



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Information Management

Cover note on XEVMPD substance controlled vocabulary following the quality control exercise

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1. Introduction

In March 2014, as part of the efforts to provide high quality Article 57(2) data, the European Medicines Agency (EMA) performed an activity to de-duplicate substance names available in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPPD) substance controlled vocabulary (CV). The objectives of this activity were as follows:

- to identify and merge all duplicated substance names;
- to collate all substance names received via Art57 helpdesk since March 2012 and substance names currently available as historical records only;
- to reconcile and include any substance names and translations reported in the Individual Case Safety Reports (ICSRs).

The following activities were out of scope of the quality control exercise:

- the validation of substance reference information available in EVWEB (e.g. CAS number, molecular formula); and
- the completion of information in the existing substance record in line with the official reference sources and addition of any missing translations.

The purpose of this document is to provide marketing authorisation holders (MAHs) with the outcome of the substance name de-duplication activity and an explanation on how to consult the [XEVMPPD substance controlled vocabulary list](#) available in the 'Controlled Vocabularies' section of the [Data submission on authorised medicines - Guidance documents webpage](#).

Following the validation performed by the Agency, the XEVMPPD substance controlled vocabulary contains the complete list of the substance assessment and mapping data. Specifically, the purpose of this file is to allow MAHs submitting Article 57 medicinal product information via the EMA Gateway to perform an analysis and plan for the implementation of the remapping of substance names in their in-house systems. In addition, the actions to be performed by EVWEB users (where applicable) are also explained.

2. General principles and definitions

Master substance

Among the cluster of potentially duplicated substance names the **master substance** is defined according to the definitions and classes referred to in the ISO 11238:2012 IDMP standard and based on the validation against internationally recognised reference sources.

The 'master substance EV Code' is selected from the 'cluster of substance names' based on the following principles:

- the substance name with the status 'validated' and most frequently referenced in Article 57(2) medicinal product submissions;
- preferably, the preferred name should be an International Nonproprietary Name (INN)/ European Pharmacopoeia (Ph. Eur.) or other internationally recognised name.

Synonym refers to a valid alternative name according to the official reference source. The synonym substance name may be used to refer to the substance preferred name.

Translation is defined as a valid alternative term of the master substance name or the associated synonym in another European language according to an official reference source. For each of the substance names assessed indication if it is a translation as well as the applicable language is available.

Duplicate substance is defined as a name that refers to the same substance and reference information where the EV Code of the name does not equal to the EV Code of the selected master substance name. This is in line with the substance definitions and classes as described in the ISO 2012:11238 IDMP standards on substances and the review of reference sources.

Invalid name

Substances in the XEVMPD should be in line with specific rules and naming conventions. Where these are not applicable, the substance name is considered not valid. Examples of not accepted substance names include multiple substance names, substance classes and product names.

These names will be removed from the XEVMPD substance CV and should not be used for future submissions.

3. XEVMPD substance controlled vocabulary description and assessment – scenarios

The following paragraph should be read in conjunction with the excel file '[EudraVigilance eXtended Medicinal Product Dictionary \(XEVMPD\) substances](#)'.

Sheet **1_Current + New Substance CV** contains the valid substance controlled vocabulary that is updated with the new substance names on regular basis. In column 'G' of this sheet, newly inserted substance names and/or EV codes since the last publication of the CV can be identified.

Sheet **2_Deprecated Substance names** includes all the substance names that have been deprecated since the last publication of the CV and sheet **3_EVCodes Nullified** includes those EV Codes nullified since the last publication.

The sheets 4-6 aim to explain the de-duplication performed by the EMA and provide guidance on the actions that need to be performed by MAHs as detailed in section 3.2 and 5 of this cover note.

3.1. Assessment - Scenarios

3.1.1. Assessment impacting EV Code

The below table describes the different scenarios following the substance validation.

	Scenario description	Action performed in the XEVMPD by the Agency	Action to be performed by the MAH
Sheet 4_Remapped EV Codes	The EV Code is a duplicate of the master substance (EV Code).	<ul style="list-style-type: none">The previous Substance EV Code 'before the substance quality control' has been remapped to the master substance EV Code 'after the substance quality control'.All products referencing the previous EV Code were re-linked to the master substance EV Code.The previous EV Code has been nullified and will not be available for use in future submissions.	<ul style="list-style-type: none">To re-align their in-house databases to link the authorised medicinal product referencing the previous EV Code to the master substance EV Code (Gateway users only).Not use the previous substance EV Code in future submissions.

Sheet 5a_EV Codes to be nullified includes substance EV Codes not used in any medicinal product(s)	The name and its EV Code are not valid, and cannot be recoded against a valid substance EV Code/Name.	<ul style="list-style-type: none"> • EV Code nullified at the end of the de-duplication activity. 	<ul style="list-style-type: none"> • Not to use the substance name/EV Code in future submissions as it is not valid.
Sheet 5b_EV Codes to be nullified includes substance EV Codes used in medicinal product(s)	The name and its EV Code are not valid, and cannot be recoded against a valid substance EV Code/Name.	<ul style="list-style-type: none"> • The EMA will ask the MAHs to re-link their medicinal product(s) to the most suitable and valid substance EV code/name; • The EMA will not perform any action in the database until the re-submission by the concerned MAHs is completed; • Following the re-submission by MAHs, the substance EV Code will be nullified, and will not be available for use in future submission. 	<ul style="list-style-type: none"> • In the context of the medicinal product maintenance submission, MAHs should re-submit the medicinal product(s) containing the EV Code to be nullified to reference the most suitable master substance EV Code.

3.1.2. Assessment impacting name

This table describes the different scenarios following the substance name validation.

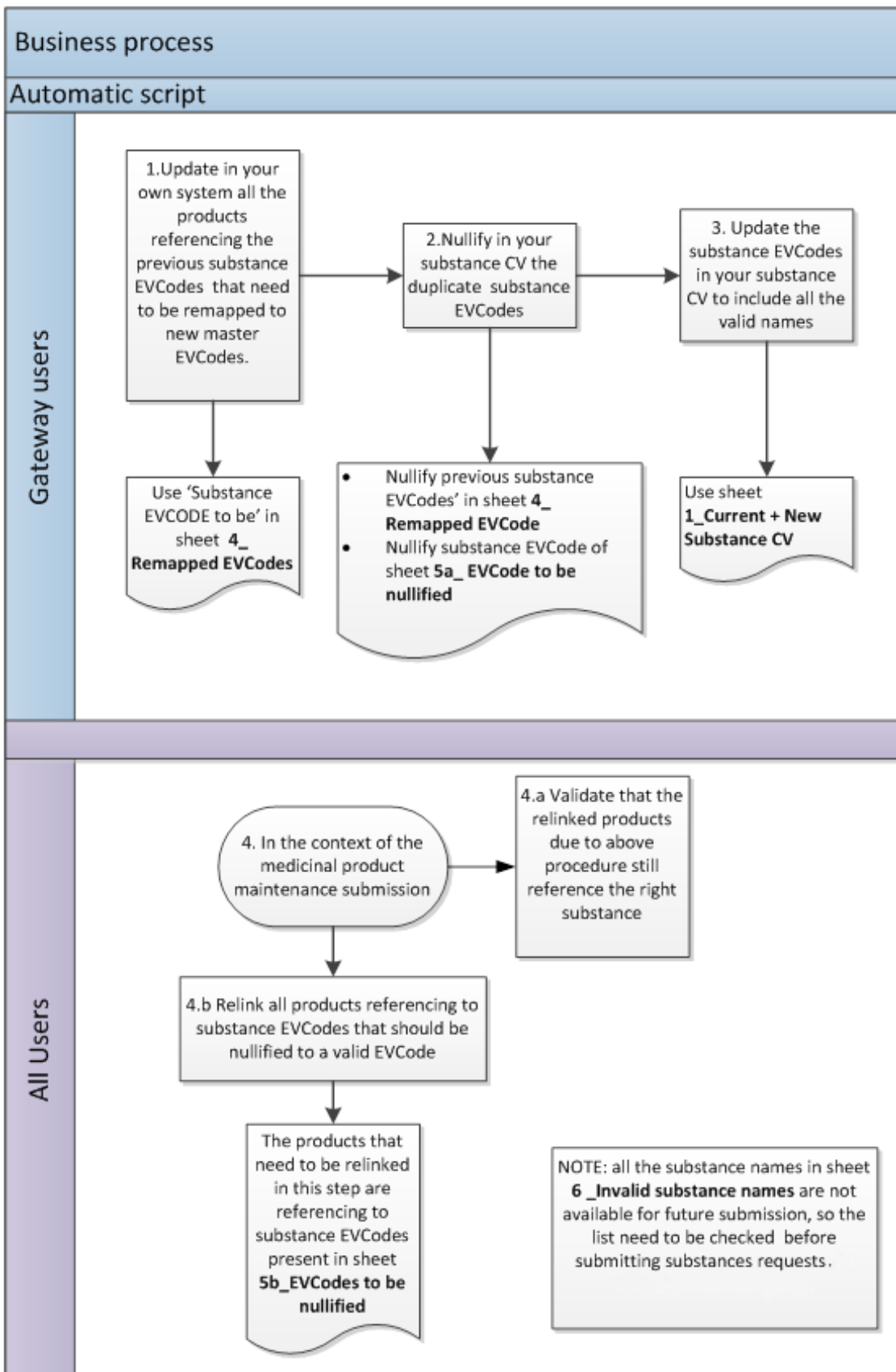
	Scenario description	Action performed in the XEVMPD by the Agency	Action to be performed by the MAH
Sheet 1_Current + New Substance CV	Valid preferred name, synonym/alias, translation according to the official reference source.	<ul style="list-style-type: none"> • The Agency reconciled all the assessed substance names and translations. The outcome of this exercise is the list of master EV Codes with their corresponding substance names and translations, which are published in the substance controlled vocabulary. 	<ul style="list-style-type: none"> • Update all substance EV Codes to include all the valid names present in sheet 1_Current + New Substance CV. • The substance EV Code 'before the substance quality control' is provided only for reference. • Sheet 1_Substance CV should be used for the maintenance of the CV.

	Scenario description	Action performed in the XEVMPD by the Agency	Action to be performed by the MAH
Sheet 6_Invalid substance names	The name is not valid according to the reference sources	<ul style="list-style-type: none"> The name has been removed from the XEVMPD substance CV, and it will not be available to users for future submission. 	<ul style="list-style-type: none"> This list is only provided to MAHs <u>for information</u> and future reference. The list needs to be checked before submitting substance requests via MDMS@ema.europa.eu the EMA Service Desk (https://servicedesk.ema.europa.eu/) (see section 6. of this document for related information). Not to use the listed substance names in future medicinal product submissions.

4. Business process for the implementation

This section describes the proposed business process to reconcile medicinal product information available in the XEVMPD with MAHs in-house systems.

In addition, it outlines the process to be followed by all users to validate the substance referenced in the Article 57 medicinal product records in the context of the medicinal product maintenance submission.



STEP	ACTION
Gateway users	
1.	<p>As regards the medicinal products submitted under Article 57(2) legal obligation, all referenced EV Codes should be replaced with the Master Substance EV Codes. Using your system, update [<i>operation type 'Update (2)'</i>] all products referencing the current substance EV Codes that need to be remapped to the new EV Codes.</p> <p>MAHs should check that the new substance name/EV Code is correct and still valid for that product, and amend as applicable as part of the maintenance submission.</p> <p>Use column " previous Substance EV CODE before the substance Quality Control" in sheet 4_ Remapped EV Codes</p> <p>NOTE: The Agency will perform the re-link of duplicated approved substances on authorised and development medicinal products in the XEVMPD.</p>
2.	<p>In your substance CV, nullify [<i>operation type 'Nullify (4)'</i>] the duplicated substance EV Codes.</p> <ul style="list-style-type: none"> • Nullify "Current substance EV Codes" in sheet 4_ Remapped EV Codes • Nullify substance EV Code of sheet 5a_ EV Codes to be nullified
3.	<p>Update [<i>operation type 'Update (2)'</i>] the substance EV Codes in your substance CV to include all valid names.</p> <p>Use sheet 1_Current + New Substance CV</p> <p>The list will be used to upload your system.</p>
All Users	
4	<p>In the context of the medicinal product maintenance submission, please check that following the process described in steps 1 – 3, the re-linked products still reference the correct substance.</p>
5	<p>Re-link all products referencing the substance EV Codes that should be nullified to a valid EV Code.</p> <p>The products that need to be re-linked in this step are referencing the substance EV Codes present in sheet 5b_ EV Code to be nullified.</p> <p>When the products are updated, these substance EV Codes will be nullified by the Agency.</p>
NOTE:	<p>All substance names in sheet 6_ Invalid substance names are not available for future submission. This list is provided for information only and should be checked before submitting substances via MDMS@ema.europa.eu the EMA Service Desk (https://servicedesk.ema.europa.eu/) (see section 6. of this document for related information).</p>

5. Next steps

From 16 June 2014, marketing-authorisation holders need to update, complete and improve the quality of the information. This involves the completion of previously submitted information with the additional data elements, as well as checking the quality of all information in line with the updated reporting requirements. MAHs were requested to complete this process by the end of 2014.

For full details on the reporting requirements during this phase, please see the [Legal Notice on the Implementation of Article 57\(2\) of Regulation \(EC\) No. 726/2004](#), and the detailed guidance documents available on the [Agency's website](#).

NOTE: During this phase, marketing-authorisation holders also need to continue to submit information on new marketing authorisations granted after 2 July 2012 as soon as possible and no later than 15 calendar days from the date of authorisation (i.e. 15 calendar days from the date of notification of the granting of the marketing authorisation by the competent authority).

Following the update, completion and improvement of the quality of data by the end 2014, marketing-authorisation holders need to maintain the data in the database. This phase began in January 2015. Marketing-authorisation holders need to:

- continue to notify the Agency of any new marketing authorisations within 15 calendar days from the date of authorisation (i.e. 15 calendar days from the date of notification of the granting of the marketing authorisation by the competent authority);
- notify the Agency of any amendments to the terms of marketing authorisation by means of the same business processes and within 30 calendar days from the date on which the changes are authorised.

For full details on the reporting requirements during this phase, please see the [Legal Notice on the Implementation of Article 57\(2\) of Regulation \(EC\) No. 726/2004](#), and the detailed guidance documents available on the [Agency's website](#).

6. Requesting a new substance/translation/synonym

The process to follow to request the insert of a new approved substance or the update of an existing approved substance in the XEVMPD is described in the [Changes to some business rules of the eXtended EudraVigilance Medicinal Product Dictionary \(XEVMPPD\): Submission of substance information](#).