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Information Management

Electronic submission of Article 57(2) data

Questions & Answers (Q&As)

Version 1.14

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Table of contents

Summary of changes

Information in the below listed section(s) was updated or added as new following the publication of version 1.13 of this document in January 2025.

Changes to existing content are highlighted in red.

Newly added Q&As are included with the text "New".

Where the answer provided to the question is included in Chapter 3.II: XEVPRM User Guidance, a reference is made to the relevant section in the Guidance. This is to avoid duplication of information.

Description of editorial changes is not included in the summary of changes.

- 1.18. Submission of information for medicinal products for which the marketing authorisation under the mutually recognised and/or decentralised procedure is pending: content updated
- 1.19. Windsor framework: *content updated*
- 5.7.8. Confidentiality of PPI: *content updated*
- 5.12.19.1. New: Module 3 extract to be provided to XEVMPD
- ~~6.12.1.3. Change of QPPV if they reside and carry out their tasks in the UK~~: *Q&A removed and replaced by Q&A 6.12.1.4*
- 6.12.1.4. New: Change of QPPV for medicinal products with marketing authorisation valid in the territory of Northern Ireland
- ~~6.13.3. PSMF located in the UK:~~ *Q&A removed and replaced by Q&A 6.13.6*
- 6.13.6. New: Change of PSMF location for medicinal products with marketing authorisation valid in the territory of Northern Ireland

1. SCOPE OF ARTICLE 57(2) of Regulation (EC) No 726/2004

1.1. Medicinal products within the scope of Article 57(2) requirements

Question: With regards to Article 57(2), which products do marketing-authorisation holders need to submit to the Agency and how?

Answer: Marketing-authorisation holders are required to submit to the Agency information on all medicinal products for which they hold a marketing authorisation in the European Union, i.e.:

- nationally authorised medicinal products (NAPs);
- centrally authorised medicinal products (CAPs);
- mutually recognised medicinal products (MRPs);
- de-centrally authorised medicinal products (DCPs).

Marketing-authorisation holders are also required to submit information concerning all medicinal products for which they hold a marketing authorisation in **EEA countries outside the EU** (i.e. Iceland, Liechtenstein and Norway), as the pharmacovigilance legislation has been incorporated into the EEA Agreement and entered into force in the EEA on 28 May 2014, and information on medicinal products for human use for which the marketing authorisation granted by the UK national authority is valid in the territory of **Northern Ireland**.

See section *Background information* of Chapter 3.II: XEVPRM User Guidance for detailed information.

Medicinal product data shall be submitted to the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD) via the eXtended EudraVigilance Medicinal Product Report Message (XEVPRM) with the operation type 'Insert' (1) based on the guidance provided for each field in Chapter 3.II: XEVPRM User Guidance. See section *1.1 Initial Submission of an Authorised Medicinal Product (AMP)* of Chapter 3.II: XEVPRM User Guidance for detailed information.

1.2. Medicinal products out of scope of Article 57(2) requirements

Question: Which medicinal products do not need to be submitted per Article 57(2) requirements?

Answer: Medicinal products falling out of scope of Article 57(2) of Regulation (EC) No 726/2004 include:

- investigational medicinal products;
- products for which the marketing authorisation is not valid;
- traditional use registration application for a herbal medicinal products (Article 16a of Directive No 2001/83/EC);
- simplified registration application for a homeopathic medicinal products (Article 14 of Directive No 2001/83/EC);
- medicinal products within the scope of Article 5 of Directive 2001/83/EC i.e. 'Named patient use' falling under Article 5(1) and 'EU Distribution Procedure' under Article 5(2);
- parallel Distributed/Imported medicinal products (Article 76(3) and (4) of Directive No 2001/83/EC);
- medicinal products authorised outside the EEA or following a non-EU procedure.

Medicinal products falling out of scope of Article 57(2) may be submitted and maintained on voluntary basis in line with the requirements and business processes described in Chapter 3.II: XEVPRM User Guidance.

1.3. Submission of centrally authorised medicinal products (CAPs)

Question: Before 2 July 2012, centrally authorised products (CAPs) were entered and maintained by the EMA. Will the EMA continue entering and maintaining CAPs on behalf of the MAHs?

Answer: Information on centrally authorised products must be submitted and maintained in the Article 57 database by the marketing authorisation holders per Article 57(2) requirements.

1.4. Submission of information on un-authorised medicinal products

Question: Should information on un-authorised medicinal products be submitted i in the XEVMPD by sponsors as per Article 57(2) requirements?

Answer: No, Article 57(2) requirements are applicable to authorised medicinal products only. Information on un-authorised medicinal product data should be submitted in the XEMVPD by sponsors in accordance with the Detailed guidance on the collection, verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use' ('CT-3') (OJ 2011/C 172/01), which applies for trials that are still ongoing under the Directive until the transition period ends (31st January 2025) and CT Regulation (EU) No 536/2014.

1.5. Submission of herbal medicinal products

Question: Our company holds several licences for herbal medicinal products. Do we need to enter those products in the XEVMPD?

Answer: In accordance with Article 57(2) of Regulation (EC) 726/2004 the electronic submission focuses on information on **authorised** medicinal products for human use. This does not include **registrations** of traditional herbal medicinal products (Chapter 2a of Directive 2001/83/EC) and registrations of homeopathic medicinal products registered according to the special, simplified registration procedure [Article 14(1) of Directive 2001/83/EC].

However, if the licence is a valid marketing authorisation granted by a national competent authority in the EU, and it is not granted following the registration of the traditional herbal medicinal products (Chapter 2a of Directive 2001/83/EC) or according to the special, simplified registration procedure [Article 14(1) of Directive 2001/83/EC], it is falling within the scope of Article 57 requirements and should be therefore submitted in line with the requirements and business processes described in Chapter 3.II: XEVPRM User Guidance. The appropriate legal basis and medicinal product type(s) must be selected.

See also the Note for clarification: Traditional herbal medicinal product and simplified registration for homeopathic medicinal products: pharmacovigilance requirements and EudraVigilance access clarifying **pharmacovigilance requirements** for traditional herbal medicinal products registered further to a simplified registration procedure (traditional use-registration) on the basis of Article 16a of Directive 2001/83/EC and homeopathic medicinal products registered further to the special, simplified registration procedure under Article 14(1) of Directive 2001/83/EC, and the process for obtaining access to adverse reaction reports in EudraVigilance for traditional use herbal medicinal products.

Moreover, to support eAF submissions, MAHs are required submit to in the Article 57 database information on herbal and homeopathic products that are required for the web-based variation form.

Related information is also available in Q&A *3.6. Recommended timelines for submission of information on traditional herbal medicinal products registered in accordance with Article 16a of Directive 2001/83/EC*.

1.5.1. Submission of herbal medicinal products authorised based on Article 20(1) of the Polish Pharmaceutical Law

Question: We are manufactures and act as a marketing-authorisation holder for several herbal medicinal products authorised based on Article 20(1) of the Polish Pharmaceutical Law that relates to the application on marketing authorisation of:

1) Unprocessed pharmaceutical raw material used for medicinal purposes;
2) Vegetable raw material in a crumbled form;
3) Therapeutic mineral;
4) Medicinal product, manufactured with the use of industrial methods, pursuant to the provisions included in the Polish Pharmacopoeia;
5) Pharmaceutical raw material, designated for manufacturing prescription and pharmaceutical medicines.
Such products are herbal substances used for medical purpose (for treatment). Our Art 20 paragraph 4 products also have its monograph in the Polish Pharmacopoeia. Such products are authorised based on simplified dossier regulated by local decree which exactly lists these products. Our Art 20 paragraph 4 herbal medicinal products are also listed in this Decree and are compliant with corresponding monographs of the Polish Pharmacopoeia.

The question is whether such herbal medicinal products have to be reported to XEVMPD in order to fulfil requirement of Article 57(2)?

Answer: Registered herbal products are exempted from the requirements of Article 57(2) of Regulation 726/2004. However, as per the description in your question, if the herbal product has been authorised following a procedure developed at national level, such product should not be exempted from the Article 57(2) requirement and therefore your company will need to comply as appropriate.

1.6. Submission of homeopathic products (HMPs) awaiting authorisation

Question: In France, we have a validation of our homeopathic products by ANSM. Products, which are already validated, have a marketing authorisation and an SmPC (with therapeutic indication, etc.). Requested data can therefore be submitted to the XEVMPD. Other medicinal products are still not validated to date and dispose of a visa (and not a MA) with no specified therapeutic indication etc.

Do we have to submit information about these products in the XEVMPD? Or do we wait for the validation of ANSM issuing of a marketing authorisation?

Answer: The addressees for the obligations laid down in Article 57(2) are "marketing-authorisation holders" and that the obligations do not extend to "registration holders". Homeopathic medicinal products (HMPs) registered according to the procedure described in Article 14 of Directive 2001/83/EC have been excluded from the obligation described in Article 57(2) of Regulation (EC0 726/2004). With regard to HMPs, pharmaceutical legislation distinguishes between "marketing authorisation" obtained on the basis of Article 8 and "registration" according to Article 14. By mentioning no specified therapeutic indication for the medicinal product in question it is much closer to Article 14 or "third way"

concept specific for the French system ("visa") than to the "full" marketing authorisation. In view of this clarification, information on homeopathic medicinal products referred to in your question will have to be provided once a marketing authorisation for those products has been obtained.

1.7. Submission of medicinal products authorised in EEA countries outside the EU

Question: Do we need to submit information on medicinal products authorised in Iceland, Liechtenstein and Norway?

Answer: Yes, since Directive 2010/84/EU, Regulation (EU) No 1235/2010 and Regulation (EU) No 1027/2012 have been incorporated into the EEA Agreement and entered into force in the EEA on 28 May 2014 and therefore now apply to the EEA countries outside the EU. See section *1.1.1. Submission of medicinal products authorised in EEA countries outside the EU* of Chapter 3.II: XEVPRM User Guidance for related information.

1.7.1. Submission of medicinal products authorised in Liechtenstein

Question: Technically, Liechtenstein does not have any registrations; it has a list of "Zugelassene Arzneimittel". These consist of all CP records, all records registered in Switzerland, and registrations in Austria since 2010 if they are registered with a special procedure. Since they are not actually registered in Liechtenstein, are these products still required for the XEVMPD?

If these registrations are indeed required, for the records which are copies of the Swiss records, who should be referenced as the appropriate QPPV? Should it be the QPPV of the EU/EEA registrations or the QPPV of the Switzerland registrations?

Answer: See section *1.1.1.1. Submission of medicinal products authorised in Liechtenstein* of Chapter 3.II: XEVPRM User Guidance for related information.

Regarding which QPPV should be referenced in the AMP entities, the following key principles, stated in "GVP Module I - Pharmacovigilance systems and their quality systems" should be taken into account in order to decide on the EU QPPV to be declared for each registration:

"As part of the pharmacovigilance system, the marketing-authorisation holder shall have permanently and continuously at its disposal an appropriately qualified person responsible for pharmacovigilance in the EU (QPPV) [DIR Art 104(3)(a)]."….

"Each pharmacovigilance system can have only one QPPV."

"In addition to the QPPV, competent authorities in Member States are legally provided with the option to request the nomination of a pharmacovigilance contact person at national level reporting to the QPPV. Reporting in this context relates to pharmacovigilance tasks and responsibilities and not necessarily to line management. A contact person at national level may also be nominated as the QPPV."

"The QPPV shall reside and operate in the EU [DIR Art 104 (3) last paragraph]. Following European Economic Area (EEA) agreements, the QPPV may also reside and operate in Norway, Iceland or Liechtenstein."

1.7.2. Submission of separate entities for medicinal products authorised in Iceland, Liechtenstein and Norway via the centralised procedure

Question: Why do we need to submit separate AMP entities for medicinal products authorised via the centralised procedure in EU and in Iceland, Liechtenstein and Norway? Is this a new requirement? This will lead to four records for a CAP.

Answer: This is not a new requirement. This has been communicated on Art57 webpages, in Chapter 3.II: XEVPRM User Guidance (section "*1.2.12.1 Authorisation Country Code*") and in this document in 2014. In December 2014, Chapter 3.II was updated to explain why the country code "EU" should not be applied for records in IC/NO/LI as these states are not member states of the EU. As per Chapter 3.II: *"The marketing authorisations granted by the European Commission have to be transposed by the competent authorities of Iceland, Liechtenstein and Norway through corresponding decisions on the basis of relevant national laws. In such a case, these marketing authorisations granted in Iceland, Liechtenstein and Norway are legally separate from the Commission's decision granting MA."* Therefore, for medicinal products authorised in Liechtenstein, Norway and Iceland via the centralised procedure, the applicable country code (i.e. LI/NO/IS) must be specified (and not the "EU" country code).

1.8. Submission of authorised but not yet marketed medicinal products

Question: Our company holds marketing authorisations for medicinal products which are not yet marketed. Do we need to enter information about these products in the XEVMPD if they are not yet on the market?

Answer: Obligations laid down in Article 57(2) apply to marketing authorisation holders regardless of whether their medicinal products are marketed or not. If your medicinal product is authorised, then the product information must be submitted in the Article 57 database.

1.9. Submission of veterinary products

Question: Do veterinary products also need to be entered in the Article 57 database as part of Article 57(2) implementation?

Answer: Veterinary medicinal products are out of scope of the requirements of Article 57(2) of Regulation (EC) 726/2004 as this is applicable to medicinal products for human use.

1.10. Submission of products registered via simplified procedure (Article 126a of Directive No 2001/83/EC)

Question: We have some products registered using the simplified procedure (Article 126a). Do these products need to be submitted in the XEVMPD? If yes, under which procedure type should we submit such products?

Answer: Medicinal product authorised according to Article 126a of Directive No 2001/83/EC fall within the category of "national procedure" and should therefore be submitted in the XEVMPD per Article 57(2) requirements.

The indication of medicinal product authorised according to Article 126a of Directive No 2001/83/EC can be provided in the XEVPRM data field 'Legal basis (AP.12.13)' by referencing the appropriate value. See section *1.2.12.13. Legal basis (AP.12.13) of* Chapter 3.II: XEVPRM User Guidance for further information.

1.11. Submission of medicinal products authorised via 'Standardzulassung'

Question: How should products authorised in Germany through the 'Standardzulassung' be provided? Should these products be entered in the XEVMPD database? If yes, which authorisation procedure is applicable?

Answer: The EMA, as well as the Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) both support the inclusion of products authorised via the 'Standardzulassung' (standard marketing authorisation) in the XEVMPD, with the exceptions of human medicinal products authorised according to Directive 2001/83/EC, article 3, number 2 and all standard registrations (traditional herbal medicinal products). The corresponding 'Fachinformation' should be provided as PPI attachment.

The authorisation procedure to be referenced in the product entry should be specified as 'EU authorisation procedures - National Procedure (4)'.

1.12. Submission of medicinal products authorised via 'Fiktive Zulassungen'

Question: Can you please advise how to enter in the XEVMPD medicinal products, which are authorised in Germany, and for which no authorisation date exists as they are so-called "Fiktive Zulassungen"?

Answer: "Fiktive Zulassungen" products, for which the procedure is pending are not authorised (or registered) in accordance with the EU legislation, and therefore do not fall within the scope of Article 57(2) requirements.

1.13. Submission of medicinal products falling within the scope of Article 5 of Directive 2001/83/EC

Question: Do Article 57(2) requirements apply to medicinal products falling within the scope of Article 5 of Directive 2001/83/EC, i.e. "Named patient use" and "EU Distribution Procedure"?

Answer: Medicinal products within the scope of Article 5 of Directive 2001/83/EC, i.e. "Named patient use" falling under Article 5(1) and "EU Distribution Procedure" under Article 5(2) are not considered "authorised" in the sense of Article 6 of Directive 2001/83/EC or Article 3 of Regulation (EC) 726/2004. They are therefore excluded from the provisions laid down in Article 57(2) of Regulation 726/2004.

1.14. Submission of 'Certain medicinal products for external use (WUM)'

Question: Sweden has a special procedure for approving/registering 'Certain medicinal products for external use (VUM)'. Are they within the scope of Article 57(2) submission requirements?

Answer: In accordance with Article 57(2) of Regulation (EC) 726/2004 the electronic submission focuses on information on medicinal products for human use authorised in the European Union. This does not include 'Certain medicinal products for external use' as referenced in your question.

1.15. Submission of medicinal product authorised as 'conditional marketing authorisations'

Question: Is a conditional approval regarded as "notification of the granting of the marketing authorisation" and therefore the 15-calendar day period given for supplying the information in the

XEVMPD starts on the date of the granting of the conditional approval, or whether it starts only once we receive the full approval?

Answer: Article 57(2) makes no distinction between conditional marketing authorisations and full marketing authorisations. Conditional marketing authorisations shall be therefore treated equally to full marketing authorisation in terms of the obligation deriving from Article 57(2). Information on such medicinal products should therefore be submitted in the Article 57 database 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).

1.16. Obligations for parallel distributors

Question: Do parallel distributors have to submit information about the authorised medicines per Article 57(2) requirements?

Answer: The obligation to electronically submit to the Agency information on all medicinal products for human use authorised in the European Union applies to marketing authorisation holders. No information needs to be submitted by parallel distributors.

1.17. Obligations for parallel importers

Question: The obligation to electronically submit to the Agency information on all medicinal products for human use authorised in the European Union applies to marketing authorisation holders. No information needs to be submitted by parallel distributors. But what about parallel imported medicinal products which are distributed under a licence obtained through a simple procedure? Must the product information in this case be submitted by each importer?

Answer: Parallel imported medicinal products are not within the scope of Article 57(2) data submission requirements. However, parallel importers may need to be registered with EudraVigilance and the XEVMPD to comply with Pharmacovigilance reporting obligations enforced at national level.

As of 16 June 2014, additional information on medicinal products is required to be provided to the Agency. The additional information includes indication whether the medicinal product is parallel distributed. Therefore, information on parallel imported medicinal products may be submitted to the XEVMPD on voluntary basis or due to national legal obligation during the transition maintenance phase and according to the business processes and submission requirements specified in Chapter 3.II: XEVPRM User Guidance. The medicinal product type *'Parallel Distributed/Imported medicinal product (Article 76(3) and (4) of Directive No 2001/83/EC) (3)'* should be selected as appropriate in the data element 'Medicinal product types (AP.12.MPT.1)'.

1.18. Submission of information for medicinal products for which the marketing authorisation under the mutually recognised and/or decentralised procedure is pending

Question: How and when can we start submitting in the Article 57 database information on medicinal products for which the marketing authorisation under the mutually recognised and/or decentralised procedure is pending?

Answer: From mid-January 2025, a new marketing authorisation value 'Valid – pending national phase' is available for use in the Article 57 database. ~~This authorisation status is to be used only when the medicinal product has been authorised by the Reference Member State (RMS) but is under evaluation in the Concerned Member States [CMS(s)]. The authorisation status in the RMS should be~~

~~'Valid' and 'Valid – pending national phase' in the CMS(s).~~ This authorisation status should only be used in newly authorised products by the Reference Member State (RMS) where the Concerned Member State(s) CMS(s) are still evaluating the Initial Marketing Authorisation application. As soon as the relevant Concerned Member State grants the approval of the medicinal product, an update should be submitted in XEVMPD to reflect the 'Valid' Authorisation status.

Please note that 'Valid – pending national phase' authorisation status is not applicable for pending national authorisation procedure approvals (such as variations or renewals).

For the pending marketing authorisations, some data might not be available, as it is to be approved by the CMS(s). Therefore, the below information should be provided in the XEVMPD product entry during the initial submission, until the time the product is formally authorised:

- **Authorisation procedure**: Use *'EU other approval/authorisation procedure' (13)* to ensure that this product record is not considered in the fee calculations.
- **Authorisation number**: The text *"Not assigned"* can be provided in this field, unless the authorisation number is already known. If this is the case, then the authorisation number can be provided.
- **Authorisation date**: The same date as the one provided for the RMS should be provided.
- **Full Presentation Name**: The proposed name can be included in the local language.
- **Product attachment(s)**: The SmPC approved by the RMS can be included.
- **Legal basis**: Reference any of the permitted legal basis values for the Authorisation procedure 'EU other approval/authorisation procedure' (13), as outlined in NOTE 6 of Chapter 3.II: XEVPRM User Guidance.
- For the **remaining product information**, the same data as those provided in the RMS (e.g. Indications, ATC codes, composition, etc.) should be provided.

Once the medicinal product is formally authorised, the MAH must perform an update of the medicinal product record in the XEVMPD to provide the correct information (e.g. authorisation procedure, correct legal basis, authorisation number and date, product name etc.).

1.19. Windsor framework

Question: With the Windsor framework coming into effect as of 01 Jan 2025, can you please confirm how this will affect our medicinal product submission in the Article 57 database and if we should submit in the Article 57 database details of our UK based QPPV and PSMF?

Answer:

~~Please refer to the information in section Background information of Chapter 3.II: XEVPRM User Guidance. With regard to the establishment requirements for the QPPV and PSMFL for medicinal products with MA valid in the territory of Northern Ireland, with the assigned country code 'XI', the QPPV and PSMF may be established in an EU member state, NO, LI, IS, XI or in the rest of the United Kingdom (GB), if the organisation does not already have a QPPV based in the EEA or Northern Ireland as per section 4. The location of the marketing authorisation holder and the qualified persons for manufacturing for pharmacovigilance with regard to medicinal products for human use of the Commission Notice – Application of the Union's pharmaceutical acquis in markets historically dependent on medicines supply from or through parts of the United Kingdom other than Northern Ireland. With regard to the establishment requirements for the QPPV and PSMFL for medicinal products~~

~~with MA valid in the United Kingdom, with the assigned country code 'GB', EU law does not apply to such authorisations. Therefore, the QPPV and PSMF may be established as per the authorisation rules applied by the MHRA.~~

Regulation (EU) 2023/1182 impacts only medicinal products authorised by the European Commission under the centralised procedure. From 1 January 2025, a marketing authorisation granted by the European Commission is no longer valid in the territory of Northern Ireland. Marketing authorisation holders must therefore apply for a marketing authorisation at the UK's national competent authority if they wish to have a medicinal product, which is authorised in the EU via a centralised procedure, authorised in the United Kingdom and/or the territory of Northern Ireland:

- If the medicinal product is authorised by the UK's national competent authority **for the territory of Norther Ireland under the EU law**, the location of the QPPV and PSMF should comply with EU requirements.
- If the medicinal product is authorised by the UK's national competent authority **for the territory of Norther Ireland under UK law**, the location of the QPPV and PSMF should comply with UK requirements.

See also Q&A *6.12.1.4. New: Change of QPPV for medicinal products with marketing authorisation valid in the territory of Northern Ireland* and *6.13.6. New: Change of PSMF location for medicinal products with marketing authorisation valid in the territory of Northern Ireland* of this document for related information.

2. PREVIOUSLY SUBMITTED (LEGACY) DATA

2.1. Definition of legacy data

Question: Which medicinal product entities are considered "legacy data"?

Answer: All authorised medicinal products (AMPs) submitted to the XEVMPD using the previous EudraVigilance Product Report Message (EVPRM) format (i.e. Pre-Article 57 format) are considered legacy data.

2.2. Visibility, ownership and maintenance of legacy product data

Question: Do product records, which were previously submitted to the EVMPD using the old EVPRM format stay visible and active in the XEVMPD? Do MAHs need to update/maintain such data?

Answer: Medicinal products previously submitted using the old EVPRM format are considered legacy data. All EVMPD legacy data were migrated to the new XEVPRM format, and the Agency assumed the XEVMPD ownership of such data (i.e. of authorised medicinal products submitted in the XEVMPD using the previous EudraVigilance Product Report Message format (i.e. Pre Article 57 format) by referencing *'**Maintained by EMA'** (Organisation EV Code ORG15457)'* as the MAH in the concerned AMPs. This is to flag medicinal products which are not compliant with Article 57(2) requirements and therefore should not be maintained by marketing-authorisation holders under the Article 57(2) obligations.

The EMA may update information within the **legacy product data** (i.e. AMPs referencing ***'Maintained by EMA'***) as part of data cleaning activities [e.g. to change the referenced pharmaceutical form(s), route(s) of administration etc.]. Whilst these changes performed by the Agency will trigger the generation of the 3rd level XEVPRM Acknowledgement, no action is required to be performed by the MAH organisation that owns the data in the XEVMPD.

Legacy product data are still visible in the XEVMPD and can be retrieved by MAHs using EVWEB Advanced Queries section - the condition 'Pre-Article 57 format' must be selected and/or ORG15457 must be specified in the "MAH Code" field (AP.4).

2.3. Use of product data previously submitted

Question: Can we use a medicinal product record previously submitted in the XEVMPD as a "template" to create a new medicinal product record?

Answer: Yes, it is possible. Marketing authorisation holders can use a medicinal product entity previously submitted in the XEVMPD to create a new medicinal product entity. Using simple or advanced queries in EVWEB retrieve the AMP record and use operation type 'Reinsert' available under 'Other operations' to move the medicinal product entity in the 'Create and Send Product Reports' section of EVWEB. Amend/populate the required data elements and submit this medicinal product via an XEVPRM with the operation type 'Insert' (1) using EVWEB (available to EVWEB users) or send the XEVPRM via EV Post functionality (available to EVWEB and Gateway users). Following a successful submission, new EV Code will be assigned.

3. ART57 SUBMISSION TIMELINES

3.1. Timeline for submission of information on newly authorised medicinal product

Question: How should MAHs submit to the EMA information on new marketing authorisations? What are the timelines?

Answer: In accordance with the Legal Notice, information on medicinal products for new marketing authorisations in the Union after 2 July 2012 shall be submitted by marketing-authorisation holders electronically to the Agency 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).

Medicinal product data shall be submitted to the Article 57 database using the eXtended EudraVigilance Medicinal Product Report Message (XEVPRM) with operation type 'Insert' (1). See section *1.1 Initial Submission of an Authorised Medicinal Product (AMP)* of Chapter 3.II: XEVPRM User Guidance for further information.

3.2. Start of 15 calendar day timeline

Question: In accordance with the published guideline, MAHs are obliged to submit information on newly authorised medicinal products "*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*" Our question is:

a) Are those 15 calendar days starting from the date when the decision is issued by the NCA (i.e. the date that is stated on the notification document issued by the NCA); or

b) 15 days from the date when the MAH actually receives the notification document from the NCA?

Answer: The compliance with the timelines stated in the Legal Notice [paragraph 2. Timelines, section 2(b)] is subject to MAHs receiving a Marketing Authorisation document issued by the National Competent Authority (NCA).

Therefore, the 15-calendar day timeline apply from the date of receipt of the Marketing Authorisation document and not the date of authorisation/renewal which is stated in the Marketing Authorisation document.

3.3. Receipt of positive XEVPRM ACK within 15 calendar days timeline

Question: MAHs shall submit to the Agency information on newly authorised medicinal products as soon as possible and no later than 15 calendar days from the date of authorisation. Are the 15 calendar days the timeline for submission of the XEVPRM with the AMP information (irrespective of the outcome of the submission), or do we need to ensure that we receive a positive XEVPRM Acknowledgement within the 15 calendar days?

Answer: If a product message (XEVPRM) is recognised successfully, an MDN (Message Disposition Notification) will be returned to the sender; the date of this MDN will serve as the official receipt date of the submission by the EudraVigilance Gateway. However, an XEVPRM can only be regarded successfully delivered if the transmission status is acknowledged by the receiver with

acknowledgement code 01, i.e. if the AMP was successfully loaded in the XEVMPD database. Therefore, a successful XEVPRM ACK must be received within the 15-calendar day timeline.

3.4. Submission of information within 15 calendar days following a transfer of marketing authorisation

Question: Does the timeline of 15 calendar days also apply to medicinal products that our company acquired following a transfer of marketing authorisation from another MAH?

Answer: The timeline of 15 calendar days from the date of authorisation applies only for newly granted marketing authorisations.

The transfer of marketing authorisation is not a new marketing authorisation and therefore should be addressed as part of the maintenance process of information on medicinal products described in section *2. Maintenance of medicinal product data* of Chapter 3.II: XEVPRM User Guidance.

3.5. Start of 30 calendar day timeline to notify the EMA following a transfer of MA

Question: The marketing authorisation of some of our medicinal products is being transferred to another MAH. The transfer was approved on 1 June 2018, but the implementation date is set for 31 December 2018, which is also the date already stated in section 10. Date of revision of the text of the SmPCs. Can you please clarify when does the 30-calendar day timeline to notify the EMA of this transfer start? It is from the approval date or from the implementation date?

Answer: Since the responsibilities of the new MAH start when the transfer is approved, the MAHs should notify the Agency of the transfer of MA using the applicable processes described in section *2.4.3. Transfer of marketing authorisation* of Chapter 3.II: XEVPRM User Guidance as soon as possible and no later than 30 calendar days from the date of approval.

3.6. Recommended timelines for submission of information on traditional herbal medicinal products registered in accordance with Article 16a of Directive 2001/83/EC

Question: Whilst the submission of traditional herbal medicinal products registered via the simplified registration procedure (traditional use-registration) on the basis of Article 16a of Directive 2001/83/EC is out of scope of Article 57(2) requirements, registration holders (RHs) should insert the information on such medicinal products in the Article 57 database to be compliant with their pharmacovigilance requirements. What is the timeline for submission of these medicinal products?

Answer: The following submission timelines are applicable:

- Submission of information on **new** herbal medicinal products registered via the simplified registration procedure (traditional use-registration): as soon as possible and no later than **15 calendar days** from the date of registration [i.e. 15 calendar days from the date of notification of the granting of the traditional herbal registration (THR) by the competent authority];
- Submission of **variations** to the initial traditional herbal registration: as soon as possible and no later than **30 calendar days** from the date of which the changes have been approved by the competent authority.

3.7. Inability to comply with medicinal product submission timelines

Question: In accordance with the information stated in the Legal Notice, information on medicinal products for which a new marketing authorisations in the Union was obtained after 2 July 2012 shall be submitted by MAHs electronically to the Agency no later than 15 calendar days from the date of authorisation and information on any amendments to the terms of the marketing authorisations following variation, transfer, renewal, suspension, revocation or withdrawal should be submitted no later than 30 calendar days from the date of which the amendments have been authorised.

If we are unable to comply with these timelines due to circumstances beyond our control, what should we do?

Answer: Organisations unable to submit medicinal product information within the 15/30 calendar day timelines should inform the Agency of their expected submission plan by sending a notification to the EMA Service Desk (https://servicedesk.ema.europa.eu/).
Please submit your notification as a "***Question***", specifying *"**Delayed Article 57 submission notification**"* in the subject. It is sufficient to send a single notification for each Headquarter/Affiliate registration ID. The following information must be provided:

- marketing-authorisation-holder name and headquarter organisation ID (the ID specified by the organisation during the registration process to uniquely identify each organisation in EudraVigilance);
- volume of data (the number of product records to be submitted during the specified timeframe);
- timeline for submission (the start date and completion date of the electronic submission)
- reason for delay in the submission of the product data.

4. SUBMISSIONS OF PACKAGE PRESENTATIONS

4.1. Multiple package presentations covered by one authorisation number

Question: How should we submit a medicinal product, for which the same marketing authorisation number covers several pack sizes?

Answer: See section *1.1. Initial submission of an authorised medicinal product (AMP) entity* of Chapter 3.II: XEVPRM User Guidance for the requested information.

4.2. Luxembourg: Registration number vs Package registration number

Question: In Luxembourg, there are two numbers mentioned in the marketing authorisation: Registration Number and Package Registration Number. In Luxembourg, we market exactly the same package(s) as in Belgium, stating the Belgian MA number. The Luxembourgish MA number is not mentioned on the package. The Belgian SmPC does not state the Luxembourgish MA number. What information should we submit to the EMA?

1. Luxembourgish Registration No + Belgian SmPC + Luxembourgish MA document
2. Luxembourgish Package Registration No + Belgian SmPC + Luxembourgish MA document
3. Luxembourgish Registration No + Belgian SmPC
4. Luxembourgish Package Registration No + Belgian SmPC

Answer: Information as per Option 1 (i.e. Luxembourgish Registration No + Belgian SmPC + Luxembourgish MA document) should be provided if you wish to submit only one product covering multiple pack sizes.

Information in Option 2 (Luxembourgish Package Registration No + Belgian SmPC + Luxembourgish MA document) should be provided if you wish to submit one product for each pack size.

4.3. Different authorisation numbers for each package presentation

Question: How should we submit a nationally authorised medicinal product for which different marketing authorisation numbers are assigned based on its pack size/pack characteristics in the XEVMPD?

Answer: If different authorisation numbers are assigned to the same product based on its pack size/description, a distinct product entity should be provided for each pack size/characteristic referring to the applicable authorisation number; a brief textual package description should be included in the 'Package Description' field (AP.13.7) as per information in section *1.2.15. Package description (AP.13.7) of* Chapter 3.II: XEVPRM User Guidance for related information.

4.4. Mandatory provision of product information based on individual pack size

Question: MAHs are now required to provide in the Article 57 database product information down to the pack size level (i.e. one product entry corresponds to one authorised pack size). Is this required for all products?

Answer: Please refer to information available in section *1.1. Initial submission of an authorised medicinal product (AMP) entity* and *Annex I: Pack size submissions* of Chapter 3.II: XEVPRM User Guidance for related information.

5. Submission principles

5.1. Submission of centrally authorised medicinal products (CAPs)

Question: For a centrally authorised medicinal product, is only one record required to be submitted in the Article 57 database to cover all countries?

Answer: For centrally authorised medicinal products, different authorisation numbers (EU numbers) exist for each medicinal product and package presentation. Therefore, for each presentation (each EU number) a separate medicinal product entity must be submitted in the XEVMPD. See *EXAMPLE 6* and section *1.2.12.1. Authorisation country code (AP.12.1)* of Chapter 3.II: XEVPRM User Guidance for related information.

5.2. Submission of reconstituted products

Question: This question is relative to the rules applying to the case of products to be reconstituted prior administration.
For instance: Concentrate (docetaxel 20 mg/0.5 ml) and solvent for solution for infusion; packaging: 1 vial + 1 vial x concentrate: 0.5 ml; solvent: 1.5 ml.
Please indicate what are the XEVMPD rules required in the following case: Is it required to describe a single pharmaceutical product in this case as follows: - Pharmaceutical form = Concentrate and solvent

for solution for infusion, Strength of API = 20 mg/ 2 ml (i.e. after reconstitution, pre-administration to the patient)? Please provide detailed specifications and comments.

Answer: In the XEVMPD, "pharmaceutical product" refers to the administrable pharmaceutical form as stated in section *1.2.17.1. Administrable Pharmaceutical form (PP.1)* of Chapter 3.II: XEVPRM User Guidance.

Therefore, the "(administrable) pharmaceutical form" should be specified as "solution for infusion" (EV Code = PHF00230MIG). The authorised pharmaceutical form should be specified as "Concentrate and solvent for solution for infusion" (EV Code = PHF827).

5.3. Submission of medicinal products without an active ingredient

Question: One of our products has no 'active' ingredient because it is a negative control solution: do we have to register such a medicinal product?

Answer: See *NOTE 10* of Chapter 3.II: XEVPRM User Guidance for the requested information.

5.4. Submission of medicinal products with multiple pharmaceutical products (e.g. combination products, KIT products)

Question: How should medicinal product information be provided in the XEVMPD when the packaged medicinal product contains different types of pharmaceutical products (e.g. KIT products that might have different pharmaceutical forms and thus different routes of administrations registered in one MA)? How should such products be entered in the XEVMPD?

For example: The active substance described in section 2. Qualitative and Quantitative Composition of the SmPC states that our product is a chemical product, on which the radioactive element is fixed after reconstitution. The pharmaceutical form defined in section 3. Pharmaceutical Form of the SmPC is 'powder for injection'. The way to reconstitute the kit is described in the SmPC. The active substance in the reconstituted product is the "chemical product-radioactive element complex" which is a solution for injection. The EMA substance list defines XEVMPD codes for both substances: the chemical product and the "chemical product-radioactive element complex".

Our question is: which substance has to be considered as the Active substance? Is it:

1) The chemical product; pharmaceutical form = powder for injection as defined in sections 2 & 3 of the SmPC with a quantity in milligrams; or

2) The "chemical product-radioactive element complex"; pharmaceutical form = solution for injection with a quantity in mega-Becquerels (radioactivity measure)?

Answer: KIT products with different pharmaceutical forms and routes of administrations should be entered in the XEVMPD as separate pharmaceutical products within one medicinal product entity. The same rule applies to combination products (i.e. where a packaged medicinal product contains two different pharmaceutical products e.g. tablet and cream).

See section *1.2.17 AMP - Pharmaceutical product elements (AP.PPs)*, *EXAMPLE 40* and *EXAMPLE 41* of Chapter 3.II: XEVPRM User Guidance for related information.

With regards to your specific example, as stated in Section 2 of the SmPC for the described medicinal product, the active substance(s) and the strength for the Kit for radiopharmaceutical preparation should be described in the XEVMPD for the finished product, i.e. after reconstitution referring to the 'chemical product-radioactive element complex', solution for injection with a quantity in mega-

Becquerels (radioactivity measure). The authorised pharmaceutical form is "Powder for injection" (EVCode = PHF00194MIG) and the administrable pharmaceutical form is "Solution for injection" (EVCode = PHF00231MIG).

5.5. Confidentiality of submitted data

5.5.1. Confidentiality of data submitted in the Article 57 database

Question: Which parts of the product data in the Article 57 database are handled confidentially? For the non-confidential data, are they be visible to a registered user group or for everybody (e.g. published on an internet website)?

Answer: All mandatory and optional data elements of an AMP flagged by the EMA as "validated", except for the QPPV name and contact details, the referenced PPI attachment(s) and the details of the PSMFL information, are visible in EVWEB to all users registered with EudraVigilance. Please refer to section *1.7.7. Data Access Policy* of the XEVMPD Data-Entity Tool (EVWEB) User Manual.

A subset of authorised medicinal product data with contact details for pharmacovigilance enquiries is also published on the 'Public data from Article 57 database' webpage.

5.5.2. Confidentiality of concentration of excipients

Question: In our AMPs submissions we included the concentration of excipients. Can you confirm that this information will be confidential and not visible to other organisations?

Answer: As stated in section *1.2.17.9. Excipient substance strength* of Chapter 3.II: XEVPRM User Guidance it is optional to describe the strength(s) of excipient(s).

As per the applicable readability rules described in section *1.7.7. Data Access Policy* of the XEVMPD Data Entry Tool (EVWEB) User Manual some information referenced in AMP entities validated by the EMA will be visible to other XEVMPD users. Therefore, if your AMP entity is flagged as validated by the EMA, other users will be able to see the strengths of your excipients.

Should you wish not to disclose this information, we recommend that you perform an update (operation type 2 = 'Update') of the affected AMP entities and remove the excipients' substance strengths.

5.6. Language requirements for XEVMPD data submission

5.6.1. Non-Latin/accented characters

Question: Does the Agency support non-Latin/accented characters in EEA languages as well? Does the EMA expect metadata in Bulgarian or Greek to be scripted in Latin characters?

Answer: Yes, the Agency expects and therefore supports non-Latin /accented characters in EEA languages. The UTF-8-character set should be used.

For WEB Trader users, the submission in non-Latin characters should be made using the XHTML version of XEVMPD Data Entry Tool (EVWEB). This option can be selected in the display setting drop down menu in the top left corner of EVWEB. The tree view in EVWEB will however not show the non-Latin characters.

Please note that non-ASCII characters are not allowed for the attachment file name.

5.6.2. Language requirements for submission of authorised medicinal product data

Question: In what language should we submit information on our authorised medicinal product data (i.e. presentation name elements, substance information, pharmaceutical forms etc.)?

Answer:

- The presentation name elements in data fields AP.13.1 - AP.13.6 must be entered in the language of the country where the marketing authorisation applies in accordance with the referenced PPI attachment (e.g. SmPC, PIL etc. as applicable). For details see Chapter 3.II: XEVPRM User Guidance, sections:
  - *1.2.13 AMP - Presentation Name element structure (AP.13),*
  - *Table 1a- Authorised Medicinal Product – language requirements,*
  - *Table 1b - Requirements for AMP records and attachments for countries with more than one national language.*
- For the following terminologies and XEVMPD Controlled Vocabularies (CVs), the English term should be used:
  - indications (English MedDRA term),
  - pharmaceutical Forms,
  - routes of administration,
  - authorisation status,
  - authorisation procedures,
  - concentration types,
  - units of presentation,
  - units of measurement
  - substance classes,
  - medical devices (for combined advanced therapy medicinal product in accordance with Regulation (EC) No 1394/2007 as applicable).
- The substance name(s) are to be specified in the language of the country where the marketing authorisation applies in accordance with the referenced PPI (e.g. SmPC, PIL etc. as applicable). For details see Chapter 3.II: XEVPRM User Guidance, sections:
  - *Table 1a- Authorised Medicinal Product – language requirements*
  - *1.2.17.4 Active ingredient substance code (PP.ACT.1),*
  - *1.2.17.8 Excipient substance code (PP.EXC.1),*
  - *1.2.17.10 Adjuvant substance code (PP.ADJ.1).*

  The preferred name of the approved substance is however entered in English. Each translation and synonym are always linked to the master substance EV Code with a preferred name in English.
- The package description should be provided in the language of the country where the marketing authorisation applies in accordance with the referenced PPI (e.g. SmPC, PIL etc. as applicable) or in English.

5.6.3. Language requirements for submission of authorised medicinal products in countries with multiple official languages

Question: What language should we use to submit medicinal product information of medicinal products authorised in countries with more than one official language? For example, in Finland we have two official languages.

Answer: Please refer to *Note 15*, *Table 1b - Requirements for AMP records and attachments for countries with more than one national language* and *EXAMPLE 68* of Chapter 3.II: XEVPRM User Guidance for the required information.

5.6.4. Language requirements for submission of medicinal products authorised in Iceland, Liechtenstein and Norway via the centralised procedure

Question: As per the latest guidance provided in Chapter 3.II: XEVPRM User Guidance, the full presentation names of medicinal products authorised centrally in Iceland, Liechtenstein and Norway are to be provided in English. Previously, these were requested in the national languages. What is the rationale behind this change? Do we need to perform a dedicated update of these AMP entities?

Answer: As per information stated in Chapter 3.II, subsequent experience over time showed that the provision of the name in English is preferable to allow the EMA group similar CAPs based on the product name information. MAHs are not required to perform a dedicated update of their product entities to amend this information as this can be done as part of a regular maintenance.

5.6.5. Substance translations

Question: Can you please confirm that the translations of substances names must be provided whenever SmPC uses them?

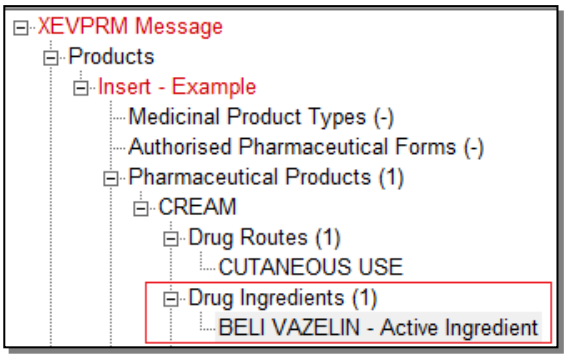
Answer: The substance information in an authorised medicinal product entity must be provided as presented in the SmPC corresponding to the language of the country where the marketing authorisation applies. The same character set as presented in the SmPC must be used. Each approved substance successfully submitted in the XEVMPD has an assigned EV Code where the preferred name of the approved substance is entered in English. Each translation and synonym are then linked to the master substance EV Code.

5.6.5.1. Visibility of substance translations in EVWEB/re-uploaded XML file

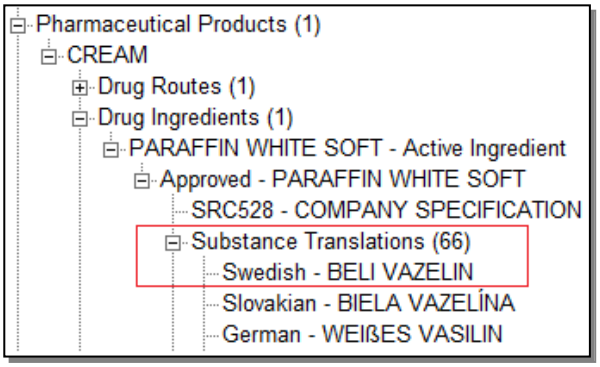
Question: We provide the translations for the active substance and excipients in the language of the SmPC, as per instructions in the guidance documents. However, when we save the XML file or re-load the AMP in EVWEB for update, the substance name does not appear in the national language (i.e. as the translation) but in English. Why is that? Do we need to amend the substance names, so they are in the national language every time we do an update of the AMP?

Answer: As per our guidance, substance information must be submitted in line with the applicable SmPC (i.e. in the language of the SmPC). Each translation and synonym are linked to a master substance code where the preferred name of the master substance is in English.

In your initial submission, when creating the XEVPRM with your AMP via EVWEB, you reference the substance name in the national language:



The name in the national language (i.e. the translation) is linked to the master substance name in English. Therefore, when you view you AMP in EVWEB and/or you perform a maintenance related operation type on that AMP entity, the master substance name in English is displayed. The list of substance translations is included in the "Substance translations" section of the approved substance entity:



You do not need to amend the substance information to "rename" the substance name back to the national language.

If the translation of the requested substance name is not available, you need to request for it to be added in the XEVMPD as per the processes described in the in the communication in section *1.4 Initial submission of an Approved Substance* of Chapter 3.II: XEVPRM User Guidancehttp://www.ema.europa.eu/docs/en_GB/document_library/Other/2013/11/WC500153998.pdf .

5.6.5.2. Language requirements for substance name for herbal/homeopathic medicinal products

Question: Can substance names for herbal medicinal products be provided in Latin? Does this apply also to homeopathic medicines?

Answer: Latin binomial plant names or Latin herbal preparation names of authorised medicinal products are acceptable if reflected in the SmPC. The substance name(s) are to be specified as reflected in the SmPC of the authorised medicinal product and in accordance with the national language(s) as applicable, or the Latin name if reflected in the SmPC.

5.6.6. Language requirements for MedDRA coding – unsupported languages

Question: Not all EEA national languages are available for the MedDRA coding - what is the expectation for those languages not supported?

Answer: The indication(s) need to be coded using MedDRA in its latest version. Supplemental MedDRA terms that will be included in the next MedDRA version can also be used.

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

5.6.7. Language requirements for package description

Question: Can MAHs use English text to provide the package description, or must this field be provided in the official language of the SmPC for national procedures?

Answer: Both is acceptable, as per information in section *1.2.15. Package description (AP.13.7)* of Chapter 3.II: XEVPRM User Guidance.

5.7. Printed product information (PPI)

5.7.1. Content and submission of PPI

Question: Is the submission of Printed Product Information (PPI) mandatory? If so, what shall we provide as a PPI for our medicinal product entity?

Answer: Yes, it is mandatory to provide the Printed Product Information (PPI) as part of the initial submission of an authorised medicinal product and/or as part of the maintenance of a medicinal product entity as per the applicable maintenance process(es) described in section *2. Maintenance of medicinal product data* of Chapter 3.II: XEVPRM User Guidance.

Please refer to section *1.10. Submission of an attachment* of Chapter 3.II: XEVPRM User Guidance for details regarding the content of the attachment.

5.7.2. Submission of an additional document if the authorisation number is not stated in the referenced SmPC/PIL

Question: Why is it necessary to provide the document granting authorisation/renewal if the authorisation number is not stated in the referenced SmPC/PIL?

Answer: This is required because the EMA needs to be able to validate the data submitted by the MAH and ensure that the data is correct. If the MAH confirms that no document stating the applicable authorisation number is available, the EMA will assume that the number stated in the "Authorisation Number" field provided by the MAH is correct.

5.7.3. Intended use of PPI

Question: Why do we need to submit the PPI attachment? What is the added value?

Answer: The provided attachment(s) is/are used for the validation of the information submitted within the AMP record (i.e. medicinal product name, marketing authorisation details, qualitative and quantitative composition of the pharmaceutical product etc.).

The added value is to have the full information (e.g. contraindications, special warnings and precautions for use, etc.) on the medicinal product in case of arising safety concerns.

There is a technical business rule where the system validates automatically if an attachment has been provided or cross-referenced for a medicinal product submission.

5.7.4. Format of PPI

Question: In which format shall the attachments be provided?

Answer: As per section *1.10. Submission of an attachment* of Chapter 3.II: XEVPRM User Guidance:

For PDF attachments, 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 we will have assurance that we will be able to open them for many years.

ISO 19005 - Document management - Electronic document file format for long-term preservation (PDF/A):

Part	*Name*	*Formal name*	*Release date*	*Standard*	*Based on PDF version*
Part 1	PDF/A-1	Use of PDF 1.4 (PDF/A-1)	2005	ISO 19005-1	PDF 1.4 (Adobe Systems, PDF Reference third edition, 2001)
Part 2	PDF/A-2	Use of ISO 32000-1 (PDF/A-2)	2011	ISO 19005-2	PDF 1.7 (ISO 32000-1:2008)
Part 3	PDF/A-3	Use of ISO 32000-1 with support for embedded files (PDF/A-3)	2012	ISO 19005-3	PDF 1.7 (ISO 32000-1:2008)

OCR (Optical Character Recognition) scanned documents may also be provided when the scanned PDF document cannot be electronically converted into an editable copy.

5.7.5. Unavailability of an SmPC

Question: Sometimes the SmPC is not available. For example, in some countries, old products do not have an approved SmPC and only an old approved leaflet is available. In case of homeopathic medicines, the SmPC is not always part of the approval process. Do companies have to provide replacement data?

Answer: Where, in exceptional circumstances, the national SmPC is not available (i.e. MRP variation approval), a similar text (i.e. the English common text, package leaflet) as authorised by the Authorising Body can be used for the submission in the XEVMPD. Please note that a proposed SmPC text should not be submitted.

5.7.5.1. Unavailability of an SmPC in the language of the country of authorisation at the time of submission

Question: We understand that an AMP authorised via national, mutually recognised and decentralised procedure must refer to the SmPC in the language of the country or authorisation. Sometimes

however, the SmPC is not available in the local language at the time of submission. Which document shall we submit in this case?

Answer: Where, in exceptional circumstances, the national SmPC for non-centrally authorised products and MRPs/DCPs/NAPs is not available, a similar text (i.e. the English text of the procedure) can be used as an attachment for the submission in the XEVMPD. The data elements AP.13.1 - AP.13.6 must however be provided in the language of the country where the marketing authorisation applies. When the SmPC in the national language becomes available, it must be provided in the context of the data maintenance, i.e. when the variations lead to changes as listed in section *2.4.1. Variations of marketing authorisation* of Chapter 3.II: XEVPRM User Guidance.

5.7.5.2. Unavailability of SmPC for medicinal products authorised before 19xx

Question: What the marketing-authorisation holder must submit in case that marketing authorisation was granted before 19xx and therefore certain information might not have been available at that time?

Answer: The information to be provided in the context of Article 57(2) is identical for all medicinal products authorised in the European Union, independent of the year of authorisation.

5.7.5.3. Unavailability of SmPC for medicinal products for Luxembourgish marketing authorisations

Question: For Luxembourgish marketing authorisations there are no approved texts (SPCs/PILs) and instead, the texts approved by the Belgian regulatory authority are circulated. Although circulated in Luxembourg, the texts do not detail the Luxembourgish licenses numbers; they only detail the Belgian license numbers.
When entering records for Luxembourgish marketing authorisations into the XEVMPD, we have submitted the Belgian texts and include the Luxembourgish authorisation numbers in the 'Authorisation number field'. Please confirm whether our approach is correct.

Answer: We can confirm that this approach is correct. Please also note that in case that the approved SmPC does not state an authorisation number, a date of authorisation/renewal or the MAH, an additional document stating the missing information (e.g. copy of the document granting or renewing marketing authorisation) should also be provided as an additional PPI attachment. This will allow the Agency to validate the information submitted by the MAH.

5.7.6. PPI naming conventions and link between XEVPRM and attachment(s)

Question: How should a PPI attachment be named? How can the link between an XEVPRM and attachment be maintained?

Answer: The file name for the attachment can be assigned by the MAH; there is no naming convention to be followed. Please note that non-ASCII characters are not allowed for the attachment file name.

The link between the product information and its PPI attachment (SmPC) is maintained via a PPI EV Code. If the SmPC of a product changes, a new PPI should be submitted via an XEVPRM, and the relevant product(s) should be updated referencing the new PPI EV Code (see section *2. Maintenance of medicinal product data* for further information of Chapter 3.II: XEVPRM User Guidance.

5.7.7. SmPC version number and version date

Question: What shall we specify as SmPC 'Version number (ATT.7)' and 'Version date (ATT.8)'? Does this information have to be actually present in the attachment (physical document i.e. SmPC) provided to XEVMPD?

Answer: Please refer to sections *1.10.7. Attachment version (ATT.7)* and *1.10.8. Attachment version date (ATT.8)* of Chapter 3.II: XEVPRM User Guidance for the requested information.

5.7.8. Confidentiality of PPI

Question: Are documents referenced in AMP entries as PPI visible to all XEVMPD users or to the public?

Answer: Attachment entities are not validated in the XEVMPD by the EMA; they are used by the EMA to support the validation of the information referenced in the AMP entry by the MAH. Therefore:

- Users logged on to EVWEB under the HQ organisation that owns the product/attachment entity in the XEVMPD can retrieve and view the attachment content.
- Users not logged on to EVWEB under the HQ organisation that owns the product/attachment entity in the XEVMPD cannot retrieve and view the attachment content.

In summary, attachments in the XEVMPD are visible to users from the organisation that owns the attachment in the XEVMPD and to the EMA.

5.8. Medicinal product entity elements

Question: What information needs to be provided for some of the data fields within each authorised medicinal product entity? The guidance provided in Chapter 3.I technical specifications is not very clear. Can you please clarify what we need to enter in e.g. "sender local code" and "info date" etc.?

Answer: Please refer to section Chapter 3.II: XEVPRM User Guidance for detailed description of what information (and when) needs to be provided for each data element.

5.8.1. Legal Basis

Question: Which value shall we select in the field Legal basis (AP.12.13) for old medicinal products?

Answer: Please refer to *Note 5* of Chapter 3.II: XEVPRM User Guidance for the requested information.

5.9. Presentation name elements

5.9.1. Population of presentation name elements

Question: How do we correctly populate the medicinal product name and name part elements of an authorised medicinal product entity in the XEVMPD?

Answer: Please refer to section *1.2.13 AMP - Presentation Name element structure (AP.13)* of Chapter 3.II: XEVPRM User Guidance.

5.9.1.1. Name in the title of an SmPC document vs. name in section 1 of the SmPC for medicinal products in Denmark

Question: The SmPC of a medicinal product authorised in Denmark often contains more information on the name of the product in the title of the document than in section 1.

EXAMPLE:

Title of the SmPC: "Prodemaz® dispergible tabletter"

Section 1 of the SmPC: "Prodemaz®"

Which of the two names should be captured in the full presentation name field?

Answer: In products from Denmark where the title contains more detailed information than section 1, the name stated in the title should be captured in the full presentation name field, with the other 'Presentation Name' data elements being derived from this name.

5.9.2. Population of presentation name elements for medicinal products with multiple trade names

Question: According to the technical specification, the product name is a mandatory field in which only one entity can be made. However, in some countries, one marketing authorisation number is granted for a product that is marketed with multiple trade names. How should we enter such medicinal products in the XEVMPD and capture the relevant name part elements of each medicinal product?
Answer: As stated in section *1.1 Initial Submission of an Authorised Medicinal Product (AMP)* of Chapter 3.II: XEVPRM User Guidance the name of the medicinal product is one of the characteristics based on which a separate medicinal product entry would be created for the authorised medicinal product in the XEVMPD. Therefore, if the same marketing authorisation covers two medicinal product names, two medicinal product entries should be submitted in the XEVMPD; the presentation name elements will be populated for each medicinal product entity as per guidance provided in section *1.2.13 AMP - Presentation Name element structure (AP.13)* of Chapter 3.II: XEVPRM User Guidance.

5.9.3. Submission of medicinal products listing the full presentation name in section 1 of the SmPC in more than one language

Question: If section 1 of the SmPC states the name of the medicinal product in more than one language as shown in the below example, should the "name fields" be populated with the Bulgarian details, the information in English, or should two separate entries be created? What are the XEVMPD rules required in the above case?

EXAMPLE

1. ИМЕ НА ЛЕКАРСТВЕНИЯ ПРОДУКТ

Кардесарт-Ко 8 mg/12,5 mg таблетки

Cardesart-Co 8 mg/12,5 mg tablets

Answer: The presentation name elements in data fields AP.13.1 - AP.13.6 must be entered in the language of the country where the marketing authorisation applies in accordance with the referenced SmPC. As in this example the authorisation country of the product is Bulgaria, the product name should be provided in Bulgarian. If the product entry is submitted via EVWEB, XHTML format should be used when inserting the product information.

5.10. Authorisation details

5.10.1. Authorisation number

Question: There are several authorisation numbers for the same product. How do we capture this in the XEVMPD? Do we create one medicinal product entity and enter all the numbers in the 'Authorisation Number field'?

Answer: Please refer to section *1.2.12.4. Authorisation number (AP.12.4)* of Chapter 3.II: XEVPRM User Guidance.

5.10.1.1. Applicable authorisation number is not stated in the relevant SmPC for a medicinal product authorised in Cyprus

Question: We have several medicinal products authorised in Cyprus using the 126a application process. As the 126a process was used, there is no Cyprus-specific SmPC, only the SmPC for the UK licence on which the 126a application was made. For these product entries we have used the Cypriot authorisation number and, as the product attachment, the SmPC for the UK licence as there is no other relevant product attachment. It that a correct approach? Or should we replace the Cypriot authorisation number with the UK product licence number (as it appears in Section 8 of the English SmPC) for these product entries?

Answer: Your approach is correct. You should not replace the Cypriot authorisation number stated in the "Authorisation Number" field (AP.12.4) with the English product licence number for these product entries. You should only update these product entries and submit an additional document stating the Cypriot authorisation number (i.e. document granting/renewing marketing authorisation in Cyprus). These medicinal product entries will therefore reference two attachments (i.e. SmPC for the UK licence and document with the Cyprus-specific authorisation number).

5.10.1.2. No authorisation number is stated in the SmPC

Question: How should we proceed if the SmPC of the AMP does not contain any authorisation number in section 8. Marketing authorisation number(s)?

Answer: If no authorisation number is stated in section 8. Marketing authorisation number(s) of the SmPC, the "Authorisation Number" field (AP.12.4) should be populated with the authorisation number assigned by the competent authority and an additional document referencing that authorisation number (i.e. document granting/renewing marketing authorisation) should be also attached to the AMP entry. The AMP entry in the XEVMPD will therefore reference two attachments (i.e. SmPC and a document showing the authorisation number).

5.10.1.3. No authorisation number assigned following granting of MA in Portugal

Question: We have a question concerning a few unusual cases of Portuguese registrations. These registrations are approved by the Portuguese authority but were not assigned any registration numbers because they are not marketed at the moment. Must these registrations be submitted to the EMA, or would we only do so once they are marketed and have an assigned registration number? In case they must be submitted immediately, please inform us how this should be done without the registration number.

Answer: Since these registrations have been authorised, even if they are not marketed, they must be submitted in the XEVMPD. You should specify the procedure number (i.e. national procedure number or

MRP/DCP number if no national procedure number has been assigned for an MRP/DCP procedure) in the authorisation number data element (AP.12.4) and attach the document granting marketing authorisation as an additional PPI attachment.

5.10.1.4. Multiple authorisation numbers stated for individual components which are part of the same package

Question: The SmPC of a medicinal product authorised in the Ireland states the following information:

1. Name of the medicinal product: "ProductX 2 million IU/mL powder and solvent for solution for injection."

3. Pharmaceutical form: "Powder and solvent for solution for injection."

8. Marketing Authorisation number(s)

PA12345/0001

PA12345/0002 (Water for injection in pre-filled syringe)

Could you please advise if we should create one XEVMPD product entity for each authorisation number or a single product entity stating both authorisation numbers in the "Authorisation Number" field?

Answer: Since the two authorisation numbers listed in Section 8 of the SmPC refer to the same authorised medicinal product (the water for injection in pre-filled syringe is part of the same product), only one XEVMPD product entity should be created. With regards to the data element AP.12.4 (Authorisation number), as the current requirement is to specify only one authorisation number for each entity, this field should conventionally be populated with the authorisation number that does not refer to the solvent preparation containing water (i.e. PA12345/0001 must be specified in AP.12.4).

5.10.1.5. Format of an authorisation number: NAP in Iceland

Question: As part of the validation performed by the EMA, we noticed changes made to the MA numbers in Iceland. In Iceland, the MA Number as granted by the local NCA can be composed of 6 digits, e.g. 123456. In the SmPC, the MA Number made of 6 digits is represented with the suffix (IS), e.g. 123456 (IS). Which MA Number should be reported? The MA Number as granted by the Icelandic NCA (i.e. the 6 digits only) or the MA Number as indicated in the SmPC (i.e. with the IS extension)?

Answer: The MA number to be reported is the MA number as granted by the Icelandic NCA (i.e. 123456).

5.10.1.6. Authorisation number: NAP in Bulgaria

Question: The MA number as granted by the Bulgarian NCA can also include the first authorisation date (i.e. II-5678/27.06.2003). Which MA number should be reported? The MA number as indicated in the SmPC (i.e. including the first authorisation date) or the MA number only, without any date?

Answer: The MA number to be reported for AMPs authorised nationally in Bulgaria is the MA number without any reference to the authorisation date (i.e. II-5678). This is because the number without the date is a unique identifier.

5.10.1.7. Authorisation number: NAP in Greece

Question: Greece has two numbers for every product, but no marketing authorisation number as recognised in other countries:

1/ a product code, a unique identifier used to identify the product during its entire life cycle which is stated on the Approval Certificate but not in the SmPC; and

2/ an approval number, which identifies the individual approval/renewal and changes with every approval, and which is stated on the Approval Certificate and in the SmPC and includes the authorisation date (e.g. 12345/11-04-2016).

Which number should be specified in the XEVPRM data element Authorisation number (AP.12.4) for medicinal product entities authorised in Greece? In case it should be the approval number, should it be submitted in the format NUMBER/ DD-MM-YYYY (i.e. including the authorisation date) or contain the MA number only (i.e. without any date)?

Answer: You can either reference the product code OR the approval number in the "Authorisation Number" field (AP.12.4) for AMPs authorised nationally in Greece.

If you decide to reference the approval number, this should be in the format NUMBER/DD-MM-YYYY (i.e. including the authorisation date). This is because the number without the date is not a unique identifier.

MAHs are not required to perform a dedicated update of their product entities in Article 57 database to amend this information; this can be done as part of a regular maintenance of the AMP entities.

5.10.1.8. Authorisation number: NAP in France

Question: For medicinal products nationally authorised in France; a "package number" is stated in section 8 of the SmPC but it does not correspond to the Marketing Authorisation number (i.e. NL number) stated in the marketing authorisation document.

Which number should be specified in the XEVPRM data element Authorisation number (AP.12.4)?

Answer: For medicinal products authorised **nationally in France**; a 'package number' is stated in section 8 of the SmPC but it does not correspond to the marketing authorisation number (i.e. NL number) stated in the marketing authorisation document. Taking into consideration that the NL number is confidential, and, as per the request of the French National Competent Authority, **from January 2025**, MAHs are required to reference either the CIS number (covering all pack sizes) or the CIP number (assigned to each individual pack size) in the 'Authorisation number' field of the product entry in the XEVMPD:

- If the MAH wishes to submit in the XEVMPD one product record for all pack sizes, then the **CIS** number must be referenced in the 'Authorisation number' field. The number is formed of 8 characters with the format *6nnnnnn*.
- If the MAH wishes to submit in the XEVMPD one product record for each individual pack size, then the **CIP** number must be referenced in the 'Authorisation number' field. The number is formed of 13 characters with the format *34009nnnnnnn*.

Records already submitted to XEVMPD and referencing the NL number should therefore be updated by the MAH to reflect either the CIP or CIS number as applicable.

5.10.1.9. Authorised medicinal products without an assigned authorisation number

Question: We are the MAH of a medicinal product which is registered through MRP procedure, and which has 11 different pack sizes (7, 14, 28, 30, 35, 42, 50, 56, 90, 98 and 100 tablets). According to the MA licence, all 11 pack sizes mentioned are approved, but not all these presentations are

marketed. The NCA issued an MA number only for the pack sizes marketed – in section 8 of the SmPC only the marketed pack sizes are listed, with the respective MA number. Until now we inserted in the XEVMPD only the marketed pack sizes since there is no MA number for the not-marketed packs. Could you confirm if I must insert information on also the not marketed presentations and if yes, what should I reference in the "Authorisation number" field?

Answer: In this specific case, since all the presentations are authorised, even if not marketed, the information for these products must be inserted in the Article 57 database. Since no authorisation number was assigned to the not marketed presentations, the procedure number assigned by the NCA or the MRP procedure number (if no procedure number is assigned by the NCA) should be referenced in the product entry.

5.10.1.10. Submission of multiple medicinal products authorised under one authorisation number (Umbrella authorisation)

Question: In some European countries, medicinal products are authorised according to an "Umbrella authorisation". It means that marketing-authorisation holders can have a marketing authorisation for instance for five strengths and ten allergens (under the same marketing authorisation number). How should this product be submitted in the XEVMPD?

Answer: Section *1.1 Initial Submission of an Authorised Medicinal Product (AMP)* of Chapter 3.II: XEVPRM User Guidance contains information on how are medicinal products are characterised for XEVPRM submissions and the guidance in that section should be followed to determine how such data should be submitted in the Article 57 database.

Question: Based on the guidance in section *1.1 Initial Submission of an Authorised Medicinal Product (AMP)* of Chapter 3.II: XEVPRM User Guidance, it seems that below is going in the direction of adopting a definition from IDMP, when a medicinal product is the same product, or when it is different and should have its own record.

The guideline shows categories a)-e) which define a medicinal product:

a) name of the medicinal product;
b) marketing-authorisation holder;
c) marketing authorisation number;
d) authorising body (i.e. Competent Authority);
e) qualitative and quantitative composition (ingredients, strength, authorised/administrable pharmaceutical form).

For b) and c) we have explicit procedures and authorisation values (valid + xxx, invalid + xxx) defined in the guideline and d) is not submitted in XEVMPD. It is also clear when differences in a) to e) constitute a different medicinal product.

It is however unclear under which conditions a change in a) and e) is a correction (same product with changed data) or when it is a change that requires a creation of new medicinal product? If a new product should be inserted, what happens to the old record? Should it be nullified?

Answer: The process to follow if the name of the medicinal product (a) or the qualitative and quantitative composition (e) changes depends on the type of the regulatory procedure:

if it is a l**ine extension** and the existing product is still marketed with the same name, composition and MA number, the existing medicinal product entity should be retained, and the new product (with the new name/composition) should be inserted (operation = 'Insert') as a standalone entity;

if it is a **variation, which changes the composition and the MA number remains unchanged**, an update should be performed on the existing medicinal product entity (operation type 'Update');

if it is a **variation, which changes the name of the medicinal product and the MA number remains unchanged**, an update should be performed on the existing medicinal product entity (operation type 'Update');

if it is a **variation, which changes the composition and the MA number**, the process described in section *2.4.1.1 Business process - Authorisation number has changed following a variation* described in Chapter 3.II: XEVPRM User Guidance should be followed.

5.10.2. MRP/DCP number format

Question: Regarding provision of information for the 'MRP/DCP/EMEA number' field (AP.12.7), we are unsure if we should enter the MRP/DCP number with the text FDC/DC" or "/MR" or not.

Chapter 3.II states that the MRP/DCP number should be stated as indicated on the Heads of Medicines Agency's website, which doesn't seem to include the text "/DC" or "/MR". However, companies with internal databases might want to distinguish the data between DCP, MRP and RUP by including the text "/DC", "/MR" or "E" in the authorisation number. Please advise how the data should be submitted to the XEVMPD.

Answer: Please refer to the updated section *1.2.12.7. MRP/DCP/EMEA number (AP.12.7)* of Chapter 3.II: XEVPRM User Guidance.

5.10.3. Authorisation/renewal date

Question: Please define what date should be entered in the "authorisation date" field; when do we submit the authorisation date and when do we submit the renewal date?

Answer: Please refer to section *1.2.12.5 Authorisation/renewal date (AP.12.5)* of Chapter 3.II: XEVPRM User Guidance for the requested information.

5.10.3.1. Authorisation date of a medicinal product authorised in Iceland via the centralised procedure

Question: Can you please confirm which date should be specified as the authorisation date for a centrally authorised product authorised in Iceland? Is it the European Commission Decision date, marketing authorisation date as assigned by the Icelandic NCA or the date of notification?

Answer: As per section *1.2.12.5. Authorisation/renewal date (AP.12.5)* of Chapter 3.II: XEVPRM User Guidance: *"The date when the first authorisation was granted by the authorising body or the date when the renewal was granted (whichever is the latest) must be specified in line with section 9. Date of first authorisation/renewal of the authorisation of the SmPC".*

Therefore, since the Icelandic NCA is the authorising body, the authorisation date to be specified is the marketing authorisation date as assigned by the Icelandic NCA.

5.10.4. Authorisation procedures

Question: How do we select the correct authorisation procedure for the submission of our medicinal product?

Answer: Please refer to section *1.2.12.2 Authorisation procedure (AP.12.2)* of Chapter 3.II: XEVPRM User Guidance for the description of available authorisation procedure values.

5.10.4.1. Authorisation procedure for a Repeat Use Procedure

Question: In a product entity, which authorisation procedure should be selected for a Repeat Use Procedure, which is in principle a second wave MRP?

Answer: For repeat-use procedure, 'EU authorisation procedures - Mutual Recognition Procedure (3)' should be selected. See also section *1.2.12.7. MRP/DCP/EMEA number (AP.12.7)* of Chapter 3.II: XEVPRM User Guidance for related information.

5.11. Pharmacovigilance details

5.11.1. Visibility/Confidentiality of Pharmacovigilance details

Question: Will the PSMF location, pharmacovigilance email/phone number and QPPV details provided for the AMP in the Article 57 database be made public by the EMA?

Answer: Please refer to the European Medicines Agency pre-authorisation procedural advice for users of the centralised procedure document, *3.4.4.9. What information will be made public on the EU web-portal regarding pharmacovigilance contact details and PSMF locations? Will details of the QPPV be made public? (Jan 2016)* for the required answer.

The PhV contact details are published in the Excel file available on the Public data from Article 57 database webpage.

5.11.2. Provision of pharmacovigilance contact details in case of nullification and withdrawal of an AMP

Question: Please confirm that it is still mandatory to include an email address in field AP.7 in case of nullification or withdrawal of a medicinal product.

Answer: From a business process perspective, enquiry phone and enquiry email remain mandatory for nullification or withdrawal although this is not enforced by technical/business rules.

5.11.3. Qualified Person responsible for Pharmacovigilance (QPPV)

5.11.3.1. Unavailability of an EU QPPV

Question: What shall we do if our company does not have an appointed EU QPPV?

Answer: MAHs are legally required to have a qualified person for pharmacovigilance (QPPV) based in the European Union (EU) in place at all times, in line with Article 103 of Directive 2001/83/EC. The EU QPPV and where such does not exist, the local QPPV (e.g. in case of purely national authorisations) must be appointed by the MAH and referenced in the respective authorised medicinal product entries in the Article 57 database.

5.11.3.2. QPPV Code

Question: Where and how can we retrieve a QPPV Code?

Answer: Please refer to section *1.2.5 Qualified Person responsible for Pharmacovigilance (QPPV) code (AP.5)* of Chapter 3.II: XEVPRM User Guidance.

5.11.3.3. Retrieval of a QPPV name in the QPPV field in EVWEB

Question: How can we find our QPPV's name in the QPPV field (AP.5) in EVWEB? It is a look-up table but when we type the name and surname of the QPPV or the code of the QPPV we don't get any results?

Answer: We recommend that in the 'QPPV' field, you just press ENTER on your keyboard (without performing a search on the name, code or surname) to retrieve the list of all QPPVs (including the QPPV Code) associated with you headquarter organisation.

See section *1.2.4. QPPV field* of the Extended EudraVigilance Medicinal Product Report Message step-by-step guide: Insert of an authorised medicinal product for details. You can also perform a search on part of the name or surname and widen the search by including an asterisk (*) after the text.

5.11.4. Pharmacovigilance System Master File (PSMF)

5.11.4.1. Submission of PSMFL information

Question: Is it mandatory to enter the location of the Pharmacovigilance System Master File in the XEVMPD? If so, how do we enter this information in the XEVMPD?

Answer: Yes, it is, from 2 July 2015. The PSMFL EV Code assigned to the PSMFL entity then must be referenced in the AMP entity.

See section *1.11 Initial submission of a Pharmacovigilance System Master File Location (PSMFL)* of Chapter 3.II: XEVPRM User Guidance for information on how to insert PSMFL information in the XEVMPD. The PSMFL EV Code can be referenced in the AMP entity during an insert or an update of the AMP as per information in section *1.2.6. Pharmacovigilance System Master File Location (PSMFL) code (AP.6)* of Chapter 3.II: XEVPRM User Guidance.

5.11.4.2. Submission of different PSMFs at the same location

Question: How many MFL EV Codes are requested in case of two different PSMFs at the same location?

Answer: In cases where a MAH hosts two different PSMFs at the same location, the MAH should obtain two separate EV Codes from the XEVMPD that relate to two different PSMF location entities.

Please refer to *Table 5 – Requesting a single/multiple PSMF EV Code(s) by the same MAH* of Chapter 3.II: XEVPRM User Guidance for further information.

5.11.4.3. Intended use of PSMFL information

Question: How will the PSMFL information submitted to the XEVMPD be used?

Answer: The PSMF location information is important for the national competent authorities and the Agency. The quotes from the legislation below indicate how the information on PSMF location is used:

- REGULATION (EC) No 726/2004, Article 18 (3) states: *The supervisory authority for pharmacovigilance shall be the competent authority of the Member State in which the pharmacovigilance system master file is located.*
- REGULATION (EC) No 726/2004, Article 26 (1) (e) states that: *The Agency shall, in collaboration with the Member States and the Commission, set up and maintain a European medicines web-portal for the dissemination of information on medicinal products authorised in the Union. By means of that portal, the Agency shall make public at least the following: ……(e) a list of the locations in the Union where pharmacovigilance system master files are kept and contact information for pharmacovigilance enquiries, for all medicinal products authorised in the Union;*
- COMMISSION IMPLEMENTING REGULATION (EU) No 520/2012Article 4 (4) states: *Without prejudice to the requirements set out in Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (1), the marketing-authorisation holder shall notify immediately the Agency of any change in the location of the pharmacovigilance system master file or changes to the contact details and name of the qualified person responsible for pharmacovigilance. The Agency shall update the Eudravigilance database referred to in Article 24(1) of Regulation (EC) No 726/2004 and, where necessary, the European medicines web-portal referred to in Article 26(1) of Regulation (EC) No 726/2004 accordingly.*

The inclusion of the PSMF location information within the XEVMPD database facilitates the implementation of Article 26 (1) (e) of Regulation (EC) No 726/2004 requirement stated above. This is explained also in the document European Medicines Agency pre-authorisation procedural advice for users of the centralised procedure document, *3.4.4.9. What information will be made public on the EU web-portal regarding pharmacovigilance contact details and PSMF locations? Will details of the QPPV be made public? (Jan 2016).*

5.11.4.4. Pharmacovigilance System Master File (PSMF) number

Question: What is the Pharmacovigilance System Master File number and where/how can we obtain it?

Answer: The Pharmacovigilance System Master File (PSMF) number is a unique code (MFL EV Code) assigned by the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD) to a specific PSMF and PSMF location. Please refer to section *1.11. Initial submission of a Pharmacovigilance System Master File (PSMF) information* of Chapter 3.II: XEVPRM User Guidance for further information.

5.11.4.5. Timelines for submission of a PSMF

Question: When should we request a PSMF number?

Answer: As per section *3.4.4.4. Pharmacovigilance system master file number (PSMF)* available in the European Medicines Agency pre-authorisation procedural advice for users of the centralised procedure: *"Applicants are encouraged to request a PSMF number (MFL EVCODE) in advance of the marketing authorisation application. If available, the PSMF number (MFL EVCODE) assigned by the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD) should be included in the statement in module 1.8.1. However, this information is not part of the compulsory elements per Article 8(3)(ia) of Directive 2001/3/EC".*

5.11.4.6. Referencing a PSMFL within an AMP entity

Question: We received an EV Code for our PSMFL, how can we reference it in our AMP entities in the XEVMPD? Can the submission of information on the PSMF location be done for all medicinal products, or shall we have to submit it for all our products impacted separately?

Answer: Regarding the electronic submission of the information on the PSMF location, the same Master File Location EV Code should be referenced in the XEVMPD in all medicinal products covered by the same pharmacovigilance system described in the same pharmacovigilance system master file declared at the one location within the European Union.

For related information see section *1.2.6. Pharmacovigilance System Master File Location (PSMFL) code (AP.6)* of Chapter 3.II: XEVPRM User Guidance.

5.11.4.7. Sharing a PSMFL EV Code between organisations

Question: Because our company is involved with business partnerships, we have 4 organisation IDs through which we submit messages. Can a PSMF EV Code that we received by the EMA through the acknowledgement process for one organisation ID be used for future XEVMPD messages for another organization ID? Or are PSMF EV Codes unique to each organization ID?

Answer: Each PSMFL entity in the XEVMPD is owned in the XEVMPD by the **Headquarter** (HQ) organisation ID of the organisation that submitted it. Therefore, it the four organisations are registered in EV under one HQ organisation, then it is possible to reference the same PSMFL entity in all product entries submitted from the various affiliate IDs. However, if the 4 organisations are registered in EV as stand-alone HQs, then each HQ will own their own PSMFL EV Code, which can only be referenced in AMP entries owned in the XEVMPD by that HQ.

Please refer to the below sections of Chapter 3.II: XEVPRM User Guidance for related information:

- *Table 5 – Requesting a single/multiple PSMFL EV Code(s) by the same MAH;* and
- *Table 6 – Requesting a single/multiple PSMFL EV Code(s) by the different MAHs.*

5.12. Substance information

5.12.1. Which substance information is to be submitted for an AMP entity

Question: What types of substances are to be captured in an authorised medicinal product entity?

Answer: All types of substances as reflected in sections *2. Qualitative and Quantitative Composition* and *6.1. List of excipients* of the SmPC [i.e. active substance(s) and/or adjuvants and/or excipients] must be specified in the relevant pharmaceutical product(s) of the AMP entity.

5.12.2. How should substance information be referenced within an AMP entity

Question: How are substances to be referenced in an AMP entity?

Answer: Please refer to *NOTE 9* of Chapter 3.II: XEVPRM User Guidance.

5.12.3. Submission of substances with multiple components

Question: For one of our AMPs, section 6.1 of the SmPC states "Opaque (containing Titanium dioxide, Lactose monohydrate, Polyethylene glycol, Macrogol 3000)". In the drug ingredient section within the XEVPRM, do we have to submit only the substance names in the parenthesis?

Answer: Please refer to *Note 10* of Chapter 3.II: XEVPRM User Guidance with regards to submission of substances containing multiple components.

5.12.4. Submission of synonyms within an AMP entity

Question: In case an SmPC references a synonym of an approved substance name, for example, "Iron oxide red" or "Red iron oxide", should we request for a new substance entity to be created in the XEVMPD for the different name, or can a substance with a similar EV Code be referenced in the AMP?

Answer: Please note that in this case, no new substance entity would be created as "Iron oxide red" and "Red iron oxide" are synonyms of the preferred substance name "IRON OXIDE RED (E172)" which is already available in the XEVMPD with the master substance EV Code SUB23080. You should therefore request that these names are added **as synonyms** of the preferred substance SUB23080 by following the process described in section *1.4. Initial submission of an approved substance* of Chapter 3.II: XEVPRM User Guidance.

See also the document European Medicines Agency substance names best practice: Procedure and principles to handle substance name in the substance management system for further information.

5.12.5. Substance names

Question: Description & coding of approved substance names should be submitted to the XEVMPD as stated in the SmPC or in the extract from the Module 3 dossier. Can we use an equivalent naming for one product to harmonize data entity across licenses and avoid creation of many new substance names for a unique ingredient?

Answer: Please refer to section *1.2.17.3 Pharmaceutical product drug ingredients and medical device(s)* and *NOTE 9* of Chapter 3.II: XEVPRM User Guidance for related information.

5.12.6. Availability of substance translations/aliases in EVWEB/substance Controlled Vocabulary

Question: Can you clarify where Gateway/EVWEB users can view the list of available synonyms/translations?

Answer: In EVWEB, substance translations and aliases are available within the approved substance entity, in sections "Substance translations" and "Substance Aliases". Simple or advanced query can also be performed on the requested substance name.

The SMS export of approved substances published on the SMS portal includes indication whether the substance name is a preferred name/alias or translation:

- **Preferred term**: Column C = TRUE
- **Alias:** Column C = FALSE & Column D = English or Latin
- **Translation:** Column C = FALSE & Column D = any other language

5.12.7. Description of the strength of the active substance(s)

Question: Can you please provide guidance on the description of the strength of active substance?

Answer: Please refer to *Table 3 - Requirements on how to reflect information on substance and strength in section 2. Qualitative and Quantitative Composition of the SmPC* and sections 1.2.17.4 Active ingredient substance code (PP.ACT.1) and *1.2.17.5 Active ingredient substance strength* of Chapter 3.II: XEVPRM User Guidance.

5.12.7.1. Description of the strength of a solution where the exact volume is unknown

Question: For authorised pharmaceutical dose forms such as effervescent tablets and granules in sachet, what should be the administrable pharmaceutical dose form and how should the strength of the active ingredient be defined? Typically, the administration instructions do not give a precise volume e.g. dissolve on half a glass of water. If the administrable pharmaceutical dose form is defined as the Oral Solution, then it is not possible to define strength as a concentration or with a suitable unit of presentation. However, if the authorised pharmaceutical dose form is also used as the administrable pharmaceutical dose form, then it does not recognise the reconstitution step.

Could you please advise how such cases should be handled?

Answer: For the authorised pharmaceutical forms such as 'effervescent tablets' and 'granules in sachet', the administrable pharmaceutical form is 'oral solution'. If it is not possible to express the strength of the oral solution with a suitable concentration or unit of presentation, the XEVMPD unit value (of measurement) 'each' (XEVMPD unit code = 1) should be used to describe the strength of the oral solution. See example below:

Administrable dose = 200 mg in an unknown volume (e.g. dissolve on half a glass of water)

Numerator value: 200

Numerator prefix: milli

Numerator unit: gram(s)

Denominator value: 1

Denominator prefix: single

Denominator unit (of measurement): each (XEVMPD unit code = 1)

See section *1.2.17.5 Active ingredient substance strength* of Chapter 3.II: XEVPRM User Guidance for related information.

5.12.8. Reference strength

Question: How should we submit substance information in case that that section 2. Qualitative and quantitative composition of the SmPC contains e.g. "*Each tablet contains Fluoxetine 20 mg as fluoxetinehydrochloride*"?

Answer: Please refer to *Note 11* of Chapter 3.II: XEVPRM User Guidance. With regards to your example, the strength of the active ingredient should be expressed as 20 mg of fluoxetine per one single tablet.

5.12.9. Submission of 'trace' substances

Question: Should substances present as "traces" in AMPs (in accordance with the contents of the SmPC) be submitted to the XEVMPD?

Answer: Substances which may be present in the medicinal product as traces (e.g. substances used during the manufacturing process) should not be entered in the composition of the medicinal product in the XEVPRM.

5.12.10. Unavailability of a substance name

Question: The substance name we need to use in our AMP entity was not found in EVWEB, so I have inserted a new substance in our XEVPRM and submitted it in the XEVMPD via Gateway. We received a negative acknowledgement. Can you please clarify why we received this ACK?

Answer: As stated in section *1.4. Initial submission of an approved substance* of Chapter 3.II: XEVPRM User Guidance only the EMA can insert/update substance entities in the XEVMPD. XEVPRM messages submitted from MAHs/sponsors and containing operation type 'Insert (1)', 'Update (2)' or 'Nullification (4)' of a substance entity will be rejected and will generate a negative XEVPRM acknowledgement.

5.12.11. Missing substances

Question: If a substance, which we need to use in our medicinal product entity, is missing in the XEVMPD, how should we request it to be added?

Answer: You should follow the process described in section *1.4 Initial submission of an Approved Substance* of Chapter 3.II: XEVPRM User Guidance.

5.12.12. Definition of substance class

Question: Could you please provide a detailed definition of the three values 'mixture', 'single' and 'specified substance'? What is expected to be entered if none of these three values is applicable?

Answer: The definitions of substance classes are provided in Chapter 6 of the Guidance documents related to data submission for authorised medicines website. EV-Post and Gateway users should also refer to the EudraVigilance eXtended Medicinal Product Dictionary (XEVMPD) substance classes controlled vocabulary.

5.12.12.1. Substance class: polymers

Question: The Substance class 'Polymer' is defined as a type of polydisperse substance that contains structural repeating units linked by covalent bound. Heparin sodium is the sodium salt of the heparin. Heparin is an anionic polysaccharide. What is the best option to classify Heparin sodium: Polymer or Chemical?

Answer: Heparin sodium should be classified as 'Polymer'.

5.12.12.2. Substance class: herbals/homeopathics

Question: What is the correct substance class for herbals/homeopathics?

Answer: The definition for herbals is provided in the 'Guideline on declaration of herbal substances and herbal preparations in herbal medicinal products /traditional herbal medicinal products'.

- For plant Latin names and where the part of the plant is described in the name, the class is: 'Structurally Diverse Substance – Herbal' (code=9)

  E.g. Valeriana Officinalis radix

- For herbal/homeopathic preparations where the form/extract or the potency is defined in the name, the class is 'Specified Substance Group 1' (Code=13)

  E.g. Arnica Montana D12, Valeriana Officinalis Radix dry extract

- For herbal/homeopathic preparation where the manufacturing process and manufacturer is described in the name, the class is 'Specified Substance Group 2' (Code=14)

  E.g. Valeriana Officinalis Radix dry extract macerated Company X

- For herbal/homeopathic preparations where the monograph is described in the name the class is 'Specified Substance Group 3' (Code=15)

  E.g. Valerina Officinalis Ph. Eur. Monograph XXX

5.12.12.3. Substance class: chemical

Question: The substance class 'chemical' is defined in the Detailed Guidance - Chapter 6, as a type of substance defined by a single molecular structure that is not a protein or a nucleic acid substance. Please confirm that the origin of the substance should not be taken into account for the substance class and consequently, an amino-acid is a chemical substance even if it is of biological origin.

Answer: According to the definition in Chapter 6 of the Guidance documents related to data submission for authorised medicines website, an amino acid can only be classified as a 'chemical' as it does not fall under the definition of any other class.

5.12.13. Description of the strength of the excipient(s)

Question: The Legal Notice on the Implementation of Article 57(2) of Regulation (EC) No. 726/2004 requires the description of active ingredient(s) and excipient(s) for the electronic submission of information on medicines. Does the amount of all excipients have to be described as a kind of composition, or is it enough to specify only the quantity of API? If the quantity of all excipients has to be provided, will this data accessible to everybody (e.g. patients and different companies, NCAs etc.)?

Answer: It is optional to describe the strength(s) of excipient(s). If this information is provided, the strength(s) of the excipient(s) as listed in section 6.1 List of excipients of the corresponding SmPC must be specified in the pharmaceutical product. Please refer to section *1.2.17.9 Excipient substance strength* of Chapter 3.II: XEVPRM User Guidance.

If the strength of the excipient is provided, it will be visible to EVWEB users registered with EudraVigilance as per the applicable visibility rights.

5.12.14. Description of the strength of adjuvant(s)

Question: Whilst it is mandatory to include information on adjuvants in the pharmaceutical product of an AMP entity, adjuvant's strength is not mentioned in Section 2 of the attached SmPC. In accordance with the SmPC guideline, it is not required to state the adjuvant in a quantitative way. How should we

submit information on the amount of the adjuvant in the XEVMPD? Can we include the strength as captured in our internal database?

Answer: The strength of the adjuvant can be based on the information you own, even if not reported in the SmPC. However, please note that if the strength of the adjuvant is provided in an AMP entry and the AMP entry is flagged as validated in EVWEB by the EMA, then this information will be visible to all EVWEB users registered with EudraVigilance. If the strength of the adjuvant substance is not mentioned in the SmPC and you do not wish to disclose the information, you should specify the concentration of the adjuvant substance as 0 grams.

5.12.15. Substance reference source

Question: Is it possible to specify more than one reference source for a substance? Some of our products contain more than one monograph, from more than one reference source. If the substance to be added is not referenced in any monograph, but only in the marketing authorisation dossier, what should we reference as the substance source.

Answer: The reference source field within the substance entity is not repeatable in the XEVPRM schema. Nevertheless, you may provide more than one reference source in your request to insert a substance/alias; the EMA will select the most suitable reference source to be referenced in the substance.

If the substance is not referenced in any monograph, but only in the marketing authorisation dossier, the reference source 'Company Specification' (SRC528) can be referenced as the substance source.

5.12.16. Submission of E Numbers for excipients

Question: How does the EMA handle E numbers that refer to excipients?

Answer: An E number as such may be requested to be inserted as an alias of the corresponding approved substance in the XEVMPD. If an excipient is already present in the XEVMPD without the E number, then the substance name with the E number can be requested to be inserted as an alias of the preferred substance.

5.12.17. Homeopathic substances

Question: For registered homeopathic substances the same registration number can correspond to a series of dilutions, different types of dilutions (CH, DH, K, LM) as well as several pharmaceutical forms. Would the XEVPRM structure consider those specificities?

Answer: In the XEVMPD, homeopathic/herbal preparations are classified as Specified substances (Group 1, 2, 3 depending on the type of substance). Each substance name containing additional information is inserted as a new substance.

E.g. the following are all different entities: Agnus Castus D6, Agnus Castus Dil D6, Agnus Castus Trit D 6, Agnus Castus (Ø 10%) D6, Agnus Castus Trit D6 (HAB 34).

The same applies for different dilutions and forms: Arnica Montana D14, Arnica Montana D12, Valeriana Officinalis Radix dry extract, Valeriana Officinalis Radix Tincture.

5.12.17.1. Expression of strength for homeopathic substances

Question: We are unsure how to submit substance information for a homeopathic product containing 15 mg of Arnica Montana D4 per tablet. Also, can a homeopathic substance be entered for a substance name or for the strength of the medicinal product? E.g. "1 tablet contains 0.1 gram of Galium aparine 4X". How should the strength be submitted in the XEVPRM? How do I express the potency in the substance?

Answer: The strength of the homeopathic preparation is 15 mg per tablet (*15mg/Tablet*). The potency of the homeopathic preparation should be reflected in the substance name (e.g. Arnica Montana D4).

As regards your second example, the potency of the homeopathic substance should be stated as part of the substance name e.g. Galium aparine 4X. The quantity of the homeopathic substance should be stated as the strength of the medicinal product e.g. 0.1 gram/tablet.

5.12.18. Submission of water for injection with tween 80

Question: One of our ingredients is "Water for injection with Tween 80". Should we submit it as one or two substances?

Answer: Two approved substances (i.e. "Water for injection" and "Tween 80") should be referenced in your medicinal product submission.

5.12.19. Submission of substance information as per Module 3 dossier

Question: In our AMP record in the Article 57 database, we referenced two substance names not as they are referenced in the SmPC but in accordance with information in Module 3 as these substances are similar to substances with SVG flag 1 in SMS. We attached to the Art57 product record the SmPC as a reference document. During the validation of the AMP, EMA data stewards updated the product record to reference both substances as they are stated in the SmPC; both substances are flagged in the SMS with SVG flag 0. Can you please clarify the rationale for this change?

Answer: EMA data stewards validate the AMP information submitted in the Art57 database by the MAH against the document(s) attached to the product entry by the MAH. If only the SmPC was attached to the product entry by the MAH, the validation was performed against the information in the SmPC.

If the MAH wishes to reference in the AMP entry the substance information as it is provided in Module 3, then the MAH should also provide an extract of the Module 3 dossier, showing the substance information for the medicinal product. Please also note that in this case, all substance information referenced in the AMP record [substance name(s) and concentration(s)] should be provided in the AMP entry as they are stated in Module 3. This will enable EMA data stewards to validate the information in consistency with the "source of truth" thus ensuring traceability and auditability of the data.

5.12.19.1. New: Module 3 extract to be provided to XEVMPD

Question: According to the most recent XEVMPD guidance, the composition of the pharmaceutical product can be submitted in the Article 57 database in accordance with Module 3 dossier; what module should be provided in the XEVMPD as an attachment? 3.2.P.1? Will this document be considered confidential?

Answer: Yes, the extract of section 3.2.P.1 Description and Composition of the Drug Product (name, dosage form) should be provided. Documents submitted as attachments in the XEVMPD are visible in

the XEVMPD only to the users from the organisation that owns that attachment/product in the XEVMPD and to the EMA.

5.13. Structured substance information (SSI)

Question: Is the SSI mandatory? If yes, can you provide a clarification on when specifically a SSG1, SSG2 or SSG3 should be included?

Answer: Marketing authorisation holders should not currently submit SSI in the XEVMPD.

5.14. Authorised/administrable pharmaceutical Forms

5.14.1. Submission of multiple authorised/administrable pharmaceutical forms within one medicinal product

Question: Our product is a gelatine capsule containing 3 tablets. How can we insert this in the pharmaceutical product section? What is the administrable pharmaceutical dose form of the product; gelatine capsule or the tablet?

Answer: If the tablets are within one capsule which is the entity administered to the patient, then the administered pharmaceutical dose form is the "capsule". Information on the distinct sub-tablets should not be provided. Therefore, the medicinal product needs to be provided with one pharmaceutical product with the dose form of the gelatine capsule; all the active and inactive ingredients (i.e. excipients) of the 3 tablets should be listed in the ingredient section of the XEVPRM altogether regardless of which tablet they are from.

If the capsule is to be opened before administration and the 3 tablets are administered separately, the authorised pharmaceutical form will have to be "capsule" and 3 administrable pharmaceutical form sections will need to be created ("tablet" three times), each of them listing the active ingredients and excipients part of the specific tablet. The standard EDQM term of the required pharmaceutical form should be reference whenever possible.

5.14.2. Submission of products where multiple authorised pharmaceutical forms are present

Question: This question is relative to the rules applying to the case of products where the SmPC states more than one authorised pharmaceutical form.

EXAMPLE A

3. Pharmaceutical form

Solution for injection.

Concentrate for solution for infusion.

Please indicate what the XEVMPD rules required are in the above case.

Answer 2: Two authorised pharmaceutical forms should be entered in the XEVMPD ("solution for injection" and "concentrate for solution for infusion"), whereas only one administrable pharmaceutical form should be specified, as the product is not a kit but a single preparation that can be used in two ways. In this case, the preferred option for the single administrable pharmaceutical form would be a term acting as a common denominator between the two authorised pharmaceutical forms, such as "solution for injection/infusion".

When it is not possible to find such a term (see example B below), only one of two authorised pharmaceutical forms should be used to populate the "Administrable Pharmaceutical Form" field.

EXAMPLE B

3. Pharmaceutical form

Solution for injection.

Oral solution.

As a suitable term acting as a common denominator between the two authorised pharmaceutical forms (like "solution" would be) is not available in the CV as a standard pharmaceutical dose form term, either "solution for injection" **or** "oral solution" should be specified as the administrable pharmaceutical form.

Multiple administrable pharmaceutical forms should only be created when different administrable pharmaceutical forms are physically present within the same product (e.g. cream and pessary in the same package) or when a product contains multiple identical pharmaceutical forms having different compositions (e.g. combined oral contraceptive tablets), as demonstrated in the following example:

EXAMPLE C

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Prodemaz® contains three different active ingredients. Each active ingredient is present in its own dosage form:

1 gastro-resistant tablet (yellow) contains 40 mg pantoprazole for oral use

1 film-coated tablet (white) contains 1000 mg amoxicillin for oral use

1 film-coated tablet (light yellow) contains 500 mg of clarithromycin for oral use

3. PHARMACEUTICAL FORM

Combination package with:

Gastro-resistant tablets: yellow, oval biconvex tablets

Film-coated tablets: white, oblong film-coated tablets with one-sided score line

Film-coated tablets: light yellow, oval film-coated tablets

In this case, the authorised pharmaceutical form should be specified as "gastro-resistant tablet" **and** "film-coated tablet", and three administrable pharmaceutical forms should be created as the product is a combination package and not a single preparation. These should be 1) "gastro-resistant tablet" (with pantoprazole as the active ingredient), 2) "film-coated tablet" (with amoxicillin) and 3) "film-coated tablet" (with clarithromycin).

5.14.3. Authorised/administrable pharmaceutical form not available in the XEVMPD

Question: How should a pharmaceutical form be provided if the standard term is not available in the XEVMPD?

Answer: Please refer to the below sections of Chapter 3.II: XEVPRM User Guidance:

- *1.2.14. Authorised pharmaceutical form (AP.APT.1);*

- *1.2.17.1 Administrable Pharmaceutical Form (PP.1);*
- *1.8 Initial submission of an Authorised/Administrable Pharmaceutical Form.*

5.14.4. Use of deprecated authorised/administrable pharmaceutical form terms

Question: Can we use deprecated pharmaceutical forms in our AMP entities?

Answer: Please note that in the context of improvement of the XEVMPD controlled vocabulary data quality, as of 2nd of August 2013, the XEVMPD privileges and rights were modified to allow MAHs to reference deprecated pharmaceutical forms within their authorised medicinal products to facilitate the Article 57(2) electronic submission of information on medicines. You can therefore use deprecated terms in your product entities. However, please note that the use of deprecated terms is discouraged; a supplementary term to be used instead of a deprecated term is available to registered users on the EDQM website.

5.14.5. Submission of medicinal products where the container/device is part of the pharmaceutical form name

Question: This question is relative to the rules applying to the case of products where the container/device is mentioned in the pharmaceutical form section of the SmPC (e.g. solution for injection in pre-filled syringe). Please indicate what the XEVMPD rules required are in the above case.

Answer: As the administrable pharmaceutical form refers to the pharmaceutical form for administration to the patient, it should preferably not include information on the container/device. Therefore, whilst the "Authorised Pharmaceutical Form" (AP.APT.1) should be specified as "solution for injection in pre-filled syringe", the "Administrable Pharmaceutical Form" (PP.1) should be specified only as "solution for injection".

5.15. Route(s) of administration

5.15.1. Multiple routes of administration

Question: Is the route of administration a mandatory field in which only one entity can be reference? What if a pharmaceutical product can be administered in two different ways?

Answer: The route of administration is a repeatable XEVPRM section and therefore multiple routes of administration can be referenced within one pharmaceutical product if applicable.

5.15.2. Route of administration not available in the XEVMPD

Question: How should a route of administration be provided if the standard term is not available in the XEVMPD?

Answer: Please refer to the below sections of Chapter 3.II: XEVPRM User Guidance:

- *1.2.17.2 Administration route (PP.AR.1);*
- *1.9 Initial Submission of a Route of Administration (RoA).*

5.15.3. Use of deprecated terms – route of administration

Question: Can we use deprecated routes of administration in our AMP entities?

Answer: Please note that in the context of improvement of the XEVMPD controlled vocabulary data quality, as of 2nd of August 2013, the XEVMPD privileges and rights were modified to allow MAHs to reference deprecated routes of administration within their authorised medicinal products to facilitate the Article 57(2) electronic submission of information on medicines. You can therefore use deprecated terms in your product entities. However, please note that the use of deprecated terms is discouraged; a supplementary term to be used instead of a deprecated term is available to registered users on the EDQM website.

5.16. Medical devices

Question: Can you please confirm that the use of medical devices in AMPs is only applicable to advanced therapy products?

Answer: The Legal Notice states that the medical device description is currently only required for ATMPs where applicable: *'A description of the medical device(s) in accordance with Regulation (EC) No 1394/2007 as applicable'.*

5.17. ATC Codes

5.17.1. ATC Code not assigned or not applicable

Question: When creating an XEVPRM with product data, what shall we insert in a product if the ATC Code is not assigned or not applicable?

Answer: Please refer to section *1.2.18 Product ATC Code(s) (AP.ATC.1)* of Chapter 3.II: XEVPRM User Guidance for information on how to proceed in this case.

5.17.2. ATC Code not available in the ATC Index

Question: Some of our medicinal products have an ATC Code, which cannot be found in the ATC Index published by the WHO. However, this ATC code is available in the list of ATC Codes published in Germany. How should we provide this information?

Answer: If the ATC Code for a medicinal product is not part of the ATC Index published by the WHO, the ATC Code should be provided as a "proposed term" via the XEVPRM.

Please refer to section *1.7 Initial submission of an ATC Code* of Chapter 3.II: XEVPRM User Guidance for information on how to request the submission of a proposed ATC Code in the XEVMPD.

5.17.3. ATC Code not available in the XEVMPD

Question: An ATC Code already published by the WHO is not available in the XEVMPD ATC Code look-up list. How can we reference this ATC Code in our product entity?

Answer: If a standard ATC Code is missing in the XEVMPD, you should request the addition of the ATC Code in the XEVMPD by following the process described in section *1.7 Initial submission of an ATC Code* of Chapter 3.II: XEVPRM User Guidance.

5.17.4. Required levels of ATC Codes

Question: Old EVMPD required 3 levels of ATC. Is this still sufficient for the XEVMPD?

Answer: All five levels of the ATC code can be used. The most specific ATC code in relation to the medicinal product needs to be specified.

5.17.5. Multiple ATC Codes in one XEVMPD product entity

Question: What shall we do in case where multiple ATC Codes are applicable for one medicinal product?

Answer: The ATC Code is repeatable section in the XEVMPRM schema. Several ATC Codes can therefore be referenced in one product entity.

5.17.6. Use of deprecated terms – ATC Codes

Question: Can we use deprecated ATC Codes in our AMP entities?

Answer: Please note that in the context of improvement of the XEVMPD Controlled Vocabulary data quality, as of 2 August 2013, the XEVMPD privileges and rights were modified to allow MAHs to reference deprecated ATC Codes within their Authorised Medicinal Products to facilitate the Article 57(2) electronic submission of information on medicines. You can therefore use deprecated terms in your product entities.

5.18. Controlled vocabularies (CVs)

5.18.1. Availability of controlled vocabularies

Question: Where can we find the list of Controlled Vocabularies to support XEVPRM submissions?

Answer:

- See the controlled vocabularies published in section *'Controlled vocabularies'* on the Guidance documents related to data submission for authorised medicines webpage. Please note that some of these files are no longer updated. Instead, MAHs should check the respective SPOR portal to obtain he most up-to-date information:
  - List of substances is available in the substance export lists (current and non-current) published in the Substance Management System (SMS) portal.
  - Organisation EV Codes can be found in the 'Mappings' section of the respective organisation on the Organisation Management System (OMS) portal.
  - EV Codes of referential terms can be found in the 'Mappings' section of the respective term on the Referentials Management System (RMS) portal.
- A copy of MedDRA needs to be obtained from the MedDRA.
- ATC Codes need be obtained from the WHO Collaborating Centre for Drug Statistics Methodology.
- Pharmaceutical forms and routes of administration are based on the standard terms published by the European Directorate for the Quality of Medicines & HealthCare (EDQM).
- The Unified Code for Units of Measure (UCUM) is maintained by the Regenstrief institute.

- The official list of ISO 3166-1 country codes is maintained by the International Organization for Standardization (ISO).
- The official list of ISO 639-1:2002 codes for the representation of names of languages: Part 1: Alpha-2 code is maintained by the International Organization for Standardization (ISO).

5.18.2. Format of CV lists published by the EMA

Question: The CV lists are currently published in an Excel format. Could they be provided in a different format?

Answer: The controlled vocabularies maintained by the Agency are published only in Excel format. However, marketing-authorisation holders can convert the CVs from Excel to the most suitable format to best suit their needs.

5.18.3. Medical device list

Question: Will a medical device table similar to the controlled vocabulary for substances be provided by the EMA? Also, the EMA technical specifications specify an integer for a medical device code, yet there is nothing in the existing CVs to define what that integer should be. Will this potentially be an integer of 0-9 with associated medical device types?

Answer: The Legal Notice states that the medical device description is currently only required for advanced therapy medicinal products (ATMPs), where applicable: "*A description of the medical device(s) in accordance with Regulation (EC) No 1394/2007 as applicable".*

Where a medical device term is required for an ATMP, the marketing-authorisation holder needs to send a request for a **term assignment** via the EMA Service Desk portal (https://servicedesk.ema.europa.eu) and the Agency will provide a code and term for the medical device to the marketing-authorisation holder.

The list of available medical devices with their assigned codes is available as part of the controlled vocabularies published on the Guidance documents related to data submission for authorised medicines webpage, in the 'EudraVigilance eXtended Medicinal Product Dictionary (XEVMPD) medical devices' file.

5.18.4. Country codes CV list

Question: Which country code should be used for United Kingdom; GB or UK? Where can we find the official list of country codes?

Answer: Please refer to *NOTE 2* of Chapter 3.II: XEVPRM User Guidance. The official list of ISO 3166-1 country codes is maintained by the International Organization for Standardization (ISO).

5.18.5. Organisations CV list

Question: Which organisations are available in the 'EudraVigilance eXtended Medicinal Product Dictionary (XEVMPD) organisations' list published on the on the Guidance documents related to data submission for authorised medicines webpage? Is it list of organisations registered with EudraVigilance?

Answer: The list contains details of marketing authorisation holder organisations available in the XEVMPD. Please note that this list is not maintained since February 2023. To retrieve MAH organisation information, including the EV Code assigned to that organisation, you should either

- search for the organisation information in EVWEB, in the 'MAH' remote look-up table; or
- perform a search for the organisation on the Organisation Management System (OMS) portal; organisation EV Codes can be found in the 'Mappings' section of the respective organisation in OMS.

5.19. MedDRA

5.19.1. Implementation of MedDRA terminology

Question: Since it is mandatory to code all indications as described in the SmPC, can you please provide more specific details about the implementation of MedDRA terminology regarding the therapeutic indication(s)?

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

Best practice for coding of indications based on information in section 4.1 of the SmPC is available in the 'Coding of indications in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD)' document published on the Guidance documents related to data submission for authorised medicines webpage.

Information on how to reference MedDRA coding information in your AMP records in the XEVMPD is available in section *1.2.19. AMP - Product Indications (AP.INDs)* of Chapter 3.II: XEVPRM User Guidance.

5.19.2. MedDRA coding consistency

Question: How will consistency of MedDRA coding be established across industry and within XEVMPD? What granularity of coding is required for utility of MedDRA codes? Can PT or higher terms be used?

Answer: Low Level Terms (LLT) must be referenced in an AMP entity in the XEVMPD. Best practice for coding of indications based on information in section 4.1 of the SmPC is available in the 'Coding of indications in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD)' document published on the Guidance documents related to data submission for authorised medicines webpage.

Information on how to reference MedDRA coding information in your AMP records in the XEVMPD is available in section *1.2.19. AMP - Product Indications (AP.INDs)* of Chapter 3.II: XEVPRM User Guidance.

The EMA validation team checks and, where necessary, corrects the indication information as part of the AMP validation process to ensure that this information is aligned with information in section 4.1 of the SmPC. See the 'Measures for Article 57 data quality assurance' document for further information.

If the MAH does not agree with the changes performed as part of the AMP validation, or in case of questions related to why a certain MedDRA term was referenced in an AMP entry during the validation, the MAH should submit a ticket via the EMA Service Desk.

- Please raise a Request for information to submit your question(s);

- in the 'Service' section of the form, reference: '*SPOR*',
- in the 'Service offering' section of the form, reference: '*XEVMPD/Art.57*';

- please raise a Request XEVMPD/Art.57 Services to submit your request for correction in case the MAH does not agree with the change(s) performed by the EMA validation team as part of the AMP validation.

5.19.3. Multiple terms in MedDRA

Question: There are many indications for products registered where qualifiers cannot be reflected by selecting one single MedDRA term. Are multiple terms permitted to cover the medical concept of the indication? Or, if there is no direct match does the nearest approaching term must be selected or the creation of a new term must be requested at MedDRA?

Example: Therapeutic indication: newly diagnosed Philadelphia chromosome positive chronic myeloid leukaemia (Ph+CML) MedDRA 14.1 LLT name: LLT-Philadelphia chromosome positive and HLT-Leukaemias chronic myeloid or LLT-Chronic myeloid leukaemia only.

Issue: Multiple terms to code an indication is not allowed (at least for AE reporting) so here only the LLT-Chronic myeloid leukaemia would be coded.

Answer: 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. underlying disease) will be possible with the implementation of the ISO IDMP standards. See examples in section *1.2.19. AMP - Product Indications (AP.INDs)* of Chapter 3.II: XEVPRM User Guidance.

5.19.4. Use of old MedDRA version(s)

Question: Which previous version of MedDRA is accepted for coding of indications? Will we need to update or medicinal product entities when a new version of MedDRA becomes available?

Answer: Please refer to section *1.2.19.1. MedDRA version (AP.IND.1)* of Chapter 3.II: XEVPRM User Guidance.

5.19.5. Indications for MRPs

Question: For an MRP, which is a generic product in a specific country, there might be a certain indication under patent. This would mean that the English Core text contains all indications (i.e. 3 indications), while the national translation contains one less (i.e. 2 indications). The additional indication would be added on a local level once the patent of the indication expires. Since 3 indications are approved on the MRP level, can you confirm that 3 indications should be entered in the AMP entity in the XEVMPD?

Answer: For MRPs where approved indications are captured in the core English SmPC but not in the national SmPC due to patent reasons, the indications should be captured as indications approved in the country of authorisation and as indicated in the national SmPC/PIL. For MRPs where the English core text contains three indications and the national SmPC contains only two indications, only two indications should be captured in the corresponding AMP entry in the XEVMPD.

6. MAINTENANCE OF MEDICINAL PRODUCT DATA

6.1. Medicinal product data ownership

Question: Who can perform updates of our medicinal product data entities submitted to the XEVMPD?

Answer: Medicinal product information submitted in the XEVMPD via an XEVPRM is "owned" in the XEVMPD by the HQ of the organisation that submitted the information. An organisation may be registered in EudraVigilance as a HQ, or as an affiliate under a HQ profile. If an affiliate, that is registered under a HQ profile of an MAH/sponsor organisation in EudraVigilance, submitted a product or organisation entity in the XEVMPD via an XEVPRM, that product/organisation entity is owned in the XEVMPD by the HQ, not by the affiliate that submitted it. The maintenance operations that can technically be performed on XEVMPD entities are described in section *'1.7.4. Data ownership and maintenance'* of the 'eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD) Data-Entry Tool (EVWEB) user manual'.

In general, amendments to XEVMPD data can be performed by:

- the HQ organisation that owns the data in the XEVMPD;
- by the affiliate(s) registered under the owner HQ organisation;
- by the EMA.

6.2. Nullification of AMP entities flagged as "valid" by the EMA

Question: Why are MAHs unable to nullify AMPs which were flagged "valid" by the EMA? MAHs are the primary owners or their AMP entities and should therefore have the rights to nullify their products irrespectively of the EMA QC status/result.

Answer: AMP entity should only be nullified in case it's a duplicate of another existing record or an incorrectly submitted record. All AMP entities flagged as "valid" are used to support signal management activities (e.g. codification of ICSRs). Before they are nullified, the EMA needs to check that a "substitute" record is available in the XEVMPD. Therefore, only the EMA can nullify AMPs flagged as "valid".

To request a nullification of AMP entities validated by the EMA, please raise a Request XEVMPD/Art.57 Services via the EMA Service Desk. Please refer to *Process map 13 – Nullification of an AMP entity*, Step 4 of Chapter 3.II: XEVPRM User Guidance for further information. If nullification is requested for more than 10 entities, please provide the EV Codes in an Excel spreadsheet, one EV Code per cell.

6.3. Update of invalidated AMP entities

Question: MAHs should be able to update an AMP entity flagged as "invalid" for example to substitute the referenced MAH or amend the invalidated date. Why is it not allowed?

Answer: Operation type "Invalidate MA" is used to indicate a transfer/revocation/withdrawal or an expiry of the marketing authorisation. Once the marketing authorisation status of an AMP entity was set as invalid, there is no need to maintain such products. As an exception, the EMA can amend information within an invalidated AMP entity (i.e. "Authorisation Status" = "Not valid") on behalf of the MAH; for example, in case when incorrect data was referenced during the invalidation (e.g. wrong invalidation date or MA status was referenced). To request such amendments, the MAH should raise a Request XEVMPD/Art.57 Services via the EMA Service Desk.

6.4. Maintenance of product entities submitted in the EVPRM format

Question: Should we maintain product entities submitted to the 'old' EVMPD using the EVPRM format (i.e. Pre-Article 57 format)?

Answer: Medicinal products previously submitted using the old EVPRM format are considered legacy data. All EVMPD legacy data were migrated to the new XEVPRM format, and the Agency assumed the XEVMPD ownership of such data (i.e. of authorised medicinal products submitted in the XEVMPD using the previous EudraVigilance Product Report Message format (i.e. Pre Article 57 format) by referencing *'**Maintained by EMA**' (Organisation EV Code ORG15457)'* as the MAH in the concerned AMPs. This is to flag medicinal products which are not compliant with Article 57(2) and that should therefore not be maintained marketing-authorisation holders under the Article 57(2) obligations.

6.4.1. Timelines for notifications of changes by the MAH

Question: What are the timelines based on which marketing-authorisation holders need to notify the Agency of changes to marketing authorisations of authorised medicinal product entities submitted to the Agency in line with Article 57(2) requirements?

Answer: As referred to the Legal Notice, section *2. Timelines*, notification of variation to the term of marketing authorisation should be submitted within 30 calendar days from the date of variation authorisation.

For CAPs, the notification is subject to the availability of the updated Product Information in all EU languages, and it should be submitted within 30 calendar days from the date of variation authorisation or finalisation of the linguistic review of the Product Information, whichever occurs last. For such products, the authorisation refers to the date of the CHMP Opinion or of the Commission Decision following the CHMP Opinion, when there is one.

Examples of the variation authorisation date are available in section *2.1 Transition maintenance phase - Electronic submission plan* of Chapter 3.II: XEVPRM User Guidance.

6.4.1.1. Start of 30 calendar day timeline following Type IB variation where implementation is delayed

Question: In accordance with the published guidance, MAHs are obliged to submit information on any changes to the terms of the marketing authorisations following variation, transfer, renewal, suspension, revocation or withdrawal of the MA "*as soon as possible and no later than 30 calendar days from the date of which the changes have been authorised by the NCA*" What should be a submission date for a variation Type IB when the NCA gives the MAH 6 months for the implementation of the variation?

Answer: The compliance with the timelines stated in the Legal Notice [paragraph 2. Timelines section 2(d)] is subject to MAHs receiving a Marketing Authorisation document issued by the National Competent Authority (NCA).

Therefore, when the implementation of the variation is delayed, the 30-calendar day timeline applies from the date of receipt of the official document issued by the NCA.

6.5. Transfer of marketing authorisation

6.5.1. Notifications of transfer of marketing authorisations

Question: Can you please advise what is the process for notifying the EMA that the marketing authorisation for a medicinal product has been transferred to another marketing-authorisation holder?

Answer: Please refer to section *2.4.3. Transfer of marketing authorisation* of Chapter 3.II: XEVPRM User Guidance which contains information on the two available processes to be followed, depending on whether the transfer of MA occurred between organisations registered in EudraVigilance under separate headquarters or between organisations registered in EudraVigilance under the same headquarter.

6.5.1.1. Change in process to notify transfer of marketing authorisation between organisations registered in EudraVigilance under separate headquarters

Question: From January 2025, when notifying a transfer of marketing authorisation between organisations registered in EudraVigilance under separate headquarters we, as the former MAH, are required to reference as the MAH in the product entry that is being invalidated the new marketing authorisation holder. Can you please explain the rationale behind this change?

Answer: This change in process was introduced to prevent transfers of product entries in PMS to the incorrect MAH. Through this change, the MAH of the medicinal product in PMS will be amended and, once the new MA holder inserts the new product in XEVMPD, the EV Code of the medicinal product inserted in the XEVMPD by the new MAH will be linked to the relevant existing medicinal product in PMS. With this approach, all information provided by the former MAH in the product entry in PMS (such as manufacturers and MBOs), will be kept when the new MAH is assigned to the product entry in PMS.

6.5.1.2. Previous EV Code cannot be received or is unknown

Question: According to the process described in section *2.4.3.1. Transfer of marketing authorisation between organisations registered in EudraVigilance under separate headquarters* of Chapter 3.II the "former MAH" must communicate to the "new MAH" the EV Codes of the medicinal product entities for which he marketing authorisation has been transferred. What shall we do when the former MAH did not provide us with the EV Codes at the time of transfer and/or the former MAH organisation no longer exists, and we are unable to find out what the EV Codes were?

Answer: You can submit a request via the EMA Service Desk portal to request the previous EV Codes. The following information must be specified:

- medicinal product name;
- authorisation number as assigned to the previous MAH;
- authorisation country;
- name of the former MAH organisation.

If the EV Codes can be retrieved from the XEVMPD, they will be provided to you. If not, the new MAH can submit the transferred AMP with the 'Insert' (01) operation type and enter value "Valid" (1) in the data element "Authorisation status" (AP.12.3), as per information in the above referenced section of Chapter 3.II.

6.5.2. Change of AMP ownership following a transfer of marketing authorisations

Questions: Does the Agency still perform change of ownership of medicinal product entities for which we are no longer the owners in the XEVMPD due to MA transfer to another MAH?

Answer: No, the Agency no longer transfers the ownership of AMP entities to another MAH's organisation ID following MA transfer. MAHs should follow the applicable process described in section *2.4.3. Transfer of marketing authorisation* of Chapter 3.II: XEVPRM User Guidance.

6.5.3. Transfer of marketing authorisation following a MA renewal

Question: It seems that whenever a renewal has been issued, the renewal date should be stated. What to do when a medicinal product with authorization status *"Valid – Renewed Marketing Authorisation (8)"* is transferred to a new MAH? Do we have to insert a new medicinal product with authorization status *"Valid - Transferred Marketing Authorisation (9)"* and select the first authorization date or the renewal date?

Answer: When a medicinal product with authorisation status "*Valid – Renewed Marketing Authorisation (8)*" is transferred to a new MAH, the new MAH has to insert a new medicinal product with authorisation status *"Valid - Transferred Marketing Authorisation (9)"* as described in section *2.4.3 Transfer of marketing authorisation* of Chapter 3.II: XEVPRM User Guidance.

The applicable renewal/authorisation date should be provided in the field *"Authorisation/Renewal date (AP.12.5)"* as it is referenced in the SmPC, section *9. Date of first authorisation/renewal of the authorisation*.

6.5.4. Transfer of marketing authorisation to an affiliate registered under the same HQ in EudraVigilance

Question: In view of United Kingdom's withdrawal from the European Union we are transferring the marketing authorisations of our medicinal products from a UK based MAH to an affiliated MAH based in another member state. Both MAH organisations are registered in EudraVigilance under the same headquarter profile. Should we follow the standard procedure described in section *2.4.3 Transfer of marketing authorisation* of Chapter 3.II to notify the EMA of this transfer (i.e. invalidate the current AMP and re-insert the AMP as new) or is there another way?

Answer: For MA transfers within the same organisation (i.e.: organisations under the same EV headquarter), where product data ownership and further maintenance in the XEVMPD is not affected by the marketing authorisation transfer, a simplified process described in section *2.4.3.2. Transfer of marketing authorisation between organisations registered in EudraVigilance under the same headquarter* of Chapter 3.II: XEVPRM User Guidance may be followed by the MAH.

6.6. Variations

6.6.1. Notifications of variations

Question: How should we amend our medicinal products submitted in the XEVMPD per Article 57(2) requirements to provide the latest information following a variation procedure?

Answer: Please refer to the below sections of Chapter 3.II: XEVPRM User Guidance for the required guidance:

- *2.4.1. Variations of marketing authorisation;*
- *Transition maintenance phase - Electronic submission plan.*

6.6.2. Change of authorisation number following a variation

Question: In some countries, the MA number changes after approval of a variation. How should this change be notified to the Agency? Do we update the current AMP record with the new number of insert a new product entity?

Answer: Please refer to section *2.4.1.1. Business process - Authorisation number (AP.12.4) has changed following a variation* of Chapter 3.II: XEVPRM User Guidance for the required guidance.

6.6.3. Submission of XEVPRM following parallel variation procedures

Question: If two parallel applications are approved at approximately the same time, is it expected to report them as one change (with merged information) or as separate changes?

Answer: Marketing-authorisation holders should submit only one XEVPRM with the operation type 'Update' (2) to reflect all changes in the medicinal product entity.

6.6.4. Variation following a marketing authorisation transfer/renewal (with a new MA number)

Question: If an AMP is transferred or renewed (with new MA number), the record receives the status "Valid-Renewed/Transferred". What happens if there is a "usual" variation afterwards? Should the authorisation status remain "Valid-Renewed/Transferred" or should it be updated to "Valid"?

Answer: The authorisation status should remain as it was following the transfer of MA/renewal.

6.6.5. Notifications of QPPV details/PSMF location via Article 57 database

Question: According to the revised variation guidance *"Once the Article 57 database is functional, changes in QPPV, including contact details (telephone and fax numbers, postal address and email address) may be updated through the Article 57 database only (without the need for a variation). Where the MAH makes use of the possibility to update this information through the Article 57 database, the MAH must indicate in the marketing authorisation that the updated information of those particulars is included in the database."* Can you please confirm if it is now possible to change our QPPV via the Article 57 database without the need of a variation?

Answer: The EMA Management Board considered the Article 57 database functionality for notifying changes to the QPPV and PSMF at its December 2015 Management Board meeting. The Board agreed that the database is functional for the purpose of notifications of changes to the QPPV and PSMF information **from 1 February 2016**. From that date MAH organisations no longer need to notify EMA or national competent authorities (as applicable) of changes to the QPPV or PSMF data by submitting a type IA_{IN} variation. No final variation is required to notify an explicit cross reference to Article 57 as the source of QPPV and PSMF information.

In line with their legal obligations, MAH should continue to ensure their AMP entries in the Article 57 database are up-to-date and reference the QPPV and PSMF information.

6.7. Revocation/Withdrawal of marketing authorisation (MA)

Question: I would like to update our XEVMPD AMP entity to indicate that a marketing authorisation (MA) has been withdrawn. How do I proceed?

Answer: Please refer to section *2.4.6 Revocation/Withdrawal/Expiry of Marketing Authorisation (MA)* of Chapter 3.II: XEVPRM User Guidance.

6.7.1. Withdrawal date

Question: When we change the authorisation status of our AMP in the XEVMPD to "Not valid - Withdrawn by marketing-authorisation holder", a withdrawal date must be provided. Which date should be specified? There are many possible options:

- Should it be the date related to the withdrawal of the MA or withdrawal from the market?
- Or is this the date that the marketing-authorisation holder intends to withdraw the MA?
- Or is it the date that the NCA accepts the withdrawal (please note that a notification is not provided in every country)?
- Is it only in case of withdrawal due to recall?

We know that it should not be the date that the product is no longer in the market, as this is impossible to trace in the distribution supply chain at local pharmacies. Please clarify.

Answer: Please refer to section *1.2.12.12 Invalidated date (AP.12.12)* of Chapter 3.II: XEVPRM User Guidance.

6.7.2. Retrieval of withdrawn medicinal product entities

Question: Can you please advise how we can retrieve our withdrawn/invalidated AMP entities in EVWEB?

Answer: Withdrawn/invalidated AMP entities can be retrieved by using the advanced queries section in the XEVMPD Data entry tool (EVWEB). In the "Conditions" section of your "Owned Authorised Products' advanced query, the following fields must be selected:

- "Art57 format" must be selected (ticked); and
- "Invalid" must be selected (ticked) in "MA validity" field.

Gateway organisations can use the xEVMPD Export tool available to registered users in the EV Restricted area to extract the list of products owned in the XEVMPD.

6.8. Renewal of marketing authorisation

6.8.1. Change of authorisation number following a renewal

Question: In some countries, following the approval of renewals, the authorisation number changes. How should this be reflected in the XEVMPD product entities?

Answer: Please refer to section *2.4.4.2 Business process - Authorisation number (AP.12.4) has changed following a renewal* of Chapter 3.II: XEVPRM User Guidance.

6.8.2. Change of authorisation status when the authorisation number does not change following a renewal

Question: The guidance states that only the date should be amended when the MA number does not change following a renewal. What about the 'Authorisation Status'? Should it remain as 'Valid' or should the authorisation status be changed to 'Valid-Renewed'?

Answer: The authorisation state should remain as 'Valid (1)'.

6.8.3. Renewal date

Question: In some countries, the NCA does not grant an official date of approval of the renewal. The renewal is submitted but no official closure is provided. What should the MAH submit as the renewal date? Date of submission of the renewal (= 6 to 9 months before renewal), the 'Expected closure date' or 'Expected expiry date' of MA?

Answer: The renewal date should be specified as the date when the renewal takes effects (i.e. the date specified in the SmPC, section 9. Date of first authorisation/renewal of the authorisation).

6.8.4. Change of authorisation procedure following a referral

Question: One of our marketing authorisations has just been switched from national to MRP following a referral. This MA relates to 3 XEVMPD product entities (i.e. to 3 active EV Codes), each referencing an individual pack size in the 'Package description' field. Each of the package presentations has got the same registration number. The authorisation number assigned to this MA is unchanged. Should these XEVMPD product entities be amended using operation type 'Update' (2) (with unchanged national authorisation number in the field AP.12.4) or with 'Invalidate MA' (6) and inserted a new AMP entity with MRP authorisation procedure?

Answer: Please refer to section *2.4.5. Change of authorisation procedure following a referral* of Chapter 3.II: XEVPRM User Guidance for the process to follow.

6.9. (Lifting of) suspension of the marketing authorisation

Question: How should we amend our medicinal product entity in the XEVMPD to indicate that a suspension of marketing authorisation for our medicinal product has been lifted?

Answer: Please refer to section *2.4.2 (Lifting of) suspension of marketing authorisation* of Chapter 3.II: XEVPRM User Guidance for the process to follow.

6.10. SmPC updates

6.10.1. Update of medicinal product entity data elements following an update of the SmPC

Question: Which changes in the SmPC should trigger an update of our AMP entities in the XEVMPD?

Answer: An updated SmPC must be provided in the context of the data maintenance, i.e. when the variations lead to changes as listed in section *2.4.1 Variations of marketing authorisation* of Chapter 3.II: XEVPRM User Guidance. See also section *Transition maintenance phase - Electronic submission plan* of Chapter 3.II for related information. The relevant data elements within the authorised medicinal product entity must be amended as applicable.

6.10.2. Update of an AMP entity following an update of section 4.1 Therapeutic indications of the SmPC

Question: Should changes in section 4.1 Therapeutic indications of the SmPC, which do not have a direct impact on the MedDRA coding of the indication, trigger an update of SmPC and therefore an AMP entity update in the XEVMPD?

Answer: Yes, the change in section 4.1 Therapeutic indications of the SmPC should be followed by an update of an SmPC referenced in an AMP entity. The data elements within the authorised medicinal product entity however do not need to be amended.

6.11. Change of Pharmacovigilance contact details

Question: Our Pharmacovigilance email address and phone number have changed. How do we amend our XEVMPD product entities so that they contain the correct PhV Email and PhV phone number?

Answer: You should retrieve the AMP entities referencing the Pharmacovigilance details you wish to change and perform an operation type 'Update' (2) to replace the no longer valid email address and phone number with the latest contact information.

6.12. QPPV details

6.12.1.1. Change of QPPV

Question: A new QPPV was appointed in our organisation. How do we inform you of this change? Our products submitted in the XEVMPD will also need to be updated, how can this be done?

Answer: Please refer to section *2.1.2. Business process to notify a change of a QPPV* and *Process map 4 – Change of a QPPV* of Chapter 3.II: XEVPRM User Guidance describing the process applicable as of 26 July 2018.

6.12.1.2. Change of QPPV's details

Question: The surname of our QPPV has changed as well as her email address. How do notify the Agency of this change?

Answer: Please refer to section *2.1.1. Business process to notify the change of QPPV's details* of Chapter 3.II: XEVPRM User Guidance describing the process applicable as of 26 July 2018.

~~***6.12.1.3. Change of QPPV if they reside and carry out their tasks in the UK***~~

~~**Question:** Will our QPPV for all active authorised products have to change once the UK is no longer in the EU?~~

~~**Answer:** As stated in section *2.2. Should I update the address information in Art. 57 database for entities located in Northern Ireland* of the 'Questions and answers to Stakeholders on the implementation of the Protocol on Ireland/Northern Ireland' document: *"The companies are reminded that from 1 January 2021 for medicinal products authorised or registered in the EU/EEA the MAH, registration holder, QPPV and PSMF must be established in the EU/EEA".*~~

~~With regards to medicinal products with marketing authorisation valid in the territory of Northern Ireland, as stated in paragraph 3 of section *4. The location of the marketing authorisation holder and the qualified persons for manufacturing for pharmacovigilance with regard to medicinal products for*~~

~~*human use* of the Commission Notice – Application of the Union's pharmaceutical acquis in markets historically dependent on medicines supply from or through parts of the United Kingdom other than Northern Ireland: *"Where the marketing authorisation is granted by the competent authority of the United Kingdom in respect of Northern Ireland, the qualified person responsible for pharmacovigilance, as well as the pharmacovigilance system master file, may exceptionally be allowed to be located and operate in parts of the United Kingdom other than Northern Ireland. This shall not apply to situations where the marketing authorisation holder already has at its disposal a qualified person established in the Union.".~~

6.12.1.4. New: Change of QPPV for medicinal products with marketing authorisation valid in the territory of Northern Ireland

Question: Are we required to update the EU-based QPPV that is currently referenced in our product entries for Northern Ireland (XI country code) to reference a QPPV located in the United Kingdom instead?

Answer: If the medicinal product is approved by the UK national competent authority under EU law, then the location of the QPPV must comply with EU law requirements. According to EU law, MAHs are legally required to have a qualified person for pharmacovigilance (QPPV) based in the European Union (EU) in place at all times, in accordance with information in Article 104 (3) of Directive 2001/83/EC. The article also further clarifies: *"By way of derogation from the second subparagraph, **where the marketing authorisation is granted by the competent authority of United Kingdom in respect of Northern Ireland**, the qualified person referred to in point (a) of the first subparagraph may reside and operate in parts of the United Kingdom other than Northern Ireland. This subparagraph shall not apply where the marketing authorisation holder already has at its disposal a qualified person who resides and operates in the Union on 20 April 2022."*

6.13. Pharmacovigilance system Master File Location (PSMFL)

6.13.1. Correction of information within a PSMFL entity

Question: We inserted a new PSMFL entity in the XEVMPD and received a positive XEVPRM ACK with the PSMFL EV Code. Following our submission, we notice that we made a mistake in the name of our city. Can we amend this PSMLF entity? Or should be nullify it and create a new one?

Answer: It is not necessary to nullify the PSMFL entity and create a new one. You can amend the PSMFL information by performing an operation type 'Update' (2).

6.13.2. Update of an AMP entity to include PSMFL information

Question: How can we update our AMP entities in the XEVMPD to include the PSMFL information?

Answer: To reference a PSMFL EV code in your AMP entities you must perform an "Update" (i.e. operation type 2) of the AMP entity and reference the EV Code assigned to the PSMFL either from the remote or local look-up table. For related information, see section *1.2.6. Pharmacovigilance System Master File Location (PSMFL) code (AP.6)* of Chapter 3.II: XEVPRM User Guidance.

6.13.3. ~~PSMF located in the UK~~

~~**Question:** The Pharmacovigilance system Master File for majority of our medicinal products is currently located in the UK. Will this have to change once the UK leaves the EU?~~

Answer: As stated in section *2.2. Should I update the address information in Art. 57 database for entities located in Northern Ireland* of the 'Questions and answers to Stakeholders on the implementation of the Protocol on Ireland/Northern Ireland' document: *"The companies are reminded that from 1 January 2021 for medicinal products authorised or registered in the EU/EEA the MAH, registration holder, QPPV and PSMF must be established in the EU/EEA".*

With regards to medicinal products with marketing authorisation valid in the territory of Northern Ireland, as stated in paragraph 3 of section *4. The location of the marketing authorisation holder and the qualified persons for manufacturing for pharmacovigilance with regard to medicinal products for human use* of the Commission Notice – Application of the Union's pharmaceutical acquis in markets historically dependent on medicines supply from or through parts of the United Kingdom other than Northern Ireland: *"Where the marketing authorisation is granted by the competent authority of the United Kingdom in respect of Northern Ireland, the qualified person responsible for pharmacovigilance, as well as the pharmacovigilance system master file, may exceptionally be allowed to be located and operate in parts of the United Kingdom other than Northern Ireland. This shall not apply to situations where the marketing authorisation holder already has at its disposal a qualified person established in the Union.".*

6.13.4. Change of location of the Pharmacovigilance system Master File

Question: We are in the process of changing our PSMF location from the UK to another EU member state for our authorised medicinal products. Should we update the PSMF location of the existing MFL entity in the XEVMPD or should we create a new PSMF entity (new EV Code will be assigned) and update the affected AMPs to reference this new PSMFL entity?

Answer: As per information in the updated Chapter 3.II: XEVPRM User Guidance, should the location of the PSMF change but the Pharmacovigilance System remains the same, the existing PSMFL EV Code should be amended using an operation type 'Update (2)' to reference the new location. No update of AMPs will be necessary as the PSMF EV Code will remain the same.

A new PSMFL entity should be submitted in the Article 57 database only in case where the Pharmacovigilance System changes; a new PSMFL EV Code will be generated. In that case, you will need to update your AMPs to reference the new assigned PSMFL EV Code.

6.13.4.1. Update of PSMFL information following a variation/renewal

Question: Should the PSMFL field in an AMP entry be updated after the PSMF has been included in the registration by means of variation/renewal, or by the time that the PSMF is applicable for the registration?

The background for this question is that PhV auditors have stated that in their opinion, the PSMF is applicable for all products, once the PSMF is available. However, would this then imply that the XEVMPD database is updated, without the notification (= variation) to the NCA/EMA?

Answer: In accordance with Article 3 of Regulation (EU) NO 1235/2010 (the pharmacovigilance legislation), the obligation on the part of the MAHs to maintain and make available on request a pharmacovigilance system master file will apply from the date on which those marketing authorisations are renewed or 2 July 2015, whichever is the earliest.

Therefore, from 2 July 2015 it is a requirement to submit the Pharmacovigilance System Master File Location (PSMFL) information to the Article 57 database. Most of the product entities in the Article 57

database already include the PSMFL information; those AMP entities that do not reference the PSMFL information should be updated.

See also Q&A *6.6.5. Notifications of QPPV details/PSMF location via Article 57 database* of this document for related information.

6.13.5. Nullification of a PSMFL entity in the XEVMPD

Question: By mistake several duplicates of the same 'Master File Locations' were created in the XEVMPD. When we tried to nullify these duplicates, we received the following acknowledgement message: *"Unsuccessful Nullify. Please contact the EMA Help Desk - This Masterfile location is referenced by one or many products".* Please advise what we need to do in this case.

Answer: It is not possible to nullify a PSMFL entity that is referenced in a medicinal product entity. You will need to amend the AMPs (not nullified and referencing any of the valid marketing authorisation statuses) to reference another PSMFL EV Code. Once the PSMFL EV Code you wish to nullify is no longer referenced in any not nullified AMPs with any of the valid marketing authorisation statuses, the nullification will be possible. To retrieve the AMPs that reference the PSMFL EV Code you wish to nullify you can perform an advanced query in EVWEB.

6.13.6. New: Change of PSMF location for medicinal products with marketing authorisation valid in the territory of Northern Ireland

Question: The PSMF for our medicinal product authorised in Northern Ireland (XI country code) is currently based in the EU. Are we required to reference a PSMF located in the United Kingdom instead?

Answer: If the medicinal product is approved by the UK national competent authority under EU law, then the location of the master file must comply with EU law requirements (please refer to section II.B.2.2. Location, registration and maintenance of Module II – Pharmacovigilance system master file). Therefore, it would be acceptable for your medicinal product to maintain its PSMF location in the EU.

6.14. Substance details

6.14.1. Insert/update of a substance preferred name in the XEVMPD

Question: In our XEVPRM, we submitted an update of a substance name available in the XEVMPD and received a negative acknowledgement stating: *"Please note that it is not possible to perform any operations on approved substances names until further notice. - If you need to insert or update substance names or translations, please contact…"* Can you please clarify why we received this ACK and what should we do to amend the substance information?

Answer: Information within a substance entity in the XEVMPD can only be update by the EMA. Please refer to the published communication Changes to some business rules of the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): Submission of substance information for the relevant information and process to follow, should you wish to insert/update or amend substance information in the XEVMPD.

6.14.2. Update of a substance entity in the XEVMPD to include a translation/synonym

Question: The substance translation and synonym we need to reference in our product entity is not available in the XEVMPD. How can we add it?

Answer: Please follow the relevant process described in section *1.4. Initial submission of an approved substance* of Chapter 3.II: XEVPRM User Guidance.

6.14.2.1. Submission of synonyms with brackets and hyphens

Question: If we are using the master EV Code for reporting of an approved substance, why is there a need to achieve a 100% match in spelling by requesting a further synonym for brackets and hyphens if the substance name to be added? Could the EMA add synonyms/translations in the XEVMPD during their QC?

Answer: If hyphens/brackets are included in an SmPC, there is a high possibility that that's how the substance could be reported in an ICSR. Therefore, the EMA must have a comprehensive controlled vocabulary list. The EMA already includes such synonyms/translations; however, this activity does not remove the responsibility of the MAH to request the translation/synonym to be added to an existing substance.

6.15. Controlled Vocabularies (CVs)

6.15.1. Organisations CV list

6.15.1.1. Organisation missing in the XEVMPD look-up table

Question: We cannot find our MAH organisation in EVWEB when trying to insert a new authorised product. We can confirm that we are registered with EudraVigilance, and our organisation is also available in OMS. What is the issue?

Answer: The MAH look-up table in the XEVMPD contains details of the MAH organisations available in the XEVMPD as inserted by marketing-authorisation holders via their submitted XEVPRMs.

It is not the same as the list of organisations registered in EudraVigilance; the list of such organisations is accessible to registered users in the restricted area of the EudraVigilance Human website.

Please also note that if your organisation is entered in OMS, it is not automatically added in the XEVMPD as there is no direct link between these two systems.

Therefore, if the requested MAH organisation does not exist in the XEVMPD, you should submit the MAH organisation entity in the XEVMPD as new; an EV Code will be assigned following your submission and provided to you via an XEVPRM acknowledgement. Please refer section *1.6 Initial Submission of a Marketing Authorisation Holder (MAH) Organisation* of Chapter 3.II: XEVPRM User Guidance for further information on how to submit an MAH organisation in the XEVMPD.

6.15.1.2. Correction of MAH organisation details

Question: Some of our organisation information in the XEVMPD is incorrect. How can we correct it?

Answer: Information within a previously submitted MAH organisation entity can be amended by performing an 'Update' of the organisation entity. See the Extended EudraVigilance Medicinal Product

Report Message step-by-step guide: Maintenance operations - Update of a marketing authorisation holder (MAH) organisation entity in the XEVMPD for detailed steps to follow.
Please refer also to section *2.2. Maintenance of a marketing authorisation holder (MAH) organisation entity* of Chapter 3.II: XEVPRM User Guidance for further related information.

6.15.1.3. Update of organisation details

Question: The address of our MAH organisation has changed. How do notify this change to the Agency? Do we amend the organisation entity in the XEVMPD using an 'Update' (2) operation type or shall we create a new MAH entity using operation type 'Insert' (1)? Do we need to amend our medicinal product entities referencing this organisation?

Answer: If only the address of the MAH changed and the legal entity remains the same, then operation type 'Update' (2) or 'Insert' (1) should be used as applicable, as per information in section *2.2.1. Notification of change of contact details, name and/or address of the MAH (i.e., no change of the legal entity)* of Chapter 3.II: XEVPRM User Guidance.
Only the owner organisation of the entity may perform maintenance related operation types. If it is not possible for the marketing-authorisation holder to amend an organisation entity, a request should be sent via the EMA Service Desk portal stating the organisation name and EV Code, and clarification of what information shall be amended in the organisation entity. The EMA will assess your request and amend the organisation information if appropriate.

6.15.1.4. Update of a legal entity

Question: To update MAH details, the MAH must update the MAH entity in the XEVMPD (i.e. EV Code) and submit an email notification to the EV Registration team to update the address in the EV Registration database. This means that there will be a duplicate effort of work (gateway submission and email notification). To avoid redundant email notification, the current MAH version in the XEVMPD should be considered as valid by the EMA.

Answer: EV Registration database contains the details of organisations registered with EV. XEVMPD contains the list of organisations indicated as MAH of an AMP. To change a name of an organisation in the registration database, several additional documents need to be provided (cover letter, extract from a trade register etc.). To change address details in the registration database, an email to the EV Registration team is sufficient. To change the details of an MAH entity in the XEVMPD, an 'Update' must be performed on the MAH entity in the XEVMPD. The EMA cannot amend the organisation details in the EV Registration database based on the information provided in the XEVMPD.

6.15.1.5. Nullification of a duplicated organisation entity in the XEVMPD

Question: Our organisation is duplicated in the XEVMPD. What shall we do?

Answer: Duplicated organisation entities in the XEVMPD should be nullified. Please refer to *Process map 6 – Notifying an MAH entity as 'non-current'* of Chapter 3.II: XEVPRM User Guidance for further related information.

6.15.1.6. Negative XEVPRM Acknowledgement received following an MAH organisation nullification

Question: We tried to nullify several organisation entities submitted and owned by our organisation, but we received a negative acknowledgement, stating "*Security Error. Insufficient Rights. Check the*

Ownership of the specified entity". Can you please advise what is the issue and how these organisation entities can be nullified?

Answer: Please note that nullification can only be performed by an organisation, which formally owns the MAH entity in the XEVMPD. Also, MAH cannot nullify organisations which they own but which are flagged as "Valid" by the EMA. Please refer to *Process map 6 – Notifying an MAH entity as 'non-current'* of Chapter 3.II: XEVPRM User Guidance for related information.

6.16. MedDRA

6.16.1. Update of AMP entities following a new MedDRA version release

Question: Do we need to update all our medicinal product entities in the XEVMPD if a new MedDRA version is available?

Answer: It is not necessary to update medicinal product entities when a new MedDRA version is released. In the context of the data submission maintenance (e.g. if there is a need of notification of a variation with an 'Update (2)' operation type), if a new MedDRA version is available, the latest current version should be used to codify the indications.

Only under special circumstances a new MedDRA version should trigger a re-coding ('significant impact'); operation type 'Update' (2) should be used.

6.16.2. Update of indications following renewal/transfer or MA

Question: Can you confirm that following a renewal, MA transfer, etc. the indication doesn't need to be updated to the latest version of MedDRA?

Answer: The latest current version of MedDRA should be used to code the indications stated in section 4.1 Therapeutic indications of the SmPC when using the operation types 'Insert (1)' and 'Update (2)' to add/amend information on a medicinal product in the context of the data submission maintenance (e.g. variation, renewal, MA-transfer, etc.).

6.16.3. Maintenance of MedDRA versions and codes

Question: When do MAHs need to start maintaining MedDRA versions and codes in their medicinal products?

Answer: From January 2015 onwards, MedDRA codes and versions should be maintained as part of the transition maintenance phase.

7. VALIDATION OF MEDICINAL PRODUCT DATA

7.1. Outlines of Art57 data validation

Question: We understand that the Agency started the validation of medicinal product data submitted in the XEVMPD by the MAHs. Where can we find more information on the process?

Answer: The EMA began systematic review of the quality and integrity of the medicinal product information submitted by marketing-authorisation holders in July 2014.

The outlines of the quality control process and the relevant details have been published and are available in the document "Quality Control of medicinal product data submitted per the legal requirement introduced by Article 57(2) of Regulation (EC) No 726/2004".

7.2. Versioning of AMP records

Question: During the validation process, does the EMA change the version that was submitted by the MAH? If so, who is responsible for the content of the version?

Answer: Where the information is erroneous, the Agency creates a new version ("the EMA version") of the product entity, which contains the corrected information. The ownership of the medicinal product data remains with the MAH organisation that owns the product entry in the XEVMPD; the version created by the Agency during the quality revision process does not interfere with the submission process or the ownership of the data. This means that, following the creation of the EMA version with amendments, any subsequent amendments of the AMP by the MAH (e.g. due to variations) can be performed on the MAH's initial version. This will generate a new version of the specific product record.

See Annex 1 of the updated document "Quality Control of medicinal product data submitted per the legal requirement introduced by Article 57(2) of Regulation (EC) No 726/2004" for details.

7.3. Visibility of validated entities

Question: The document "Outlines of the Quality Control process" states that: *"Only the versions flagged as "Valid" are visible to other EVWEB users as per the applicable visibility rules."* Could you please explain the term "applicable visibility rules"? Or could you let us know where these are mentioned?

Answer: Please refer to section *1.7.7. Data Access Policy* of the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD) Data-Entry Tool (EVWEB) user manual. Please note that the term "Valid" was formerly known as "Checked".

7.4. Retrieval of validated entities

Question: How can I identify AMP records that were validated?

Answer: In EVWEB, go to "Advanced Queries" and select "Authorised Products (Valid version)". In the "Conditions (AND)", select "Owned" and run the query (using "Run" or "Run to Excel"). The list of AMPs which have a product validity set to "Valid" will become available.

- To identify AMPs, which were not updated (i.e. operation type "Update" was not applied for that AMP) by the MAH following a validation by the Agency:
  - In EVWEB, go to "Advanced Queries" and select "Owned Authorised Products".

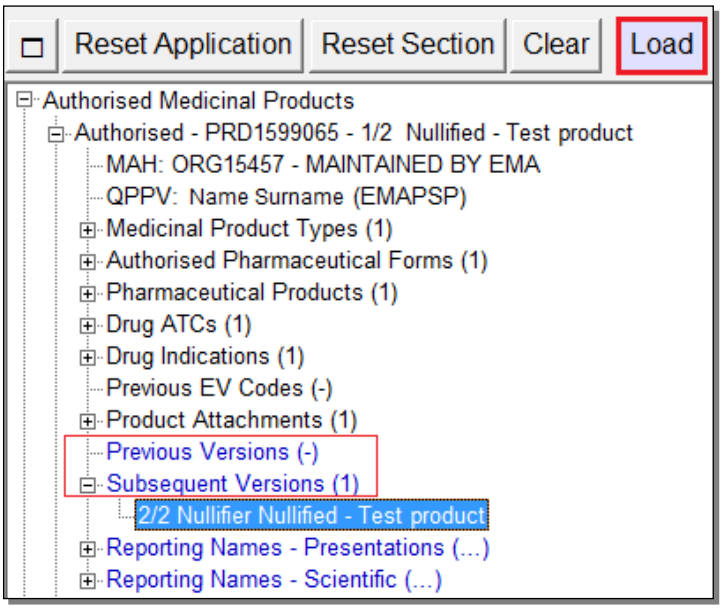
- In the "Conditions (AND)", select the field "Product Validity" and set the value to "Valid". Also, select the field "Product Pending" and set the value to "Assessed".
- Then run the query (using "Run" or "Run to Excel").

- To identify AMPs, which were updated (i.e. operation type "Update" was applied for that AMP) by the MAH following a validation by the Agency:
  - In EVWEB, go to "Advanced Queries" and select "Owned Authorised Products".
  - In the "Conditions (AND)", select the field "Product Validity" and set the value to "Valid". Also, select the field "Product Pending" and set the value to "Pending Update".
  - Then run the query (using "Run" or "Run to Excel").

7.5. Visibility of individual versions

Question: Can we view individual versions of our AMP entity?

Answer: Yes. Go to EVWEB and retrieve your AMP entity. In the tree-view area (under "Product Attachments"), sections "Previous Versions" and "Subsequent Versions" are available. Open the applicable version, select the version you wish to view and click on "Load":



8. EVWEB APPLICATION

8.1. Location of the XEVMPD Data Entry Tool (EVWEB)

Question: Where do we find the link to the XEVMPD Data Entry Tool (EVWEB)?

Answer: The XEVMPD Data Entry Tool (also known as EVWEB) can be accessed by users registered with EudraVigilance from the EudraVigilance production or test environment (XCOMP) of the EudraVigilance Human Restricted area, under 'EV Services'.

- XEVMPD production: https://eudravigilance.ema.europa.eu/x
- XEVMPD XCOMP: https://evtest.ema.europa.eu/x

8.2. Access to EVWEB application

Question: How can we access EVWEB?

Answer: EVWEB can be accessed in Google Chrome and Microsoft Edge via an IE Tab extension. You will also need to download ActiveX, which is a software provided by the EMA, and have a multi-factor authentication set up. The steps to follow are described on the 'xEVMPD support' page in the EudraVigilance restricted area. Please note that since IE TAB is not compatible with MAC computers; users will not be able to access EVWEB using a MAC computer.

8.3. Use of ZIP file during XEVPRM submission

Question: Could a standalone XEVPRM be transmitted through the gateway? Or is the ZIP file format mandatory, even when we sent only an XEVPRM without any attachment?

Answer: The use of ZIP file format by Gateway users is always mandatory for consistency, and to help reduce the size of the file.

8.4. Use of different transmission modes

Question: Several companies intend to use a different system and different transmission mode for the submission of XEVPRMs and submission of ICSRs. As a single organisation cannot be both, a Gateway user and an EVWEB user, what do you advise us to do to deal with this difficulty?

Answer: The proposed approach is to request the creation of a virtual affiliate under the headquarter (HQ) of the marketing authorisation holder profile. Marketing authorisation holders can have a main profile set as Gateway user and a virtual affiliate set as WEB Trader user or vice versa. The WEB Trader profile can be used to perform manual maintenance through the XEVMPD Data Entry Tool (EVWEB) and/or the Gateway profile can be used to perform XML uploads. Please review the EudraVigilance: how to register website for more information on how to register a virtual affiliate.

8.5. XEVPRM Acknowledgements

Question: Can you please confirm that XEVPRM ACKs will be sent 'immediately' to the senders, based on a technical validation (using the parsing rules detailed in the Detailed Guidance), and not delayed (if based on a human validation)? Can the tracking of the message delivery notifications (MDN) serve as a proof of compliance, in addition to the tracking of the XEVPRM ACK?

Answer: The 1st and 2nd XEVPRM Acknowledgements confirming if the submitted XEVPRM was processed by EMA gateway and the information was successfully loaded in the XEVMPD are sent to the sender organisation within 24 hours since the initial submission by the sender organisation.
The 3rd XEVPRM Acknowledgment related to the validation of your authorised medicinal product information in the Article 57 database is generated when the EMA validation team performs the product validation in the Article 57 database:

- The first validation of a newly submitted AMP is performed within 2 weeks since the initial submission of the AMP.
- There is no defined timeline for a subsequent validation following an update of the AMP information. This is due to large volumes of data and prioritisation of newly entered products. Therefore, re-validation of previously validated AMPs is performed as needed and max within 2 years since last validation.

With regards to proof of compliance, please refer to Q&A *3.3. Receipt of positive XEVPRM ACK within 15 calendar days timeline* of this document.

8.5.1. XEVPRM Acknowledgement not received

Question: We submitted an XEVPRM to the XEVMPD via EVWEB. Until now we have not received an acknowledgement. Furthermore, we are wondering why this XEVPRM cannot be seen in the EVWEB Outbox. Can you please investigate?

Answer: Please note that XEVPRMs and XEVPRM Acknowledgements are available in the WEB Trader Inbox/Outbox for 7 days; they are moved to the "Archive" section 7 days after their submission/receipt. Please follow the steps described in section *3.10.5. Archive* of the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD) Data-Entry Tool (EVWEB) user manual to retrieve your XEVPRM/XEVPRM ACK in the Archive section of your WebTrader Inbox/Outbox.

If you are still unable to find your acknowledgement, please raise a Request XEVMPD/Art.57 Services ticket via the EMA Service Desk portal to request the ACK. In the ticket, please provide all the relevant information (e.g. XEVPRM name, sender ID, date of submission) or the XML of the submitted XEVPRM. Please allow 24 hours since your XEVPRM submission before contacting the helpdesk regarding an ACK which was not received.

8.6. Access to EVWEB for Gateway users

Question: Can Gateway users use the XEVMPD Data Entry Tool (EVWEB)? We need to perform queries, to be able to manually enter IMPs etc. Please confirm that a unique user's account will allow us to perform transactions using both, the XEVMPD Data Entry Tool (EVWEB) and using our Gateway (XCOMP environment and Human EV production environment).

Answer: Gateway users can access the XEVMPD Data Entry Tool (EVWEB) and to retrieve medicinal product information. Depending on their organisation's profile set-up, they can also create an XEVPRM using EVWEB but not to submit XEVPRM messages (the 'Send' button is not available in the 'Create and Send Product Reports' section). To submit the XEVPRM created via EVWEB, Gateway users should save the XEVPRM as a ZIP file and submit it via the EV POST functionality available in the EV restricted area.

If a marketing authorisation holder registered as a gateway user wishes to send XEVPRMs directly via the XEVMPD Data Entry Tool (EVWEB), the marketing authorisation holder needs to register a virtual

affiliate. Please review the EudraVigilance: how to register website for more information on how to register a virtual affiliate.

8.7. Access to the test environment (XCOMP) for IT vendors

Question: Is access to the XEVMPD test environment (XCOMP) granted to software vendors?

Answer: Software vendors were able to test their software systems directly in the XEVMPD test environment (XCOMP), between 16 June and 31 December 2014, following the XEVPRM schema change. After this period, to access XCOMP, software vendors must be registered as third-party service providers for marketing authorisation holder or sponsor organisations.

8.8. Change of transmission mode

Question: Is it possible for an MAH organisation to switch from being an EVWEB user to a Gateway trader?

Answer: Yes, this is possible; however, changes in the registration profile and technical set-up are required. To change the transmission mode of a profile, the registered QPPV/ Trusted Deputy must send a request addressed to the Gateway support team via the EMA Service Desk.

8.9. Use of two different organisation IDs

Question: Using the Gateway, can marketing-authorisation holders use two different interchange IDs (one for ICSRs and one for XEVPRMs) or does it need to be the same interchange ID for both types of transmission?

Answer: The IDs can be different within the same EudraVigilance Group.

8.10. Upload of XEVPRMs via EVWEB

Question: Is it possible to load into the XEVMPD an existing XML to create a new XEVPRM? How does it work?

Answer: In the WEB Trader section of the XEVMPD Data Entry tool (EVWEB), a '**Local Import**' function is available. This function allows uploading XML files previously created. Once imported, the message is loaded in the '*Create and Send Product Report*' section of EVWEB, where the information can be edited as necessary. This function is available only to users registered as Web trader users in the EudraVigilance system. Please refer to the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD) Data-Entry Tool (EVWEB) user manual for information how to use EVWEB functionalities.

9. XEVMPD Bulk Update Manager tool

9.1. Bulk update of XEVMPD records

Question: We are EVWEB users, and we would like to update several AMP records in the XEVMPD at the same time. How can this be done?

Answer: In November 2014, the Agency released a 'Bulk Update Manager' tool to enable marketing authorisation holders submitting information using EVWEB to perform bulk data operations on their

products in the XEVMPD. The tool facilitates editing of key data fields and supports the re-submission of this data to the XEVMPD repository. This tool is not available for organisations registered as Gateway users.

For details see the XEVMPD Bulk Update Manager user guide available in the restricted area of the EudraVigilance website.

9.2. Access to the Bulk Update Manager tool

Question: How can we access the Bulk Update Manager tool?

Answer: The Bulk Update Manager tool is available in the EV restricted area, under 'EV Services'. The technical set-up to access this tool is the same as for EVWEB; the tool can be accessed in Google Chrome and Microsoft Edge via an IE Tab extension. You will also need to have ActiveX, which is a software provided by the EMA, downloaded on your computer and have a multi-factor authentication set up.

9.3. Changes submitted via the Bulk Update tool are not visible in XEVMPD

Question: We have applied several changes to our product data via the Bulk Update tool. However, when we submitted the changes via the Bulk Update tool, they were not visible in the products in the XEVMPD. Can you please clarify why?

Answer: Using the Bulk Update Manager tool, you can apply the same change(s) to multiple AMPs that your organisation owns in the XEVMPD. The tool will apply the changes to the product entries and generate an XEVPRM file, but the file is not automatically sent by the Bulk update tool. You need to retrieve the newly generated file from the 'WEB Trader' section of EVWEB, re-upload it in the 'Create and Send Product Reports section', assign the 'Message Number' to the XEVPRM, check that the changes were applied as requested, validate and submit the file using the 'Send' button. Refer to steps 16 to 20 of section *10.2. Step by Step Guide – Change of "MAH" and "MedDRA version"* of the XEVMPD Bulk Update Manager user guide for detailed instructions.

10. XEVMPD Product Export tool

10.1. Access to the XEVMPD Product Export tool

Question: How can we access the XEVMPD Product Export tool?

Answer: In May 2014, the Agency made available an 'XEVMDP product export' tool to enable marketing authorisation holders to export the product data owned by their HQ organisation in the XEVMPD.

The XEVMPD Product Export tool is available in the EV restricted area, under 'EV Services'. The technical set-up to access this tool is the same as for EVWEB; the tool can be accessed in Google Chrome and Microsoft Edge via an IE Tab extension. You will also need to have ActiveX, which is a software provided by the EMA, downloaded on your computer and have a multi-factor authentication set up.

For more information, see the XEVMPD product export tool user manual available in the restricted area of the EudraVigilance website.

10.2. Inability to download an export from the XEVMPD Product Export tool

Question: In the XEVMPD Product Export Tool, we fail to download an export (XML and Excel files). When we select the button "Download", after performing a request, a window opens for one second and automatically closes. No file is downloaded. We use Internet Explorer 8. Please advise what may be the issue.

Answer: This may be related to the settings on your computer. Please ensure that the following actions are followed:

- Only use MS IE versions 8, 9, 10 or 11;
- Install ActiveX (supplied by EMA Service desk);
- IE Settings for two EudraVigilance WEB Sites (Test and Production):
    - https://evtest.ema.europa.eu/human/restricted/PublicView/list2.asp
    - https://eudravigilance.ema.europa.eu/human/restricted/PublicView/list.asp
- Disable Blocker (Tools/Pop up Blocker/Pop up Blocker settings);
- Include these sites into the list of the trusted sites (Tools > Internet Options > Security > Trusted Sites > Sites).
- In the IE security settings (Tools > Internet Options > Security > Custom Level), enable the following: ActiveX controls and plug-ins, Java VM, Scripting.

If you are still unable to download the files, please submit an enquiry via the EMA Service Desk portal (https://servicedesk.ema.europa.eu).