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Information Management

Guidance on the electronic submission of information on investigational medicinal products for human use in the Extended EudraVigilance medicinal product dictionary (XEVMPD)

Extended EudraVigilance Medicinal Product Report (XEVPRM) user guidance for sponsors of clinical trials

Version 1.5

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Summary of changes

Following the publication of version 1.4 in December 2024, the below listed sections of this document were updated in this version; significant changes are highlighted in red and strikethrough text and/or described below:

- Throughout the document:
  - References to the current user interface (EVWEB-XEVMPD/Art.57), were replaced with reference to the upgraded XEVMPD user interface (XEVMPDweb)
  - Information related to the 'Local Number' for individual entities was removed and added in the 'Introduction and general principles' section.
- About this document: Content updated
- Introduction and general principles: Content updated
- XEVMPD data access policy: Table replaced
- Pre-submission requirements: Content updated
- 1.8.2. MedDRA level (DP.IND.2): Content updated
- 2. Initial submission of a reference source: Content updated; sub-sections 2.1 – 2.4 were removed as applicable to users from the EMA only.
- 3. Initial submission of a sponsor information: Content re-structured and updated
- 4.1. Request for an insert of a standard or a proposed ATC Code: Content updated
- 5. Initial submission of a pharmaceutical form: Content updated
- 6. Initial submission of a route of administration: Content updated
- 7.2. Attachment File: Section added
- Process maps 4, 5 and 6 were updated to reference "RMS change request via EMA Service Desk" instead of 'change request via RMS"

Glossary

Development term: confidential term used in a clinical trial. These terms are entered and maintained in the XEVMPD by sponsors. Development terms can only be referenced in development medicinal products.

EudraVigilance (EV) Organisation ID: is the ID under which an organisation is registered in the EudraVigilance database to uniquely identify each organisation in EudraVigilance. This ID is used to send/receive product/safety reports as per the organisation's profile.

Upon login in the XEVMPD User Interface, the organisation ID is located in the right-hand corner of the screen in the following format *username* (**ORGANISATION ID**) followed by @ Human Production (for XEVMPD production environment) or @Human XComp (for XEVMPD test environment).

Local look-up table: allows users to search locally and refer to entities existing in the Extended EudraVigilance Medicinal Product Report Message (XEVPRM) to be sent to the XEVMPD, such as proposed and/or development terms concerning administration routes, pharmaceutical dose forms etc.

OMS organisation ID: a reference ID of an organisation (as a legal entity) registered in the Organisation Management Services (OMS) system.

Owner organisation: The HQ organisation that owns the data in the XEVMPD.

For example:

- Organisation A is registered with EudraVigilance as a headquarter under EV organisation ID 'ORGA'. A development medicinal product entity submitted to the XEVMPD from that organisation ID is therefore owned in the XEVMPD by 'ORGA'.
- Organisation B is registered with EudraVigilance as an affiliate under the HQ profile organisation A. EV organisation ID of organisation B is 'ORGB'. Since 'ORGB' is registered as an affiliate under the HQ profile of 'ORGA', a development medicinal product entity submitted to the XEVMPD from 'ORGB' will be owned in the XEVMPD by 'ORGA'.
- Organisation C is an affiliate registered with EudraVigilance with their own HQ profile with EV ID 'ORGC' instead of being registered as an affiliate under the HQ profile of Organisation A. A development medicinal product entity submitted to the XEVMPD by Organisation C is therefore owned in the XEVMPD by 'ORGC'.

Proposed term: Term for which there is an application to the maintenance organisation, but the term is not yet approved or published. These terms used to be entered and maintained in the XEVMPD by sponsors and MAHs. From 18 January 2024, only the EMA can insert and maintain proposed terms in the XEVMPD. Proposed terms can be used either in development medicinal products or authorised medicinal products.

Remote look-up table: allows users to search remotely and refer to entities existing in the XEVMPD, such as substances, administration routes, etc.

Standard term: term published as a term of standard terminology by an official maintenance body [e.g. European Directorate for the Quality of Medicines (EDQM)] used in the XEVMPD. This information is entered and maintained in the XEVMPD by the European Medicines Agency (EMA). Standard terms can be used either in development medicinal products or authorised medicinal products.

(Substance) Preferred name: is the preferred name of the substance associated with an EV Code and it is selected based on the review of reference sources. E.g., paracetamol, maize starch etc.

About this document

The purpose of this document is to provide consolidated **business guidance** to users from sponsor organisations registered with the European Medicines Agency (EMA) for the submission of medicinal product information in the Extended EudraVigilance medicinal product dictionary (XEVMPD).

This guidance describes how the information for each XEVPRM data element related to an unauthorised medicinal product, referred to in the XEVMPD as a 'development medicinal product' (DMP), must be included during the submission of the information via the **XEVMPD User Interface (XEVMPDweb).**

The list of all data elements applicable for an initial insert the various data elements and technical guidance on how each of the data elements should be completed is described in Chapter 3.I: Technical specifications.

For convenience, this document also contains screenshots of how information is presented in an XML file and/or how it is presented in the XEVMPDweb.

Where relevant, the name of the data field in XEVMPDweb is referenced together with the technical reference number of that data field in an XEVPRM; the technical reference number is entered in the brackets after the text, e.g., "Sponsor Name (O.2)", "Active ingredient substance code (PP.ACT.1)" etc.

All medicinal product names/sponsor organisation names and examples used in this document were created for demonstration purposes only.

Introduction and general principles

As per Article 81(3) of CT Regulation (EU) No 536/2014: *"The EU database shall support the recording and submission to the Medicinal Product Dictionary, contained in the Eudravigilance database, of all the data on medicinal products without a marketing authorisation in the Union and substances not authorised as part of a medicinal product in the Union, that are necessary for the maintenance of that dictionary. To this effect and also with the purpose of enabling the sponsor to cross-refer to prior applications, an EU medicinal product number shall be issued for every medicinal product without a marketing authorisation and an EU active substances code shall be issued for each new active substance not previously authorised as part of a medicinal product in the Union. This shall be done before or during the application for authorisation of the first clinical trial with that product or active substance submitted in accordance with this Regulation. Those numbers shall be mentioned in all subsequent applications for clinical trials and for substantial modifications.*

The data submitted, in accordance with the first subparagraph, describing medicinal products and substances shall comply with Union and international standards for the identification of medicinal products and active substances. When an investigational medicinal product which already has a marketing authorisation in the Union and/or an active substance which is part of a medicinal product with a marketing authorisation in the Union, is to be used in a clinical trial, the relevant product and active substance numbers shall be referred to in the application for that clinical trial"

Directive 2001/20/EC, Article 2 (d), provides the following definition for an IMP: *"a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including products already with a marketing authorisation but used or assembled (formulated or packaged) in a way different from the authorised form, or when used for an unauthorised indication, or when used to gain further information about the authorised form."*

- Information on authorised medicinal products (AMPs) is entered in the XEVMPD (also known as 'Article 57 database') by marketing authorisation holders (MAHs). The guidance and principles for the submission of AMP information are described in the Chapter 3.II: XEVPRM User Guidance of the Detailed guidance on the electronic submission of information on medicinal products for human use by marketing authorisation holders to the European Medicines Agency in accordance with Article 57(2) of Regulation (EC) No. 726/2004. When an authorised medicinal product is successfully inserted in the XEVMPD by the MAH, an EV Co
- Information on un-authorised medicinal products used in a clinical trial conducted in the EU/EEA is entered in the XEVMPD by sponsors of clinical trials.

In general:

- If an **active substance** is used in a clinical trial **in a new pharmaceutical dose form and/or new strength**, a new DMP must be entered in the XEVMPD by the sponsor organisation.
  - In the Clinical Trial Application (CTA) form, the sponsor makes a reference to the DMP entered in the XEVMPD by the sponsor organisation by providing the unique number, known as an EV Code, assigned to the DMP by the XEVMPD.
- If a **medicinal product authorised in the EEA** is used in a clinical trial **in its authorised form** (i.e., the pharmaceutical dose form, active ingredient and its concentration remain unchanged) **for different indications and/or via a new route of administration(s)**, no DMP needs to be submitted to the XEVMPD by the sponsor.
  - In the CTA form, the sponsor makes a reference to the AMP entered in the XEVMPD by the marketing authorisation holder.
  - Information on medicines authorised in the EEA as present in the Article 57 database is published in the form of an excel document on the 'Public data from Article 57 database' webpage.
  - Registered XEVMPD users can also perform queries in XEVMPDweb to retrieve the AMP information and EV Code.
- If a medicinal product **not authorised in the EEA** is used in a clinical trial in the EEA **in its authorised form** (i.e., the pharmaceutical dose form, active ingredient and its concentration remain unchanged), the sponsor submits a new DMP in the XEVMPD.
  - In the CTA form, the sponsor then makes a reference to the DMP entered in the XEVMPD by the sponsor organisation.
- If a **medicinal product not authorised in the EEA** is used in a clinical trial in the EEA **for different indications and/or via new routes of administration(s),** the sponsor can update their existing DMP with the new indication/route of administration.
  - In the CTA form, the sponsor makes a reference to the existing DMP entered in the XEVMPD by the sponsor by providing the EV Code assigned to the DMP by the XEVMPD.

A process map of the principles to follow to determine if a sponsor should submit information about the medicinal product used in their clinical trial in the XEVMPD is available in *Process map 2: DMP submission principles and retrieval of XEVMPD EV Codes for CTIS submission* of this document.

Information on how to perform searches in CTIS is available in the Sponsor handbook.

Information on how to perform searches in XEVMPDweb is available in the 'User manual for the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD) user interface (XEVMPDweb)'.

In the XEVMPD, the information to be provided for the individual data elements of a development product entry must be in line with the information in the **Investigator's Brochure (IB)**.

Medicinal product information can be submitted to the XEVMPD using the **EudraVigilance Gateway** or via the Agency's XEVMPD user interface **XEVMPDweb**. Further information is available on the 'How to submit information' webpage.

Technical business rules are described in Chapter 3.I: XEVPRM Technical Specifications of the Detailed guidance on the electronic submission of information on medicinal products for human use by marketing authorisation holders to the European Medicines Agency in accordance with Article 57(2), second subparagraph of Regulation (EC) No 726/2004.

The data elements to be completed for the electronic submission of information on medicinal products used in clinical trials in the European Economic Area (EEA) are based on the Extended EudraVigilance Medicinal Product Report Message (XEVPRM) schema.

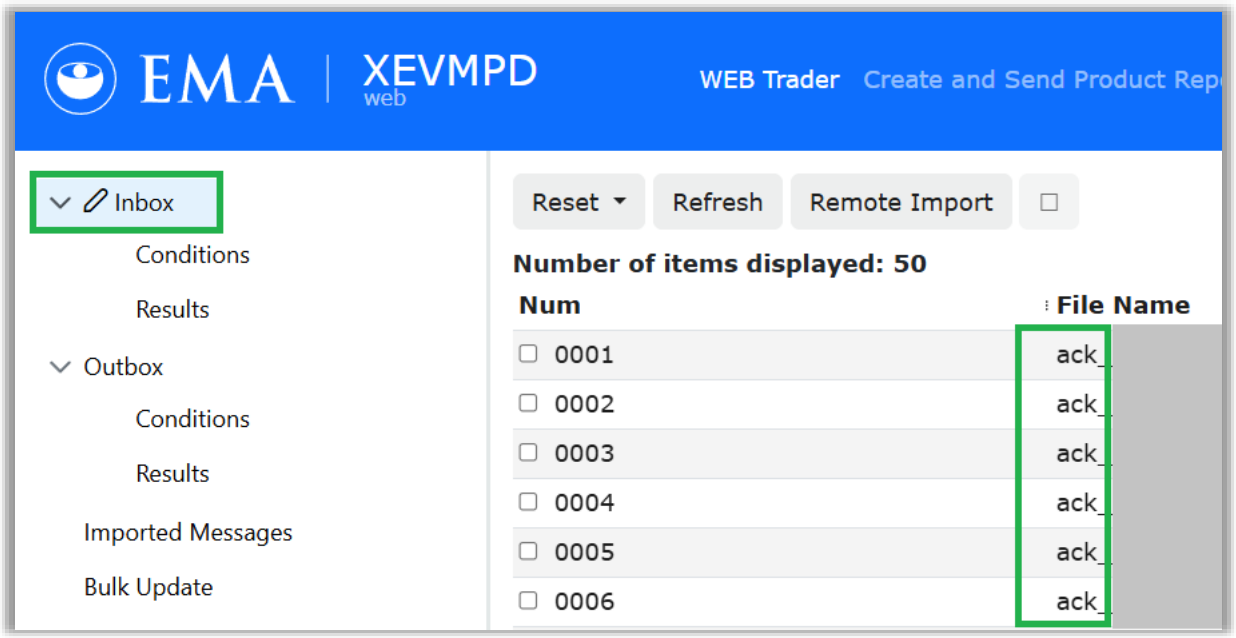
Following the submission of medicinal product information in the XEVMPD via an XEVPRM, an XEVPRM Acknowledgement is returned to the sender organisation. A **local code** will be assigned as an internal reference code for the inserted entities (e.g. an organisation, product, attachment etc.) until an EV Code has been provided as part of the acknowledgement process:

- If the insert is performed via an XEVPRM created in XEVMPDweb, the local number is generated automatically by the system.
- If the insert is performed by Gateway users, their internal submission tool should generate and assign the local number.

Once the entity is successfully inserted in the XEVMPD, a unique number known as an **EV Code** for the submitted entity will be received in the XEVPRM Acknowledgement:

```
<reportacknowledgment>
  <reportname>ATTACHMENT</reportname>
  <localnumber>3</localnumber>
  <ev_code>ATT51994</ev_code>
  <operationtype>1</operationtype>
  <operationresult>2</operationresult>
  <operationresultdesc>Entity inserted successfully</operationresultdesc>
</reportacknowledgment>
<reportacknowledgment>
  <reportname>ORGANISATION</reportname>
  <localnumber>2</localnumber>
  <ev_code>ORG11190</ev_code>
  <operationtype>1</operationtype>
  <operationresult>2</operationresult>
  <operationresultdesc>Entity inserted successfully</operationresultdesc>
</reportacknowledgment>
<reportacknowledgment>
  <reportname>DEVELOPMENTPRODUCT</reportname>
  <localnumber>1</localnumber>
  <ev_code>PRD137234</ev_code>
  <operationtype>1</operationtype>
  <operationresult>2</operationresult>
  <operationresultdesc>Entity inserted successfully Version 1 </operationresultdesc>
</reportacknowledgment>
</acknowledgment>
```

- If the sender organisation is a WEB Trader user, the XEVPRM Acknowledgement will be sent to the WEB Trader 'Inbox' in XEVMPDweb:



- Gateway users should check with their Gateway providers where their XEVPRM Acknowledgements are received.

Type of data that can be submitted by sponsors to the XEVMPD

Sponsors can submit the following type of data to the XEVMPD via an XEVPRM:

- Development product entities;
- Sponsor organisation entities;
- ATC Codes (development);
- Pharmaceutical form entities (development);
- Routes of administration entities (development);
- Attachments;
- Pharmacovigilance Master File Locations (PSMFLs), however, these are not applicable for development product submissions.

Operation types that can be performed by sponsors in the XEVMPD

- Operation type **'Insert' (1)**: allows the sender organisation to insert medicinal product information to the XEVMPD.
- For XEVMPDweb users, a command button **'Reinsert' (1)** is also available. This operation type allows users to re-insert an existing XEVMPD entity, whilst retaining the previous information. Following the modification of the required data elements, the XEVPRM is then submitted to the XEVMPD with the operation type 'Insert' (1).
- Operation type **'Update' (2)**: allows the owner organisation to amend medicinal product information previously submitted. Maintenance operation type 'Update' can only be performed on current (i.e., not nullified) entities that the sponsor organisation owns in the XEVMPD (the data was submitted by an organisation registered under the same headquarter). For example, sponsor X cannot update an XEVMPD entity submitted to the XEVMPD by sponsor Y.
- Operation type **'Nullification' (4)**: allows the owner organisation to flag medicinal product information as 'non-current' providing that the medicinal product information is:
  - not referenced in any current (i.e., not nullified) product entities, and
  - has not been validated by the EMA[1].

XEVMPD data access policy

Data entered in the XEVMPD as 'development' is considered, in the XEVMPD, confidential.

In the XEVMPD, data is owned by the HQ of the organisation that entered such data (i.e. the HQ profile of the MAH/sponsor organisation in EudraVigilance).

Only users registered under the owner organisation profile [i.e., under the HQ profile or under an affiliate profile registered under the HQ profile in EV] with 'Browse Medicinal Product Reports (MPRs)'

[1] Exceptions apply, see section *9.5. Nullification of duplicated or obsolete information* for details

can see such data, while those with 'Browse and Send Medicinal Product Reports (MPRs)' can view and maintain such data.

An organisation registered with the EudraVigilance system and that is not a national competent authority (NCA) can view:

- data for which they are the owners (product data, substance data etc.);
- authorised medicinal products, approved substances and proposed terms that have been validated by the EMA;
- all standard terms present in the look-up tables and maintained by the EMA.

Development substances, development products and development terms not owned by the organisation, even if flagged as 'Valid' by the EMA, remain strictly confidential in the XEVMPD and cannot be accessed by other applicants, MAHs or sponsors.

Sponsors should note that, while details of the active substance and pharmaceutical product composition (including the pharmaceutical form and the route of administration) are not made publicly available in the XEVMPD, they are made publicly available through CTIS upon decision date on the clinical trial application, for all kinds of trials except for the early development phase trials, for which their publication occurs 30 months after the trial completion in European Economic Area (more information in the quick user guide on the CTIS transparency rules).

In the XEVMPD, the general **visibility rules** applicable to any MAH/sponsor/applicant registered with the EudraVigilance system are summarised in the following table:

XEVMPD entity	Users from owner organisation	Non-owner users	Users from national competent authorities
Approved substance	Not applicable, as owned by EMA	All substance information	All substance information
Attachment	All information	No information	No information
Attachment referenced in AMP	All information	No information	No information
Attachment referenced in DMP	All information	No information	No information
Authorised medicinal product (AMP)	All information from every version of the AMP entity	Restricted information from validated versions of the AMP entity	All information from validated versions of the AMP entity
Development ATC Code	All information	No information	No information
Development medicinal product (DMP)	All information from every version of the DMP entity	No information	All information from validated versions of the DMP entity

Development Pharmaceutical Form (PhF)	All information	No information	No information
Development Route of Administration (RoA)	All information	No information	No information
Development substance	All information	No information	All substance information
MAH organisation	All information	All information from a validated version	All information
Master File Location (MFL)	All information	Restricted information	All information
Proposed ATC Code	All information	All information	All information
Proposed PhF	All information	All information	All information
Proposed RoA	All information	All information	All information
Source	All information	No information	All information
Sponsor organisation	All information	All information from validated version	All information
Standard ATC Code	Not applicable, as owned by EMA	All information	All information
Standard PhF	Not applicable, as owned by EMA	All information	All information
Standard RoA	Not applicable, as owned by EMA	All information	All information

Pre-submission requirements

To submit medicinal product information to the XEVMPD, sponsor organisations must be registered with EudraVigilance for **medicinal product reporting** either via Gateway or via the XEVMPD user interface, which allows registered users to create and send XEVPRMs, receive XEVPRM acknowledgements, view medicinal product information and perform queries.

During the registration process of the organisation, a *'Notification of successful completion of the XEVMPD knowledge evaluation'* is requested from at least one user from the organisation. This is to ensure that the data submitted to the XEVMPD is of good quality. To obtain the notification, the XEVMPD training course must be completed.

Organisations need to register electronically via the Organisation Management System (OMS) in the SPOR portal.

User registration and user account management is performed via the EMA Account Management portal. The following XEVMPD only related base roles can be requested via the EMA Account Management portal by users from a sponsor organisation:

- EV Human CS/NCS **Responsible**: Request this role if you work for a Commercial Sponsor or a Non-Commercial Sponsor and you are the main responsible for Pharmacovigilance in your organisation profile. This role allows you to grant and revoke access to users and manage the organisation hierarchy. This role grants you full access.

- EV Human MAH/CS/NCS **Trusted Deputy**: Request this role, if you work for an MAH, Commercial Sponsor or Non-Commercial Sponsor and you are supporting the main responsible person for Pharmacovigilance in the administrative tasks. This role allows you to grant and revoke access to users and manage the organisation hierarchy. This role grants you full access. Please note, this role will be rejected, if your organisation does not have an EV MAH EU QPPV or an EV CS/NCS Responsible.

- EV Human NCA/MAH/CS/NCS **Browse MPR**: Request this role if you need only access to browse Medicinal Products in the XEVMPD.

- EV Human MAH/CS/NCS **Browse & Send MPR**: Request this role, if you work for an MAH, Commercial Sponsor or Non-Commercial Sponsor and you need only functionalities related to the Medicinal Products: create queries, create and send extended Medicinal Products Reports or generate acknowledgement messages.

The EMA EudraVigilance Registration Manual provides comprehensive information on how to register with EudraVigilance; information on all available roles is available in Annex 1 - EV "base" and "supplementary" roles of the document.

Process map 1: Sponsor organisation registration process and the below simplified process describes the steps to be followed by a sponsor organisation before the submission of DMP information in the XEVMPD can begin.

Step 1. A user participates in the XEVMPD training course.

Step 2. A user not yet registered with the EMA Account Management portal creates a new EMA account; the role of SPOR *'Unaffiliated user'* is automatically assigned to the user.

Step 3. Using the EMA Account Management credentials, the user logs in to the SPOR portal and performs a search in OMS for the required organisation:

a. If the organisation is present, continue with Step 5;

b. If the required organisation is not found, continue with Step 4.

Step 4. The creation of a new organisation is requested via the **OMS change request** submitted via the EMA Service Desk portal as per instructions in the document A6 - Alternative access solution available in section 'Documents' of the OMS portal.

Step 5. Once the organisation is created, login to your EMA account via the EMA Account Management portal and request the role of **'EV Human CS/NCS Responsible'** for that organisation.

Step 6. Note your request ID.

Step 7. Connect to the EMA Service Desk portal and create a **request for registration with EudraVigilance** providing the EMA Account Management request ID and the required documents.

Please note that all new organisations are registered with the Web Trader transmission mode by default once the registration of the responsible person (RP) is completed.

Step 8. When your RP registration is completed, go to the EudraVigilance restricted area and complete the missing information in the "**Manage your profile**" section.

Step 9. Once other users from the sponsor organisation create their own EMA accounts and request the relevant role(s) in the EMA Account Management portal, the RP approves them as required.

Step 10. The organisation is now registered with EudraVigilance for product reporting; the RP and/or the users registered under your organisation profile can log on to the XEVMPD user interface to create an XEVPRM through which your medicinal product data and organisation data will be submitted to the XEVMPD.

Access to the XEVMPD user interface (XEVMPDweb)

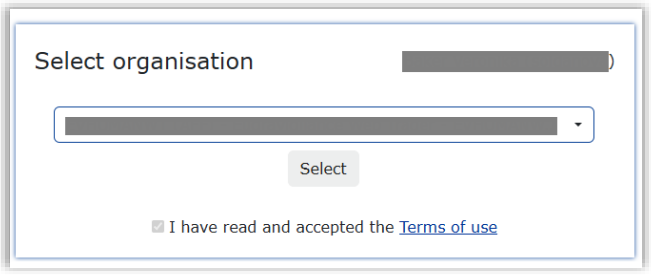
To access XEVMPDweb, users are required to have:

- set up a multi-factor authentication (MFA);
- requested access to the XEVMPD production environment via the EMA Account Management portal.

Registered users can access **XEVMPDweb production** environment:

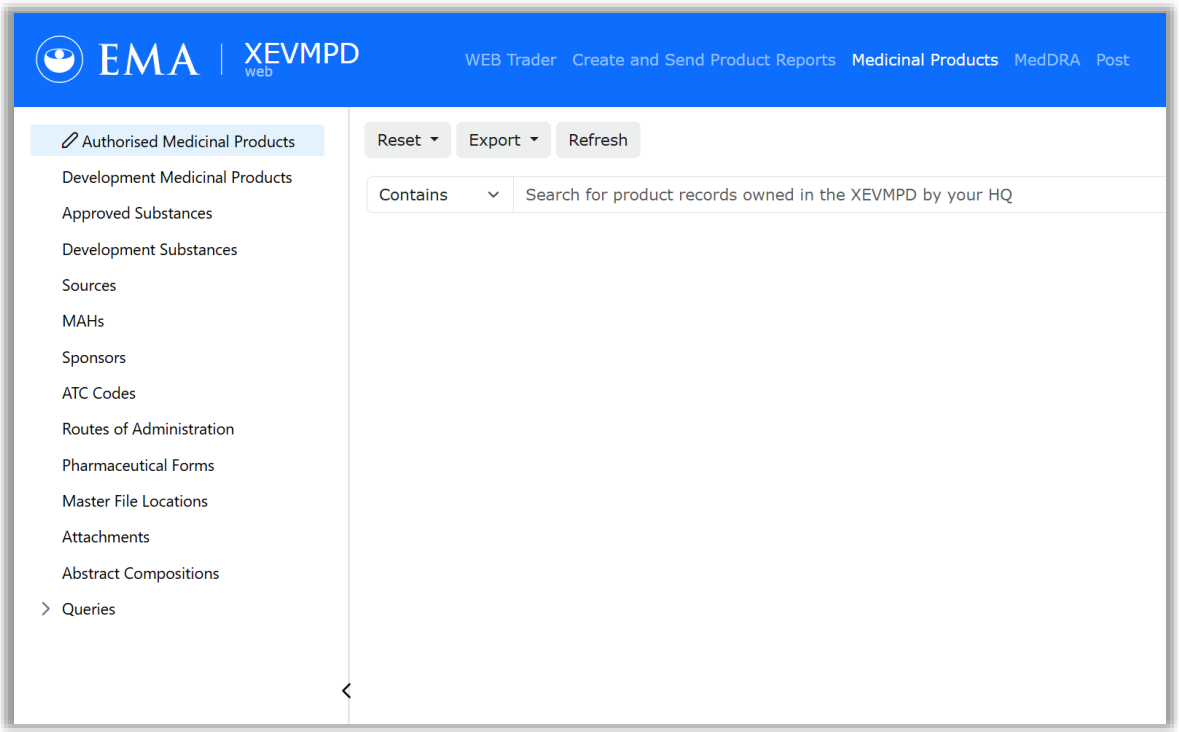
- directly via the URL: https://eudravigilance-xevmpd.ema.europa.eu/login or
- via the EudraVigilance (production) restricted area; the link to 'XEVMPDweb (New UI)' is available under 'EV Services'.

Once the user is authenticated, the list of organisations **for which the user is registered in the EMA Account Management portal** will be displayed:



The user should select the required organisation, under which they wish to log on to the user interface and, if logging in for the first time, accept the terms and conditions.

Once the required organisation is selected, the user interface opens; the 'Medicinal Product' section is displayed by default:



For information on how to use the XEVMPDweb user interface please refer to the 'User manual for the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD) user interface (XEVMPDweb)'.

1. Initial submission of a development medicinal product

Development medicinal product (DMP) information must be submitted to the XEVMPD in an XEVPRM with the operation type 'Insert'.

This section describes the data elements to be provided by sponsors during their **initial insert** of **development medicinal product** information in the XEVMPD via XEVMPDweb.

The information to be provided during the **initial insert** of a DMP entity in the XEVMPD via an XEVPRM created in XEVMPDweb includes the below information [the symbol (*) means mandatory]:

- (*) Type
- Sender Local Code
- (*) Sponsor
- (*) Product Code or Product Name
- Product Other Name
- Comment
- (*) Pharmaceutical dose form(s)
- (*) Route of administration(s)
- Drug Ingredients:
- (*) Active ingredient(s)
- (*) Strength of the Active Ingredient(s)
- Excipient information
- Excipient substance strength
- (*) Adjuvant(s) information, if applicable
- (*) Adjuvant substance strength, if applicable
- Old Drug Ingredient(s)
- Medical devices
- Product ATC code(s)
- Product indications (using MedDRA coding)
- Product Attachment(s) including validity declaration (if applicable and as per relevant business rules) (DP.PPIs)

Process map 3: Submission of DMP entity in the XEVMPD provides a basic overview of the information to be included for a DMP submission.

1.1. Type

Mandatory information

'Development' must be referenced in this field when submitting a DMP information in the XEVMPD.

1.2. Sender Local Code (DP.4)

Optional information

The sender local code for the DMP used by the sponsor for internal reference purposes may be specified in this data element.

The sender local code specified by the sponsor is not used in the XEVMPD for maintenance and it can be any technical code.

1.3. Sponsor (DP.5)

Mandatory information

The EV Code assigned to the sponsor of the clinical trial, as indicated in the IB, must be provided.

- If the sponsor organisation was successfully submitted to the XEVMPD, an EV Code was assigned to the organisation entity. In XEVMPDweb, the sponsor organisation EV Code can be retrieved from the available **remote look-up table**.
- If the sponsor organisation does not exist in the XEVMPD, the sponsor information must be added using the 'Organisation' section of the XEVPRM and referenced in the DMP entry using the **local look-up table**.

  See section *3. Initial submission of a sponsor information* for information how to submit sponsor organisation information in the XEVMPD.

1.4. Product Code, Product Name, Product Other Name

Mandatory information

Either the name or the code of the medicinal product, as indicated in the IB, must be provided, as applicable.

1.4.1. Product Code (DP.6.1)

Mandatory optional information

The code of the product, as referenced in the IB, must be specified, if available.

If a product name is available for the medicinal product and entered in data element DP.6.2, then it is optional to provide the product code.

The maximum number of characters to be entered in the Product Code (DP.6.1) data element is 60.

Examples:

XYZ-1234

1.4.2. Product name (DP.6.2)

Mandatory optional information

The name of the product, as referenced in the IB, must be specified, if available.

If a product code is available for the medicinal product and entered in data element DP.6.1, then it is optional to provide the product name.

If the sponsor does not yet have a specific product name, and only the active substance name or code is available to identify the product in the clinical trial, the product name may reference the substance code or name.

Please note: Development medicinal product may be associated to a clinical trial application in the Clinical Trial Information System (CTIS) and, in compliance with the clinical trial Regulation No. 536/2014 and CTIS transparency rules[2], some of the structured data are made public on the CTIS public portal.

The name of the DMP is published once the trial application has been decided by the member state, while other DMP details (e.g. strength) follow publication rules that are described in Annex I of the relevant Guidance document. It is therefore recommended that the product name created and entered in the XEVMPD **does not** include those details, as the timing of their disclosure on CTIS varies depending on the trial's development phase and does not always occur at decision date.

The maximum number of characters to be entered in the Product name (DP.6.2) data element is 2000.

Examples:

Xyznumab

XYZ

1.4.3. Product Other Name (DP.6.3)

Optional information

Any other name used to identify the product may be specified in this data element by the sponsor.

The maximum number of characters to be entered in the Product Other Name (DP.6.3) data element is 500.

Examples:

XYZ-1234

ABC-123/01

1.5. Comment (DP.7)

Mandatory optional information

During the initial insert of the DMP entity, no information needs to be provided in this field.

[2] Note that the CTIS transparency rules have been revised in a new version; more information on their applicability here

1.6. Pharmaceutical product (DP.PPs)

The number and composition of pharmaceutical product(s) within the development medicinal product must be provided in accordance with the information stated in the Investigator's Brochure.

Each development medicinal product entity in the XEVMPD must contain at least one pharmaceutical product.

The technical concept of a 'pharmaceutical product' refers to the qualitative and quantitative composition of a medicinal product in the pharmaceutical form for administration in line with the product information.

A medicinal product may contain one or more 'pharmaceutical products' (e.g., a kit containing two sets of tablets containing different active ingredients and/or concentration, such as day and night flu tablets, contraceptive tablets etc.). In these instances, a pharmaceutical product section is to be completed for each 'pharmaceutical product' in an XEVPRM.

Where applicable, the technical concept of a 'pharmaceutical product' can also include information on a medical device if it is an integral part of the medicinal product; for example, the scaffolding or net for a cell therapy medicinal product in accordance with Regulation (EC) No 1394/2007.

The administrable pharmaceutical form refers to the pharmaceutical form for administration to the patient, after any necessary transformation of the manufactured pharmaceutical form has been carried out.

Examples:

- DMP containing **one pharmaceutical product**:

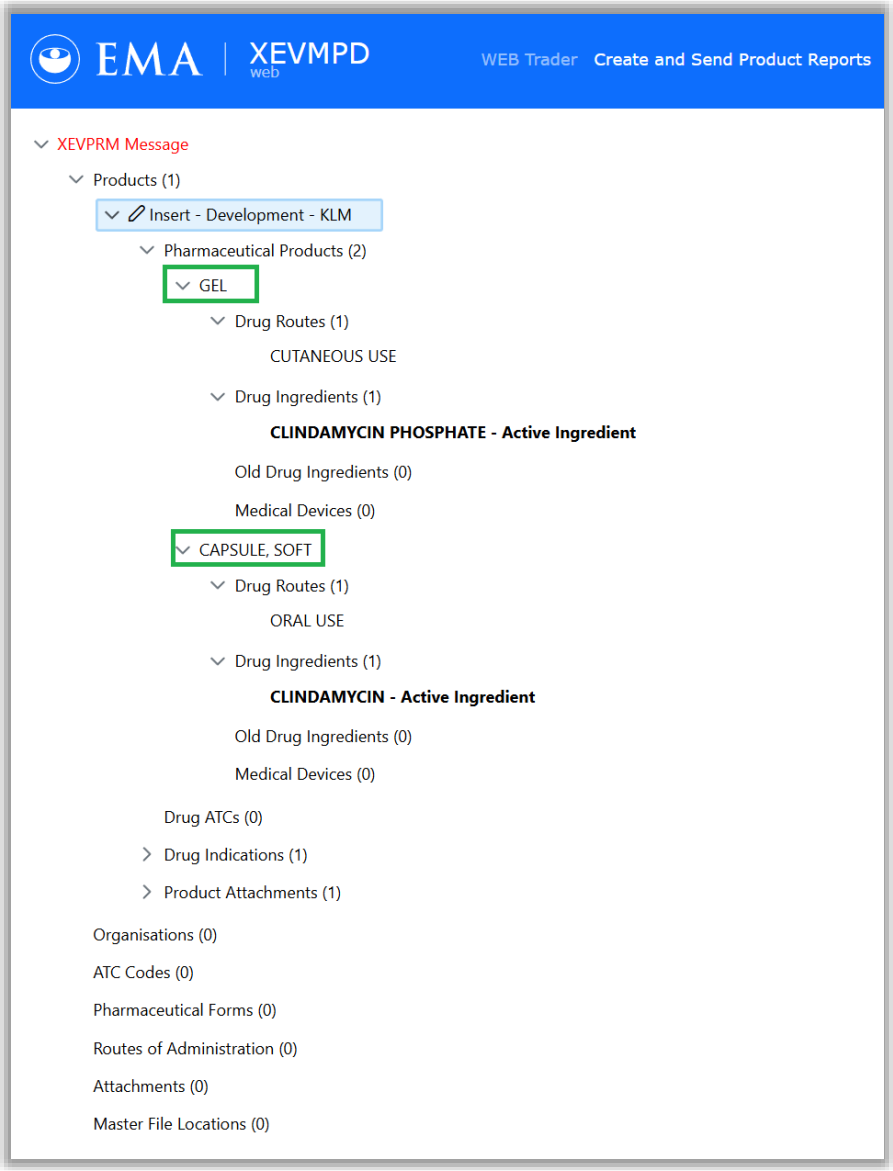
  DMP 'ABC' is presented as one tablet containing 100 mg of active ingredient 'paracetamol'

- DMP containing **multiple pharmaceutical products**:

  DMP 'KLM' is presented as:

  - a gel containing 1.2% w/w of Clindamycin Phosphate

  - one soft capsule containing 200 mg of clindamycin



1.6.1. Administrable pharmaceutical form (PP.1)

Mandatory information

The administrable pharmaceutical form(s) must be specified in accordance with the pharmaceutical product information indicated in the IB.

The 'Administrable pharmaceutical form' refers to the pharmaceutical form for administration to the patient, **after any necessary transformation of the manufactured pharmaceutical form has been carried out.**

The administrable pharmaceutical form is identical to the authorised pharmaceutical form in cases where no transformation is necessary prior administration to the patient.

Examples:

Manufactured pharmaceutical form	*Administrable pharmaceutical form*
Tablet	Tablet
Capsule	Capsule
Inhalation powder	Inhalation powder
Powder for solution for injection	Solution for injection
Concentrate for solution or infusion	Solution for infusion
Granules for oral solution	Oral solution
Effervescent tablet	Oral solution

The administrable pharmaceutical form may differ from the standard term included in the European Directorate for the Quality of Medicines (EDQM) standard term list. In such cases, the EDQM standard term as available in the XEVMPD must be selected. I.e., it is not necessary to request the addition of a new proposed term for the pharmaceutical form as it is stated in the IB in the XEVMPD; see the below example.

Example:

The IB states: *hard capsule*

EDQM standard term available in the XEVMPD: *Capsule, hard (PHF00006MIG)*

With regards to referencing a pharmaceutical form in the DMP in the XEVMPD, the below guidance should be followed:

- If a not-nullified **standard term** of the requested administrable pharmaceutical form **is available** in the XEVMPD look-up table, sponsors should reference the standard term in their pharmaceutical product entity within their DMP.
- If a not-nullified **standard term** of the pharmaceutical form **is NOT available** but a **not-nullified proposed term** of the pharmaceutical form **is available** in the XEVMPD look-up table, sponsors should reference the proposed term in their pharmaceutical product entity within their DMP.
- If the pharmaceutical form is n**ot available as a standard or proposed term** in the XEVMPD look-up table **and**:
  - the term is flagged as "Pending" on the EDQM website; or
  - an application for a new pharmaceutical form was/will be submitted to the maintenance Organisation (i.e., EDQM) via the NCA or EMA (as applicable) with the request of adding it to the standard term list; and
  - the requested pharmaceutical form **is not included in the list of proposed pharmaceutical forms re-mapped to standard pharmaceutical forms** in the pharmaceutical form mapping

list named **'D1 - XEVMPD-RMS_EDQM Pharmaceutical Dose Form terms mapping'** and available in the 'Documents' section of the Referentials Management Service (RMS) portal then

the pharmaceutical form should be inserted in the XEVMPD by the EMA as a new **proposed** term**.** See section *5.1. Request for an insert of a standard or proposed pharmaceutical form* for further information.

- If the pharmaceutical form is still under development in a clinical trial and therefore considered confidential, it should be submitted in the XEVMPD by the sponsor as a new **development term**. See section *5.2. Insert of a development pharmaceutical form via an XEVPRM* for further information.

An overview of the above information on how to reference a pharmaceutical form term in a DMP entity in the XEVMPD is provided in *Process map 4: How to reference a pharmaceutical form term in a DMP*.

To find EV Code(s) of pharmaceutical dose form terms available in the XEVMPD, users should check:

- the 'Pharmaceutical Forms' look-up table in XEVMPDweb; or
- the 'Mappings' section of the pharmaceutical form term in the Referentials Management System (RMS).

1.6.1.1. Route of administration (PP.AR.1)

Mandatory information

The route of administration of the administrable pharmaceutical form must be specified in accordance with the pharmaceutical product information indicated in the IB.

Administration route section describes the route(s) of administration i.e., the path by which the medicinal product (described as technical concept of a 'pharmaceutical product') is taken into/makes contact with the body.

Examples:

Oral use (ADR00048MIG), intravenous use (ADR00042MIG), oromucosal use (ADR00069MIG), ocular use (ADR00068MIG)

The route of administration stated in the IB may differ from the standard term included in the EDQM standard term list. In such cases, the EDQM standard term available in the XEVMPD must be selected. I.e., it is not necessary to request the addition of a new proposed term for the route of administration as it is stated in the IB in the XEVMPD; see the below example.

The IB SmPC states: *"This product should be administered orally…".*

Since "orally" is not a standard EDQM term, the DMP should reference the standard term "Oral use" instead:

- Oral use (ADR00048MIG)

- Sponsors may reference deprecated route(s) of administration in a development medicinal product entry to facilitate the submission of information on medicines in the XEVMPD.
- If a not-nullified **standard term** of the route of administration **is available** in the XEVMPD look-up table, sponsors should reference the standard term in their pharmaceutical product entity within their DMP.

- If a not-nullified **standard term** of the route of administration **is NOT available** but a **not-nullified proposed term** of the route of administration **is available** in the XEVMPD look-up table, sponsors should reference the proposed term in their pharmaceutical product entity within their DMP.
- If the route of administration **is not available as a standard or proposed term** in the XEVMPD look-up table and
  - the term is flagged as "Pending" on the EDQM website; or
  - an application for a new route of administration term was/will be submitted to the maintenance Organisation (i.e., EDQM) via the NCA or EMA (as applicable) with the request of adding it to the standard term list; and
  - the requested route of administration **is not included in the list of proposed routes of administration re-mapped to standard routes of administration** in the route of administration mapping list named "**D2 - XEVMPD-RMS_EDQM Route of Administration terms mapping**" and available in the document section of the Referentials Management Service (RMS) portal, then

  the route of administration should be inserted by the EMA as a new **proposed term.**

  See section *6.1. Request for an insert of a standard or proposed route of administration* for further information.
- If the route of administration is still under development in a clinical trial and therefore considered confidential, it should be submitted in the XEVMPD by the sponsor as a new **development term**. See section *6.2. Insert of a development route of administration via an XEVPRM* for further information.

An overview of the above information on how to reference a route of administration term in a DMP entity in the XEVMPD is provided in *Process map 5: How to reference a route of administration term in a DMP.*

To find the EV Code(s) of the route of administration terms available in the XEVMPD, users should check:

- the 'Routes of Administration' remote look-up table in XEVMPDweb; or
- the 'Mappings' section of the route of administration term in the Referentials Management System (RMS).

1.6.1.2. Pharmaceutical product drug ingredients and medical device(s)

The IB will indicate the composition of the pharmaceutical product(s) within the medicinal product.

- Each approved substance successfully submitted to the XEVMPD has an assigned EV Code. The preferred name of the substance is entered in English.
- The name(s) of the substance in individual national languages is/are listed as "Translations". The Agency supports non-Latin /accented character set EEA languages.
- Any synonym(s)/alias(es) of the substance is/are listed as "Synonyms"/"Alias(es)".
- When a substance contains multiple components, the substance and the individual components should be submitted, providing that the substance has a descriptive level of information relevant to

excipient in medicinal products (e.g., general terms not indicative of excipients in medicines are not accepted such as thickeners, ink, emulsifiers).

Example:

- *Thickeners (methylcellulose, xanthan gum);*

- *Stearate emulsifiers (polyethylene glycol sorbitan tristearate, macrogol stearate, glycerides);*

- *Lemon flavour (maltodextrin, arabic gum, lactose, triethyl citrate).*

All substance names should be referenced separately since they are substance names referenced in the supporting document (e.g., the IB or an SmPC); i.e., methylcellulose, xanthan gum, stearate emulsifiers, polyethylene glycol, sorbitan tristearate, macrogol stearate, glycerides, lemon flavour, maltodextrin, arabic gum, lactose and triethyl citrate.

1.6.1.2.1. Active ingredient information

Mandatory information

Each pharmaceutical product must contain information on the active ingredient(s). Active ingredient substance name(s) and its/their concentration(s) can be found in the relevant section of the IB.

1.6.1.2.1.1. Active ingredient substance code (PP.ACT.1)

The EV Code(s) of the substance(s) indicated as the active ingredient(s) of the medicinal product according to the description provided in the IB must be specified.

Each substance record successfully submitted to the XEVMPD has an assigned EV Code. The **preferred name** of the approved substance is entered in English.

Each **translation and synonym** are linked to the master substance EV Code.

The substance name referenced in the pharmaceutical product must correspond to the substance name used in the IB and should provide the description of the substance within the medicinal product irrespective of national naming convention or any symbols, commas, and additional brackets, hyphens.

- If a substance record was successfully submitted to the XEVMPD and a substance EV Code was assigned, the substance name can be selected from the available XEVMPD look-up table.

  List of substance names available in the XEVMPD, with their assigned EV Code, can be found:

  - in the XEVMPD look-up table in XEVMPDweb;
  - on the Substances Management Services (SMS) portal, under the links: Download SMS Export (current) and Download SMS Export (non-current).

- If the required substance name/substance translation or a synonym/alias is not available in the XEVMPD, please refer to section *8. Initial submission of substance information* of this document for information how the substance information should be submitted to the XEVMPD.

Guidance on how to handle substance names is included in the 'EMA Substance names best practice' document published in section "Data Quality-control methodology" of the 'Guidance documents related to data submission for authorised medicines' webpage.

'SMS guidance for external users' document is also available for related information.

1.6.1.2.1.2. Active ingredient concentration type Code (PP.ACT.2)

'Concentration Type Code' corresponding to the selected concentration type value must be specified.

The strength of the substance indicated as 'active' must be specified as a quantity of the substance present in the pharmaceutical product.

The following concentration type values (amount value types) are available for use in the XEVMPD look-up table/CV list *'Extended EudraVigilance product report message concentration types'* on the 'Guidance documents related to data submission for authorised medicines' webpage:

- equal;
- range;
- up to;
- not less than;
- approximately;
- average.

Examples:

Each capsule contains 50 mg of substance X: for this example, the value should be set to "Equal", and the strength should be expressed per unit of presentation, as 50 mg per 1 single capsule.

After reconstitution, each ml of solution contains 10 mg of substance X: for this example, the value should be set to "Equal", and the strength should be expressed per unit of measurement, as 10 mg per 1 ml.

After dilution, the concentration of substance X will be 100 mg/ml to 200 mg/ml depending on the age of the patient: for this example, the value should be set to "Range" and the strength should be expressed as unit of measurement, as 100 mg per 1 ml to 200 mg per 1 ml.

1.6.1.2.1.3. Active ingredient substance strength

The strength of the substance specified as the active ingredient in the IB must be entered.

Whenever possible, the substance strength should be expressed as a unit of measurement.

Strength must be entered in the XEVMPD in accordance with the ISO IDMP standards based on a numerator and denominator.

Strength can be therefore expressed in two ways:

- As a **unit of Measure**

  When the strength of a medicinal product described as a technical concept of a pharmaceutical Product that has undergone a transformation (for example reconstitution) is to be specified, it is to be specified using the strength resulting from the transformation.

  Examples:

10 milligrams per 100 millilitres, 10 milligrams per 1 single day

- As a **unit of Presentation**

  The unit of presentation is a qualitative term describing the discrete unit in which a pharmaceutical product is presented to describe strength or quantity in cases where a quantitative unit of measurement is not appropriate.

  Examples:

  250 milligrams per 1 single tablet, 10 millilitres per one single spoon

Unit of presentation can be expressed as **strength** (e.g., spray/puff contains 100 mcg per actuation, the unit of presentation = actuation) or **quantity** (e.g., bottle contains 100 ml per bottle, the unit of presentation = bottle).

Where an ingredient is present in the form of a salt or hydrate, the quantitative composition may be expressed in terms of the mass [or biological activity in International (or other) units where appropriate] of the active moiety (base, acid or anhydrous material).

The strength declared should be included in the IB. No calculations/conversions should be performed to obtain a figure.

- If the strength is declared as the amount of base, then the base is the substance to be declared as the ingredient
- If the strength is declared as the amount of the salt, then the salt is the substance to be declared as the ingredient

In the rare examples where the strength of the salt and the base are both declared, then the salt is the substance to be declared as the ingredient. This is in line with IDMP where the both the substance (salt) and the reference substance (base/active moiety) will need to be defined.

Where the active ingredient is an ester or pro-drug, the quantitative composition may be stated in terms of the quantity of that ester or pro-drug.

1.6.1.2.1.4. Active ingredient substance value(s)

A numerator value and numerator unit, as well as a denominator value and denominator unit, must be specified during the submission of active ingredient concentration.

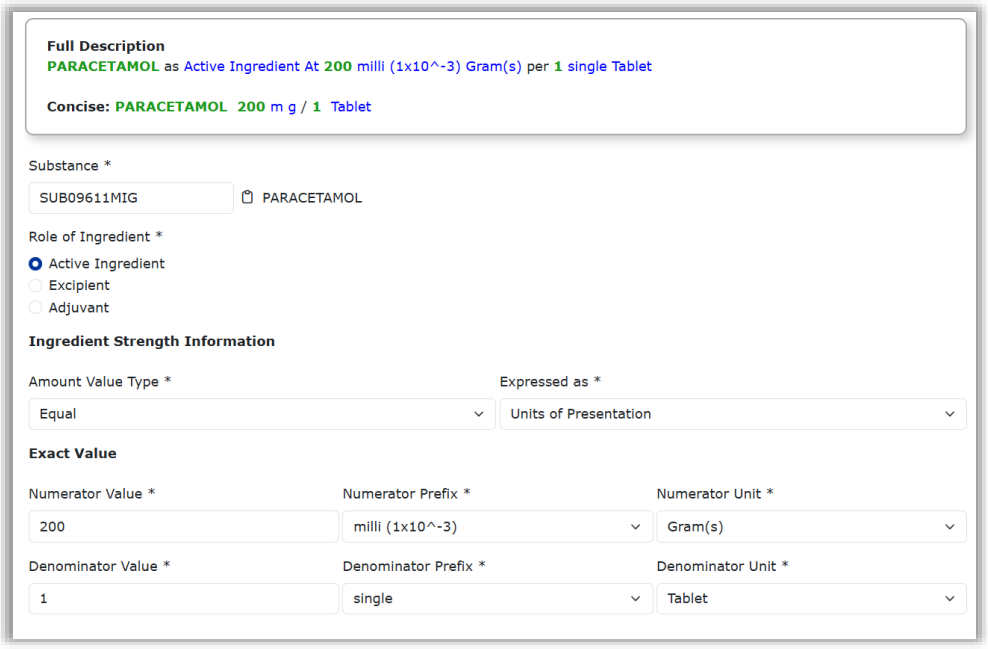
- **(Low Amount) Numerator Value (PP.ACT.3)** refers to the strength of the active substance expressed in a ratio scale. It refers to the numerator value of the strength of the active substance.
- **(Low Amount) Numerator Prefix (PP.ACT.4)** refers to the strength of the active substance expressed in a ratio scale. It refers to the numerator unit prefix value of the strength of the active substance.
- **(Low Amount) Numerator Unit (PP.ACT.5)** refers to the strength of the active substance expressed in a ratio scale. It refers to the numerator unit value of the strength of the active substance.
- **(Low Amount) Denominator Value (PP.ACT.6)** refers to the strength of the active substance expressed in a ratio scale. It refers to the denominator value of the strength of the active substance

- **(Low Amount) Denominator Prefix (PP.ACT.7)** refers to the strength of the active substance expressed in a ratio scale. It refers to the denominator unit prefix value of the strength of the active substance.
- **(Low Amount) Denominator Unit (PP.ACT.8)** refers to the strength of the active substance expressed in a ratio scale. It refers to the denominator unit value of the strength of the active substance
- **High Amount Numerator Value (PP.ACT.9**) refers to the strength of the active substance expressed in a ratio scale. It refers to the numerator value of the strength of the active substance.
- **High Amount Numerator Prefix (PP.ACT.10)** refers to the strength of the active substance expressed in a ratio scale. It refers to the numerator unit prefix value of the strength of the active substance.
- **High Amount Numerator Unit (PP.ACT.11)** refers to the strength of the active substance expressed in a ratio scale. It refers to the numerator unit value of the strength of the active substance.
- **High Amount Denominator Value (PP.ACT.12)** refers to the strength of the active substance expressed in a ratio scale. It refers to the denominator value of the strength of the active substance.
- **High Amount Denominator Prefix (PP.ACT.13)** refers to the strength of the active substance expressed in a ratio scale. It refers to the denominator unit prefix value of the strength of the active substance.
- **High Amount Denominator Unit (PP.ACT.14)** refers to the strength of the active substance expressed in a ratio scale. It refers to the denominator unit value of the strength of the active substance.

Examples:

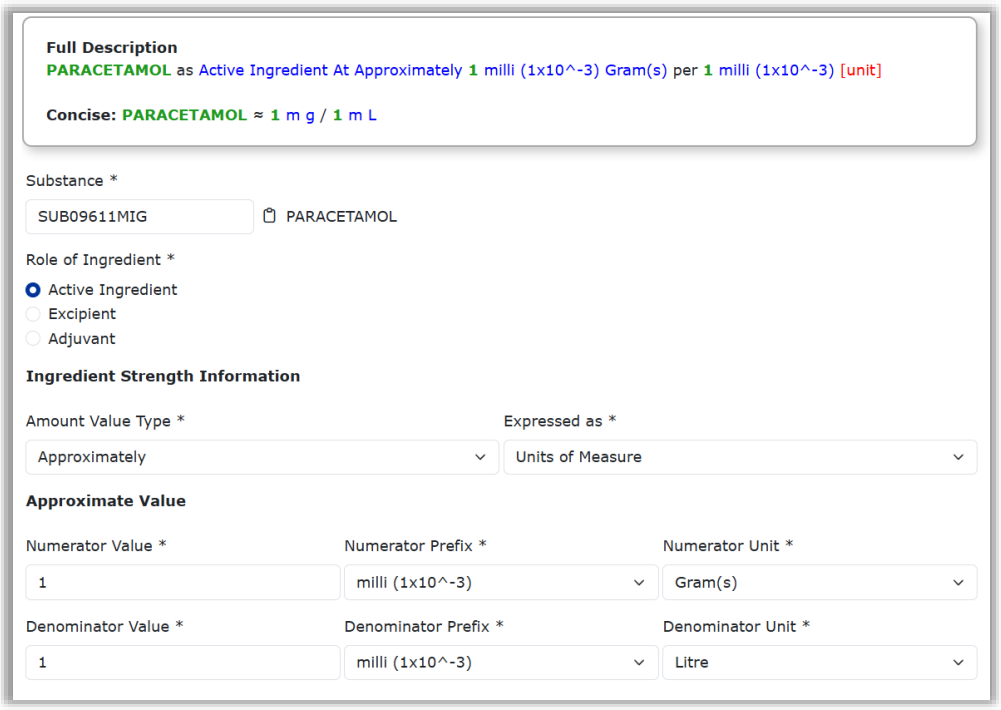
Each tablet contains 200 mg of paracetamol

The strength of the active ingredient should be expressed as per unit of presentation. The value should be set to "Equal" and the strength should be expressed as 200 milligrams per 1 single tablet.



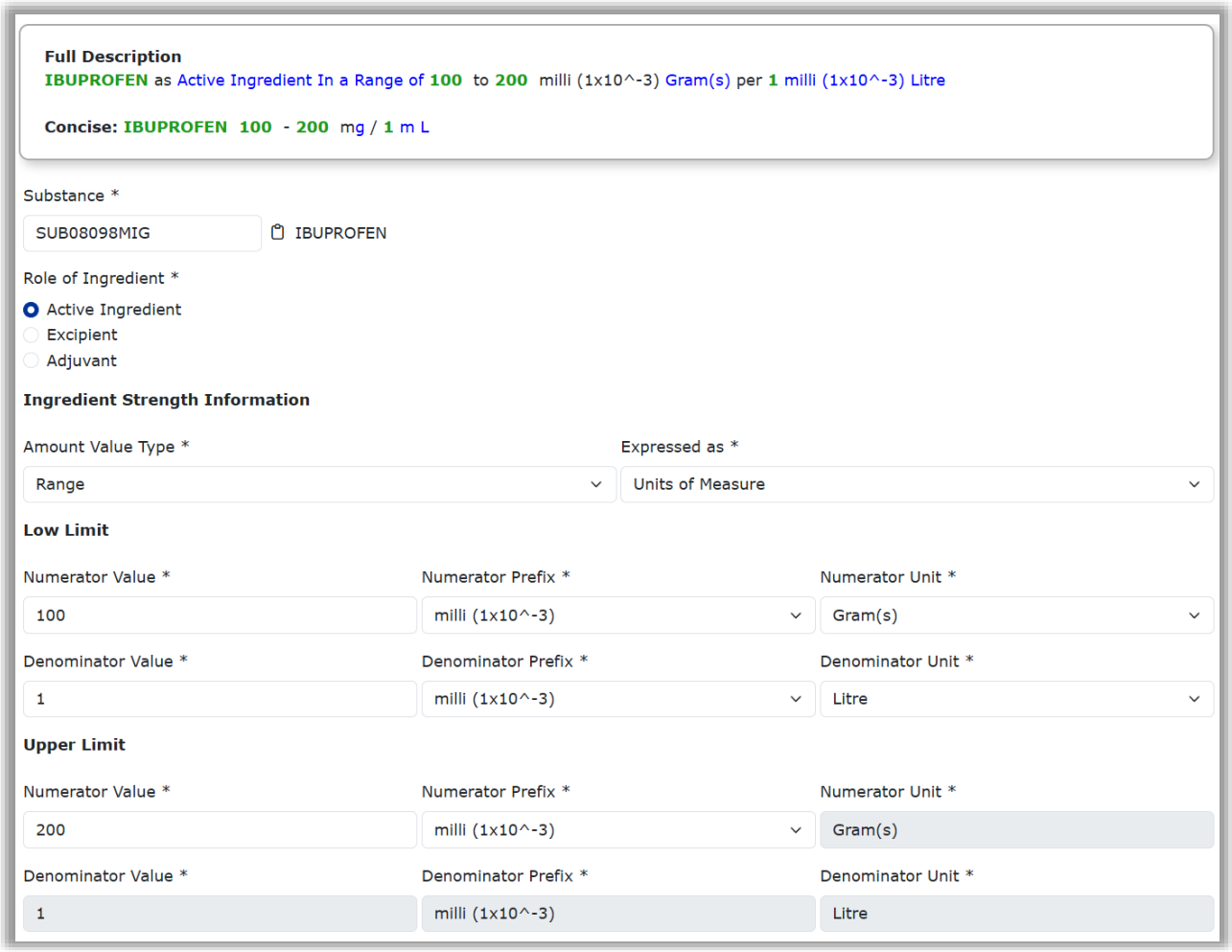
Each vial contains 10 mg of Paracetamol; after reconstitution, each ml of solution contains approximately 1 mg of Paracetamol.

The strength of the active ingredient should be expressed as per unit of measure. The value should be set to "Approximately" and the strength should be expressed as 1 milligram per 1 millilitre.



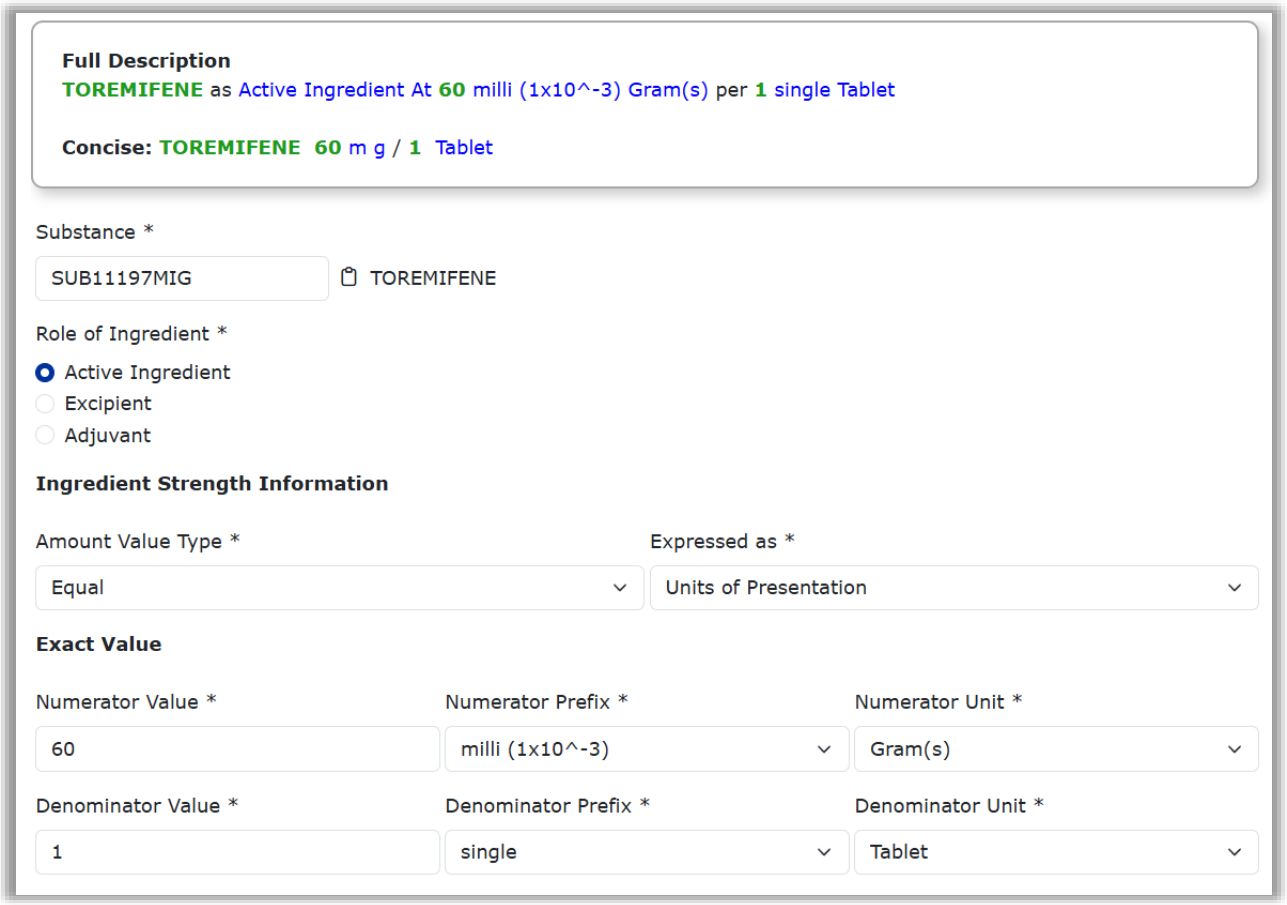
The concentrate for solution for infusion contains 1000 mg/ml Ibuprofen; after dilution, the concentration of Ibuprofen will be 100 mg/ml to 200 mg/ml depending on the age of the patient.

The strength of the active ingredient should be expressed as per unit of measure. The value should be set to "Range" and the strength should be expressed as 100 milligrams per 1 millilitre to 200 milligrams per 1 millilitre.



Each tablet contains 60 mg toremifene (as citrate)

The substance 'toremifene' should be specified as the active ingredient in the pharmaceutical product; the strength of the active ingredient should be expressed as per unit of presentation. The value should be set to "Equal" and the strength should be expressed as 60 milligrams per 1 tablet.



1.6.1.2.2. Excipient information

Optional information

It is optional to submit information on excipient(s) and their concentration for a pharmaceutical product within a DMP entity. If these are provided, the information must be entered in accordance with the information stated in the IB.

1.6.1.2.2.1. Excipient substance code (PP.EXC.1)

The EV Code(s) of the substance(s) indicated as excipient(s) of the medicinal product according to the information in the IB may specified.

The same principles as described in section *1.6.1.2.1.1. Active ingredient substance code (PP.ACT.1)* of this document apply if the sponsor wishes to provide this information.

1.6.1.2.2.2. Excipient concentration type Code (PP.EXC.2)

'Concentration Type Code' corresponding to the selected concentration type value may be specified.

The same principles as described in section *1.6.1.2.1.2. Active ingredient concentration type Code (PP.ACT.2)* of this document apply if the sponsor wishes to provide this information.

1.6.1.2.2.3. Excipient substance strength

The strength of the substance(s) indicated as excipient(s) of the medicinal product according to the information in the IB may specified.

The same principles as described in section *1.6.1.2.1.3. Active ingredient substance strength* of this document apply if the sponsor wishes to provide this information.

1.6.1.2.2.4. Excipient substance values

A numerator value and numerator unit, as well as a denominator value and denominator unit, may be specified during the submission of excipient ingredient concentration.

The same principles as described in section *1.6.1.2.1.4. Active ingredient substance value(s)* of this document apply if the sponsor wishes to provide this information.

Example:

Excipient with known effect: Each tablet contains 91.20 mg of lactose

The strength of the ingredient should be expressed as per unit of presentation. The value should be set to "Equal" and the strength should be expressed as 10 milligrams per 1 single capsule.

1.6.1.2.3. Adjuvant(s) information

Mandatory information

In some instances, the pharmaceutical product can also contain **adjuvants**. Adjuvant substance(s) and its/their concentration(s) can be found in the relevant IB.

It is mandatory to submit information on adjuvants and their concentration for a pharmaceutical product within a DMP entity. If these are provided, the information must be entered in accordance with the information in the IB.

1.6.1.2.3.1. Adjuvant substance code (PP.ADJ.1)

The EV Code(s) of the substance(s) indicated as adjuvant(s) of the medicinal product according to the information in the IB must specified.

The same principles as described in section *1.6.1.2.1.1. Active ingredient substance code (PP.ACT.1)* of this document apply to provide this information.

1.6.1.2.3.2. Adjuvant concentration type Code (PP.ADJ.2)

'Concentration Type Code' corresponding to the selected concentration type value may be specified.

The same principles as described in section *1.6.1.2.1.2. Active ingredient concentration type Code (PP.ACT.2)* of this document apply to provide this information.

1.6.1.2.3.3. Adjuvant substance strength

The strength of the substance(s) indicated as adjuvant(s) of the medicinal product according to the information in the IB must specified.

The same principles as described in section *1.6.1.2.1.3. Active ingredient substance strength* of this document apply to provide this information.

1.6.1.2.3.4. Adjuvant substance values

A numerator value and numerator unit, as well as a denominator value and denominator unit, must be specified during the submission of an adjuvant ingredient concentration.

The same principles as described in section *1.6.1.2.1.4. Active ingredient substance value(s)* of this document apply to provide this information.

Example:

*A medicinal product contains 20 micrograms/ml of Hepatitis B surface antigen**

**adjuvanted on aluminium hydroxide (0.2 micrograms/ml Al3+)*

The adjuvant (i.e., EV code of the adjuvant substance) to be referenced in the pharmaceutical product section of the DMP entity in the XEVMPD must be "aluminium hydroxide" (i.e., EV Code SUB33625) and the strength is to be specified as "0.2 micrograms/ml".

1.6.1.3. Old Drug Ingredient(s)

This information is related to legacy data; it is not to be used/provide by sponsors.

1.6.1.3.1. Medical device Code (PP.MD.1)

Optional information

Where a medical device forms an integral part of the mode of action of a medicinal product, the EV code of the medical device may be specified in this data element.

Medical device description is currently only required for Advanced Therapy Medicinal Products (ATMPs), where applicable (see Regulation (EC) No 1394/2007).

Example(s):

collagen scaffold, cochlear implant

Where a medical device term is required for an ATMP, the sponsor should submit a request for a term assignment via the EMA Service Desk portal. The EMA will assess the request and, if the term should be included, provide a code and term name for the medical device to the sponsor.

List of available medical devices with their assigned codes can be found:

- in the 'Medical devices' remote look-up list in XEVMPDweb;
- in the 'EudraVigilance eXtended Medicinal Product Dictionary (XEVMPD) medical devices' controlled vocabulary list published on the 'Guidance documents related to data submission for authorised medicines' webpage; or
- in the 'XEVMPD Medical Devices' list in the Referentials Management System (RMS).

1.7. ATC

Optional information

It is optional to reference an ATC Code for a development medicinal product in the XEVMPD.

For XEVMPDweb users, the list of ATC Codes is available in the corresponding XEVMPD look-up table in the XEVMPD.

Gateway users can obtain the list of ATC Codes from the WHO Collaborating Centre for Drug Statistics Methodology.

If the sponsor wishes to reference an ATC Code in their DMP, the ATC Code should be entered as per information in the IB, and the following guidance should be considered:

- A 'standard' ATC code must be specified whenever possible.
- All five levels of the ATC code can be used.
- In case that multiple ATC Codes are applicable for one development medicinal product, multiple ATC Codes can be referenced within one DMP entity.
- Where, for certain types of medicinal products, an ATC Code is usually not the ATC Code, value NOTAPPLIC may be specified.
- If the ATC Code for a medicinal product is not part of the ATC Index published by the WHO, the company should request the ATC code to be added in the Index by submitting an application to the WHO. Once a confirmation on whether the ATC code will be published either as provisional or final is received from the WHO, the company can then send a request through the RMS portal with the confirmation from WHO. The EMA will then publish the ATC Code in RMS before the official yearly update from WHO. The EMA will also enter the ATC code in the XEVMPD to allow marketing authorisation holders/sponsors to reference it in their medicinal product entity. See section *4.1. Request for an insert of a standard or a proposed ATC Code* for further information.
- If the ATC Code is still under development and therefore considered confidential, it should be submitted in the XEVMPD by the sponsor as a new **development ATC Code**. See section *4.2. Insert of a development ATC Code* for further information.

For an overview of the above information on how to reference an ATC Code in a DMP entity in the XEVMPD see *Process map 6: How to reference an ATC Code in a DMP.*

1.8. Product indications (DP.INDs)

Optional information

It is optional to reference indications for a development medicinal product in the XEVMPD.

Guidance on coding of indications using MedDRA terminology is available in the document 'Coding of indications in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD)' published on the 'Guidance documents related to data submission for authorised medicines' webpage and also in the latest to MedDRA Term Selection: Points to Consider document available on the MedDRA website.

A license for MedDRA needs to be acquired by commercial sponsors from the MSSO.

Non-commercial sponsors are eligible for a fee waiver for MedDRA subscription.

If the sponsor wishes to reference product indications in their DMP, the following guidance must be considered:

1.8.1. MedDRA version (DP.IND.1)

The indication(s) is/are to be coded using MedDRA in its latest version in use. The next official MedDRA version can also be used if a term of that version is required and is not present in the latest version in use.

The following MedDRA versions are included in the XEVMPD:

- the latest version of MedDRA in use;
- the two previous versions of MedDRA;
- the last published MedDRA version (for supplemental terms).

New MedDRA versions are implemented in XEVMPD on the 1st Monday of May and November of each year.

1.8.2. MedDRA level (DP.IND.2)

Low Level Terms (LLT) or Preferred Terms (PTs) may be specified. ~~must be specified. PT or higher terms cannot be used.~~

1.8.3. MedDRA Code (DP.IND.3)

The indication(s) is/are to be coded using a term and corresponding code.

Where a specific language is not supported in MedDRA, the MedDRA Code associated with the English equivalent term should be used.

Multiple terms can be used to code the medical concepts of indication(s), the signs, symptoms or intended effects. The use of qualifiers (e.g., comorbidities, population specifics) will be possible with the implementation of the ISO IDMP standards.

It is not necessary to update medicinal product entries when a new MedDRA version is released. In the context of the data submission maintenance, if a new MedDRA version is in use at the time of submission, the latest version in use should be used to code the indications.

As a general principle, when updating the product information, terms which are 'non-current' in a new version of MedDRA cannot be referenced in any XEVPRM submitted thereafter and current terms are to be provided instead.

For coding instructions, please refer to MedDRA Term Selection: Points to Consider document available on MedDRA website. Summary of Changes to MedDRA Term Selection are also available on MedDRA website.

Efforts should be made to capture the most granular and comprehensive level of information available in MedDRA; where the stage or type of a disease is available, this should be captured as well.

Examples:

See examples 62 – 64.3 of Chapter 3.II: XEVPRM user guidance document and the examples available in the document 'Coding of indications in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD)'.

1.9. PPI attachments (DP.PPIs)

Optional information

It is optional to provide printed product information (PPI) attachments for a development medicinal product in the XEVMPD.

If the sponsor wishes to reference a PPI attachment in their DMP, the attachment referenced should be the Investigator's Brochure.

Each PPI section contains a reference to a document in a specific language either submitted with the product in the same XEVPRM or referring to a document already present in the XEVMPD (i.e., an attachment EV Code has already been assigned).

1.9.1. Attachment EV Code (DP.PPI.1)

The EV Code of the attachment relevant for the development medicinal product must be specified.

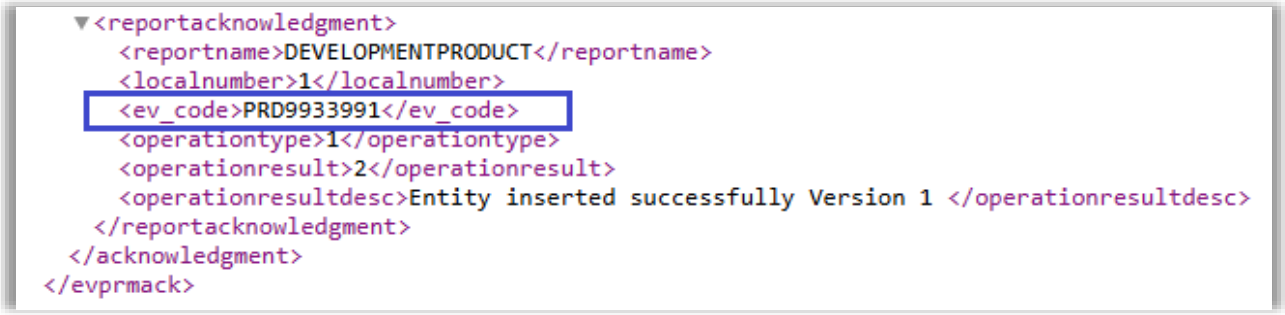
- If the attachment to be referenced in the DMP entity was already successfully submitted to the XEVMPD and an attachment EV Code has been assigned, the attachment can be selected from the **remote look-up table in XEVMPDweb**.
  - Gateway users should populate the 'Attachment EV Code' field (DP.PPI.1) with the assigned attachment EV Code received in the XEVPRM Acknowledgement.
- If the required attachment is not available in the XEVMPD, the attachment can be added using the attachment section of the XEVPRM and selected from the **local look-up table in XEVMPDweb**.

For information on how to insert an attachment in the XEVMPD please refer to section *7. Initial submission of an attachment* of this document.

1.9.2. Attachment validity declaration (AP.PPI.2)

Validity confirmation that the referenced attachment is the latest version of the documentation must be provided for an existing attachment entity by entering the value 'Valid (1)'.

Following a successful insert of a development medicinal product, an EV Code is assigned to the product entity and provided to the sender organisation in an XEVPRM ACK. The pattern of the EV Code for a medicinal product is 'PRD' followed by a number:



2. Initial submission of a reference source

List of available reference sources with their allocated EV Codes can be found in the XEVMPD look-up table 'Sources'.

From 18 January 2024, if the required reference source is not available in the published controlled vocabulary/XEVMPD look-up list, the EMA may enter the reference source information in the XEVMPD by submitting an XEVPRM with operation type 'Insert (1)' assigned to the reference source information.

It is recommended that any request for a new reference source is submitted to the EMA as part of the request for an insert of a new substance or an update of an existing substance.

If the required reference source does not exist in the XEVMPD, sponsors can request the addition of a new reference source in the XEVMPD via an **RMS change request** submitted via the EMA Service Desk:

- If the required reference source is available in RMS list named **'Source of Information'** (RMS ID: 100000000009) but it is not available in the XEVMPD, users should submit an **'Update Term'** RMS change request via ~~RMS~~ the EMA Service Desk portal to request the insert of the reference source in the XEVMPD.
- If the required reference source is not available in either system (i.e., RMS and XEVMPD), users should submit **an 'Add Term'** RMS change request via ~~RMS~~ the EMA Service Desk portal to request the addition of the reference source in the RMS list named **'Source of Information'** (RMS ID: 100000000009) and in the XEVMPD.

~~An 'RMS user manual' is available for download from section 'Documents' of the RMS portal. Please refer to section *3.7. Change Requests* of the RMS user manual for further information.~~

Further information and guidance on how to submit change requests via the EMA Service Desk portal is available in section **3.3. RMS Change requests** of the document **'A6 – Alternative access solution**' under the 'Documents' section of the RMS portal.

RMS data stewards will assess the change request and provide the requestor with the EV Code of the reference source term, as applicable.

3. Initial submission of a sponsor information

New sponsor organisation information must be submitted to the XEVMPD by the sponsor in an XEVPRM with operation type 'Insert'.

The organisation information (i.e., sponsor name and address) corresponding to the sponsor organisation referenced in the Investigator's Brochure (IB) must be entered in the individual XEVMPD data fields:

- as referenced in the IB using the below guidance for each data element, or
- as entered in the Organisation Management System (OMS), i.e. in accordance with the data quality standards for the organisation name and address specified by OMS.
  - Data quality principles for submission of organisation information in OMS are available in the OMS portal, section 'Document's, in the document '**C - OMS Data Quality standards**'.
  - Guidance on how to request the addition of an organisation information in OMS using an OMS change requests in the EMA Service Desk portal is available in section **3.1. OMS Change requests** of the document **'A6 – Alternative access solution**' under the 'Documents' section of the OMS portal.

The sponsor information stated in the IB may differ from the organisation information entered in the OMS.

To indicate in the organisation record in the XEVMPD that the organisation information is reflected as it is entered in OMS, the location ID (LOC ID) must be referenced in the 'Comment' field (0.18) of the sponsor organisation entity in the XEVMPD.

3.1. Initial insert of sponsor information via an XEVPRM

The information to be provided during the **initial insert** of a sponsor organisation in the XEVMPD via an XEVPRM created in XEVMPDweb includes the below information [the symbol (*) means mandatory]:

- (*) Type
- (*) Sponsor Name
- Sponsor Sender ID
- (*) Address
- (*) City
- State
- (*) Postcode
- (*) Country Code
- Telephone Number
- Telephone Extension
- Telephone Country Code
- Fax Number
- Fax Extension

- Fax Country Code
- E-mail Address
- Comment

3.1.1. Type (O.1)

Mandatory information

'Sponsor' must be referenced in this field when submitting a sponsor organisation information in the XEVMPD.

3.1.2. Sponsor Name (O.2)

Mandatory information

The name of the sponsor of the clinical trial, as indicated in the IB/OMS, must be provided.

3.1.3. Sponsor Sender ID (O.5)

Optional information

The ID of the organisation that corresponds to the same organisation, as assigned in the registration system, may be provided.

3.1.4. Address (O.6)

Mandatory information

The address (e.g., street name and number) of the sponsor of the clinical trial, as indicated in the IB/OMS, must be provided.

3.1.5. City (O.7)

Mandatory information

The city where the sponsor of the clinical trial is located, as indicated in the IB/OMS, must be provided.

3.1.6. State (O.8)

Optional information

The county/region where the sponsor of the clinical trial is located, as indicated in the IB/OMS, may be provided.

3.1.7. Postcode (O.9)

Mandatory information

The postcode of the location of the sponsor organisation, as indicated in the IB/OMS, must be provided.

3.1.8. Country Code (O.10)

Mandatory information

The country code of the country where the sponsor of the clinical trial is located, as indicated in the IB/OMS, must be provided.

The country code is to be specified using the ISO-3166-1 standard. The official list of ISO 3166-1 country codes is maintained by the International Organization for Standardization (ISO).

- The country code '**GR**' (not 'EL') corresponding to 'Greece' should be used for locations in Greece as the officially assigned code in accordance with the ISO country codes.
- The country code '**GB**' (not 'UK') corresponding to 'United Kingdom' should be used for locations in England, Wales, and Scotland. 'UK' is a "reserved code" assigned at the request of the national ISO member bodies, governments, and international organisations. This applies to certain code elements required to support a particular application as specified by the requesting body and limited to such use. Any further use of such code elements is subject to approval by the ISO 3166/MA. More information about the reserved codes can be found on the ISO website.
- The country code "**XI**" corresponding to 'United Kingdom (Northern Ireland)' should be used for locations in Northern Ireland.

3.1.9. Telephone Number (O.11)/Telephone Extension (O.12)/Telephone Country Code (O.13)

Optional information

The telephone number, extension and country code for the sponsor organisation may be specified.

3.1.10. Fax Number (O.14)/Fax Extension (O.15)/Fax Country Code (O.16)

Optional information

The fax number, extension and country code for the sponsor organisation may be specified.

3.1.11. E-mail Address (O.17)

Optional information

The email address to be used as a contact point with the sponsor organisation may be specified.

3.1.12. Comment (O.18)

Mandatory Optional information

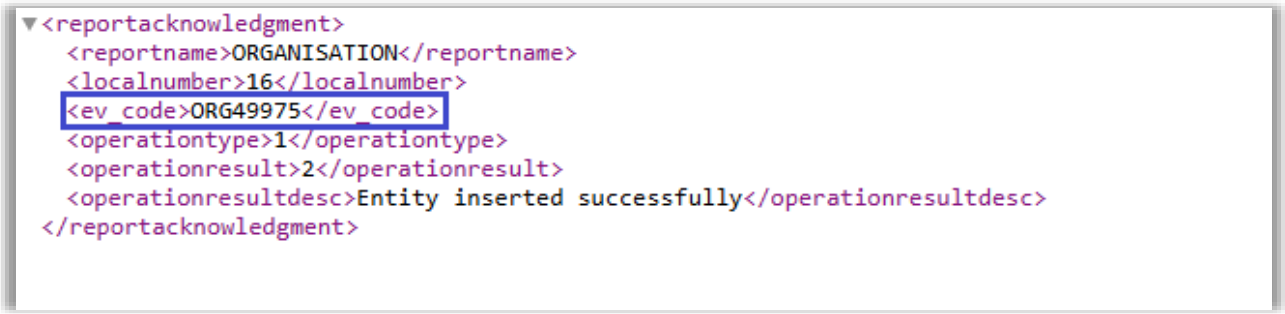
- During the initial insert of the sponsor organisation entity, no information needs to be provided in this field if the sponsor information is provided as per information in the IB.
- When the organisation details are inserted as entered in OMS, the OMS location ID must be entered in this field to facilitate the validation of this information with the organisation details in OMS.

Examples of information to be referenced as applicable:

LOC-100012345

Following a successful insert of an organisation entity in the XEVMPD, an EV Code is assigned to the organisation and provided to the sender organisation in an XEVPRM ACK.

The pattern of the EV Code for an organisation is 'ORG' followed by a number:



4. Initial submission of an ATC Code

Standard and proposed ATC Codes are submitted and maintained in the XEVMPD by the EMA.

From 18 January 2024, only the EMA can insert and maintain proposed ATC Codes in the XEVMPD.

- If the required **standard or proposed ATC Code** does not exist in the XEVMPD, sponsors can request the addition of a new ATC Code in the XEVMPD via an **RMS change request** submitted via the EMA Service Desk.
- If the ATC Code is still under development and information about such ATC is considered confidential, the sponsor can submit a new **development ATC Code** in the XEVMPD. This must be done via an XEVPRM with the operation type 'Insert (1)'. Development ATC Codes are entered and maintained in the XEVMPD by the sponsor; such ATC Codes can be referenced only in the development medicinal product entries owned in the XEVMPD by that sponsor organisation.

Prior to submitting an RMS change request for the addition of a new ATC Code in the XEVMPD or inserting a new development ATC Code in the XEVMPD via an XEVPRM, sponsors are advised to consult the ATC code mapping list named **'D3 - XEVMPD-RMS_WHO-National ATC codes mapping**' available in the 'Documents' section of the Referentials Management Service (RMS) portal to determine if an existing standard ATC code can referenced in the DMP instead.

4.1. Request for an insert of a standard or a proposed ATC Code via an RMS change request

The addition of a standard or proposed ATC Code in the XEVMPD should be requested via an RMS change request.

1. If an **ATC code is included in the ATC Index** published by the WHO but is missing in RMS and/or in the XEVMPD, continue with step 2a and 2b, as applicable.
2. If an **ATC code is not included in the ATC Index** published by the WHO and the sponsor would like to request for this ATC Code to be added in the Index, the sponsor should request the ATC code to be added in the Index by submitting an application to the WHO.

   Once a confirmation on whether the ATC code will be published either as provisional or final is received from the WHO, the sponsor should send an RMS 'change request' through the ~~RMS portal~~ EMA Service Desk portal (**with the confirmation from WHO as an attachment**) to include the ATC code in the RMS list:

   a. If the required ATC Code is available in RMS but it is not available in the XEVMPD, an **'Update term'** change request should be submitted to request the insert of the ATC Code in the XEVMPD.

   b. If the required ATC code is not available in RMS nor in the XEVMPD, a **'New term'** change request should be submitted to request the insert of the ATC Code in RMS and in the XEVMPD.

      If the ATC code is not yet published on the WHO ATC website, please provide a letter from WHO confirming the ATC code as an attachment.

Instructions on how to submit a change request in EMA Service Desk are available in the document A6 - Alternative access solution under the 'Documents' section of the RMS portal.

The EMA will then enter the ATC Code in RMS/XEVMPD before the official yearly update from WHO and inform the requestor.

4.2. Insert of a development ATC Code via an XEVPRM

Sponsors can submit information for an ATC Code that is still under development, and therefore considered as confidential term, in the XEVMPD via an XEVPRM either from the XEVMPD user interface or from their gateway solution.

The 'development' ATC Code that the sponsor wishes to insert in the XEVMPD must not match a current standard or proposed ATC Code already present in the XEVMPD.

The information to be provided during the **initial insert** of a development ATC Code in the XEVMPD via an XEVPRM created in XEVMPDweb includes the below information [the symbol (*) means mandatory]:

- (*) Type
- (*) ATC Code
- (*) ATC Code Description
- Version Date
- Comment

4.2.1. Type (ST.ATC.1)

Mandatory information

The type of term must be specified as 'Development'.

4.2.2. ATC Code (ST.ATC.2)

Mandatory information

The ATC Code must be specified.

The development ATC Code must not match a current standard or proposed ATC Code already inserted in the XEVMPD.

The maximum number of characters to be entered in the ATC Code (ST.ATC.2) data element is 10.

4.2.3. ATC Code Description (ST.ATC.4)

Mandatory information

The ATC code description in English must be specified.

Example:

tetracycline, oxytetracycline, combinations

4.2.4. Version Date (ST.ATC.6)

Optional information

The date of the last update of the specified ATC code may be specified.

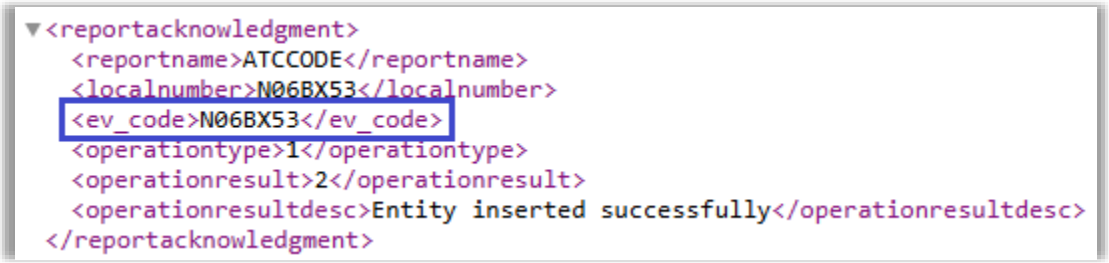
Format of the version date must correspond to 'dd/mm/yyyy'.

4.2.5. Comment (ST.ATC.7)

Optional information

During the initial insert of the ATC entity, no information needs to be provided in this field.

Following a successful insert of the development ATC Code in the XEVMPD, an EV Code is assigned to the ATC Code and provided to the sender organisation in an XEVPRM ACK:



5. Initial submission of a pharmaceutical form

Standard and proposed pharmaceutical form terms are inserted and maintained in the XEVMPD by the EMA.

From 18 January 2024, only the EMA can insert and maintain proposed terms in the XEVMPD.

- If the required **standard or proposed pharmaceutical form** does not exist in the XEVMPD, sponsors can request the addition of a new pharmaceutical form in the XEVMPD via an **RMS change request** submitted via the EMA Service Desk.
- If the pharmaceutical form is still under development and information about such pharmaceutical form is considered confidential, the sponsor can submit a new **development pharmaceutical form** in the XEVMPD. This must be done via an XEVPRM with the operation type 'Insert (1)'. Development pharmaceutical forms are entered and maintained in the XEVMPD by the sponsor; such pharmaceutical forms can be referenced only in the development medicinal product entries owned in the XEVMPD by that sponsor organisation.

Prior to submitting a request for an addition of a new pharmaceutical form in the XEVMPD or inserting a new (development) pharmaceutical form in the XEVMPD, sponsor users are advised to consult the pharmaceutical form mapping list named **'D1 - XEVMPD-RMS_EDQM Pharmaceutical Dose Form terms mapping'** available in the 'Documents' section of the Referentials Management Service (RMS) portal first to determine if an existing standard pharmaceutical form term can be referenced in the DMP instead.

5.1. Request for an insert of a standard or proposed pharmaceutical form via an RMS change request

The addition of a standard or proposed pharmaceutical form in the XEVMPD should be requested via an RMS change request.

1. Check if the required pharmaceutical form is available in RMS:
    a. If yes, and it is missing in XEVMPD only, submit an **'Update term'** change request to request the insert of the pharmaceutical form in the XEVMPD.
    b. If no, and the pharmaceutical form is missing in RMS and in the XEVMPD, submit a **'New term'** change request to request the insert of the pharmaceutical form in RMS and in the XEVMPD.

        As an attachment to the change request, provide as much information as possible to support the inclusion of the term (e.g. product information, investigator´s brochure, etc.).

Instructions on how to submit a change request in EMA Service Desk are available in the document A6 - Alternative access solution under the 'Documents' section of the RMS portal.

RMS data stewards will assess the change request and provide the requestor with the EV Code of the pharmaceutical form as applicable.

5.2. Insert of a development pharmaceutical form via an XEVPRM

Sponsors can submit information for a pharmaceutical form that is still under development, and therefore considered as confidential term, in the XEVMPD via an XEVPRM either from the XEVMPD user interface or from their gateway solution.

The 'development' pharmaceutical form that the sponsor wishes to insert in the XEVMPD must not match any current standard or proposed pharmaceutical form already present in the XEVMPD.

The information to be provided during the **initial insert** of a development pharmaceutical form in the XEVMPD via an XEVPRM created in XEVMPDweb includes the below information [the symbol (*) means mandatory]:

- (*) Type of term
- (*) Pharmaceutical Form Name
- Previous EV Code
- Version Date
- Comment

5.2.1. Type (ST.PF.1)

Mandatory information

The type of term must be specified as 'Development'.

5.2.2. Pharmaceutical Form Name (ST.PF.5)

Mandatory information

The name of the pharmaceutical form in English must be specified.

5.2.3. Previous EV Code (ST.PF.8)

Optional information

This field should remain empty for a pharmaceutical form entered as a development term.

5.2.4. Version Date (ST.PF.7)

Optional information

The date of the last update of the specified pharmaceutical form may be specified.

Format of the version date must correspond to 'dd/mm/yyyy'.

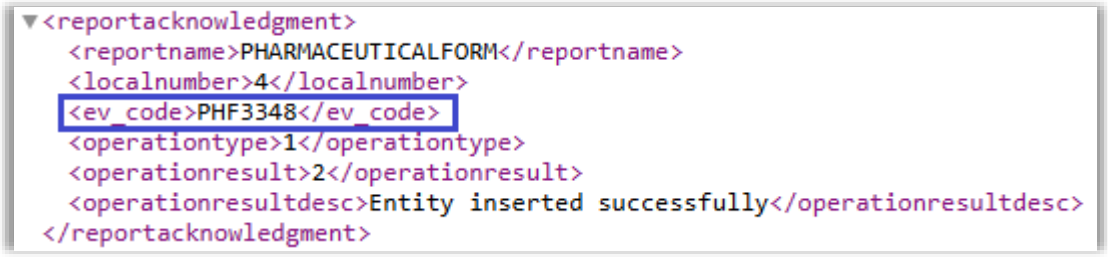
5.2.5. Comment (ST.PF.9)

Mandatory Optional information

During the initial insert of the pharmaceutical form entity, no information needs to be provided in this field.

Following a successful insert of the or development pharmaceutical form in the XEVMPD, an EV Code is assigned to the pharmaceutical form and provided to the sender organisation in an XEVPRM ACK.

The pattern of the EV Code for a pharmaceutical form is 'PDF' followed by a number:



6. Initial submission of a route of administration

Standard and proposed routes of administration terms are submitted and maintained in the XEVMPD by the EMA.

From 18 January 2024, only the EMA can insert and maintain proposed terms in the XEVMPD.

- If the required **standard or proposed route of administration** does not exist in the XEVMPD, sponsors can request the addition of a new route of administration in the XEVMPD via an **RMS change request** submitted via the EMA Service Desk.
- If the route of administration (RoA) is still under development and information about such route of administration is considered confidential, the sponsor can submit a new **development route of administration** in the XEVMPD. This must be done via an XEVPRM with the operation type 'Insert (1)'. Development routes of administration are entered and maintained in the XEVMPD by the sponsor; such routes of administration can be referenced only in the development medicinal product entries owned in the XEVMPD by that sponsor organisation.

Prior to submitting a request for an addition of a route of administration in the XEVMPD or inserting a new (development) route of administration in the XEVMPD, sponsor users are advised to consult the route of administration mapping list named **'D2 - XEVMPD-RMS_EDQM Route of Administration terms mapping '** available in the 'Documents' section of the Referentials Management Service (RMS) portal first to determine if an existing standard pharmaceutical form term can be referenced in the DMP instead.

6.1. Request for an insert of a standard or proposed route of administration via an RMS change request

The addition of a standard or proposed route of administration in the XEVMPD should be requested via an RMS change request.

1. Check if the required route of administration is available in RMS:
    a. If yes, and it is missing in XEVMPD only, submit an **'Update term'** change request to request the insert of the RoA in the XEVMPD.
    b. If no, and the RoA is missing in RMS and in the XEVMPD, submit a **'New term'** change request to request the insert of the route of administration in RMS and in the XEVMPD.

    As an attachment to the change request, provide as much information as possible to support the inclusion of the term (e.g. product information, investigator´s brochure, etc.).

Instructions on how to submit a change request in EMA Service Desk are available in the document A6 - Alternative access solution under the 'Documents' section of the RMS portal.

RMS data stewards will assess the change request and provide the requestor with the EV Code of the pharmaceutical form as applicable.

6.2. Insert of a development route of administration via an XEVPRM

Sponsors can submit information for a route of administration that is still under development, and therefore considered as confidential term, in the XEVMPD via an XEVPRM either from the XEVMPD user interface or from their gateway solution.

The 'development' route of administration that the sponsor wishes to insert in the XEVMPD must not match any current standard or proposed route of administration already present in the XEVMPD.

The information to be provided during the **initial insert** of a development route of administration in the XEVMPD via an XEVPRM created in XEVMPDweb includes the below information [the symbol (*) means mandatory]:

- (*) Type
- (*) Administration Route Name
- Version Date
- Previous EV Code
- Comment

6.2.1. Type Term (ST.AR.1)

Mandatory information

The type of term must be specified as 'Development'.

6.2.2. Administration Route Name (ST.AR.5)

Mandatory information

The name of the route of administration in English must be specified.

6.2.3. Version Date (ST.AR.7)

Optional information

The date of the last update of the specified route of administration may be specified.

Format of the version date must correspond to 'dd/mm/yyyy'.

6.2.4. Previous EV Code (ST.AR.8)

Optional information

This field should remain empty for a RoA entered as a development term.

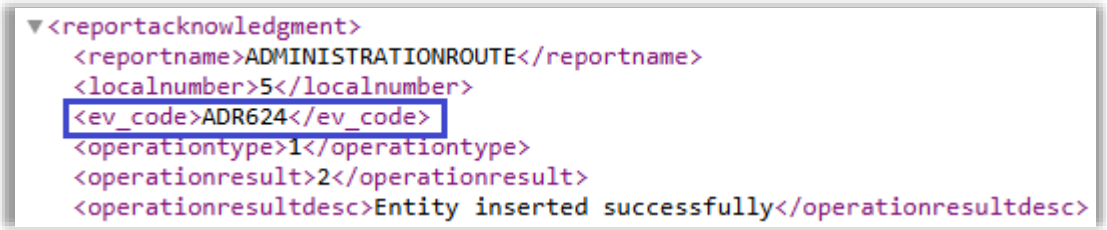
6.2.5. Comment (ST.RA.9)

Mandatory Optional information

During the initial insert of the RoA entity, no information needs to be provided in this field.

Following a successful insert of the development route of administration in the XEVMPD, an EV Code is assigned to the RoA entity and provided to the sender organisation in an XEVPRM ACK.

The pattern of the EV Code for a route of administration is 'ADR' followed by a number:



7. Initial submission of an attachment

If the sponsor wishes to submit an attachment in the XEVMPD, this must be done via an XEVPRM sent either from the XEVMPD user interface or from their gateway solution.

At least one of the medicinal products (i.e. DMP entity) referencing the new attachment must also be present in the same XEVPRM.

Printed Product Information (PPI) attachments submitted to the XEVMPD for development products are considered confidential in the XEVMPD and visible in XEVMPDweb only to users registered under the profile of the sponsor organisation that owns the data in the XEVMPD, and to registered users from the EMA.

Gateway user organisations creating their own XEVPRMs should be aware of the following:

- Attachments are to be provided in a single ZIP file, which also includes the XEVPRM with the PPI(s);
- Zip file includes:
  - 1 XML file containing the XEVPRM,
  - Zero or more attachments;
- The ZIP file can be of a maximum size of 60 MB;
- Each file within the ZIP file can be a maximum size of 25 MB;
- The ZIP file must not contain folders;
- File names must be less than 200 characters in length.

Format of an attachment

The allowed file types for PPI are: .PDF (1), .DOC (2), .DOCX (3), .XLS (4), .XLSX (5).

The expected format of the provided IB is PDF (1), .DOC (2) or .DOCX (3).

With respect to pdf documents, sponsors should not attach scanned PDF documents; the documents should be a "genuine" PDF documents. PDF file version 1.4 or 1.7 should be used, as these are the only two versions that are ISO standards compliant. They are used for long term preservation of information and therefore the EMA and/or sponsor will have the assurance that they will be able to open them for years to come.

Content of an attachment

A copy of the IB should be provided, if the sponsor wishes to reference an attachment in their DMP entity.

Content of attachments cannot be updated. Updated attachment(s) must be re-submitted when necessary. E.g., if the IB is updated with new route of administration, the updated IB must be inserted in the XEVMPD as a new entity; new attachment EV Code will be assigned. The DMP entity must then be updated to reference the new attachment and RoA.

It is not possible to nullify attachment entities in the XEVMPD. Obsolete attachments submitted by error, or duplicated attachment entities, will remain in the XEVMPD.

The information to be provided during the **initial insert** of a PPI attachment in the XEVMPD via an XEVPRM created in XEVMPDweb includes the below information [the symbol (*) means mandatory]:

- (*) Type
- (*) Attachment File
- (*) Attachment Name
- (*) File Type
- (*) Language
- Second Language
- (*) Version Number
- (*) Version Date

7.1. Type (ATT.5)

Mandatory information

The type of attachment for a development medicinal product entity must be specified as Printed Product Information (PPI).

Printed Substance Information (PSI) is only applicable for the EMA, during a submission of substance information in the XEVMPD.

7.2. Attachment File

Mandatory information

The attachment file must be uploaded by selecting the file from the relevant location on user's computer.

7.3. Attachment name (ATT.4)

Mandatory information

The name of the attachment must be specified to allow the user easily identify the attachment when associating it with their product.

7.4. File type (ATT.3)

Mandatory information

The file type of the attachment must be specified as applicable.

The allowed file types for PPI are: .PDF, DOC, .DOCX.

7.5. Language (ATT.6)

Mandatory information

The language of the attachment must be specified.

7.6. 2nd Language (ATT.7)

Optional information

If the content of the attachment is provided in two languages, this field should reference the second language.

If the content of the attachment is provided in one language only, this field should remain blank.

7.7. Attachment version (ATT.8)

Mandatory information

The version number of the PPI attachment must be specified.

The version number refers to the 'internal' reference of the sponsor and does not need to appear on the physical document (i.e., the IB attached). The version number should allow the sponsor and EMA to understand if the version of the attachment has changed over time.

7.8. Attachment version date (ATT.9)

Mandatory information.

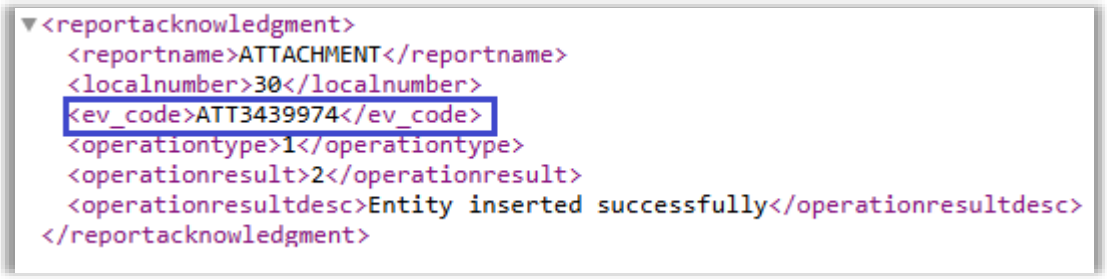
The date of the last update of the document must be specified.

The version date refers to the 'internal' reference of the sponsor and does not need to appear on the physical document (i.e., the IB attached). The version number should allow the sponsor and EMA to understand if the version of the attachment has changed over time.

Format of the version date must correspond to 'dd/mm/yyyy'.

Following a successful insert of an attachment in the XEVMPD, an EV Code is assigned to the attachment and provided to the sender organisation in an XEVPRM ACK.

The pattern of the EV Code for an attachment is 'ATT' followed by a number:



8. Initial submission of substance information

New or updated substance information can be submitted/maintained in the XEVMPD only by the EMA.

Historically, sponsor organisations were able to insert 'approved' and 'development' substance information in the XEVMPD. Since July 2019, when the Substance Management Service (SMS) went live[3], all substances are entered in the XEVMPD as 'approved' by the EMA on request via the EMA Service Desk portal. Any commercially sensitive information is entered in SMS as 'restricted' and is not visible in the XEVMPD substance look-up list. All legacy ' development ' substances have been nullified in SMS and XEVMPD and, most of them, have been replaced by an 'approved' substance, with new substance EV Code. That EV Code should be used in all future submissions.

Any XEVPRM message submitted by an MAH or sponsor organisation containing operation type 'Insert', 'Update' or 'Nullification' of an approved or development substance in the XEVMPD **will be rejected and will generate a negative XEVPRM acknowledgement**.

8.1. Request for an insert or an amendment of a substance entity via an SMS change request

If the required substance is not available in the XEVMPD remote look-up table and in the file Download SMS Export (current):

1. Check that the required substance is not listed as a 'non-current' substance in the file 'Download SMS Export (non-current)' on the Substances Management Services (SMS) portal:

- If yes, reference the 'replacement' substance EV Code (column F: Comment) from that file in your product submission instead.
- If no, continue with step 2.

2. Complete and submit a 'Request SMS services' form via the EMA Service Desk portal:

- Complete and attach the substance request form to the request;
  - company code can be set as the substance preferred term, only if the substance is not in the public domain,
  - privacy settings can be adjusted for all additional names and molecular formula; additional information on substance confidentiality is available on 'SMS guidance for external users' document, section 3 "Substance Confidentiality".
- Attach supporting documentation for the substance (e.g., copy of the Investigator's Brochure or the SmPC) to the request;
  - An EV Code of an attachment, or an EV Code of the medicinal product entry in the XEVMPD referencing the document where the requested substance name is included, can also be provided instead of the actual document within the request;
- if requesting an alias to be added to the substance entry, the required alias must be included in the request.

The substance request will be processed by SMS Data Stewards, who will validate the request in accordance with the Service Level Agreements (SLAs) below:

[3] Please refer to the Substance Management Service (SMS) webpage for the most up to date information.

Type of request	75% of requests	90% of requests
Creation of a new substance, addition of an English alias or change in a preferred term (up to 20)	Resolved within 5 working days	Resolved within 10 working days
Creation of new substance, addition of English alias, change in preferred term or addition of translation (over 20)	No guaranteed SLA	No guaranteed SLA

Once the substance is registered, the user will receive an **e-mail confirmation** from the EMA Service Desk. The substance data will be available for selection in the eAF, XEVMPD, IRIS, EudraCT and EudraGMDP automatically.

Guidance on how to handle approved substance names is included in the 'SMS guidance for external users' document, Annex 1: Business Rules per Substance type

9. Maintenance of medicinal product information

9.1. Update of a DMP if studied for different indications

If a medicinal product not yet authorised in the EEA is used in a clinical trial for different indications, the sponsor can update their existing DMP to include the new indication(s).

The below process describes the actions to be performed in XEVMPDweb by users from organisations registered as Web Trader users:

Step 1. Using simple or advanced queries in XEVMPDweb, retrieve the development medicinal product entry in the XEVMPD.

Step 2. Perform an UPDATE (operation type 2) on the DMP entry.

Step 3. Reference the indications in the 'Drug Indications' section of the pharmaceutical product(s) as required.

Step 4. Validate and send the XEVPRM.

Step 5. Retrieve the XEVPRM ACK to confirm that the update of the DMP information was successful. In case of negative XEVPRM acknowledgement, correct the information that led to the negative acknowledgement as per the 'operation result' message and resubmit the XEVPRM.

9.2. Update of a DMP if studied for different route(s) of administration

If a medicinal product not yet authorised in the EEA is used in a clinical trial for different routes of administration, the sponsor can update their existing DMP to include the new route(s) of administration.

The below process describes the actions to be performed in XEVMPDweb by users from organisations registered as Web Trader users:

Step 1. Using simple or advanced queries in XEVMPDweb, retrieve the development medicinal product entry in the XEVMPD.

Step 2. Perform an UPDATE (operation type 2) on the DMP EV Code.

Step 3. Reference the route(s) of administration in the 'Drug Routes' section of the pharmaceutical product(s) as required.

Step 4. Validate and send the XEVPRM.

Step 5. Retrieve the XEVPRM ACK to confirm that the update of the DMP information was successful. In case of negative XEVPRM acknowledgement, correct the information that led to the negative acknowledgement as per the 'operation result' message and resubmit the XEVPRM.

9.3. Transfer of a DMP to a new sponsor

If a development medicinal product was transferred to a new sponsor, the following process should be followed by the 'former' and 'new' sponsor to reflect this transfer in the XEVMPD:

Step 1. The 'new' sponsor inserts (operation type 1 = INSERT) a new development medicinal product entry in the XEVMPD; a new EV Code will be assigned for the submitted DMP.

Step 2. The 'former' sponsor submits an update (operation type 2 = UPDATE) of their existing DMP entry in the XEVMPD to include a comment in the 'Comment' data element (DP.7) that the product is no longer in use and has been replaced by the one created by the new sponsor.

9.4. Correction of information erroneously submitted

An XEVMPD entity, which was submitted with erroneous information, can be **updated** by the **owner organisation** to reference the correct data, providing that the entity is not nullified in the XEVMPD.

As a general rule, sponsors can update the following not nullified **owned** XEVMPD entities:

- Development product entities;
- Sponsor organisation entities;
- Development ATC Codes;
- Development Pharmaceutical form entities;
- Development routes of administration entities.

The below process describes the actions to be performed in XEVMPDweb by users from organisations registered as Web Trader users:

Step 1. Using simple or advanced queries in XEVMPDweb, retrieve the entity in which you wish to amend the existing information.

Step 2. Perform an UPDATE (operation type 2) on the XEVMPD entity.

Step 3. Correct the erroneous information as required.

Step 4. Validate and send the XEVPRM.

Step 5. Retrieve the XEVPRM ACK to confirm that the update of the DMP information was successful. In case of negative XEVPRM acknowledgement, correct the information that led to the negative acknowledgement as per the 'operation result' message and resubmit the XEVPRM.

9.5. Nullification of duplicated or obsolete information

An XEVMPD entity, which is duplicated (i.e., multiple EV Codes are assigned to the same entity) or erroneously submitted (e.g., the entity was not supposed to be submitted) can be **nullified** in the XEVMPD.

9.5.1. Nullification of development product entities

Only the **owner organisation** can nullify DMPs, regardless of whether they are flagged as validated or not in the XEVMPD, providing that they are **not referenced in any current** (i.e., not-nullified) **AMP(s)**.

NOTE: *If a medicinal product submitted to the XEVMPD in its development form (i.e., as a development medicinal product) becomes authorised, the EV Code of the DMP entity may be referenced by the MAH in the Previous EV Code section (AP.PEV.1) of the AMP. If the sponsor wishes to nullify the DMP EV Code, the current AMP will need to be amended, so that the DMP to be nullified is no longer referenced in that AMP. The amendment can be performed by the MAH organisation that owns the AMP record in the XEVMPD. If the AMP is invalidated (i.e., the product references a 'not-valid' marketing authorisation status) the EMA can amend the AMP upon request via the* EMA Service Desk portal*.*

To nullify a DMP entity not referenced in any current AMP entity in XEVMPDweb, a user from the owner organisation should follow the below process:

Step 1. Using simple or advanced queries in XEVMPDweb, retrieve the DMP you wish to nullify.

Step 2. Perform a NULLIFY (operation type 4) on the product entity.

Step 3. Enter the reason for nullification in the 'Comment' field of the DMP.

Step 4. Validate and send the XEVPRM.

Step 5. Retrieve the XEVPRM ACK to confirm that the nullification of the DMP was successful. In case of negative XEVPRM acknowledgement, correct the information that led to the negative acknowledgement as per the 'operation result' message and resubmit the XEVPRM.

For the overall process, please see *Figure 1: Nullification process of a DMP entity*.

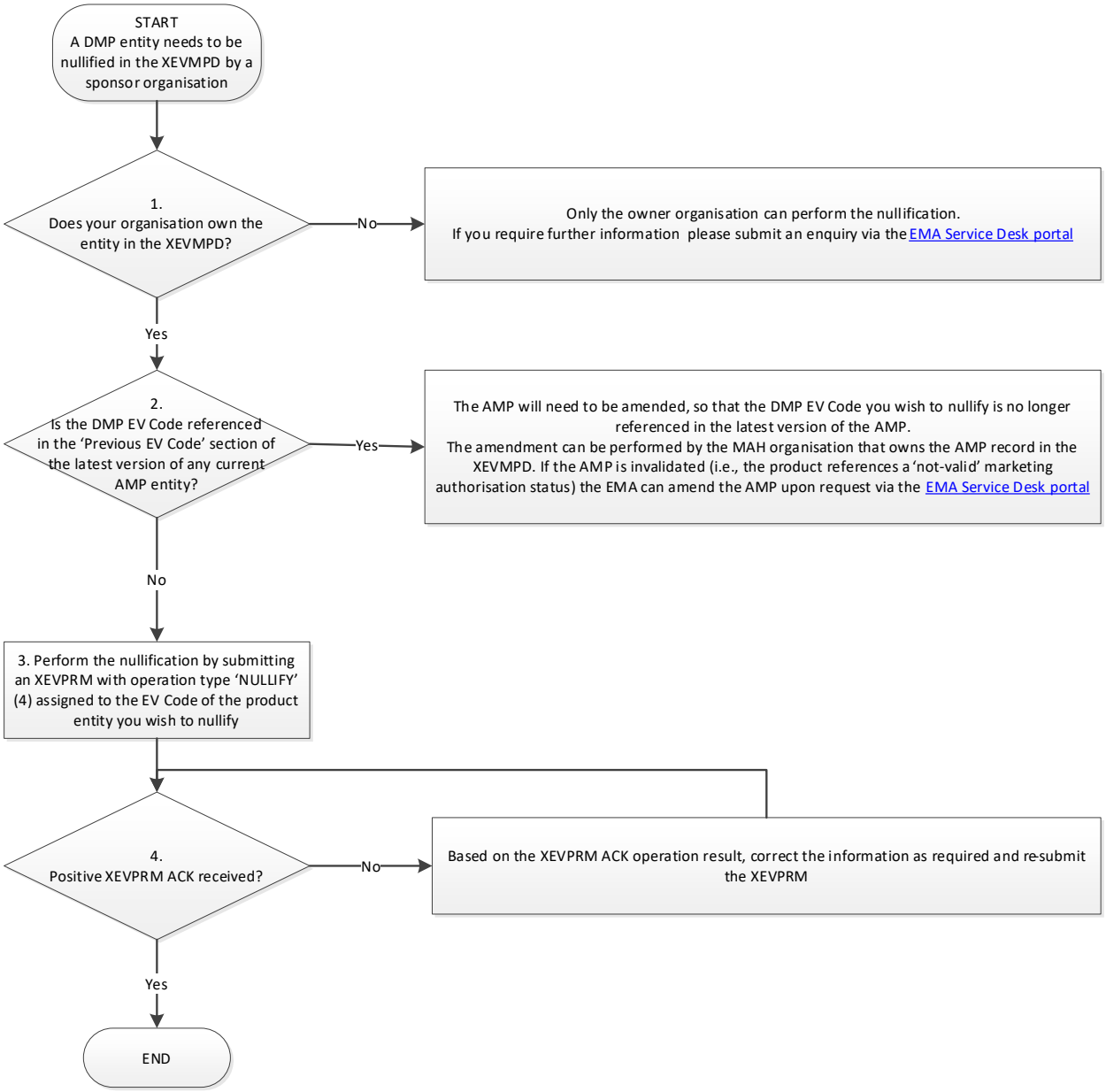


Figure 1: Nullification process of a DMP entity

9.5.2. Nullification of entities in XEVMPD

Sponsors can nullify sponsor organisations entities and development terms (ATC Codes, pharmaceutical forms, routes of administration) in the XEVMPD, providing that:

- they are owned in the XEVMPD by their organisation;
- they are not flagged as **validated** in the XEVMPD and/or
- they are **not referenced** in any current (i.e., not-nullified) product entity.

NOTE: *If a controlled vocabulary entity to be nullified is referenced in any current (i.e.: not nullified) XEVMPD entity (e.g.: a DMP, AMP), that entity will need to be amended, so that the entity to be*

nullified is no longer referenced in that entity. The amendment can be performed by the organisation that owns the entity in the XEVMPD, or by the EMA upon request via the EMA Service Desk portal.

Controlled vocabulary entities validated by the EMA and/or entered by the EMA can only be nullified by the EMA upon request via the EMA Service Desk portal, providing that they are not referenced in any current (i.e., not-nullified) AMP or DMP entity.

To nullify an owned XEVMPD entity, not referenced in any current XEVMPD entity using XEVMPDweb, a user from the owner organisation should follow the below process:

Step 6. Using simple or advanced queries in XEVMPDweb, retrieve the entity you wish to nullify.

Step 7. Perform a NULLIFY (operation type 4) on the XEVMPD entity.

Step 8. Enter the reason for nullification in the 'Comment' field of the nullified entity.

Step 9. Validate and send the XEVPRM.

Step 10. Retrieve the XEVPRM ACK to confirm that the nullification of the entity was successful. In case of negative XEVPRM acknowledgement, correct the information that led to the negative acknowledgement as per the 'operation result' message and resubmit the XEVPRM.

For the overall processes, please see *Figure 2: Nullification of a sponsor organisation and development terms* in the XEVMPD.

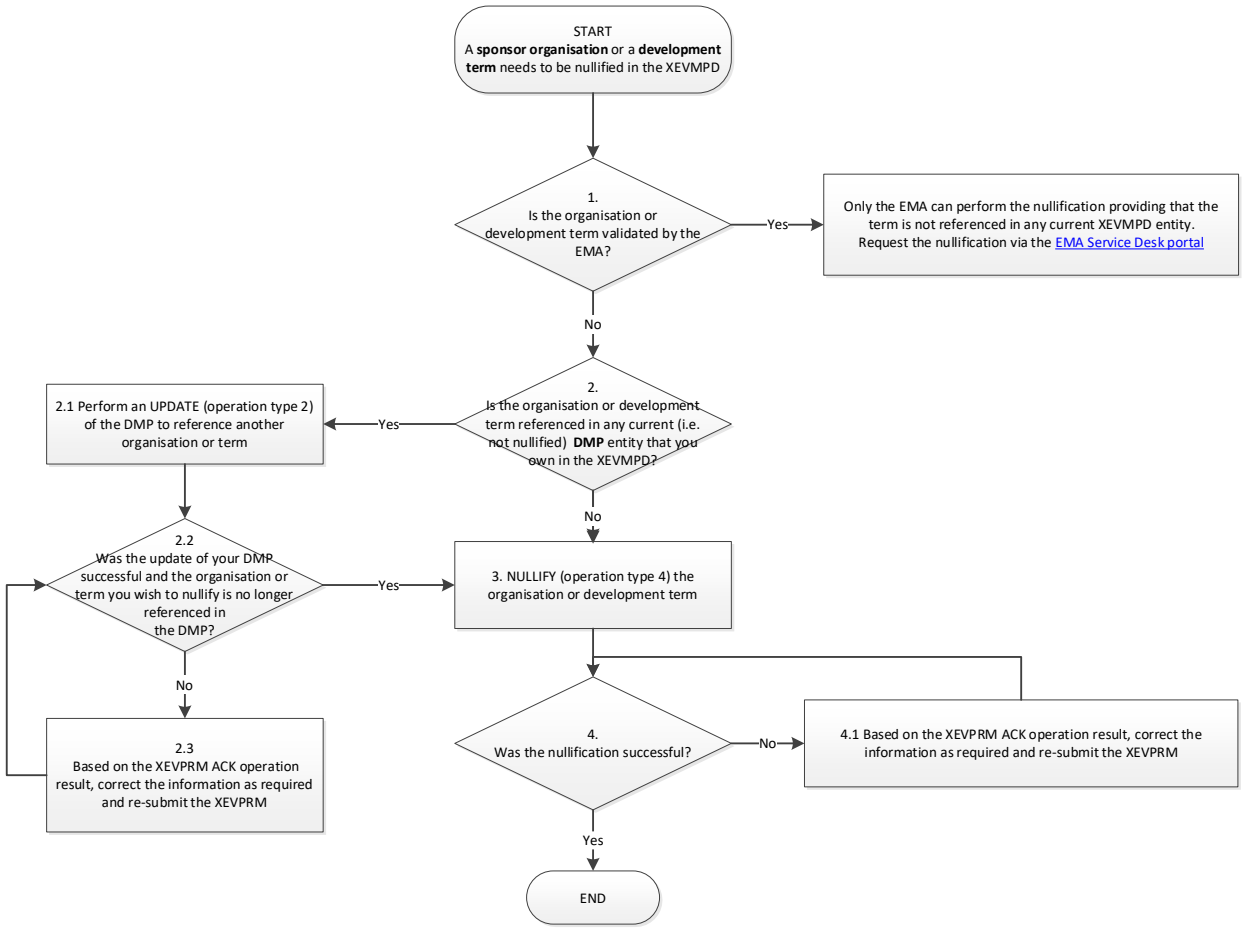


Figure 2: Nullification of a sponsor organisation and development terms in the XEVMPD

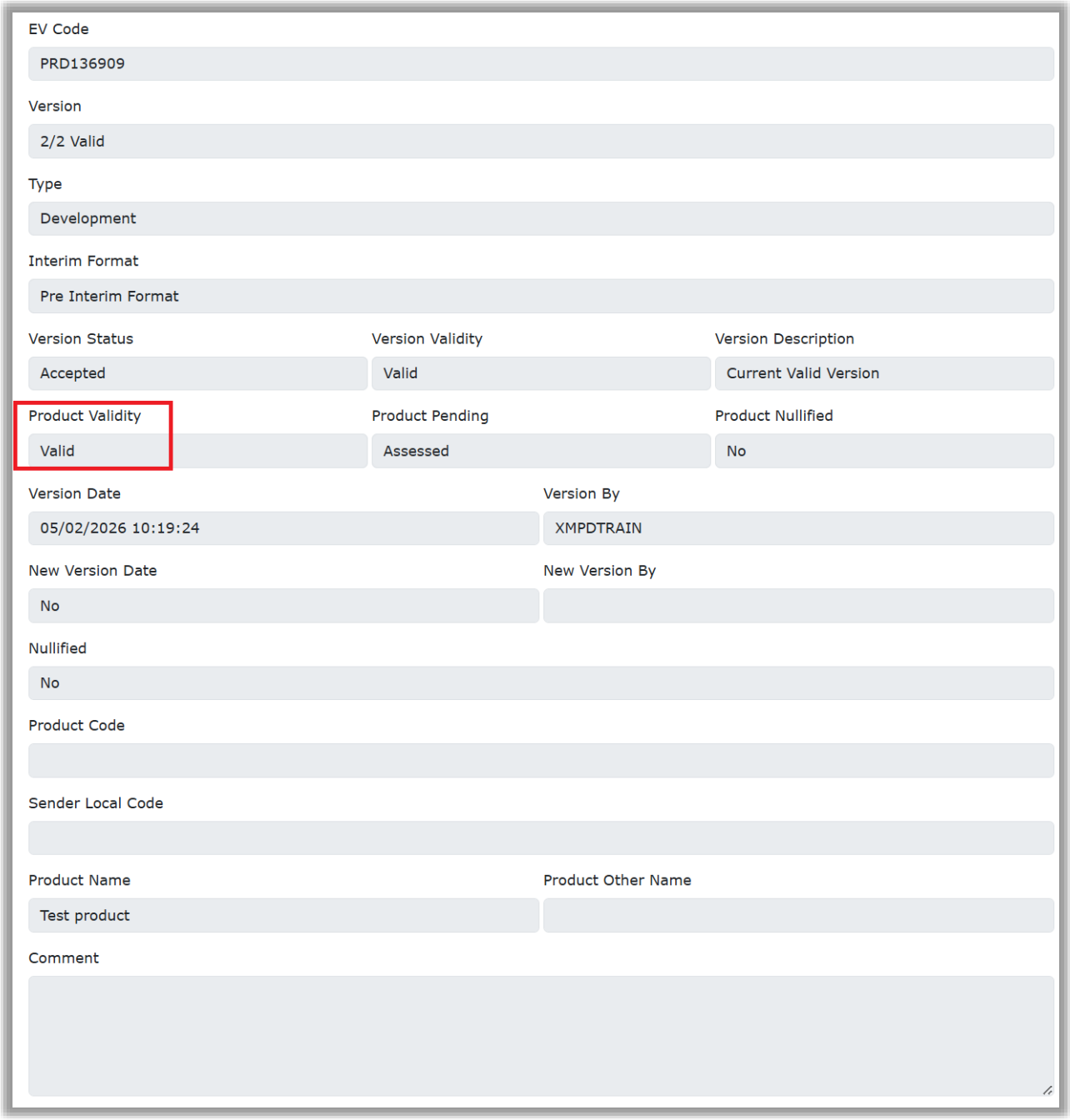
9.5.3. Nullification of attachments

It is not possible to nullify attachments in the XEVMPD. If an attachment is obsolete or duplicated, it will remain in the XEVMPD.

10. Validation of DMP information in the XEVMPD

The EMA performs validation of authorised medicinal product entities, however, there is no dedicated validation of DMP information in the XEVMPD.

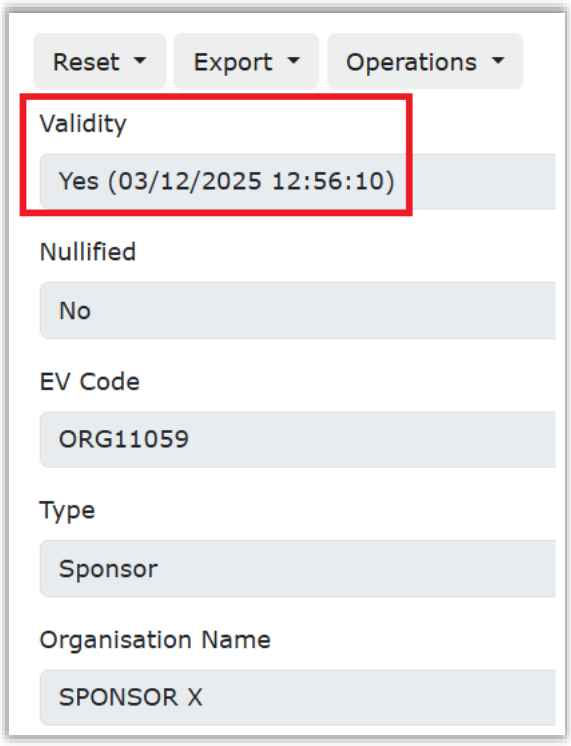
- DMP entities are automatically flagged as valid (i.e., the 'Product Validity' field in XEVMPDweb displays 'Valid') upon their initial submission by the sponsor organisation. This is to allow for the DMP to be available for the recoding of Suspected unexpected serious adverse reactions reports (SUSARs):



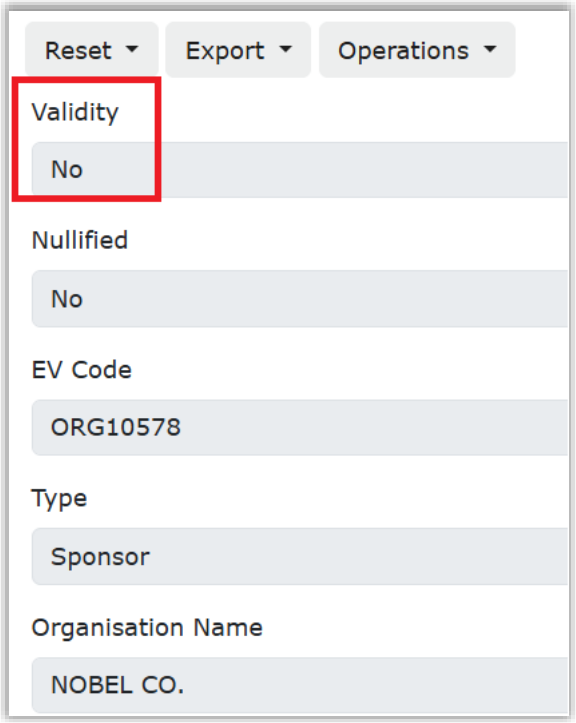
Some development product entities **submitted historically** (up to 2016) may display 'Not assessed' in the 'Product Validity' field.

- Historically, sponsor organisation entities became validated (i.e., the 'Validity' field displays the value 'Valid') if the sponsor organisation entity was inserted or updated (only in specific scenarios per request) by the EMA.

  Currently, when a development product is updated in the XEVMPD, and the sponsor organisation referenced in the DMP is not validated (i.e. the 'Validity' field displays 'No'), the sponsor organisation entity will become automatically validated:

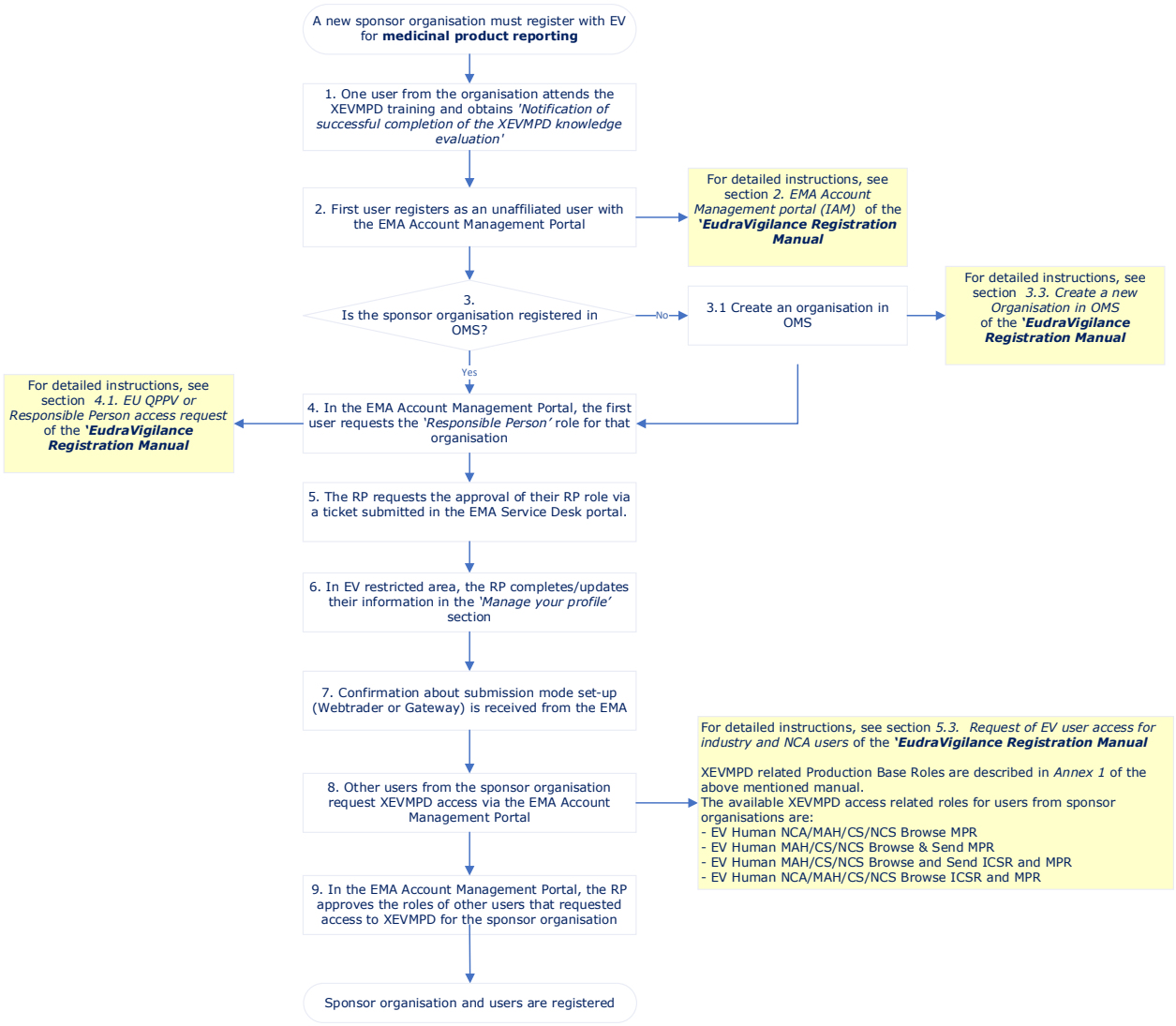


  Sponsor organisation entities not validated by the EMA will display 'No' in the 'Product Validity' field:

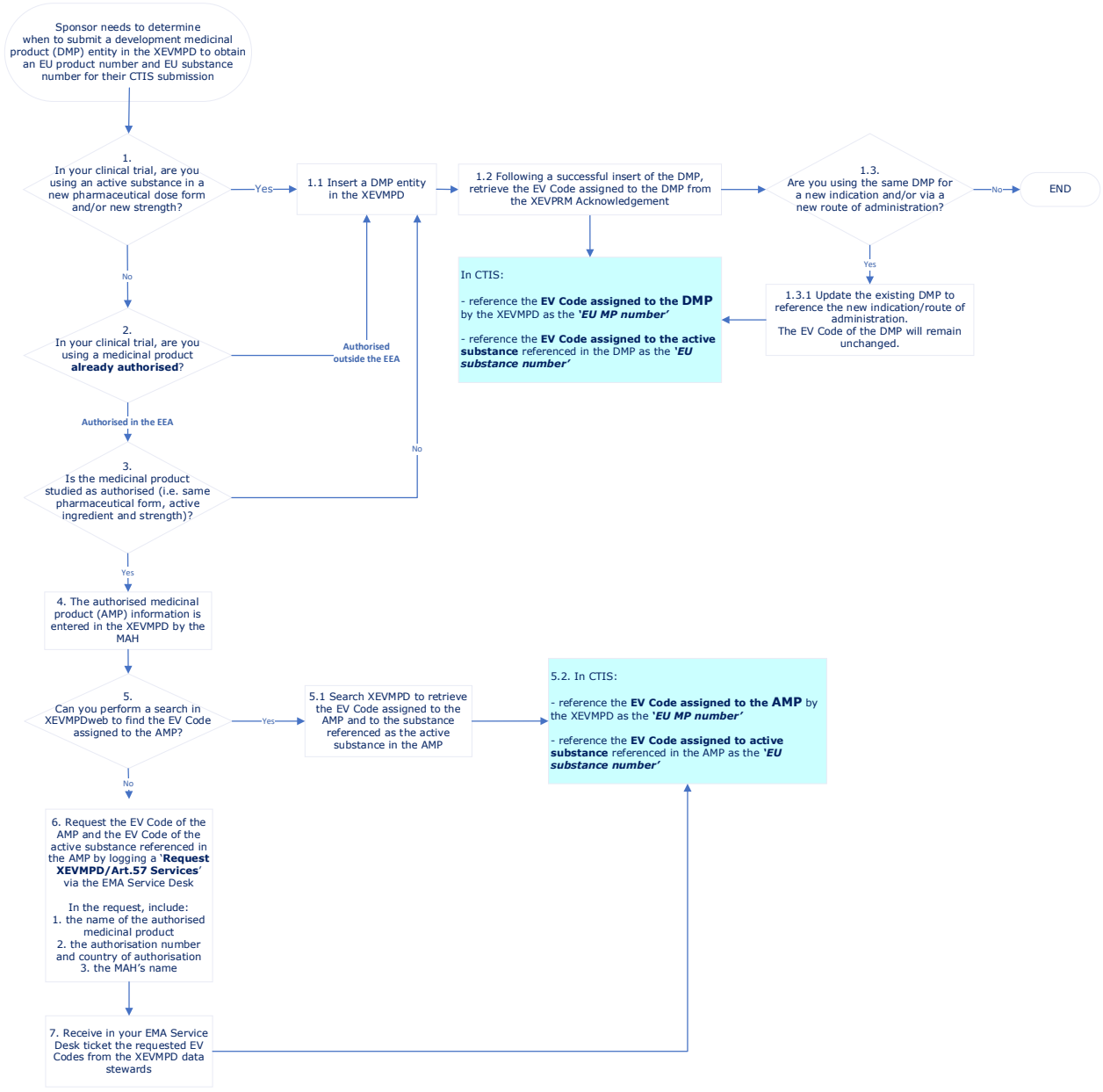

Reset
Export
Operations
Validity
No
Nullified
No
EV Code
ORG10578
Type
Sponsor
Organisation Name
NOBEL CO.

Annex I: Process maps

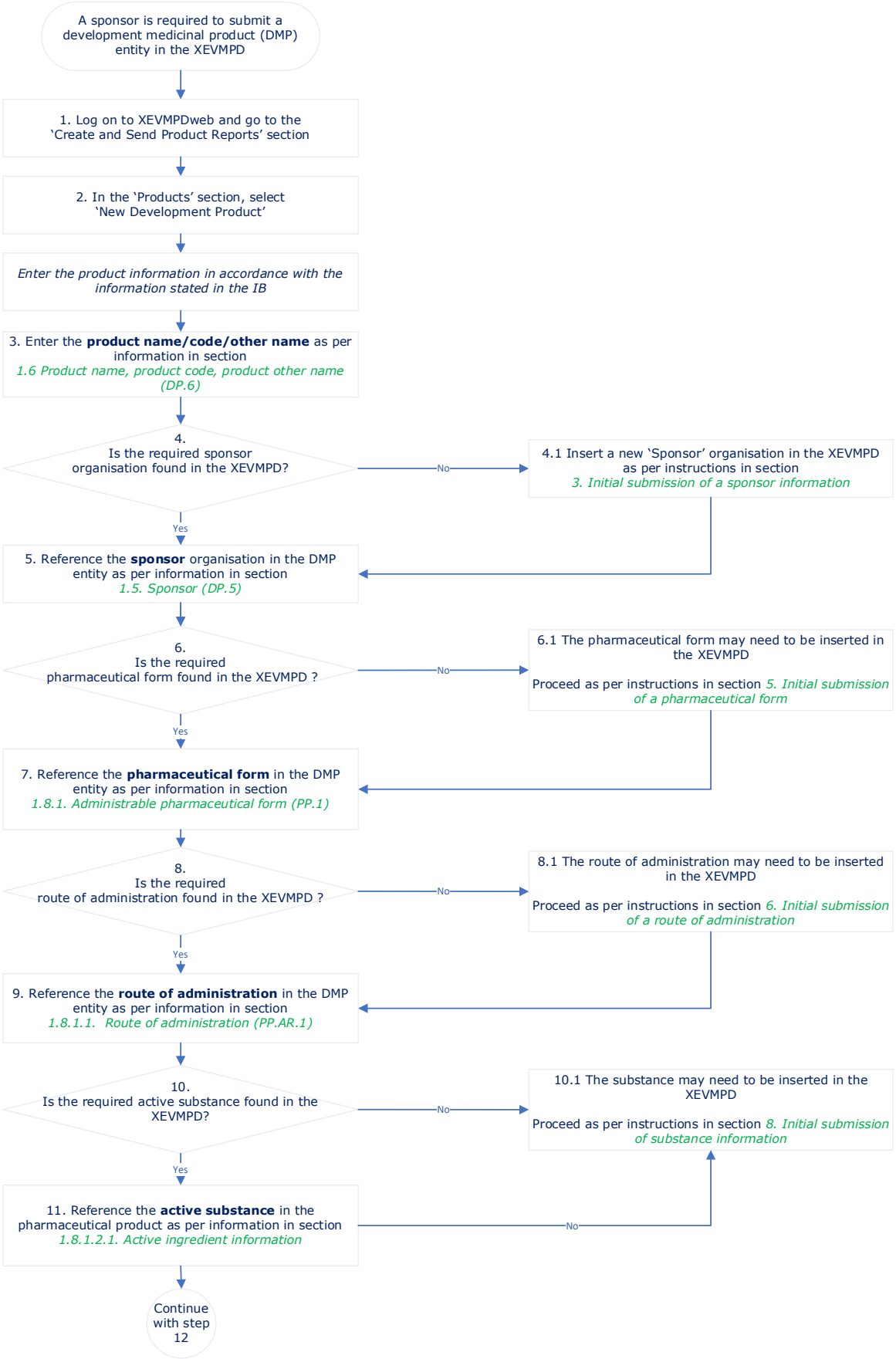
Process map 1: Sponsor organisation registration process

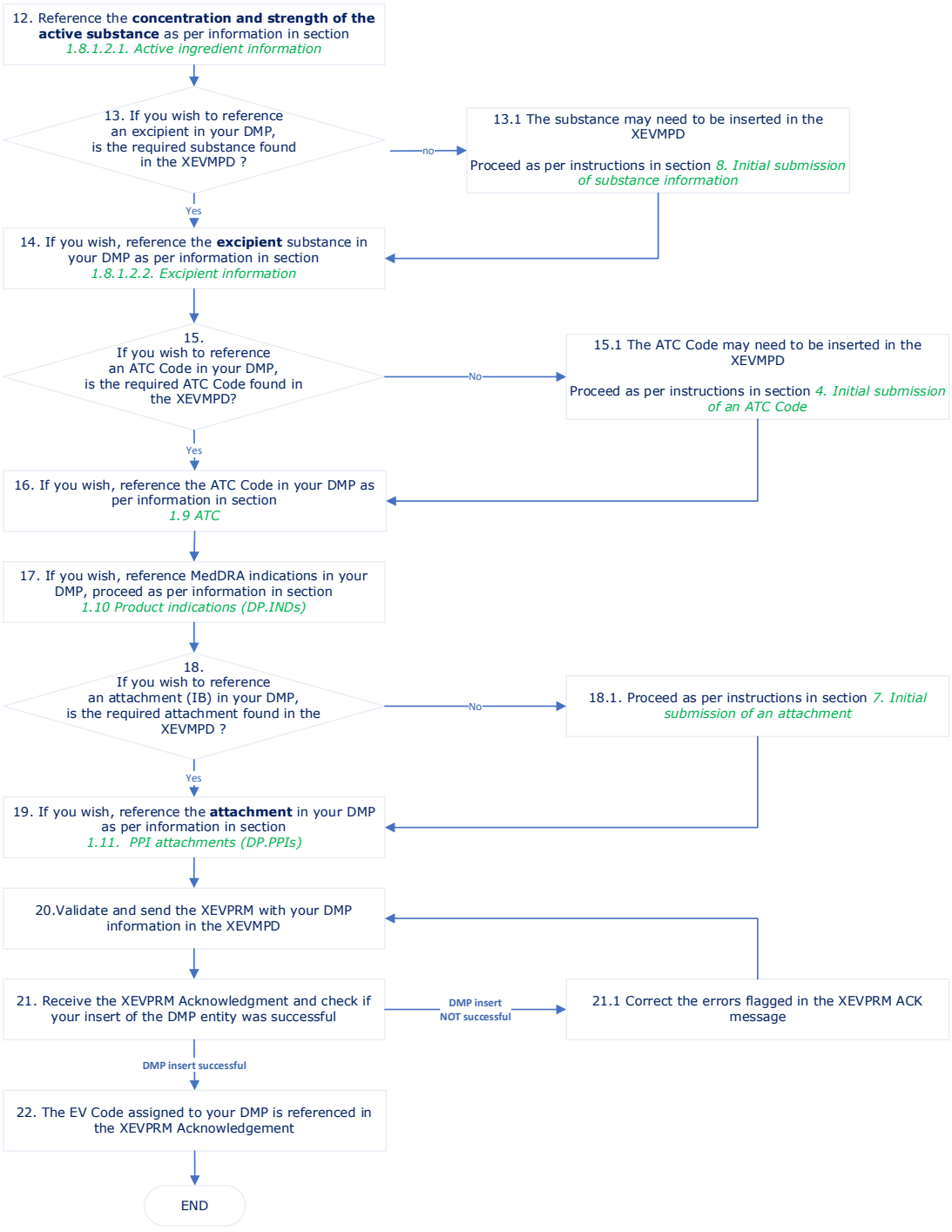


Process map 2: DMP submission principles and retrieval of XEVMPD EV Codes for CTIS submission

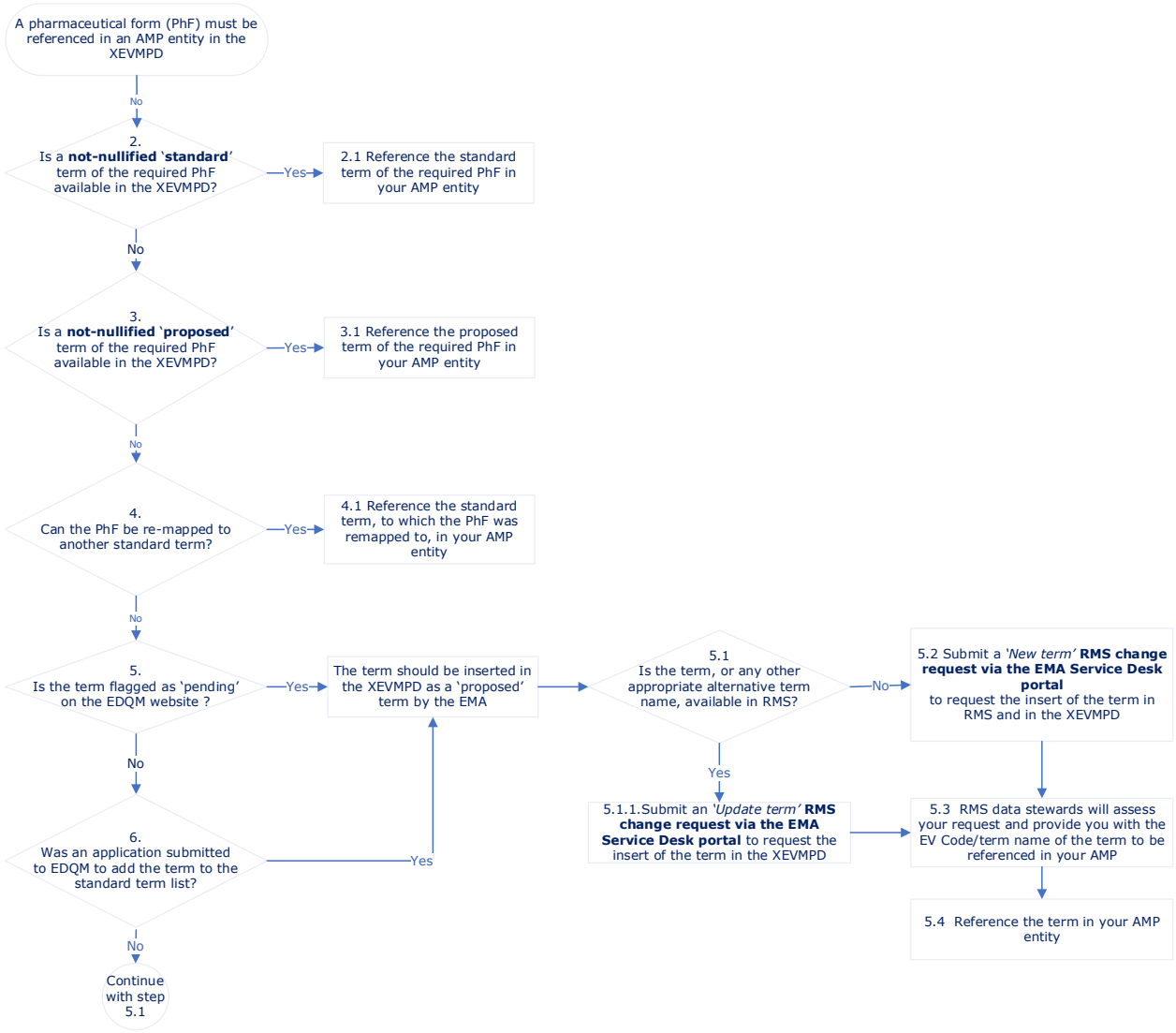


Process map 3: Submission of DMP entity in the XEVMPD using XEVMPDweb

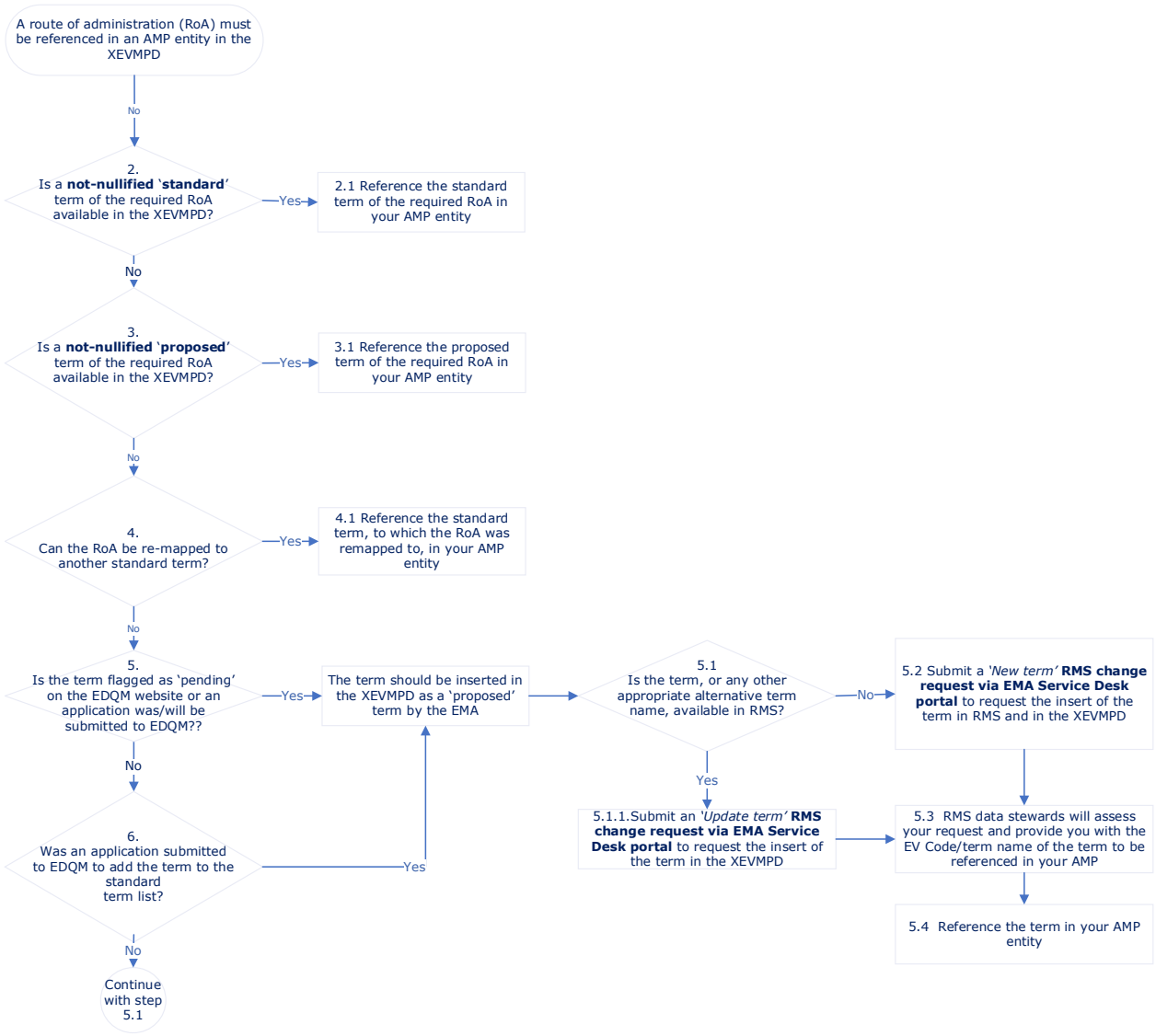



12. Reference the **concentration and strength of the active substance** as per information in section *1.8.1.2.1. Active ingredient information*
13. If you wish to reference an excipient in your DMP, is the required substance found in the XEVMPD ?
no
13.1 The substance may need to be inserted in the XEVMPD
Proceed as per instructions in section *8. Initial submission of substance information*
Yes
14. If you wish, reference the **excipient** substance in your DMP as per information in section *1.8.1.2.2. Excipient information*
15. If you wish to reference an ATC Code in your DMP, is the required ATC Code found in the XEVMPD?
No
15.1 The ATC Code may need to be inserted in the XEVMPD
Proceed as per instructions in section *4. Initial submission of an ATC Code*
Yes
16. If you wish, reference the ATC Code in your DMP as per information in section *1.9 ATC*
17. If you wish, reference MedDRA indications in your DMP, proceed as per information in section *1.10 Product indications (DP.INDs)*
18. If you wish to reference an attachment (IB) in your DMP, is the required attachment found in the XEVMPD ?
No
18.1. Proceed as per instructions in section *7. Initial submission of an attachment*
Yes
19. If you wish, reference the **attachment** in your DMP as per information in section *1.11. PPI attachments (DP.PPIs)*
20.Validate and send the XEVPRM with your DMP information in the XEVMPD
21. Receive the XEVPRM Acknowledgment and check if your insert of the DMP entity was successful
DMP insert NOT successful
21.1 Correct the errors flagged in the XEVPRM ACK message
DMP insert successful
22. The EV Code assigned to your DMP is referenced in the XEVPRM Acknowledgement
END

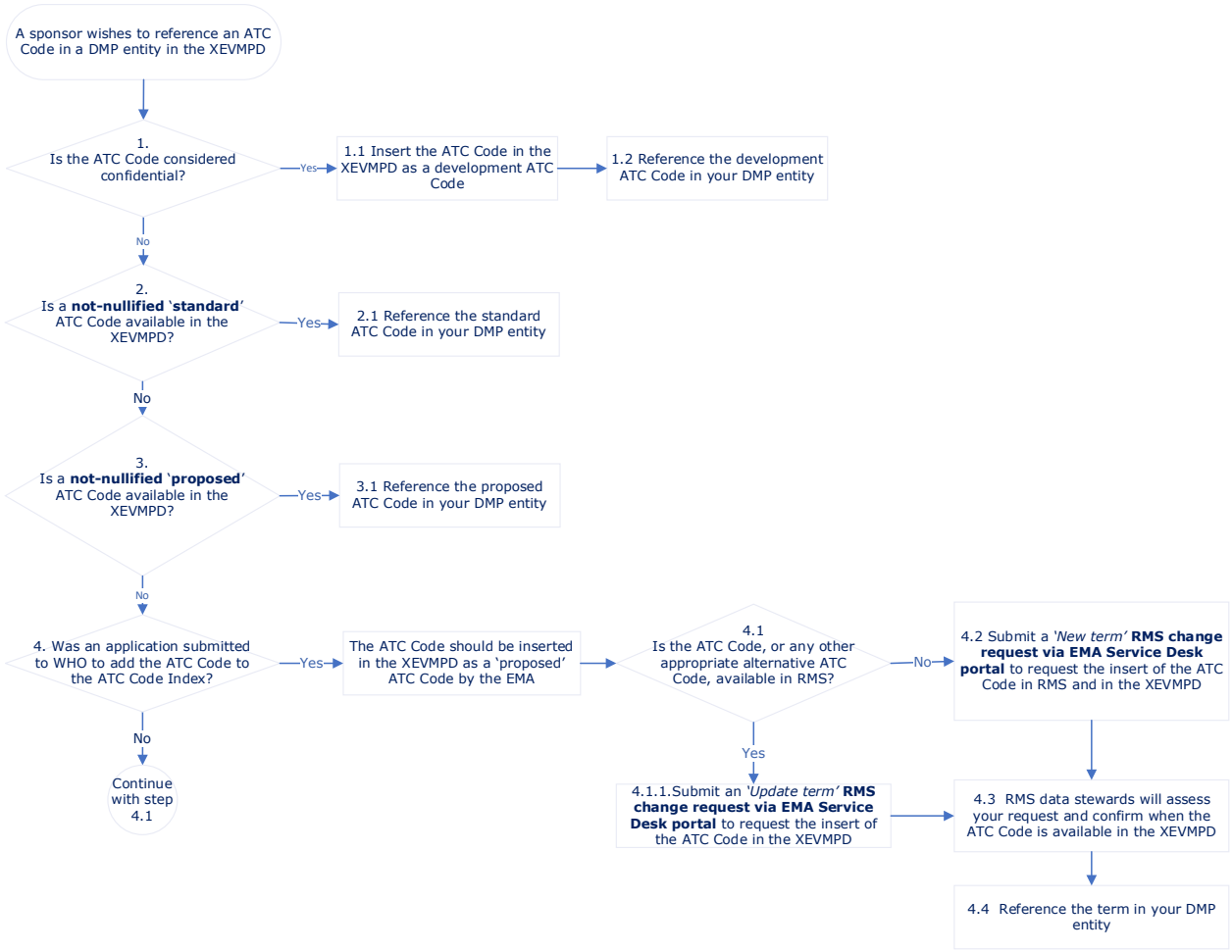
Process map 4: How to reference a pharmaceutical form term in a DMP



Process map 5: How to reference a route of administration term in a DMP



Process map 6: How to reference an ATC Code in a DMP



Annex II: XEVMPD support

Support related to submission of information in the XEVMPD is provided via the EMA Service desk.

- **Request *(for)* XEVMPD/Art.57 Services** should be submitted to request:
  - XEVMPD data (e.g., EV Code of an AMP/DMP, substance EV Code, copy of the XEVPRM ACK if not received by the sponsor etc.).
  - Support with XEVMPD data management (e.g., nullification of validated entries, data amendment in XEVMPD on behalf of the organisation etc.).
  - Registration for XEVMPD e-learning training (initial registration, assessment evaluation).
  - Support with using the XEVMPD user interface (XEVMPDweb)

The timeframe applicable to the XEVMPD support team to address such request is ***5 working days*** since the ticket was assigned to the XEVMPD support team.

- **Request for information** referencing "*SPOR*" as the 'Service' and "*XEVMPD/Art.57*" as the 'Service Offering' should be submitted to request information or ask a question related to:
  - XEVMPD processes in use;
  - guidance on how to submit data in XEVMPD;
  - where to find XEVMPD related information;
  - how to use XEVMPD Data entry tool;
  - XEVMPD e-learning training process (initial registration, assessment evaluation).

- **Request for information** referencing "*SPOR*" as the 'Service' and "*XEVMPDweb*" as the 'Service Offering' should be submitted to request information or ask a question related to using the XEVMPD user interface (XEVMPDweb).

The timeframe applicable to the XEVMPD support team to respond to requests for information is ***22 working days*** since the ticket was assigned to the XEVMPD support team.

- **Report *(of)* a technical issue with XEVMPD/Art.57** should be submitted to notify the EMA of a **technical issue** with:
  - XEVMPD (production or XCOMP environment);
  - XEVMPD additional tools (e.g., XEVMPD Data Export tool, XEVMPD Bulk update tool);
  - Technical issues in the XEVMPD user interface (XEVMPDweb).

The timeframe applicable to the responsible team to respond to such report is ***5 working days*** since the ticket was assigned to the responsible team.