6 July 2017
EMA/159776/2013
Information Management

Electronic submission of Article 57(2) data
Questions & Answers (Q&As)

Version 1.11

Table of contents

Summary of changes

Information in the below listed section(s) has been updated or added as new following the publication of version 1.10 of this document in April 2017. The changes are highlighted.

- 1.5. Submission of herbal medicinal products

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

- 3.11. NEW: Inability to comply with medicinal product submission timelines

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

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

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

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

Answer: Article 57(2) of Regulation (EC) No. 726/2004 as amended by Regulation (EU) 1235/2010 and Regulation (EU) 1027/2012 requires:

(a) the Agency shall, by 2 July 2011 at the latest, make public a format for the electronic submission of information on medicinal products for human use;

(b) marketing-authorisation holders shall, by 2 July 2012 at the latest, electronically submit to the Agency information on <u>all medicinal products for human use authorised in the Union</u>, using the format referred to in point (a);

(c) from the date set out in point (b), marketing-authorisation holders shall inform the Agency of any new or varied marketing authorisations granted in the Union, using the format referred to in point (a).'

Therefore, 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.

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). For further information see Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance section *1.1 Initial Submission of an Authorised Medicinal Product (AMP).*

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

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: Extended EudraVigilance product report message (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: As stated in section *1.1. Medicinal products within the scope of Article 57(2)* of this document, centrally authorised products are to be submitted by the marketing-authorisation holder per Article 57(2) requirements.

1.4. Submission of Investigational Medicinal Products (IMPs)

Question: How should we handle submission of investigational medicinal products per requirements of Article 57(2)?

Answer: As stated in section *1.2. Medicinal products out of scope of Article 57(2)* of this document, the submission of information on IMPs is outside the scope of Article 57(2). IMPs should be electronically submitted as required 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) published by the Commission on 11 June 2011.

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 <u>authorised</u> medicinal products for human use. This does not include <u>registrations</u> 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 <u>marketing authorisation</u> 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: Extended EudraVigilance product report message (XEVPRM) user guidance of the

Guidance documents published at the [Agency's website](#). The appropriate legal basis and medicinal product type(s) must be selected.

For further information, reference is made to 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.

Related information is also available in 3.2. NEW: 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 a number of 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: As per section *1.2.* of this document, 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 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. Marketing-authorisation holders are therefore required to electronically submit to the Agency information on medicinal products authorised in the EEA countries outside the EU (i.e. Iceland, Liechtenstein and Norway.

See section *1.1.1. Submission of medicinal products authorised in EEA countries outside the EU* of Chapter 3.II: Extended EudraVigilance product report message (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: Extended EudraVigilance product report message (XEVPRM) user guidance.

Regarding which QPPV should be referenced in your 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 (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 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 if their medicinal products are being marketed or not. As per information stated in section *1.1. Medicinal products within the scope of Article 57(2)* of this document, your authorised medicinal products should therefore be submitted to the XEVMPD per Article 57(2) requirements.

1.9. Submission of veterinary products

Question: Do veterinary products also need to be entered 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.

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)'. See Chapter 3.II: Extended EudraVigilance product report message (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 Agency, 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 provided in the XEVPRM data field 'Authorisation procedure (AP.12.2)' 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: Please note that 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). Therefore, information on medicinal products authorised 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).

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: Extended EudraVigilance product report message (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)'.

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 Agency 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. 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. DATA SUBMISSIONS PER ARTICLE 57(2) REQUIREMENTS

3.1. Timelines for submission of authorised medicinal product information

Question: How should MAHs notify the Agency of <u>new</u> marketing authorisations? What are the timelines?

Answer: In accordance with the [Legal Notice on the Implementation of Article 57(2) of Regulation (EC) No. 726/2004](#), 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 eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD) 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: Extended EudraVigilance product report message (XEVPRM) user guidance*](#) for further information.

3.1.1. Start of 15 calendar day timeline

Question: In accordance with the published guideline, MAH is 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.

3.1.2. 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.

3.1.3. 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 NEW 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: Extended EudraVigilance product report message (XEVPRM) user guidance](#).

3.2. NEW: 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: As per information stated in the [Note for clarification: Traditional herbal medicinal product and simplified registration for homeopathic medicinal products: pharmacovigilance requirements and EudraVigilance access](#): "*holders of traditional use registrations for herbal medicines should submit the information for these medicines using the electronic format referred to as Article 57 format or eXtended EudraVigilance Product Report Message (XEVPRM) format. Registration holders should also ensure that the information is kept up to date. The Article 57 database already allows for data submission for traditional use registrations for herbal medicines in line with the requirements and business processes described in Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance.*"

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.

3.3. 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: Please refer to section *1.1 Initial Submission of an Authorised Medicinal Product (AMP)* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance for information on how are medicinal products are characterised for XEVPRM submissions.

Question: Based on the guidance stated in Chapter 3.II: Extended EudraVigilance product report message (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 line 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, please follow the process described in section *2.1.8.1.1. Business process - Authorisation number (AP.12.4) has changed following a variation* described in Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance. It is a two-step process, in which the MAH must retire the authorised medicinal product for which the marketing authorisation number is no longer valid by using the

operation type 'Invalidate MA' and a new AMP entity must be submitted in the XEVMPD using the operation type 'Insert'.

3.4. Submission of medicinal products with 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 EXAMPLE 2 of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance for the requested information.

3.4.1. Submission of medicinal product information in Luxembourg

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 should be provided if you wish to submit one product for each pack size.

3.5. Submission of medicinal products with different authorisation number 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).

See EXAMPLE 3 of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance for related information.

3.6. Submission of 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 of 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. Up to now I have inserted in the XEVMPD only the marketed pack sizes since there is no MA number for the not-marketed packs.

Could you please advise how to handle this situation? If I have to insert all of the not-marketed presentations what should I insert in the "Authorisation number" field?

Answer: In this specific case, since all of the presentations are authorised, those without the assigned authorisation number must be inserted in the XEVMPD with the procedure number assigned by the NCA or the MRP procedure number (if no procedure number is assigned by the NCA).

3.7. Submission of centrally authorised medicinal products (CAPs)

Question: For a centrally authorised medicinal product, is only one XEVMPD record required 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 should be submitted in the XEVMPD. See *EXAMPLE 6* and section *1.2.12.1. Authorisation country code (AP.12.1)* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance for related information.

3.8. 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: Extended EudraVigilance product report message (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).

3.9. 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: Extended EudraVigilance product report message (XEVPRM)](#) [user guidance](#) for the requested information.

3.10. 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: Extended EudraVigilance product report message (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).

3.11. NEW: Inability to comply with medicinal product submission timelines

Question: In accordance with the information stated in the [Legal Notice on the Implementation of](#) [Article 57(2) of Regulation (EC) No. 726/2004](#), 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 this 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).

3.12. Confidentiality of submitted data

3.12.1. Confidentiality of data submitted in the XEVMPD

Question: Which parts of the data in the XEVMPD will be handled confidentially? For the non-confidential data - will 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 [with the exception of the QPPV name and contact details and the referenced PPI attachment(s)] in the XEVMPD entities flagged as "Valid" are in the XEVMPD visible and accessible to all stakeholders registered with EudraVigilance (i.e. there are no user restrictions). Please refer to section *1.7.7. Data Access Policy* of the XEVMPD Data-Entity Tool (EVWEB) User Manual.

3.12.2. Confidentiality of excipients' concentration

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: Extended EudraVigilance product report message (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-Entity Tool (EVWEB) User Manual AMP entities flagged as "Valid" will be visible to other XEVMPD users. Therefore, if your AMP entity is flagged as "Valid", 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.

3.13. Language requirements for XEVMPD data submission

3.13.1. 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 XEVMPD Data Entry Tool (EVWEB) will however not show the non-Latin characters.

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

3.13.2. 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 s*ee* [Chapter 3.II: Extended EudraVigilance product report message (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: Extended EudraVigilance product report message (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).*

Each approved substance successfully submitted in the XEVMPD has an assigned EV Code. The preferred name of the approved substance is entered in English. Each translation and synonym is linked to the master substance EV Code.

List of available substances with their assigned EV Codes can be found in the XEVMPD look-up table and in the Controlled Vocabulary (CV) lists published on the [Agency's website](#) - see "*eXtended Eudravigilance Product Dictionary (XEVMPD) substances*". The list contains substance data available in the XEVMPD at the time of publication.

If a new approved substance/substance translation or a synonym needs to be submitted in the XEVMPD, please refer to the process described in the communication [Changes to some business rules of the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): Submission of substance information](#) or in section *1.4 Initial submission of an Approved Substance* [Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance](#).

3.13.3. 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, where we do have two official languages, the SmPCs for medicinal products authorised via the national procedure exist only in Finnish. Package leaflets are available in Finnish and Swedish.

Answer: Please refer to *Note 15, Table 1b - Requirements for AMP records and attachments for countries with more than one national language* and *AMPLE 68* of [Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance](#) for the required information.

3.13.4. 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 <u>centrally</u> in Iceland, Liechtenstein and Norway are now 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 in order to allow the Agency 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.

3.13.5. Substance translations

Question: Can you please confirm that the translations of substances names have to 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. The preferred name of the approved substance is entered in English. Each translation and synonym is linked to the master substance EV Code.

EVWEB users should select the requested substance name in the EudraVigilance remote look-up table.

Gateway users should populate the 'Active ingredient substance code' data element (PP.ACT.1), 'Excipient substance code' data element (PP.EXC.1) or 'Adjuvant substance code' data element (PP.ADJ.1) with the assigned substance EV Code as per the available "eXtended Eudravigilance Product Dictionary (XEVMPD) substances" CV list.

If a new approved substance/substance translation or a synonym needs to be submitted in the XEVMPD, please refer to the process described in the communication Changes to some business rules of the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): Submission of substance information or in section *1.4 Initial submission of an Approved Substance* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance.

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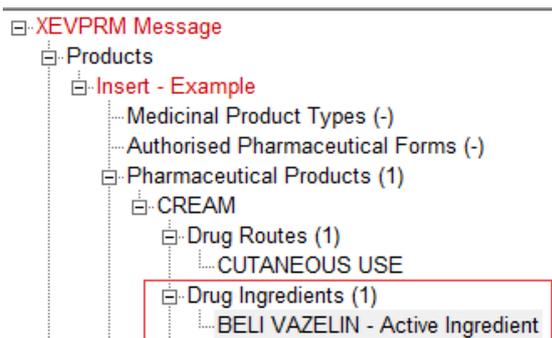
The name in the national language (i.e. the translation) is linked to the master substance name in English. Therefore, when you view you AMP in EVWEB and/or you perform a maintenance related operation type on that AMP entity, the master substance name in English is displayed. The list of substance translations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

```
Pharmaceutical Products (1)
  CREAM
    Drug Routes (1)
    Drug Ingredients (1)
      PARAFFIN WHITE SOFT - Active Ingredient
        Approved - PARAFFIN WHITE SOFT
          SRC528 - COMPANY SPECIFICATION
        Substance Translations (66)
          Swedish - BELI VAZELIN
          Slovakian - BIELA VAZELÍNA
          German - WEIßES VASILIN
```
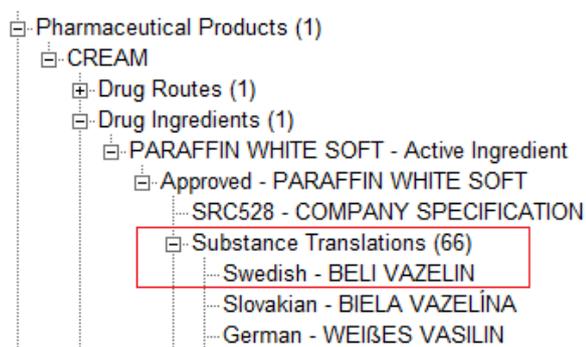
You do not need to amend the substance information to "rename" the substance name back to the national language.

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 Changes to some business rules of the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): Submission of substance information or in section *1.4 Initial submission of an Approved Substance* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance..

3.13.5.2. 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: 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 registrations of traditional herbal medicinal products (Chapter 2a of Directive 2001/83/EC) and registrations of homeopathic medicinal products registered according to the simplified registration procedure (Article 14 of Directive 2001/83/EC).

Traditional herbal medicinal products and homeopathic medicinal products may be submitted in the XEVMPD on voluntary basis in line with the requirements and business processes described in Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance.

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.

List of available substances with their assigned EV Codes can be found in the XEVMPD look-up table and in the Controlled Vocabulary (CV) lists published on the Agency's website - see "*eXtended Eudravigilance Product Dictionary (XEVMPD) substances*". The list contains substance data available in the XEVMPD at the time of publication.

If a new approved substance/substance translation or a synonym needs to be submitted in the XEVMPD, please refer to the process described in the communication Changes to some business rules of the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): Submission of substance information or in section *1.4 Initial submission of an Approved Substance* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance.

3.13.6. 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. Also supplemental MedDRA terms that will be included in the next MedDRA version can be used.

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

3.13.7. 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: Please refer to section *1.2.15. Package description (AP.13.7)* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance for the requested information.

3.14. Printed product information (PPI)

3.14.1. 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: Extended EudraVigilance product report message (XEVPRM) user guidance.

Please refer to section *1.10. Submission of an attachment* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance for details regarding the content of the attachment.

3.14.2. Submission of an additional document

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: The Agency 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 Agency will assume that the number stated in the "Authorisation Number" field provided by the MAH is correct.

3.14.3. 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.

3.14.4. 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: Extended EudraVigilance product report message (XEVPRM) user guidance:

The attachments can be provided in the following formats: .PDF, .DOC, .DOCX, .XLS and .XLSX.

Marketing-authorisation holders are not to send PDF scanned documents, but need to provide "genuine" PDF documents.

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.

3.14.5. 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.

3.14.5.1. 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 <u>for non-centrally authorised products and MRPs/DCPs/NAPs</u> 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 *2.1.8.1. Variations of marketing authorisation* of <u>Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance</u>.

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

Question: What the marketing-authorisation holder has to 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.

3.14.5.3. 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.

3.14.6. 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: Extended EudraVigilance product report message (XEVPRM) user guidance.

3.14.7. 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: Extended EudraVigilance product report message (XEVPRM) user guidance for the requested information.

3.14.8. Confidentiality of PPI

Question: Will the PPI be visible to all XEVMPD users or to the public?

Answer: With regards to the visibility of PPI, only the latest version of the SmPC for a medicinal product is retrievable/visible in the XEVMPD by users registered with EudraVigilance. Non-current PPI versions will be archived.

3.15. 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 *1.2 Authorised medicinal product - element structure* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance for detailed description of what information (and when) needs to be provided for each data element.

3.15.1. 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: Extended EudraVigilance product report message (XEVPRM) user guidance for the requested information.

3.16. Presentation name elements

3.16.1. 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: Extended EudraVigilance product report message (XEVPRM) user guidance.

3.16.1.1. Name in the title of an SmPC document vs. name in section 1 of the SmPC

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.

3.16.2. 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: Extended EudraVigilance product report message (XEVPRM) user guidance:

"Medicinal products are being characterised as part of the initial XEVPRM submissions based on the main following characteristics:
> *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)*

Whenever any of the characteristics described above (point a. to e.) for a medicinal product are different, a separate medicinal product entity should be submitted in the XEVMPD. This also applies to medicinal products for which one marketing authorisation has been issued with the same marketing authorisation number.

Therefore, 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: Extended EudraVigilance product report message (XEVPRM) user guidance.

3.16.3. 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 <u>in the language of the country where the marketing authorisation applies</u> in accordance with the referenced SmPC. As in this example the authorisation country of the product is Bulgaria, only the product name in Bulgarian language should be used.

3.17. Authorisation details

3.17.1. 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 of the numbers in the 'Authorisation Number field'?

Answer: Please refer to section *1.2.12.4 Authorisation number (AP.12.4)* of <u>Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance</u>.

3.17.1.1. Applicable authorisation number is not stated in the relevant SmPC

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).

3.17.1.2. 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 stating that authorisation number (i.e. document granting/renewing marketing authorisation) should be also attached. The AMP entry in

the XEVMPD will therefore reference two attachments (i.e. SmPC and a document showing the authorisation number).

3.17.1.3. 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.

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

Question: The SmPC of a medicinal product authorised in the United Kingdom 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)

PL 12345/0001

PL 12345/0002 (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. PL 12345/0001 must be specified in AP.12.4).

3.17.1.5. Format of an authorisation number: NAP in Iceland

Question: As part of the EMA QC, 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).

3.17.1.6. 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.

3.17.1.7. 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 <u>OR</u> 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.

3.17.1.8. 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: If you wish to submit only one XEVMPD product entity for all the pack sizes covered by the NL number, you should specify the NL number in the data element Authorisation number (AP.12.4).

If you wish to submit multiple XEVMPD product entities (i.e. one for each pack size), you may specify the NL number or the package number stated in section 8 of the SmPC in the data element AP.12.4.

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.

3.17.2. 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: Extended EudraVigilance product report message (XEVPRM) user guidance.

3.17.3. 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: Extended EudraVigilance product report message (XEVPRM) user guidance for the requested information.

3.17.3.1. 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: Extended EudraVigilance product report message (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.

3.17.4. 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: Extended EudraVigilance product report message (XEVPRM) user guidance for the description of available authorisation procedure values.

3.17.4.1. *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: Extended EudraVigilance product report message (XEVPRM) user guidance](#) for related information.

3.18. Pharmacovigilance details

3.18.1. Visibility/Confidentiality of Pharmacovigilance details

Question: Will the PSMF location, pharmacovigilance email/phone number and QPPV details be made public?

Answer: Please refer to the [European Medicines Agency pre-authorisation procedural advice for users of the centralised procedure document](#), section *3.4.3.9. 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?*

3.18.2. 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.

3.18.3. Qualified Person responsible for Pharmacovigilance (QPPV)

3.18.3.1. *Unavailability of an EU QPPV*

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

Answer: A QPPV is mandatory. The EU QPPV and where such does not exist, the local QPPV (e.g. in case of purely national authorisations) should register with EudraVigilance.

3.18.3.2. *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: Extended EudraVigilance product report message (XEVPRM) user guidance](#).

3.18.3.3. *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 of the QPPV or the code of the QPPV we don't get any results?

Answer: EVWEB users should not type the name or the code of the QPPV in the look-up table of the 'QPPV Code' field (AP.5). Instead, click on the 'QPPV' field, press ENTER (do not perform a search on

name, code or part of the name). A list of all registered QPPVs (including the QPPV Code) for the Organisation, for which the user has been registered will be displayed.

3.18.4. Pharmacovigilance System Master File (PSMF)

3.18.4.1. 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: Please refer to:

- The [European Medicines Agency pre-authorisation procedural advice for users of the centralised procedure document](#), *question 3.4.3.4. Pharmacovigilance system master file number (PSMF);*

- section *1.11 Initial submission of a Pharmacovigilance System Master File Location (PSMFL)* of [Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance](#).

3.18.4.2. 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 EVCODEs from the XEVMPD that relate to two different PSMF location entities. These two PSMF locations will be identical but the comment field within the PSMF location of the XEVMPD should be used by the MAH to include an internal MAH reference to distinguish which PSMF is related the specific PSMF Location EVCODE (MFL EVCODE)."

Please refer to section *1.11 Initial submission of a Pharmacovigilance System Master File Location (PSMFL)* of [Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance](#) for further information.

3.18.4.3. 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 are used/will be 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 will facilitate 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, *question 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).*

3.18.4.4. 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 *1.2.6 Pharmacovigilance System Master File Location (PSMFL) code (AP.6)* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance for further information.

3.18.4.5. Timelines for submission of a PSMF

Question: When should we request a PSMF number?

Answer: As per section 3.4.3.4. Pharmacovigilance system master file number (PSMF) available in the European Medicines Agency pre-authorisation procedural advice for users of the centralised procedure document: *"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".*

3.18.4.6. Referencing a PSMFL within an AMP entity

Question: We received an EV Code for our PSFML, how can we reference it in out 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 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.

To facilitate the correct PSMF EV Code assignment:

- if the PSMF is submitted together with the AMP(s) in the same XEVPRM file, AMP(s) covered by the same PSMFL should reference the same 'local number' for the PSMFL;

- if the AMP(s) and the PSMFL were submitted via separate XEVPRMs (an EV Code was assigned for each entity), the PSMFL can be referenced in the AMP entity by amending the AMP entity as per the process described in section *2.2.2. Amendment of an AMP entity following a change in the referenced PSMFL information* of <u>Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance</u>.

3.18.4.7. *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: It is necessary to create 1 PSMF for each Headquarter Organisation ID registered in the system. Two affiliates within the same Headquarter can share the same PSMF. Please refer to section *1.11 Initial submission of a Pharmacovigilance System Master File Location (PSMFL)* of <u>Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance</u> and specifically:

- *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.*

3.19. Substance information

3.19.1. Substance information to be submitted within an AMP entity

Question: What types of substances are to be captured in an authorised 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), adjuvants where applicable and excipients) need to be specified.

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 section *1.2.17.4 Active ingredient substance code (PP.ACT.1)* of <u>Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance</u>.

3.19.2. Referencing substance information within an AMP entity

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

Answer: Please refer to *NOTE 9* of <u>Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance</u>.

3.19.3. Submission of substances with multiple components

Question: For one of our AMP 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 <u>Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance</u> with regards to submission of substances containing multiple components.

3.19.4. Submission of synonyms within an AMP entity

Question: In case that the SmPC states: "Iron oxide red" or "Red iron oxide"; should we request for new substance entity to be created as per the process described in the communication Changes to some business rules of the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): Submission of substance information, or can a substance with a similar EV Code be used?

Answer: Please note that in this particular 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. "Iron oxide red" or "Red iron oxide" should be requested to be added as synonym of the preferred substance SUB23080 as per the process described in Changes to some business rules of the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): Submission of substance information.

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.

3.19.5. Substance names

Question: Description & coding of approved substance names should be submitted to the XEVMPD as named in the SmPC. Can we use an equivalent naming for one product in order 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)* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance.

3.19.6. 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 controlled vocabulary list EudraVigilance eXtended Medicinal Product Dictionary (XEVMPD) substances includes the column 'Name Type', in which the designation of the substance name is specified (i.e. " Substance Preferred Name", "Substance Translation", "Substance Alias").

3.19.7. 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: Extended EudraVigilance product report message (XEVPRM) user guidance.

3.19.7.1. *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) must 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)

3.19.8. 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 *Table 3 - Requirements on how to reflect information on substance and strength in section 2. Qualitative and Quantitative Composition of the SmPC* and section *1.2.17.4 Active ingredient substance code* (PP.ACT.1) of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance.

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

Taking the example of a salt and an active moiety (base):

– If the strength is declared as the amount of base then the base is the substance to be declared as the ingredient

– If the strength is declared as the amount of the salt then the salt is the substance to be declared as the ingredient

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

Therefore, as per your example, the strength of the active ingredient should be expressed as 20 mg of fluoxetine per one single tablet.

3.19.9. Submission of 'trace' substances

Question: Do the substances present as "traces" in AMPs (in accordance with the contents of the SmPC) have to 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.

3.19.10. 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. We received a negative acknowledgement stating: *"Please note that it is not possible to perform any operations on approved substances names until further notice…."*Can you please clarify why we received this ACK?

Answer: Please refer to the published communication on Changes to some business rules of the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): Submission of substance information.

3.19.11. Missing substances

Question: If a substance, which we need to use in our medicinal product entity, is missing in the available controlled vocabulary substance list, how should we request a new substance EV Code? Can the substance be submitted through XEVMPD Data Entry Tool (EVWEB) and/or Gateway?

Answer: If a new approved substance/substance translation or a synonym needs to be submitted in the XEVMPD please follow the process described in the communication Changes to some business rules of the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): Submission of substance information or in section *1.4 Initial submission of an Approved Substance* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance.

3.19.12. Definition of substance class

Question: Could you please provide a detailed definition of the three values 'mixture', 'aingle' and 'apecified aubstance'? 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 Detailed Guidance available on the Agency's website. EV-Post and Gateway users should also refer to the EudraVigilance eXtended Medicinal Product Dictionary (XEVMPD) substance classes controlled vocabulary.

3.19.12.1. 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'.

3.19.12.2. 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

3.19.12.3. 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: The definitions provided in [Chapter 6](#) of the Detailed Guidance available on the Agency's website should be used to decide what the most relevant substance class is. According to these definitions, an amino acid can only be classified as a 'chemical' as it does not fall under the definition of any other class.

3.19.13. 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: Extended EudraVigilance product report message (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.

3.19.14. 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, it will be visible to EVWEB users registered with EudraVigilance as per the applicable visibility rights. 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.

3.19.15. 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: No, the reference source field 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 Agency will select the most suitable reference source to be referenced in the substance. Please refer to the Controlled Vocabulary list *"eXtended Eudravigilance Product Dictionary (XEVMPD) reference sources"* published on the [Agency's website](#).

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.

3.19.16. Submission of E Numbers for excipients

Question: How does the Agency handle E numbers referring 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 as per the process described in the communication [Changes to some business rules of the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): Submission of substance information](#) or in section *1.4 Initial submission of an Approved Substance* of [Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance](#).

3.19.17. 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 take into account those specificities?

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 simplified registration procedure (Article 14 of Directive 2001/83/EC). Such medicinal products can be provided in the XEVMPD on voluntary basis in line with the requirements and business processes described in of [Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance](#).

In 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.

3.19.17.1. *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.

3.19.18. 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.

3.20. 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 do not need to submit structured substance information (SSI) until an agreement on a collaborative way forward to coordinate entity of high quality structured substance information is reached with the European Union Regulatory Network and European Pharmaceutical Industry Associations. Specific aspects will be addressed as part of the ISO IDMP Road Map development.

3.21. Authorised/administrable pharmaceutical Forms

3.21.1. 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 - the 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 to 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.

3.21.2. 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).

3.21.3. 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 published controlled vocabulary list "*Extended EudraVigilance product report message (XEVMPD) pharmaceutical dose forms*" available at the Agency's website?

Answer: Please refer to the below sections of Chapter 3.II: Extended EudraVigilance product report message (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.*

3.21.4. 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.

3.21.5. 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".

3.22. Route(s) of administration

3.22.1. Multiple routes of administration

Question: According to Chapter 3.I: Technical specifications, the route of administration is a mandatory field in which only one entity can be made. What if a pharmaceutical product can be administered in two different ways?

Answer: Route of administration is a repeatable XEVPRM section and therefore two routes of administration can be referenced within one pharmaceutical product.

3.22.2. 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 published controlled vocabulary list "*Extended EudraVigilance product report message (XEVMPD) routes of administration*" available at the Agency's website?

Answer: Please refer to the below sections of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance:

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

3.22.3. 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.

3.23. 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'.*

3.24. ATC Codes

3.24.1. 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: Extended EudraVigilance product report message (XEVPRM) user guidance.

3.24.2. 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: Extended EudraVigilance product report message (XEVPRM) user guidance.

3.24.3. ATC Code not available in XEVMPD

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

Answer: 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: Extended EudraVigilance product report message (XEVPRM) user guidance.

3.24.4. 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.

3.24.5. 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 in the schema. Several ATC Codes can be therefore referenced in one product entity.

3.24.6. 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 2nd of 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.

3.25. Controlled vocabularies (CVs)

3.25.1. Availability of controlled vocabularies

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

Answer:

- The available controlled vocabularies are published on the [Agency's website](), section *"Controlled vocabularies"*.

- 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)]().

3.25.2. 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.

3.25.3. Identification of changes in the published controlled vocabularies

Question: How can I determine what has changed in the substance CV list available on the Agency's website? Is it possible to get a list of just the changes to the previous versions of the CV please?

Answer: The published updated versions of the substance and organisations CVs contain a sheet named "EV Codes Added". This sheet contains the extract of the new EV Codes added in the controlled vocabulary since the last publication. In subsequent publications the tracking of the changes will be enhanced so that users of the CVs can also view EV Codes that were nullified since the last publication as well as identify which EV Codes where updated (e.g. substance name updated or translation added).

3.25.4. 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 on the Implementation of Article 57(2) of Regulation (EC) No. 726/2004 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 Agency's website, section *"Controlled vocabularies"* – see *"EudraVigilance eXtended Medicinal Product Dictionary (XEVMPD) medical devices"*.

3.25.5. 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: Extended EudraVigilance product report message (XEVPRM) user guidance.

3.25.6. Organisations CV list

Question: Which organisations are available in the published 'Organisations' list? Is it list of organisations registered with EudraVigilance?

Answer: The *"Extended EudraVigilance product report message (XEVMPD) Organisations"* list available as part of the Controlled Vocabularies published on the Agency's website, section *"Controlled vocabularies"* contains details of the marketing-authorisation holder organisations available in the XEVMPD.

See NOTE *1* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance for further information.

3.26. MedDRA

3.26.1. 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: See section *1.2.19. AMP - Product Indications (AP.INDs)* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance.

For 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.

3.26.2. 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: See section *1.2.19. AMP - Product Indications (AP.INDs)* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance.

For 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.

3.26.3. 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: Extended EudraVigilance product report message (XEVPRM) user guidance.

3.26.4. 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: Extended EudraVigilance product report message (XEVPRM) user guidance.

3.26.5. 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.

4. MAINTENANCE OF MEDICINAL PRODUCT DATA

4.1. Medicinal product data ownership

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

Answer: Medicinal product information provided via an XEVPRM is "owned" by the sender organisation and its headquarter that submitted the information. The operation types which can be technically performed by the sender organisation are described in section *Data Operations and Ownership* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance.

4.2. 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 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 refer to Process map 13 – Nullification of an AMP entity, Step 3 of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance. If nullification is requested for more than 10 entities, please provide the EV Codes in an Excel spreadsheet.

4.3. 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 revocation/withdrawal or an expiry of MA. There is no need to maintain such products. As an exception, the EMA can amend an invalidated (i.e. "Authorisation Status" = "Not-valid") AMP on behalf of the MAH to enable the MAH to clean the list of their MAH entities (e.g. to enable the MAH a nullification of incorrectly submitted MAH entity referenced in an AMP) and in case when incorrect data was provided during the invalidation (e.g. wrong invalidation date was stated).

4.4. Maintenance of product entities submitted in the EVPRM format

Question: Should we maintain product entities submitted to the 'old' EVMPD using in the EVPRM 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.

4.4.1. 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 on the Implementation of Article 57(2) of Regulation (EC) No. 726/2004](#), 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: Extended EudraVigilance product report message (XEVPRM) user guidance](#).

4.4.1.1. 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 <u>when the NCA gives the MAH 6 months for the implementation of the variation</u>?

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.

4.5. Transfer of marketing authorisation

4.5.1. Notifications of transfer of marketing authorisations

Question: Can you please advise what is the process for updating our product entity in the XEVMPD to indicate that the marketing authorisation for this medicinal product has been transferred to another marketing-authorisation holder?

Answer: Please refer to section *2.1.8.3. Transfer of marketing authorisation* of [Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance](#).

4.5.1.1. Previous EV Code cannot be received as former MAH no longer exists

Question: According to the process described in section *2.1.8.3. Transfer of marketing authorisation* of the published 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 since the former MAH organisation no longer exists, we are unable to find out what the EV Codes were?

Answer: If the "former MAH" organisation no longer exists and the EV Codes cannot therefore be communicated to the "new MAH", the "new" MAH should submit a request via the EMA Service Desk portal (https://servicedesk.ema.europa.eu) 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.

4.5.1.2. Previous EV Code is unknown

Question: We are the new MAH of a medicinal product that was transferred to us from another MAH. We have not received the "previous" EV Code of this product from the former MAH and are unable to retrieve this product in the XEVMPD. We don't know if the previous MAH submitted this AMP in the XEVMPD at all. This is preventing us from inserting this AMP in the XEVMPD. Could you please advise how we should proceed?

Answer: To check if the previous MAH entered the AMP in the XEVMPD, please submit a request via the EMA Service Desk portal (https://servicedesk.ema.europa.eu) to request the previous EV Code. 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.

In case the former MAH was not compliant with the Article 57 requirements and therefore there is no AMP in the XEVMPD to be referenced (i.e. no previous EV Code was assigned), the new MAH can submit the transferred AMP with the 'Insert' (1) operation type and the value "Valid" (1) must be specified in the data element "Authorisation status" (AP.12.3).

4.5.2. 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 process described in section *2.1.8.3. Transfer of marketing authorisation* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance.

4.5.3. 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 *2.1.8.3. Transfer of marketing authorisation* of Chapter 3.II: Extended EudraVigilance product report message (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*.

4.6. Variations

4.6.1. 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: Extended EudraVigilance product report message (XEVPRM) user guidance:

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

4.6.2. 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 *2.1.8.1.1. Business process - Authorisation number (AP.12.4) has changed following a variation* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance.

4.6.3. 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.

4.6.4. 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 Authorization Status remain "Valid-Renewed/Transferred" or should it updated to "Valid"?

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

4.6.5. 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.

Please see the corresponding [press release](#) for related information.

4.7. 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 *2.1.8.6. Revocation/Withdrawal/Expiry of Marketing Authorisation (MA)* of [Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance](#).

4.7.1. 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 has to be given. Which date should be specified? There are many possible options:

- It should 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: Extended EudraVigilance product report message (XEVPRM) user guidance.

4.7.2. 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. Go to "Queries", in "Conditions", the following fields must be selected:

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

4.8. Renewal of marketing authorisation

4.8.1. 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 *2.1.8.4.2. Business process - Authorisation number (AP.12.4) has changed following a renewal* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance.

4.8.2. 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)'.

4.8.3. 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*).

4.8.4. 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 (=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 *2.1.8.5. Change of authorisation procedure following a referral* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance.

4.9. (Lifting of) suspension of 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 *2.1.8.2 (Lifting of) suspension of marketing authorisation* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance.

4.10. SmPC updates

4.10.1. 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 *2.1.8.1 Variations of marketing authorisation* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance. See also section *2.1. 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.

4.10.2. 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?

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.

4.11. 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.

4.12. QPPV details

4.12.1.1. 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 to reflect this change. How can this be done?

Answer: Please refer to section *2.1.6.2. Business process to notify the change of a QPPV within the organisation* and *Process map 10 – Amendment of an AMP entity following a change of QPPV* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance.

4.12.1.2. Change of QPPV details

Question: The surname of our QPPV has changed as well as her email address. How do we amend these details in the EV registration database? Our medicinal products submitted in the XEVMPD will also need to be updated to reflect this change. How can we make these changes?

Answer: Please refer to section *2.1.6.1. Business process to notify the change of QPPV details* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance.

4.13. Pharmacovigilance system Master File Location (PSMFL)

4.13.1. 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).

4.13.2. Update of an AMP entity to include PSMFL information

Question: We electronically submitted our authorised medicinal products in the XEVMPD in the new XEVPRM format without including information on the PMFL as it is not mandatory information. Now we would like to add this information to the AMP entity. What shall we do?

Answer: Please refer to section *2.2.2. Amendment of an AMP entity following a change in the referenced PSMFL information* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance.

4.13.3. Update of PSMFL information referenced in an AMP entity

Question: We electronically submitted our authorised medicinal products in the XEVMPD in the new XEVPRM format with information on the corresponding PSMFL. The location of our pharmacovigilance system master file has changed and we submitted new PSMFL information in the XEVMPD. A positive XEVPRM ACK containing the new PSMFL was received. How do we amend the AMP entities to reference the new PSMFL?

Answer: Please refer to section *2.1.7.2. Maintenance of Pharmacovigilance System Master File Location (PSMFL)* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance.

4.13.3.1. 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. The majority of 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 *4.6.5. Notifications of QPPV details/PSMF location via Article 57 database* of this document for related information.

4.13.4. Nullification of 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, which is referenced in a medicinal product entity. You need to retrieve the AMP entities, in which the incorrect PSMFL is referenced and amend the medicinal product entity using an operation type 'Update' (2) to change the referenced PSMFL.

Please refer to section *2.2.4.3. Nullification of PSMFL entity* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance for related information.

4.14. Substance details

4.14.1. Insert/update of a substance preferred name

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: Approved substance preferred name 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 approved substance name.

4.14.2. Update of a substance entity to include a translation/synonym

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

Answer: Providing that an approved substance is not listed in the XEVMPD substance controlled vocabulary list (sheets *1_Substance CV* and *4b_ Invalid substance names*), or in the XEVMPD substance look-up table, MAHs should submit their requests to the email address MDMS@ema.europa.eu using the processes described in the published communication Changes to some business rules of the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): Submission of substance information.

4.14.2.1. 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.

4.15. Controlled Vocabularies (CVs)

4.15.1. Organisations CV list

4.15.1.1. Organisation missing in the published CV list/XEVMPD look-up table

Question: Our MAH organisation is not included in the published Organisation CV list and we cannot find it in EVWEB when trying to insert a new authorised product. We can confirm that we are registered with EudraVigilance. What is the issue?

Answer: The published Organisation CV list/MAH look-up table are different from the list of organisations registered in EudraVigilance. The list of organisations registered in EudraVigilance is accessible to registered users in the restricted area of the EudraVigilance Human website.

The published Extended EudraVigilance product report message (XEVMPD) Organisations list contains details of the MAH organisations available in the XEVMPD as inserted by marketing-authorisation holders via their submitted XEVPRMs.

If the requested MAH organisation does not exist in the XEVMPD, the organisation can be added using the Organisation section of the XEVPRM. Please refer section *1.6 Initial Submission of a Marketing Authorisation Holder (MAH) Organisation* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance for further information on how to submit an MAH organisation in the XEVMPD.

4.15.1.2. Correction of MAH organisation details

Question: Some of our organisation information published in the Organisation CV list and available in the 'MAH' look-up table is incorrect. How can we correct it?

Answer: It is the responsibility of the marketing-authorisation holder to ensure that the information associated with the Organisation EV Code is up to date and accurate. Information within a previously submitted MAH organisation entity must be amended or additional information must be added (as applicable) by submitting an XEVPRM with the operation type 'Update' (2).

Please refer to section *2.1.7.1. Maintenance of a Marketing Authorisation Holder (MAH) Organisation entity* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance for related information.

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 (https://servicedesk.ema.europa.eu) stating the Organisation name and EV Code, and clarification of what information shall be amended in the organisation entity.

4.15.1.3. 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 changes and the legal entity remains the same, then operation type 'Update' (2) should be used. Please refer to section *2.1.7.1. Maintenance of a Marketing Authorisation Holder (MAH) Organisation entity* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance for related information.

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 (https://servicedesk.ema.europa.eu) stating the Organisation name and EV Code, and clarification of what information shall be amended in the organisation entity.

4.15.1.4. 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 submitted for the MAH entity. The EMA cannot amend the organisation details in the EV Registration database based on the information provided in the XEVMPD.

4.15.1.5. Nullification of a duplicated organisation entity

Question: Our organisation is duplicated in the published Organisation CV list. What shall we do?

Answer: MAH organisation entity which is no longer valid and which will not be used in any future medicinal product submission can be nullified by submitting an XEVPRM with the operation type 'Nullification' (4). Please refer to Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance, sections:

- *2.1.7.1. Maintenance of a Marketing Authorisation Holder (MAH) Organisation entity;* and

- *2.2.4.2. Nullification of MAH organisation entities.*

4.15.1.6. Negative XEVPRM Acknowledgement received following 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 section *2.2.4.2. Nullification of MAH organisation entities* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance for further information.

4.16. MedDRA

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

Question: Do we need to update all of 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.

4.16.2. 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.).

4.16.3. 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.

5. VALIDATION OF MEDICINAL PRODUCT DATA

5.1. 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 found more information on the process?

Answer: Please be informed that the Agency 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".

5.2. 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 sender organisation; 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 detailed process map.

5.3. 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".

5.4. Retrieval of validated entities

Question: How can I identify AMP records that we have 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").

5.5. 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":
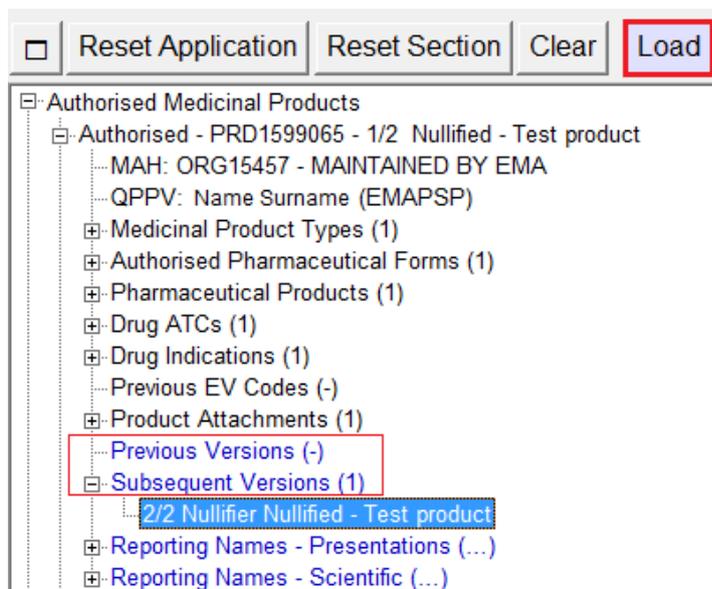
6. EVWEB APPLICATION

6.1. Location of 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'.
EudraVigilance production environment: https://eudravigilance.ema.europa.eu/x
XCOMP: https://evtest.ema.europa.eu/x

6.2. Access to EVWEB application using Internet Explorer 9, 10 and 11

Question: Can we access EVWEB using any other IE version but 8?

Answer: The EVWEB application currently only supports Internet Explorer 8. If you cannot use this older version of IE, you can still use EVWEB with IE9, IE10 and IE 11 using the link here to access the XHTML version of the application directly. You will need to set your IE browser to compatibility view. More information on how to change Internet Explorer compatibility view settings is available from the Microsoft website.

6.3. 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 is always mandatory for consistency, and to help reduce the size of the file.

6.4. 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. 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 Registration website (http://eudravigilance.ema.europa.eu/human/phase2.asp) for more information on how to register a virtual affiliate.

6.5. 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: Please refer to *chapter III.2. Processing and Acknowledgement of Receipt of Medicinal Product Report Messages* of the [Note for guidance on the electronic data interchange (EDI) of individual case safety reports (ICSRs) and medicinal product reports (MPRs) in pharmacovigilance during the pre-and post-authorisation phase in the European Economic Area (EEA)](#) (Doc. Ref: EMEA/115735/2004).

Marketing-authorisation holders need to identify if the received acknowledgements (ACKs) are positive or with warnings only.

ACKs with errors require the marketing-authorisation holders to correct and resubmit the medicinal product(s) affected using the same operation type.

An XEVPRM can contain several entities such as substances, organisations, attachments that are referenced in the medicinal products present in the same XEVPRM. If the loading of any of those entities fails, the entire message will be rolled back and the marketing-authorisation holders will need to resubmit the amended message with the same operation type with all the entities.

If all those entities are successfully loaded and all the products except one or more products are not loaded successfully, only the one or more products should be resubmitted in a new XEVPRM, because all the other products and entities would have been loaded.

6.5.1. 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 below steps to retrieve your XEVPRM/XEVPRM ACK:

1. Select the appropriate Archived Inbox/Outbox
2. Click on 'Run'
3. Wait until Results Node is populated with a list of XEVPRMs/XEVPRM ACKs
4. Select Results node to see results in the right panel

If you are still unable to find your ACK please send an enquiry via the EMA Service Desk portal (https://servicedesk.ema.europa.eu) providing the relevant information (e.g. XEVPRM name, sender ID, date of submission). Please allow 24 hours since your XEVPRM submission before contacting the helpdesk regarding an ACK which was not received.

6.6. 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 EV POST.

If a marketing-authorisation holder registered as a gateway user desires 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 Registration website (http://eudravigilance.ema.europa.eu/human/phase2.asp) for more information on how to register a virtual affiliate.

6.7. 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. To access XCOMP, software vendors must be registered as third party service providers for marketing-authorisation holder organisations.

6.8. Change of transmission mode

Question: Is it possible for 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 in the form of a cover letter to the Registration team (EudraVigilanceRegistration@ema.europa.eu).

6.9. 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.

6.10. Upload of XEVPRMs via EVWEB

Question: Will it be possible to load into the XEVMPD an existing XML in order 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 "XEVMPD Data-Entry Tool (EVWEB) User Manual" available in the restricted area of the EudraVigilance website or under the link https://eudravigilance.ema.europa.eu/human/docs/EVWEB_User_Manual_XEVMPD.pdf for information how to use EVWEB functionalities.

7. XEVMPD Bulk Update Manger tool

7.1. NEW: 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.

For details, see the XEVMPD Bulk Update Manager user guide available in the restricted area of the EudraVigilance website or under the link
https://eudravigilance.ema.europa.eu/human/docs/Guidance/EudraVigilance%20xEVMPD%20Bulk%20Update%20User%20Guide.pdf.

7.2. Bulk Update Manger tool system requirements

Question: With which version of Internet Explorer does the Bulk Update Manger works with?

Answer: The bulk update manager tool is designed to work on machines operating under Windows 7 using Internet Explorer 8 (IE8) or above. Earlier versions of Windows, Internet Explorer and other operating systems/browsers will not receive support for the export tool should issues arise. If the tool is used in IE8, it is necessary to disable compatibility mode for the browser as described here: http://windows.microsoft.com/en-gb/internet-explorer/use-compatibility-view#ie=ie-8.

7.3. "Create Change" button not visible in the Bulk Update Manager tool

Question: I have tried to carry out a bulk update for several of our products however, when I view the bulk update screen operations page, as per figure 18 in the user guide, I am unable to select the "Create Change" button as it is not visible. Can you please advise?

Answer: This is related to the compatibility view. Please try to toggle the current setting for "Compatibility View". The toggle button is available in the Internet Explorer Address Bar.

Disabled:

Enabled:

8. XEVMPD Product Export tool

8.1. Availability of XEVMPD Product Export tool and system requirements

Question: Is the XEVMPD data export tool available? Does it work with Internet Explorer version 8 and above?

Answer: In May 2014, the Agency made available an "XEVMDP product export tool" to enable marketing-authorisation holders to export their own data during the transition maintenance phase. The data export functionality only works with Internet Explorer versions 8 and above.

For more information, see the XEVMPD product export tool user manual available in the restricted area of the EudraVigilance website or under the link https://eudravigilance.ema.europa.eu/human/docs/Guidance/XEVMPD%20Export%20tool%20user%20manual.pdf.

8.2. Inability to download an export from 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):

    o https://evtest.ema.europa.eu,

    o https://eudravigilance.ema.europa.eu;

- 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).