanici corticis aetheroleum (Ceylon cinnamon bark oil) 0.24 g Menthae arvensis aetheroleum partim mentholi privum field mint oil (with a reduced content of menthol) 0.24 g Lavandulae aetheroleum (lavender oil) 0.24 g Citronellae aetheroleum (citronella oil) 0.1 g Caryophylli floris aetheroleum (clove oil) 0.1 g Excipient with known effect: ethanol The product contains 63% - 72% (V / V) of ethanol.
3. POSTAĆ FARMACEUTYCZNA Koncentrat do sporządzania roztworu do płukania jamy ustnej i gardła, roztwór doustny, do stosowania na skórę i do sporządzania inhalacji parowej. Bezbarwny, klarowny płyn.	Concentrate for the preparation of a solution to rinse the mouth and throat, oral solution, for use on the skin and for the preparation of steam inhalation. Colourless, clear liquid.

4.2 Dawkowanie i sposób podawania Dawkowanie Produkt przeznaczony dla osób dorosłych i młodzieży powyżej 12 lat. 1 g roztworu odpowiada objętości ok. 1,1 mililitra lub 27 kroplom produktu. Podanie doustne W dolegliwościach trawiennych (zaburzeniach dyspeptycznych): np. niestrawności, wzdęciach: 1 do 3 razy na dobę przyjmować 10 do 15 kropli produktu Aromatol zmieszanych z wodą. Podanie na skórę Do nacierań: 1 do 3 razy na dobę nacierać produktem, aż powierzchnia skóry stanie się sucha. W celu zmniejszenia dolegliwości po ukąszeniach owadów miejsce po ukąszeniu przetrzeć wacikiem nasączonym produktem Aromatol. Do płukania gardła Około 5 ml (1 łyżeczka) produktu Aromatol rozcieńczyć w około 250 ml (szklanka) ciepłej wody, płukać gardło i jamę ustną 1 do 3 razy na dobę. Stosowanie w postaci inhalacji (przy przeziębieniu) Około 5 ml (1 łyżeczka) produktu Aromatol rozcieńczyć w około 250 ml (szklanka) gorącej wody i wdychać przez kilka minut powstające opary. Inhalacje powtarzać do 3 razy na dobę. Sposób podawania Podanie doustne, podanie na skórę, do płukania gardła, lub w postaci inhalacji z parą wodną.	4.2 Posology and method of administration Dosage: The product is intended for adults and adolescents over 12 years of age. 1 g of the solution corresponds to the volume of approximately 1.1 milliliters or 27 drops of the product. Oral use, in digestive ailments (dyspeptic disorders): e.g., indigestion, flatulence: take 10 to 15 drops of Aromatol mixed with water 1 to 3 times daily. Cutaneous use, for rubbing, rub the product 1 to 3 times a day until the skin surface becomes dry. In order to reduce the discomfort of insect bites, rub the area after the bite a cotton ball moistened with Aromatol. For gargling, dilute approximately 5 ml (1 teaspoon) of Aromatol in approximately 250 ml (a glass) of warm water, rinse the throat and mouth 1 to 3 times a day. Use in the form of inhalation (with colds), dilute approximately 5 ml (1 teaspoon) of Aromatol in approximately 250 ml (a glass) of hot water and inhale the resulting vapors for a few minutes. Repeat the inhalation up to 3 times a day. Method of administration: Oral use, cutaneous use, gargling or inhalation with steam

The Authorized Pharmaceutical Dose Form to report are concentrate for oral solution, concentrate for gargle, cutaneous solution and inhalation vapour, solution. The manufactured dose forms are similar to the authorised Pharmaceutical dose forms.



3.5. Alignment of Manufactured Item Quantity, Unit of Presentation and Pack Size

This section provides guidance with examples on encoding medicinal product packaging information, together with the relationship between Pack Size, Package Item (container) quantity, and unit of presentation and quantity of the manufactured item as per ***EU IG Chapter 2 – Data elements for the electronic submission of information on medicinal products for human use***.

Topic	Topic description
Description of the challenge	How to record values for Pack size, Package Item (immediate container) Quantity, Manufactured Item Quantity and Unit of Presentation including multi-packs and multi-dose packs.
Chapter 2 References	4.4 Pack Size 4.8.5 Package Item (container) Quantity 4.11.1 Unit of Presentation 4.11.2 Manufactured Item Quantity
Out of scope	Not applicable
Additional reference(s)	ISO 11615, Health informatics — Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated medicinal product information. ISO/TS 20443, 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 *Note: The information contained in these references is non-exhaustive. Companies should refer to all relevant European Union legislation and **guidelines** when drawing up applications and used the information in the SmPC and regulatory documents (e.g., eAF) to complete medicinal product data.*

The following table shows how to record Pack Size, Manufactured Item Quantity and Unit of Presentation, respectively for different product types and package presentations.

Product examples	Packaged Medicinal Product Description	Package Item Container Quantity	Manufactured Item (MI) - Quantity	Pack size	Manufactured item - Unit of Presentation
Tablets in a blister: Ciflox 500 mg	10 tablets in a blister, 1 blister in a box	1 (*blister*)	10 countable unit	10 Tablets	Tablet
Tablets in a blister, multiple blisters: Exforge	10 tablets in a blister, 9 blisters in a box	9 (*blister)*	10 countable unit	90 Tablets	Tablet
LOSEC – Cfr full example	7 tablets in a blister, 4 blisters in a box	4 (*blister*)	7 countable unit	28 Tablets	Tablet
Tablets in a blister with unknown or variable number of blisters: Diamicron MR 30 mg	Tablets in a blister, pack of 60 tablets	*<blank>*	60 countable unit	60 Tablets	Tablet
Tablets with different active ingredient in a monthly dose pack: Qlaira – cfr example	Solid/contraceptive – 1 box with 1 blister with 5 different tablets (different number of tablets)	1 (*blister*)	2 countable unit5 countable unit17 countable unit 2 countable unit 2 countable unit	28 Tablets	Tablet Tablet Tablet Tablet Tablet
Tablets with different active ingredient in a monthly dose pack, multi pack: Qlaira	Solid/contraceptive – 1 box with 3 blisters with 5 different tablets (different number of tablets)	3 (*blister*)	2 countable unit 5 countable unit 17 countable unit 2 countable unit 2 countable unit	84 Tablets	Tablet Tablet Tablet Tablet Tablet
Inhaler multi-dose pack: Relvar Elipta (dry powder inhaler)	1 inhaler including 1 strip of 30 doses	1(*strip*)	30 countable unit	30 actuations	actuation

Product examples	Packaged Medicinal Product Description	Package Item Container Quantity	Manufactured Item (MI) - Quantity	Pack size	Manufactured item - Unit of Presentation
Inhaler, multi-dose pack, administerable dose measured by actuation (pressurised metered dose inhaler)	1 inhaler containing 60 actuations	1 (*inhaler*)	60 countable unit	60 Actuations	Actuation
Liquid: Synflorix	1 vial of 0.5 ml, single dose pack	1 (*vial*)	0.5 ml	1 vial	Vial
Liquid in a vial, multi dose pack : Synflorix	1 vial of 2 ml, 4 dose pack	1 (*vial*)	2 ml	1 vial (4 doses)	Vial
Liquid and powder for reconstitution: Varivax	1 vial (of powder) and 1 Pre-filled Syringe of 1ml of solvent	1 (*vial*) 1 (*pre-filled syringe*)	1 countable unit (powder) 1 ml (solvent)	1 vial (powder) + 1 syringe (solvent)	Vial Syringe
Solution for injection in a pre-filled syringe, single dose	1 pre-filled syringe and needle device, 1 box	1 (*pre-filled syringe*)	0.5 ml	1 syringe	Syringe
Solution in a vial, multi-pack	Vial containing 0.5 ml solution, 10 vials in a box	10 (*vials*)	0.5 ml	10 vials	Vial
Solution in a bottle, administrable dose is measured per 'drop' not by defined unit of measure	5 ml solution in a bottle, 1 bottle in a box, multi-dose pack	1 (*bottle*)	5 ml	1 bottle (multidose)	Bottle

3.5.1. **Product with multiple package configurations**

The example below (**Exforge 5 mg/80 mg film-coated tablets**) contains different approved packaged medicinal products including simple packs, unit-dose configurations and multipacks.

The following principles apply when completing packaged medicinal product information:

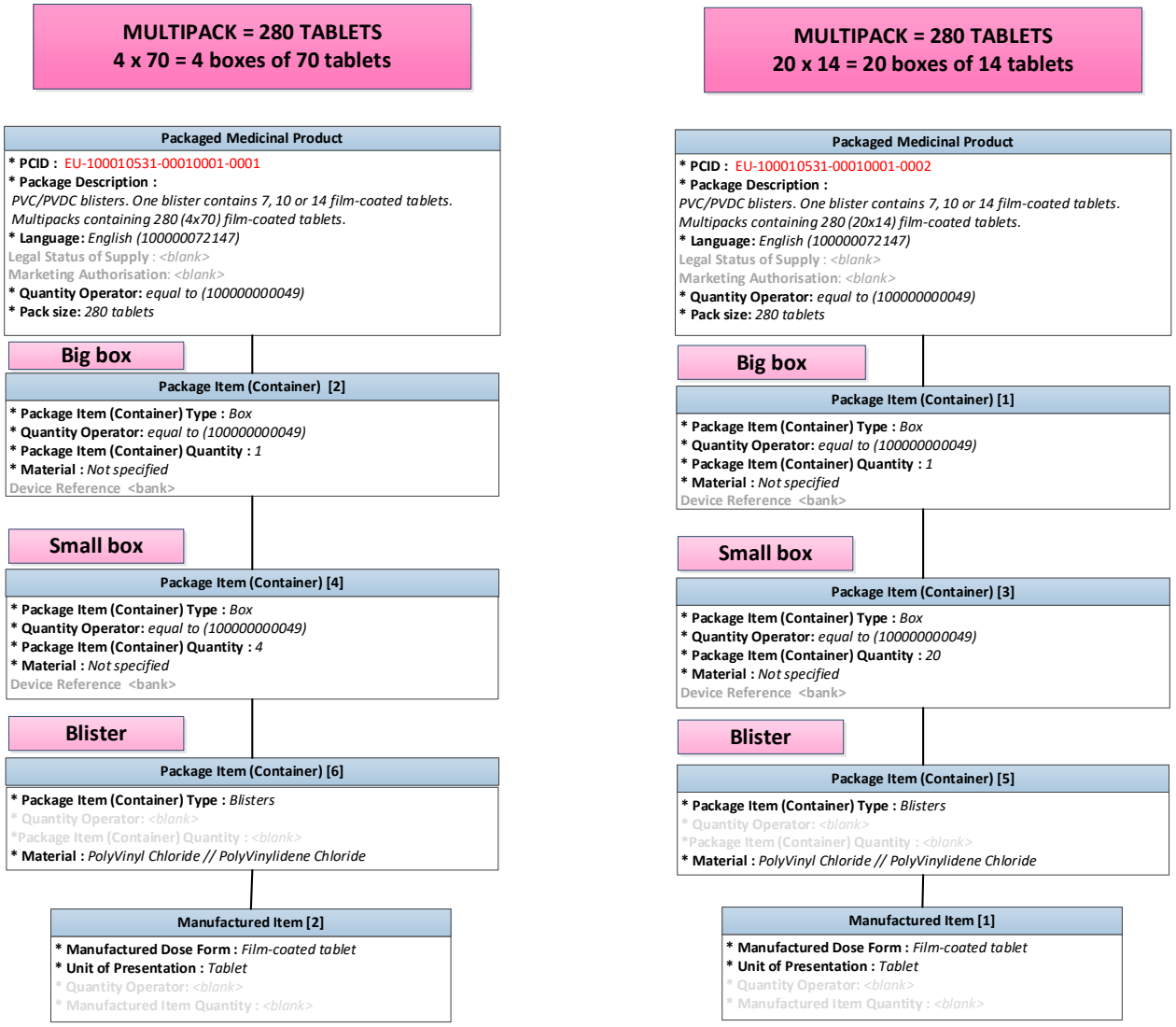
- package Medicinal Product Domain (Section 4 EU IG Chapter 2) must be repeated once per each medicinal product;
- multiple PCID identifiers are generated by the system upon submission of the medicinal product information. One PCID is generated for each medicinal product package submitted;
- for solid dosage forms, there are situations where the number of blisters (immediate packaging) is not reported to regulatory authorities. This is related to the fact that one package, whilst presenting the same immediate packaging characteristics (material) and number of manufactured item (total number of tablets in the pack), may present different package configurations in terms of number of immediate blisters associated to the same package authorisation or PCID (e.g., 1x28 or 2x14 or 4x7). In these cases, Package Item (Container) Quantity and Manufacturing Item Quantity must be left blank while Pack size must reflect the total number of the unit of presentation (tablet);
- unit-dose and multipack pack sizes present some differences when recording the information. The following diagrams provide examples of how to encode these differences.

3.5.2. **Multipacks**

Multipack packaged medicinal product presentation examples are included below. In this example two Multipacks with 2 different configurations are presented:

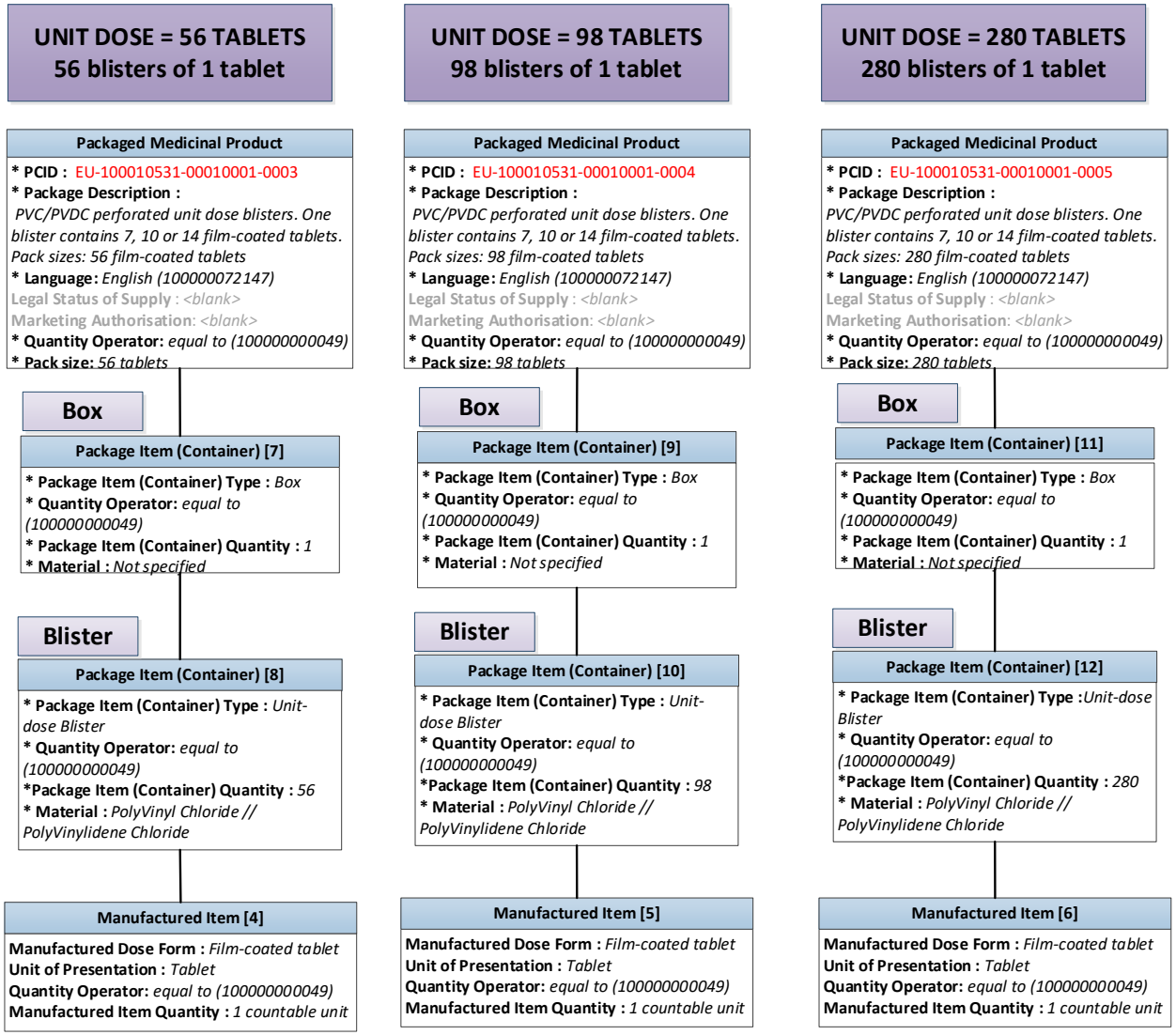
- 280 tablets (20 boxes of 14 tablets)
- 280 tablets (4 boxes of 70 tablets)

This purpose of this example of Exforge **5 mg/80 mg film-coated tablets** is to show how to represent a multipack product with more than one layer of secondary packaging.


MULTIPACK = 280 TABLETS
4 x 70 = 4 boxes of 70 tablets
Packaged Medicinal Product
* PCID : EU-100010531-00010001-0001
* Package Description :
PVC/PVDC blisters. One blister contains 7, 10 or 14 film-coated tablets.
Multipacks containing 280 (4x70) film-coated tablets.
* Language: English (100000072147)
Legal Status of Supply : <blank>
Marketing Authorisation: <blank>
* Quantity Operator: equal to (100000000049)
* Pack size: 280 tablets
Big box
Package Item (Container) [2]
* Package Item (Container) Type : Box
* Quantity Operator: equal to (100000000049)
* Package Item (Container) Quantity : 1
* Material : Not specified
Device Reference <bank>
Small box
Package Item (Container) [4]
* Package Item (Container) Type : Box
* Quantity Operator: equal to (100000000049)
* Package Item (Container) Quantity : 4
* Material : Not specified
Device Reference <bank>
Blister
Package Item (Container) [6]
* Package Item (Container) Type : Blisters
* Quantity Operator: <blank>
*Package Item (Container) Quantity : <blank>
* Material : PolyVinyl Chloride // PolyVinylidene Chloride
Manufactured Item [2]
* Manufactured Dose Form : Film-coated tablet
* Unit of Presentation : Tablet
* Quantity Operator: <blank>
* Manufactured Item Quantity : <blank>
MULTIPACK = 280 TABLETS
20 x 14 = 20 boxes of 14 tablets
Packaged Medicinal Product
* PCID : EU-100010531-00010001-0002
* Package Description :
PVC/PVDC blisters. One blister contains 7, 10 or 14 film-coated tablets.
Multipacks containing 280 (20x14) film-coated tablets.
* Language: English (100000072147)
Legal Status of Supply : <blank>
Marketing Authorisation: <blank>
* Quantity Operator: equal to (100000000049)
* Pack size: 280 tablets
Big box
Package Item (Container) [1]
* Package Item (Container) Type : Box
* Quantity Operator: equal to (100000000049)
* Package Item (Container) Quantity : 1
* Material : Not specified
Device Reference <bank>
Small box
Package Item (Container) [3]
* Package Item (Container) Type : Box
* Quantity Operator: equal to (100000000049)
* Package Item (Container) Quantity : 20
* Material : Not specified
Device Reference <bank>
Blister
Package Item (Container) [5]
* Package Item (Container) Type : Blisters
* Quantity Operator: <blank>
*Package Item (Container) Quantity : <blank>
* Material : PolyVinyl Chloride // PolyVinylidene Chloride
Manufactured Item [1]
* Manufactured Dose Form : Film-coated tablet
* Unit of Presentation : Tablet
* Quantity Operator: <blank>
* Manufactured Item Quantity : <blank>

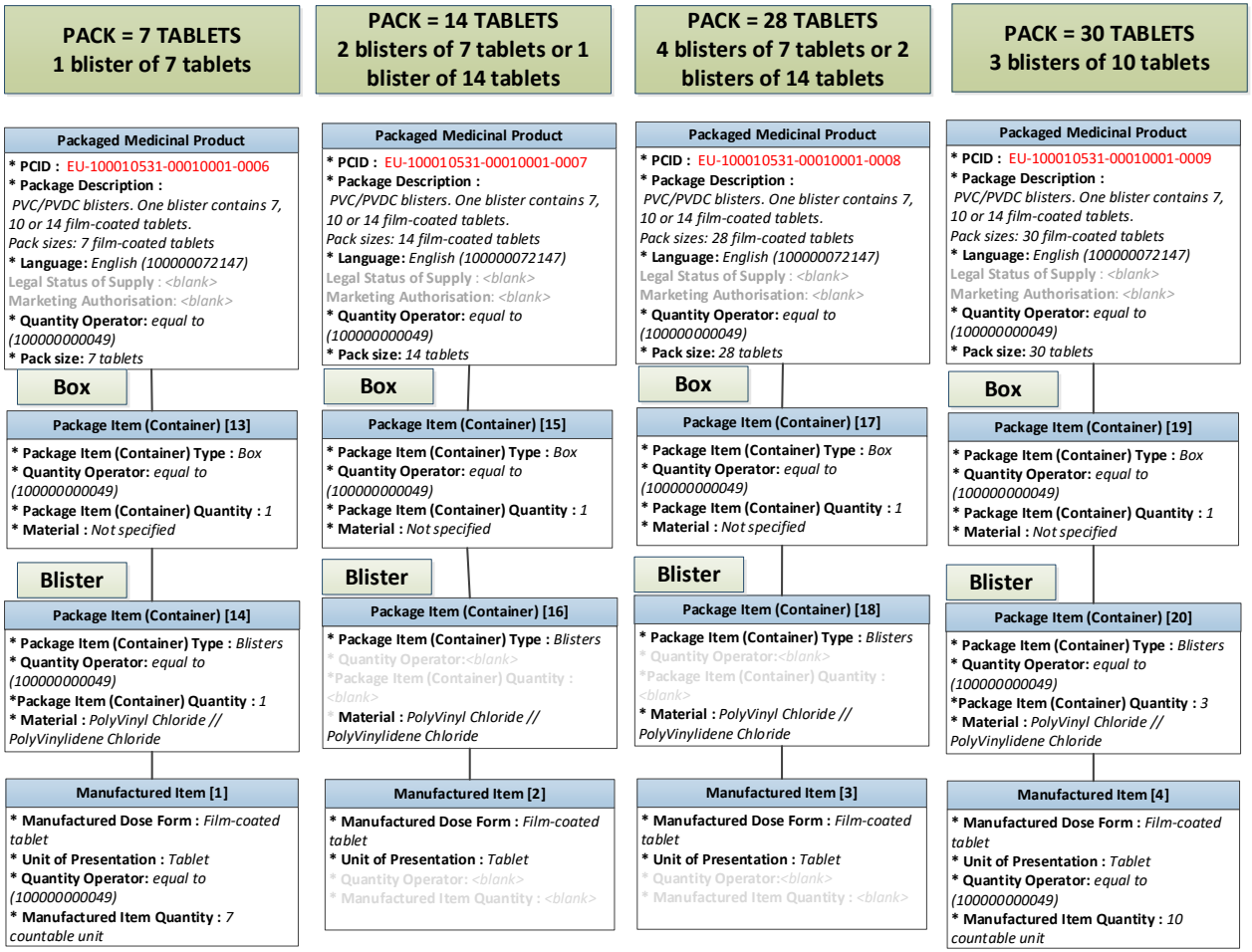
When the number of tablets and/or blisters is unspecified in the SmPC, the fields ‘Package Item (Container) Quantity’ (blister) and ‘Manufactured Item Quantity should be left blank. This is because the individual blister may contain 7, 10 or 14 tablets (or any other number) and the only quantity specified is the total number of tablets in the box (280). The 280 is encoded at Package Medicinal Product level as the pack size. Unit dose package configuration

The example below depicts a unit dose package presentation, where the package item (container) quantity for blisters equals the total pack size (number of tablets) of the packaged medicinal product. In this case, the manufactured item quantity will always be 1.


UNIT DOSE = 56 TABLETS
56 blisters of 1 tablet
Packaged Medicinal Product
* PCID : EU-100010531-00010001-0003
* Package Description :
PVC/PVDC perforated unit dose blisters. One blister contains 7, 10 or 14 film-coated tablets. Pack sizes: 56 film-coated tablets
* Language: English (100000072147)
Legal Status of Supply : <blank>
Marketing Authorisation: <blank>
* Quantity Operator: equal to (100000000049)
* Pack size: 56 tablets
Box
Package Item (Container) [7]
* Package Item (Container) Type : Box
* Quantity Operator: equal to (100000000049)
* Package Item (Container) Quantity : 1
* Material : Not specified
Blister
Package Item (Container) [8]
* Package Item (Container) Type : Unit-dose Blister
* Quantity Operator: equal to (100000000049)
*Package Item (Container) Quantity : 56
* Material : PolyVinyl Chloride // PolyVinylidene Chloride
Manufactured Item [4]
Manufactured Dose Form : Film-coated tablet
Unit of Presentation : Tablet
Quantity Operator: equal to (100000000049)
Manufactured Item Quantity : 1 countable unit
UNIT DOSE = 98 TABLETS
98 blisters of 1 tablet
Packaged Medicinal Product
* PCID : EU-100010531-00010001-0004
* Package Description :
PVC/PVDC perforated unit dose blisters. One blister contains 7, 10 or 14 film-coated tablets. Pack sizes: 98 film-coated tablets
* Language: English (100000072147)
Legal Status of Supply : <blank>
Marketing Authorisation: <blank>
* Quantity Operator: equal to (100000000049)
* Pack size: 98 tablets
Box
Package Item (Container) [9]
* Package Item (Container) Type : Box
* Quantity Operator: equal to (100000000049)
* Package Item (Container) Quantity : 1
* Material : Not specified
Blister
Package Item (Container) [10]
* Package Item (Container) Type : Unit-dose Blister
* Quantity Operator: equal to (100000000049)
*Package Item (Container) Quantity : 98
* Material : PolyVinyl Chloride // PolyVinylidene Chloride
Manufactured Item [5]
Manufactured Dose Form : Film-coated tablet
Unit of Presentation : Tablet
Quantity Operator: equal to (100000000049)
Manufactured Item Quantity : 1 countable unit
UNIT DOSE = 280 TABLETS
280 blisters of 1 tablet
Packaged Medicinal Product
* PCID : EU-100010531-00010001-0005
* Package Description :
PVC/PVDC perforated unit dose blisters. One blister contains 7, 10 or 14 film-coated tablets. Pack sizes: 280 film-coated tablets
* Language: English (100000072147)
Legal Status of Supply : <blank>
Marketing Authorisation: <blank>
* Quantity Operator: equal to (100000000049)
* Pack size: 280 tablets
Box
Package Item (Container) [11]
* Package Item (Container) Type : Box
* Quantity Operator: equal to (100000000049)
* Package Item (Container) Quantity : 1
* Material : Not specified
Blister
Package Item (Container) [12]
* Package Item (Container) Type :Unit-dose Blister
* Quantity Operator: equal to (100000000049)
*Package Item (Container) Quantity : 280
* Material : PolyVinyl Chloride // PolyVinylidene Chloride
Manufactured Item [6]
Manufactured Dose Form : Film-coated tablet
Unit of Presentation : Tablet
Quantity Operator: equal to (100000000049)
Manufactured Item Quantity : 1 countable unit

Simple package configurations

The example below depicts simple package configurations for solid dosage forms, comprising an outer box (secondary packaging) and blisters (primary/immediate packaging). These are very common.



In the example above, the pack of 7 tablets can only contain 1 blister of 7 tablets. In this case, the Manufactured Item Quantity = 7 units and the Package Item (Container) Quantity = 1.

Multiplying the Manufactured Item and Package Item (Container) quantities should equal the quantity encoded in the Pack Size of the Package Medicinal Product. However, the 14-tablet pack can contain either 2 blisters of 7 or 1 blister of 14 tablets. When this is the case, the fields 'Manufactured Item Quantity' and 'Package item (Container) Quantity' are left blank, and the number of tablets (14 in this case) is encoded in the 'Pack size' at 'Packaged Medicinal Product.

3.6. Combination products where medical devices are an integral part of the medicinal product

This section provides guidance on how to structure the information for medicinal products submission as per ***EU IG Chapter 2 – Data elements for the electronic submission of information on medicinal products for human use*** with a focus on the definition and relationship of packaged medicinal product and medical devices.

Topic	Topic description
Description of the challenge	How to describe medical devices that are integrated and contain the medicinal product already as packaged for sale (e.g., pre-filled syringes, pre-filled pen). How to represent their relationship with package items. How to describe package component(s) of the integrated medical device.
Chapter 2 References	Device(s) which are an integral part of a medicinal product are described in the following sections: Packaged medicinal product 4.8 Package item (container) 4.8.4 Device reference(s). This attribute is for mandatory completion where the package medicinal product contains a medical device. In the case of integrated medical devices, the relationship of the medical device with the package item is established at the level of the primary packaging (e.g., pen, syringe). As consequence, the device (e.g., pen, syringe) will be both a package item container and a medical device. 4.9 Package (component) 4.10 Medical Device
Out of scope	Devices that are not co-packaged with the medicinal product (e.g., spoons, syringe) Medical devices that support the pharmacological/metabolic/immunological action of the medicinal product (e.g., collagen scaffold), as described in section 4.9 - Device
Additional reference(s)	https://www.ema.europa.eu/en/human-regulatory/overview/medical-devices#medicinal-products-that-include-a-medical-device-('combination-products')-section *Regulation (EU) 2017/745 on medical devices- Article 1(8) and Article 1(9)* *Note: The information contained in these references is non-exhaustive. Companies should refer to all relevant European Union legislation and **guidelines** when drawing up applications and use the information in the SmPC and regulatory documents (e.g., eAF) to complete medicinal product data.*

Examples of **pre-filled syringe** and **pre-filled pen** are shown below for illustration purposes.

In each case, information found in section 6.5 of the SmPC is used as a basis for the **integrated medical device** description and the **package item(s)** of the package medicinal product.

Pre-filled syringe example

Nucala 100 mg solution for injection in pre-filled syringe

6.5 Nature and contents of container

1 ml solution in a Type 1 glass syringe with a fixed needle (stainless steel) and passive safety needle guard.

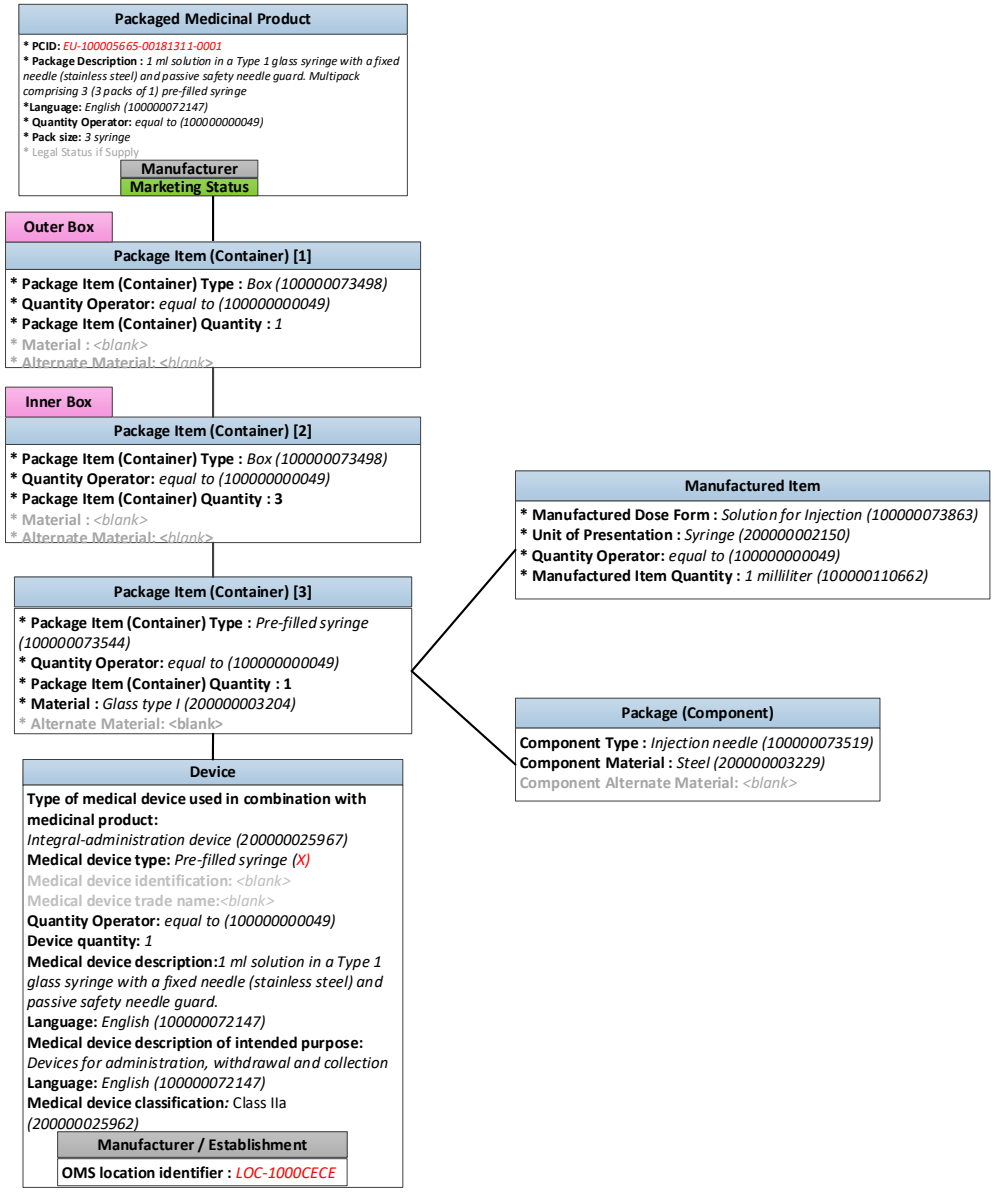
Pack sizes: 1 pre-filled syringe. Multipack comprising 3 (3 packs of 1) pre-filled syringe.

In the following graphical representation, only the multipack is shown below – 3(3 packs of 1) pre-filled syringe.

The pre-filled syringe is both a package item and a device.

The injection needle is a package component of the syringe. If the needle is not a fixed component of the syringe but provided separately, it should be considered as a (separate) device.

The safety needle guard is part of the pre-filled syringe and as such not considered as a separate item or device.


Packaged Medicinal Product
* PCID: EU-100005665-00181311-0001
* Package Description : 1 ml solution in a Type 1 glass syringe with a fixed needle (stainless steel) and passive safety needle guard. Multipack comprising 3 (3 packs of 1) pre-filled syringe
*Language: English (100000072147)
* Quantity Operator: equal to (100000000049)
* Pack size: 3 syringe
* Legal Status if Supply
Manufacturer
Marketing Status
Outer Box
Package Item (Container) [1]
* Package Item (Container) Type : Box (100000073498)
* Quantity Operator: equal to (100000000049)
* Package Item (Container) Quantity : 1
* Material : <blank>
* Alternate Material: <blank>
Inner Box
Package Item (Container) [2]
* Package Item (Container) Type : Box (100000073498)
* Quantity Operator: equal to (100000000049)
* Package Item (Container) Quantity : 3
* Material : <blank>
* Alternate Material: <blank>
Package Item (Container) [3]
* Package Item (Container) Type : Pre-filled syringe (100000073544)
* Quantity Operator: equal to (100000000049)
* Package Item (Container) Quantity : 1
* Material : Glass type I (200000003204)
* Alternate Material: <blank>
Device
Type of medical device used in combination with medicinal product:
Integral-administration device (200000025967)
Medical device type: Pre-filled syringe (X)
Medical device identification: <blank>
Medical device trade name:<blank>
Quantity Operator: equal to (100000000049)
Device quantity: 1
Medical device description:1 ml solution in a Type 1 glass syringe with a fixed needle (stainless steel) and passive safety needle guard.
Language: English (100000072147)
Medical device description of intended purpose:
Devices for administration, withdrawal and collection
Language: English (100000072147)
Medical device classification: Class IIa (200000025962)
Manufacturer / Establishment
OMS location identifier : LOC-1000CECE
Manufactured Item
* Manufactured Dose Form : Solution for Injection (100000073863)
* Unit of Presentation : Syringe (200000002150)
* Quantity Operator: equal to (100000000049)
* Manufactured Item Quantity : 1 milliliter (100000110662)
Package (Component)
Component Type : Injection needle (100000073519)
Component Material : Steel (200000003229)
Component Alternate Material: <blank>

Pre-filled pen example

Victoza 6 mg/ml solution for injection in pre-filled pen

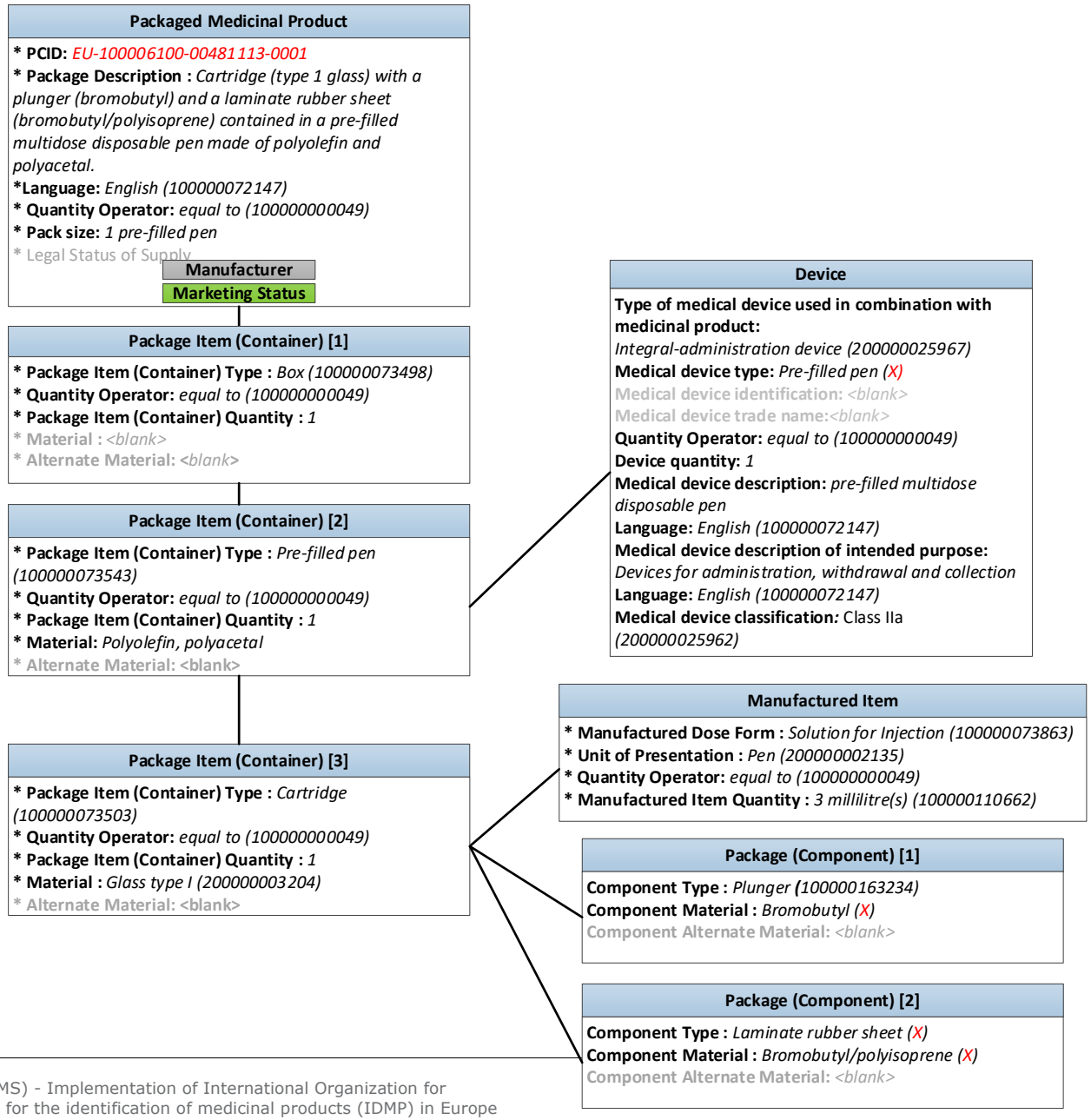
6.5 Nature and contents of container

Cartridge (type 1 glass) with a plunger (bromobutyl) and a laminate rubber sheet (bromobutyl/polyisoprene) contained in a pre-filled multidose disposable pen made of polyolefin and polyacetal.

Each pen contains 3 ml solution, delivering 30 doses of 0.6 mg, 15 doses of 1.2 mg or 10 doses of 1.8 mg.

Pack sizes of 1, 2, 3, 5 or 10 pre-filled pens.

The pack size of one pre-filled pen is shown below.


Packaged Medicinal Product
* PCID: EU-100006100-00481113-0001
* Package Description : Cartridge (type 1 glass) with a plunger (bromobutyl) and a laminate rubber sheet (bromobutyl/polyisoprene) contained in a pre-filled multidose disposable pen made of polyolefin and polyacetal.
*Language: English (100000072147)
* Quantity Operator: equal to (100000000049)
* Pack size: 1 pre-filled pen
* Legal Status of Supply
Manufacturer
Marketing Status
Package Item (Container) [1]
* Package Item (Container) Type : Box (100000073498)
* Quantity Operator: equal to (100000000049)
* Package Item (Container) Quantity : 1
* Material : <blank>
* Alternate Material: <blank>
Package Item (Container) [2]
* Package Item (Container) Type : Pre-filled pen (100000073543)
* Quantity Operator: equal to (100000000049)
* Package Item (Container) Quantity : 1
* Material: Polyolefin, polyacetal
* Alternate Material: <blank>
Package Item (Container) [3]
* Package Item (Container) Type : Cartridge (100000073503)
* Quantity Operator: equal to (100000000049)
* Package Item (Container) Quantity : 1
* Material : Glass type I (200000003204)
* Alternate Material: <blank>
Device
Type of medical device used in combination with medicinal product:
Integral-administration device (200000025967)
Medical device type: Pre-filled pen (X)
Medical device identification: <blank>
Medical device trade name:<blank>
Quantity Operator: equal to (100000000049)
Device quantity: 1
Medical device description: pre-filled multidose disposable pen
Language: English (100000072147)
Medical device description of intended purpose:
Devices for administration, withdrawal and collection
Language: English (100000072147)
Medical device classification: Class IIa (200000025962)
Manufactured Item
* Manufactured Dose Form : Solution for Injection (100000073863)
* Unit of Presentation : Pen (200000002135)
* Quantity Operator: equal to (100000000049)
* Manufactured Item Quantity : 3 millilitre(s) (100000110662)
Package (Component) [1]
Component Type : Plunger (100000163234)
Component Material : Bromobutyl (X)
Component Alternate Material: <blank>
Package (Component) [2]
Component Type : Laminate rubber sheet (X)
Component Material : Bromobutyl/polyisoprene (X)
Component Alternate Material: <blank>

Pre-filled pens may be assembled using different immediate packaging (e.g., cartridges, pre-filled syringe within a pen). The example above shows a pre-filled pen (package item container 2) containing a cartridge where the cartridge acts as immediate packaging (package item container 3) in contact with the medicinal product.

Other medicinal products may consist of different types of pre-filled pens, e.g., pens containing a pre-filled syringe. In such cases, both the pen and the pre-filled syringe should be captured in the model as a device and a package item container.

3.7. Shelf Life and Storage Conditions

This example shows how to record values for Shelf Life Type and Storage Conditions related to the authorized medicinal product.

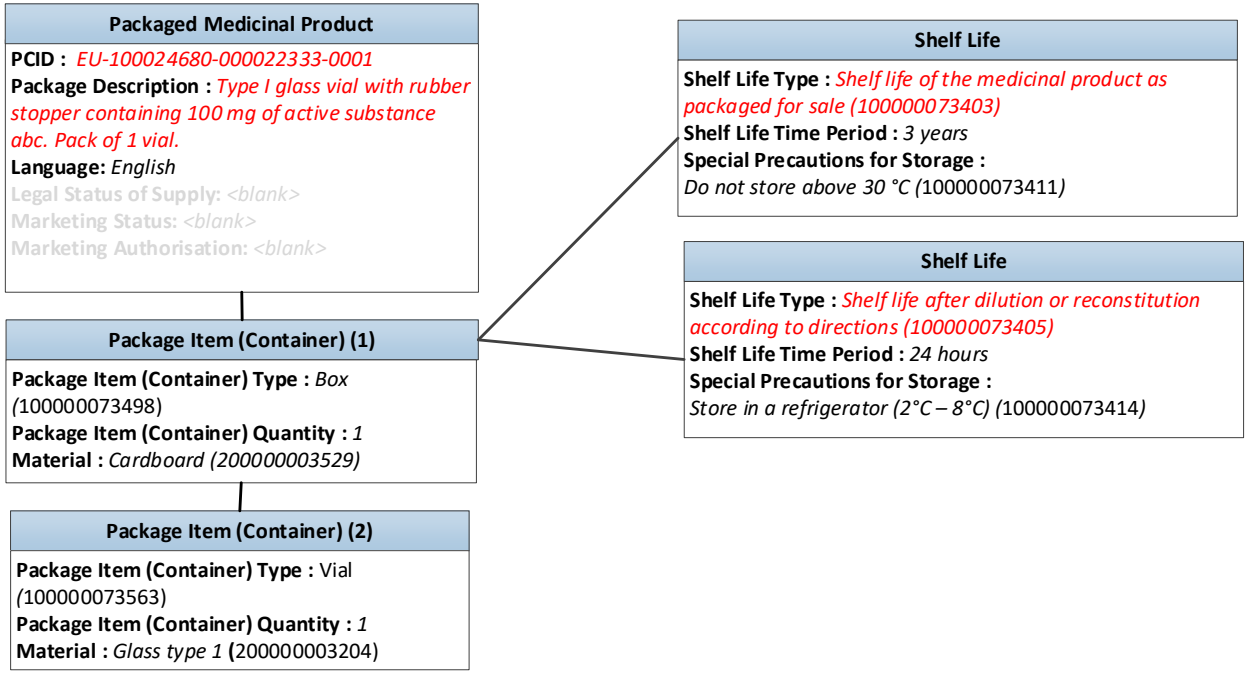
Topic	Topic description
Description of the challenge	• How to capture multiple shelf-life types and different storage conditions. • How to record Shelf-life Type and Storage Conditions when an equivalent term is not included in the corresponding RMS List.
Chapter 2 References	Shelf life and storage conditions/scenarios are described in the product information and section 2.2.3 of the electronic application form (eAF). This includes shelf life and storage conditions as packaged for sale, shelf life/storage conditions after dilution or reconstitution or any other scenario. This entity is repeatable to allow the introduction of different shelf-life/storage conditions in the same product (e.g., shelf life and storage conditions for medicinal products as packaged for sale and after dilution or reconstitution). Shelf Life/ Storage should be linked to the overall packaged medicinal product (outer-most package item).
Out of scope	Examples do not include Shelf Life and Special Conditions for Storage that do not fall within scope of QRD guidelines. Statements that relate to Safety but not Shelf Life or Storage Conditions, such as general safety statements, are not required e.g., ‘‘Keep out of reach and sight of children". Shelf Life data related to excursions in temperature are not required e.g., if it is indicated in the SmPC that a product is "to be stored at 2-8°C but can also be stored ≤ 25°C for a shorter time period while still unopened", only the Shelf Life Type and duration for the storage temperature at 2-8°C should be recorded.
Additional reference(s)	*QRD guidelines:* https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/product-information/product-information-templates

Topic	Topic description
	https://www.ema.europa.eu/documents/template-form/appendix-iii-quality-review-documents-templates-human-medicinal-products_en.doc https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/product-information/product-information-templates *Note: The information contained in these references is non-exhaustive. Companies should refer to all relevant European Union legislation and **guidelines** when drawing up applications and use the information in the SmPC and regulatory documents (e.g., eAF) to complete medicinal product data.*

1. Multiple Values for Shelf Life Types and Storage Conditions

The example shown below is aligned with the data used in Chapter 2, section 4.11. It reflects two values for Shelf Life based upon the product as it is packaged for sale and after first opening, and associated Storage Conditions.

Product example from Chapter 2, section 4.11



Note that, although in principle a shelf-life after reconstitution refers more to the Pharmaceutical Product, the model only allows shelf lives for the package object and so after reconstitution shelf-lives must be recorded there.

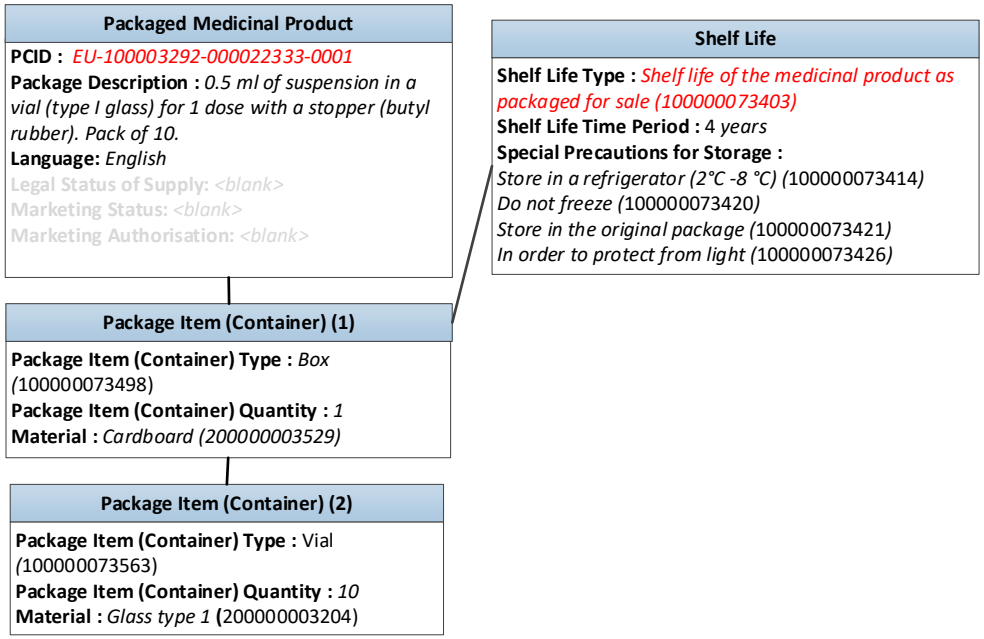
In the following case, the Packaged Medicinal Product Shelf Life and Storage Conditions are changed after opening (Synflorix). Shelf life and Storage Conditions are different based upon pack size..

Pack type	Shelf Life of the medicinal product as packaged for sale	Shelf Life of the medicinal product after first opening the immediate packaging	Special Precautions for Storage
Single dose pack	4 years		Store in the original container
2-dose pack	4 years	6 hours	

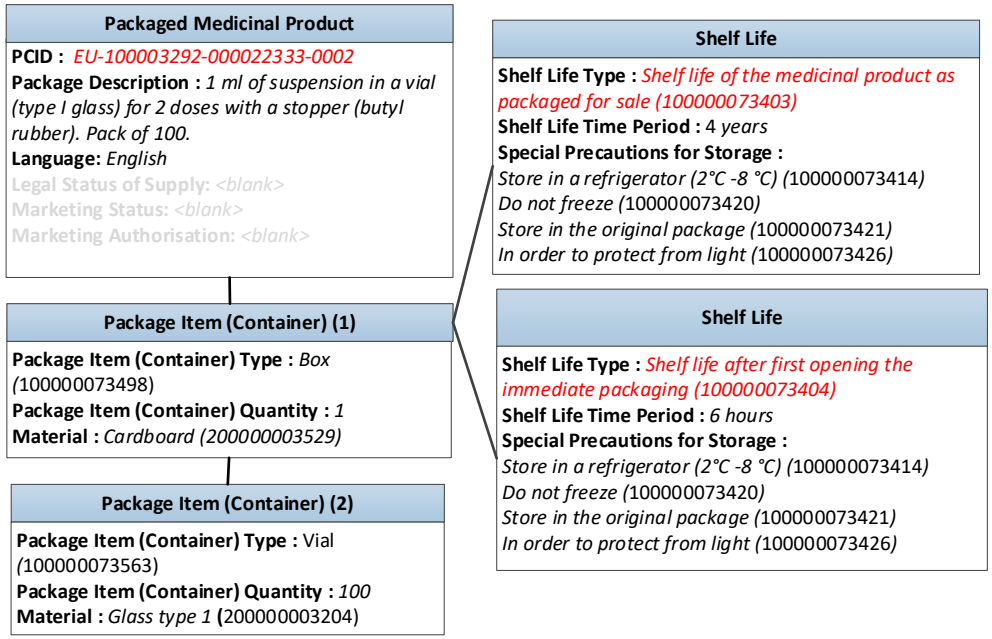
4-dose pack	3 years	28 days	in order to protect from light Store in a refrigerator (2°C – 8°C) Do not freeze

Link to the associated SmPC: https://www.ema.europa.eu/en/documents/product-information/synflorix-epar-product-information_en.pdf

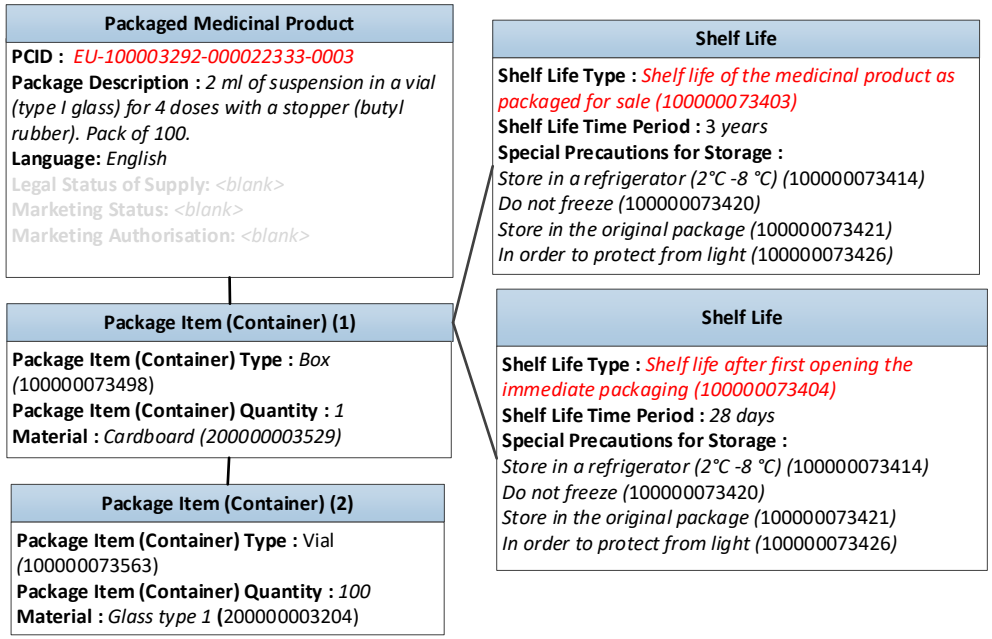
Synflorix 0.5 ml suspension in a vial



Synflorix 1 ml suspension in a vial (2 doses)



Synflorix 2 ml suspension in a vial (4 doses)



2. Encoding Shelf-life information for a medicinal product comprising several pharmaceutical products, each with its own shelf life

Shelf life/storage information shall be encoded in the shelf life/storage conditions section at the package item box level when an authorised medicinal product comprises pharmaceutical product(s) with more than one administrable dose form and different shelf lives once reconstituted. This is a repeatable entity, enabling different shelf-life/storage conditions to be entered for the same product.

Although the shelf-life of a reconstituted product relates to Pharmaceutical Product, it is not expected to link this information to a specific pharmaceutical product. Consequently, the information should not be repeated at the php description field level.

In the example below the medicinal product comprises reconstituted pharmaceutical products, with different administrable dose forms and shelf-life information; however, all shelf-life information is captured at package item box level.

Vancocin 500 mg powder for solution for infusion and oral solution

Section 3 Pharmaceutical form: Powder for solution for infusion and oral solution

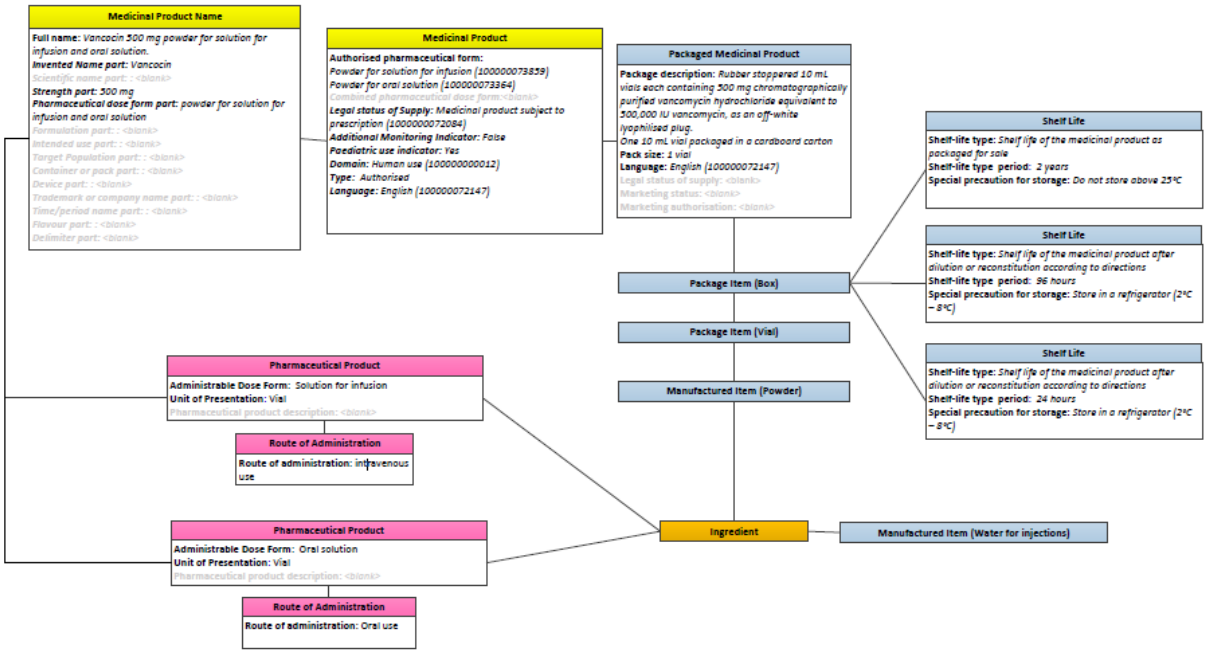
Section 6.3 Shelf-life: 2 years

Section 6.4 Special precaution for storage:

- Do not store above 25°C
- After reconstitution: may be stored in a refrigerator (2°C-8°C) for 24 hours […] Solutions of the parenteral powder intended for oral administration may be stored in a refrigerator (2°C-8°C) for 96 hours

Section 6.5 Nature and contents of the container:

Rubber stoppered 10 ml vial each containing 500 mg chromatographically purified vancomycin hydrochloride equivalent to 500,000 IU vancomycin, as an off-white lyophilised drug. One 10 mL vial packaged in a cardboard carton.



3. How to record Shelf Life Type and Special Precautions for Storage when the exact term is not available in the RMS List

Shelf Life Type and Special Precautions for Storage are expected to conform to QRD guidelines however, when completing the product information users must follow the approved/under approval regulatory documents (e.g., SmPC, eAF).

In the event that there is no exact match with the text specified in the SmPC and the values within the RMS List for "Shelf Life Type" or "Special Conditions for Storage", the user is advised to evaluate whether a synonymous term is available and select the most appropriate value.

If there is no appropriate value in the RMS List, assess whether the term included within the SmPC is aligned with QRD guidelines. If not aligned, it is advisable to discuss this with the local relevant competent authority issuing the marketing authorisation.

If the SmPC term is in accordance with QRD guidelines, follow the RMS Maintenance procedure as regards requesting new terms. If the request is refused, select the most appropriate/closest match on the RMS list.. Additional information can be found at the RMS Document section of the SPOR portal.

Note: Special Precautions for Storage may be satisfied by selecting more than one value.

Example - "Store in the original package in order to protect from light"

- *Store in the original package (100000073421)*
- in order to protect from light (100000073426)

4. Relationship between PMS ID, MPIDs and PCIDs

Example of seasonal vaccines

This example of influenza vaccines describes the relationship between MPID and PCID in seasonal vaccines, as regards the active substances, at initial submission and their evolution during their lifecycle.

These vaccines are composed of certain strains of seasonal influenza viruses (subtypes A(H1N1), A(H3N2) and lineages B/Yamagata and/or B/Victoria). These can evolve each season per subtype and lineage, thus changing the vaccine's composition.

A type II variation is submitted for the change in composition (new circulating strains) without any change to the marketing authorisation.

In this scenario, as stated in the EU IG Chapter 2, the PMS ID remains stable, whereas new MPID and PCID are assigned. The assignment of the relevant identifiers is determined by the following considerations:

- The composition of the vaccine medicinal product can evolve each season due to the change in strains
- This change impacts one of the MPID defining elements: the active substance (s)/active moieties
- The change in the medicinal product ID code segment directly impacts the PCID assignment

For further information related to the defining elements for the assignment of the relevant identifiers in PMS, refer to the Identifiers and defining characteristics of a medicinal product entry in PMS section in EU IG Chapter 2.

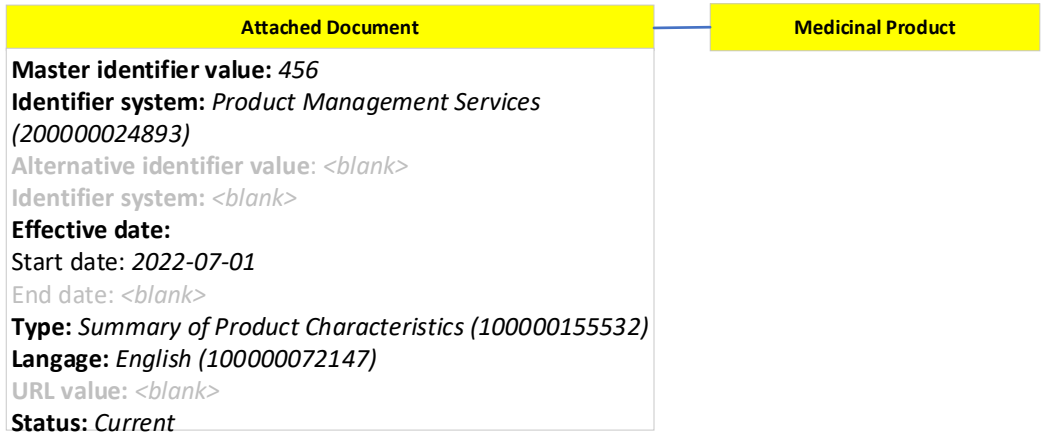
Action	Procedure number	Version	Content	Medicinal product	Package	MAH name/ID	PMS ID	MPID	Marketing Authorisation number (Medicinal Product Level)	PCID	Marketing Authorisation number (Package Medicinal Product Level)
Submission in Ireland	IE/H/1939/002	v1	initial submission via MRP; MPID is generated	Influenza Vaccine, <strains season **Y**>, suspension for injection, MAH A, IE	Pre-filled syringe (Type I glass) with a plunger stopper (grey butyl rubber) with 1 needle: pack sizes of 1 Pre-filled syringe (Type I glass) with a plunger stopper (grey butyl rubber) with 1 needle: pack sizes of 10	MAH A/100000797 (IE)	00005678	IE-100000797-00000001	PA1095/256/001	IE-100000797-00000001-0001 IE-100000797-00000001-0002	Not applicable - Blank
Type IA variation	IE/H/1939/002	v2	change of admin data	no change	no change	no change	no change	no change	no change	no change	Not applicable - Blank
Type II variation	IE/H/1939/002	v3	**change of strains (change in section 2 of the SmPC)**	Influenza Vaccine, <strains season **Y+1**>, suspension for injection, MAH A, IE	no change	no change	no change	IE-100000797-**00000002**	no change	IE-100000797-**00000002-0001** IE-100000797-**00000002-0002**	Not applicable - Blank

5. Examples of submission of attached document

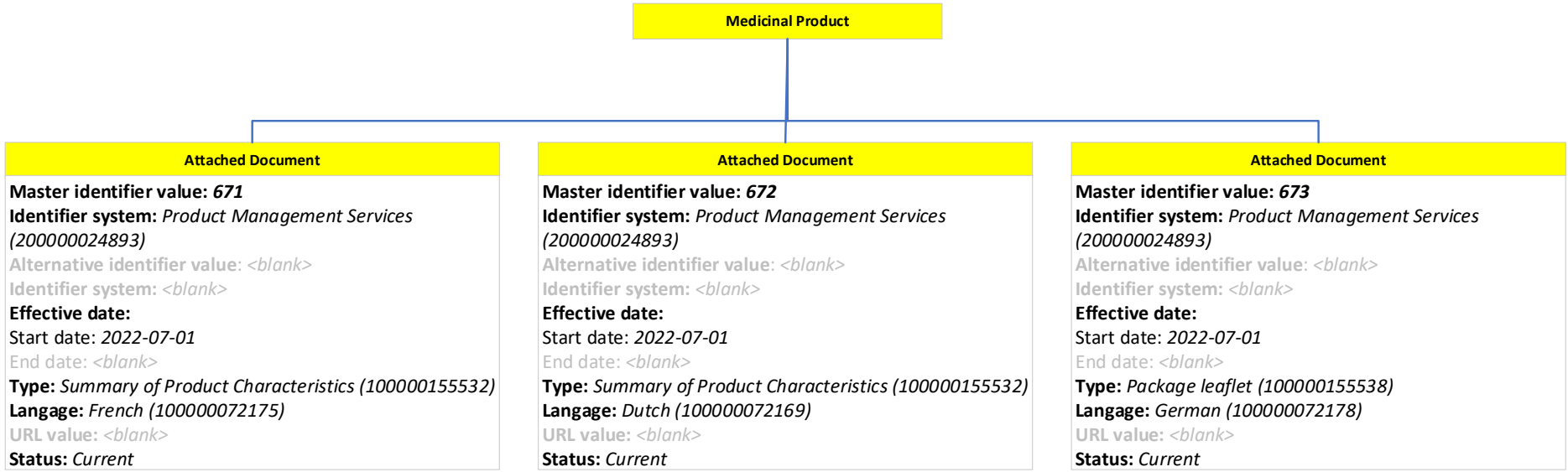
The examples listed below are presented with a simplified representation.

Initial Submission for a centralised product:

In case of the initial submission of a centralised authorised product, at least one document shall be referenced, and it will have a Master Identifier value.

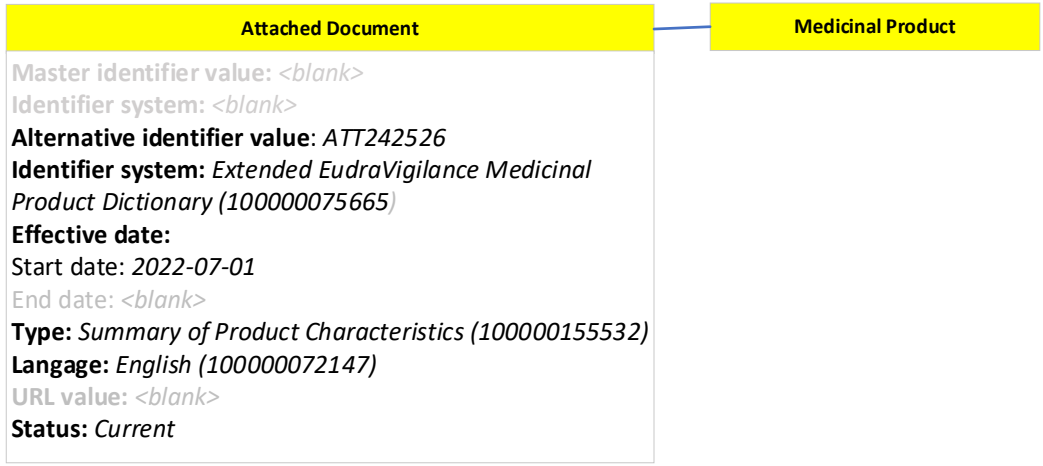


Initial Submission for a national product in a country with multiple languages, e.g., Belgium:



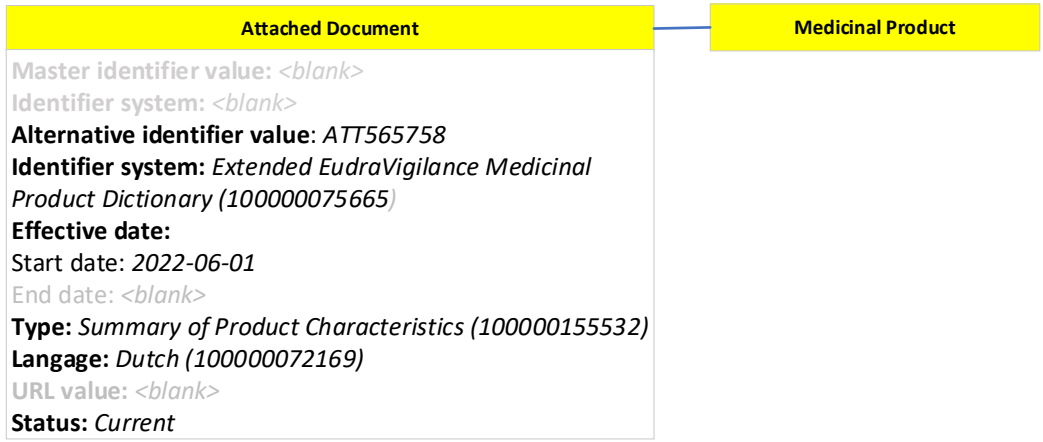
In case of national initial submission, in a multilingual country, e.g., Belgium, the French and Dutch SmPCs, along with the German patient leaflet, will have master identifier value.

Migration submission of centralised product:



In case of xEVMPD data load for a centralised product, the English version of the SmPC will be migrated with the alternative identifier value.

Migration submission of national product:



In case of xEVMPD data load, for a national product in Netherlands, the SmPC in Dutch will be migrated with the alternative Identifier value.