EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Inspections and Human Medicines Pharmacovigilance

# Measures for Article 57 Data Quality Assurance

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# 1. Introduction

The Article 57 database delivers structured and quality assured information on medicinal products authorised in the EU that can support EU terminologies of products, substances, and organisations used to power pharmacovigilance and regulatory systems in the EU.

The primary objectives comprise the facilitation and coordination of regulatory decisions to safeguard public health and the fulfilment of regulatory actions and legal obligations including:

- support identification of products and substances in reports of suspected adverse drug reactions (ADRs);
- literature monitoring service;
- repository of periodic safety update reports (PSURs);
- support referral procedures;
- support collection of pharmacovigilance fees.

# 2. Document purpose

The purpose of this document is to detail the measures taken by the European Medicines Agency (hereinafter the 'Agency') at the pre-submission, submission, and post-submission phases of data entry into the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD) to improve data quality in the Article 57 database. The document details the methodologies used by the Agency to validate the medicinal product information submitted to the Article 57 database.

The optimal approach to engage national competent authorities in the quality assurance of Article 57 product submissions received by the Agency is being explored within the Network.

# 3. Intended audience

The audience of the document is all Article 57 stakeholders.

# 4. Definition of terms

**Agency**: European Medicines Agency

**AMP**: Authorised Medicinal Product

**CAP**: Centrally Authorised Product

**DCP**: Decentralised Procedure

**EEA**: European Economic Area

**EMA**: European Medicines Agency

**EVDAS:** EudraVigilance Data Analysis System

**EVWEB**: XEVMPD Data-Entry Tool

**MA**: Marketing Authorisation

**MAH**: Marketing Authorisation Holder

**MRP**: Mutual Recognition Procedure

**NAP**: Nationally Authorised Product

**Non-CAP**: Products which are not centrally authorised (MRP / DCP / NAP)

**PPI**: Printed Product Information

**SmPC**: Summary of Product Characteristics

**XEVPRM**: eXtended EudraVigilance Product Report Message

**XEVMPD**: eXtended EudraVigilance Medicinal Product Dictionary

# 5. Legal basis

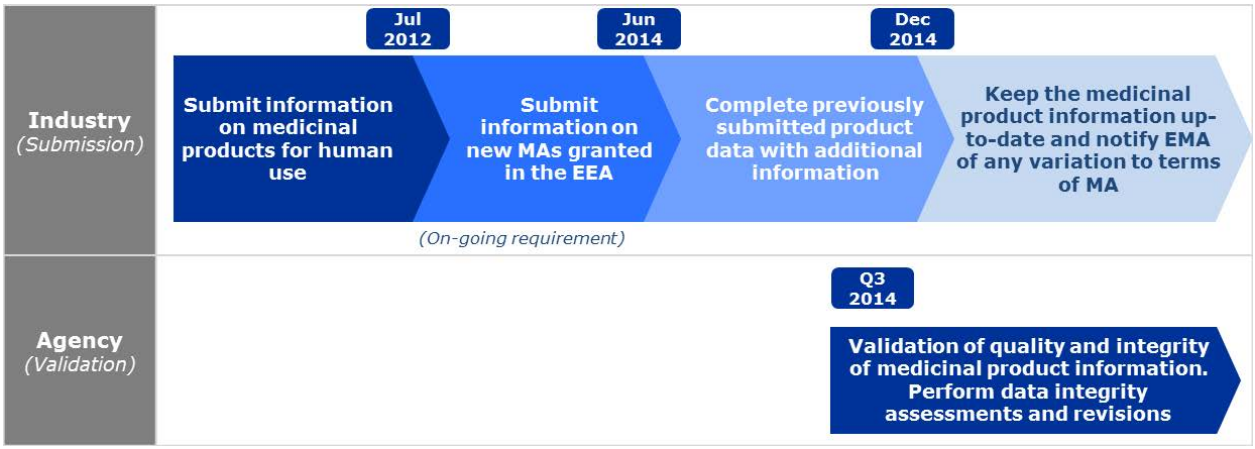
The submission of data on medicines by marketing-authorisation holders is a legal requirement from the 2010 pharmacovigilance legislation, Regulation (EU) No 1235/2010.

As outlined in the Legal Notice on the Implementation of Article 57(2), of Regulation (EC) No. 726/2004, marketing-authorisation holders (MAHs) shall:

- use the XEVPRM as the format to electronically submit to the Agency information on all medicinal products for human use authorised in the Union;
- after 2 July 2012, submit information on medicinal products for new marketing authorisations in the Union to the Agency immediately 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);
- ensure that information on all medicinal products for human use authorised in the Union, which is submitted electronically to the Agency using the format and content as referred to in point 1, 3 and 4 of the Legal Notice on the Implementation of Article 57(2), of Regulation (EC) No. 726/2004 is accurate and up to date;
- respond to requests of the Agency immediately and no later than 15 calendar days following receipt of such request.

MAHs are also required to submit and maintain 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 is part of the EEA Agreement.

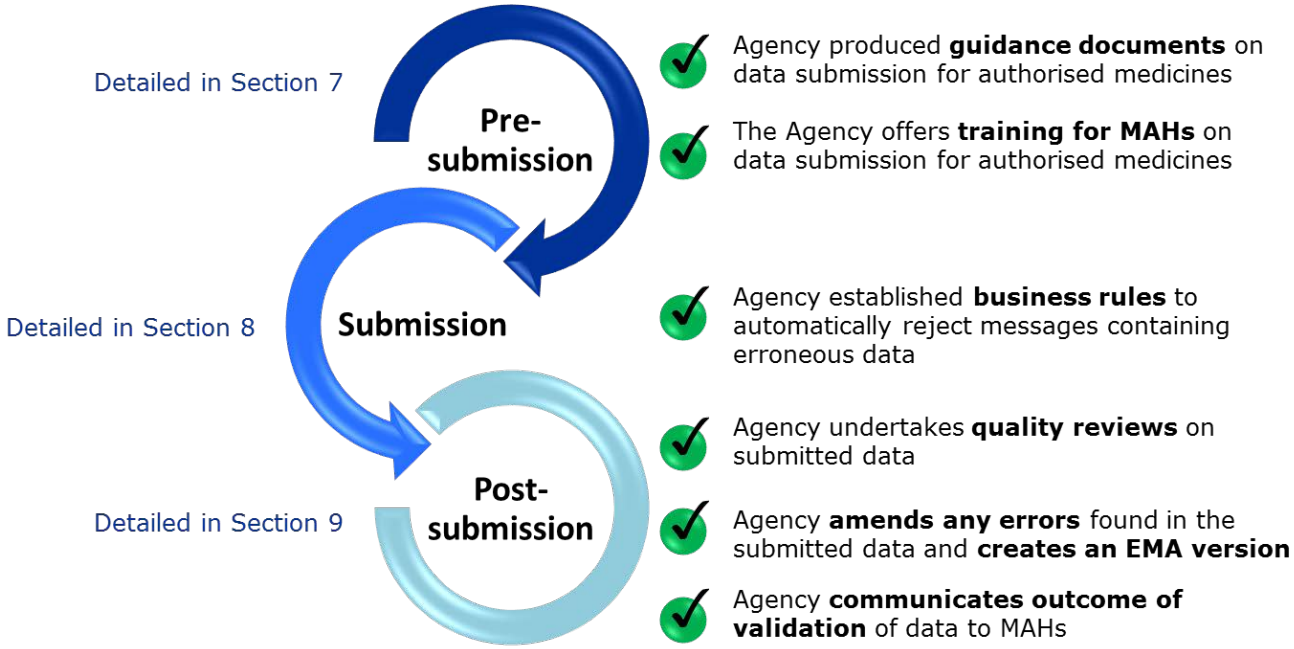
In Q3 2014, the Agency commenced the review of the quality and integrity of the medicinal product information submitted in line with the amended XEVPRM format and specifications.




Additionally, the Article 57 database is referenced in the pharmacovigilance implementation regulation and pharmacovigilance fees legislation.

# 6. Overview of quality assurance measures

The Agency has put in place a range of measures to support Industry with the submission of high quality data. Robust processes are in place to verify the quality of the submitted data and update any incorrectly populated fields to ensure that the Article 57 database is up-to-date, accurate and fit for use.



# 7. Pre-submission phase quality assurance measures

To support Industry with their legal obligations, and to promote the accurate submission of data, the Agency has produced the following **guidance documents:**

- Article 57 Guidance documents which include:
  - Legal notice,
  - Detailed guidance on electronic submission of information on medicinal products,
  - Article 57(2) requirements: Frequently asked questions,
  - Controlled Vocabularies (CVs) / CVs Quality Control;
- Reporting requirements for marketing-authorisation holders.

The Agency offers **training for MAHs** on data submission for authorised medicines. At least one user from each MAH should receive training. The training focuses on explaining the guidance on data submission. The training is provided as e-learning modules and as face-to-face training. This further assists Industry with submitting high quality data to the XEVMPD.

Further information can be found on the Article 57 webpage (Training and Best Practice).

- XEVMPD training
- XEVMPD e-learning
- Data-Entry Tool (EVWEB) User Manual


# 8. Submission phase quality assurance measures

Business rules are enforced in the XEVPRM Schema to strive for a better quality of data initially received in the database and to automatically reject messages containing incomplete or erroneous data. For example, the system will not allow entering of a non-EU country with an EU authorisation procedure.

These rules have been introduced and improved over years of experience in handling product data submission and data analysis related to identification of preventable errors.

# 9. Post-submission quality assurance measures

## *9.1. Validation*

### *Data fields subject to Agency validation*

A subset of the Article 57 data fields are validated by the Agency. These data fields are identified in *Annex I – Data fields subject to validation and high level validation process summary.* The data fields which have been selected to be validated are those fields which are most critical to ensuring that the

pharmacovigilance business needs of the Agency are efficiently and effectively addressed based on reliable, up-to-date and accurate data.

***Validation processes used by the Agency***

The Agency performs data integrity assessments and, where necessary, revisions of the incorrect data. Systematic assessments of the latest version of the received medicinal product data is performed by checking each data field using one of the three validation processes. The process used depends on the type of field and the public availability of that particular information. The validation processes used by the Agency processes are:


**Full Validation (PPI):** Submitted data validated against printed product information, usually the SmPC;

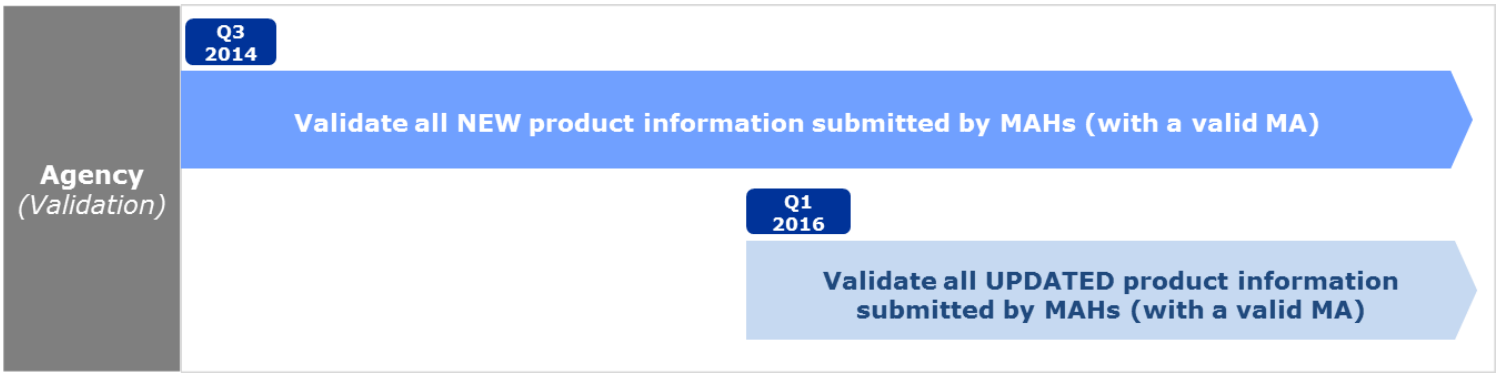

**Full Validation (other):** Submitted data validated against a data source (Agency or other);


**Logical Validation:** Rational assessment of the validity of the submitted data based on expert knowledge and a sense check against other relevant fields within the database.

The validation activity is a manual process and all entities are validated based on their names (readable information). Their respective identifiers are listed in Annex I for completeness, but their validation status is not meaningful (e.g.: the substance name will be assessed as correct or will be modified - the identifier associated with it will be correct or modified implicitly). Refer to *Annex I – Data fields subject to validation and high level validation process* summary for validation details on each field.

If the Agency cannot perform the data quality assessment because incorrect or invalid document(s) was/were provided during the submission process, the QPPV of the MAH organisation is informed by email with the request to review their medicinal product entity/entities and attach a valid reference document(s) or additional document(s) that allow the data quality assurance process, within 15 calendar days as per paragraph 6(b) of the Legal notice.

If correct and valid document(s) is/are attached, the Agency performs the quality assessment on the medicinal product available in the Article 57 database of the XEVMPD. Provided that the medicinal product entity was submitted by the MAH correctly and in line with principles outlined in Chapter 3.II: XEVPRM User Guidance, the Agency flags the assessed version of the medicinal product entity as "Valid".




It should be noted that:

- MAHs are not required to wait for the Agency to flag their AMP entity as *"Valid"* in the XEVMPD before their next maintenance related submission;
  - MAHs can submit XEVPRMs with operation types 'Update (2)' or 'Invalidate MA (6)' irrespective of the validity assessment status,
  - Authorised medicinal product entities that have been flagged *"Valid"* can be nullified by the Agency upon request;
- All versions of the AMP entity are visible to the users registered under the ID of the owner organisation in EVWEB;
- Only the versions flagged as "*Valid*" are visible to other EVWEB users as per the applicable visibility rules described in the Data Access Policy section of the Data-Entry Tool (EVWEB) User Manual.

**Q3 2014 to 2016**

- All new AMPs with a valid marketing authorisation (MA) are validated when an MAH has made an *insert* of the AMP due to a new marketing authorisation being granted or due to a transfer of a MA to a new MAH (If correct and valid document(s) is/are attached).
- Validation is performed only on Valid Marketing Authorisations (i.e. Marketing Authorisation Status is equal to "Valid" or "Valid - Suspended").
- The data elements which are subject to validation are identified in *Annex I – Data fields subject to validation and high level validation process summary*.
- By 31st October 2015, all new AMPs with a valid marketing authorisation submitted by 1st March 2015 will be validated. There will be continuing validation of new inserts throughout 2016.
- When one or more data fields identified within *Annex I – Data fields subject to validation and high level validation process summary* which are subject to 'Full Validation' are updated by the MAH, the updated field and any other impacted data field (as per Annex I) are validated by the Agency (if correct and valid document(s) is/are attached).
- All AMPS with a valid MA, validated by the Agency, which have had subsequent updates made, will be validated within 12 months of the last validation being undertaken.

## *9.2. Correcting errors found during validation (creation of EMA versions)& follow up actions*

All data fields that are subject to amendment by the Agency in the event that an error is identified during the validation process are defined within *Annex I – Data fields subject to validation and high level validation process summary.*

If the medicinal product entity was not submitted correctly by the MAH organisation, the Agency corrects the submitted information so that it is in line with the information outlined in the Article 57 guidance documents. This action results in a new version (Agency version) being created and flagged as "*Valid*", and becomes the current version of the medicinal product entity in the database.

Should the marketing-authorisation holder object to any of the changes/corrections made by the Agency or to receive further clarifications on the performed amendments, an email should be submitted to the Article 57 Quality Control Inbox (Art57-QC@ema.europa.eu) providing feedback / clarification. The Art57-QC team will assess the comments or objections raised by MAHs and provide explanation on the rationale of the changes made by the EMA. If corrective actions need to be taken by the EMA, the Art57-QC team will perform an amendment of the AMP information in the Article 57 database by creating a new version of the AMP entity and then inform the MAH. Art57-QC mailbox responds to the received queries within 15 working days.

- If a medicinal product entity has been amended by the Agency during the quality control process, no further action needs to be performed by the MAH organisations using WEB Trader for submissions of their data until their next maintenance submission is performed (e.g. to reflect any changes to the terms of the marketing authorisations following variation, transfer, renewal, suspension, revocation or withdrawal of the marketing authorisation procedure or to nullify the entity).
- If an MAH organisation submitting via the WEB Trader functionality also maintains a local database, the users are advised to review and retrieve the medicinal product entities in which information was amended by the Agency using the XEVMPD Product Export tool and amend this information in their internal systems prior to their next maintenance submission due to changes to the terms of the marketing authorisations.
- MAH organisations that use Gateway for the submissions of their data are advised to retrieve and review the medicinal product entities in which information was amended by the Agency using the XEVMPD Product Export tool and update this information in their internal systems prior to their next maintenance submission due to changes to the terms of the marketing authorisations.

## 9.3. Communication of validation status


**1st level Acknowledgement: On receipt of new or updated data by the Agency**


**2nd level Acknowledgement: On processing of the new or updated data**

Once an XEVPRM is processed by the EudraVigilance system, Gateway and WEB Trader users receive an XML message acknowledgement confirming the result of the load of the message; i.e.:

- '01' XEVPRM processed successfully;
- '02' XEVPRM not processed successfully;

and the result of the operation type assigned to each medicinal product entity in that XEVPRM.

The description text also includes information on:

- The applicable version number
  - Medicinal product submitted in an XEVPRM with an operation type 'Insert (1)' is assigned with a version number (i.e. version number 1). Any subsequent amendment(s) to the medicinal product entity via an operation type 'Update (2)', 'Invalidate MA (6)' or 'Nullification (4)' lead to a new version number being assigned.
  - MAHs can view each individual version available for the EV Code of their AMP entity in the sections "Previous Versions"/"Subsequent Versions" within the AMP entity.
- The quality control activity that the Agency will perform
  - I.e. *"The product will be validated by the EMA in due course. When validated you will receive a further acknowledgement with the message number: "Product Validated XXXX Version [Version Number] / [Date and Time]"."*


**3rd level Acknowledgement: On validation of the new or updated data by the Agency**

Following the validation performed by the Agency, a summary report of changes made by the EMA to the medicinal product entities submitted by the MAH organisation has been sent to the QPPVs via email.

As per agreement at the level of the Article 57 Implementation Working Group, as of 4 November 2015, the manually produced report will be replace by an additional XEVPRM XML Acknowledgement message, sent to the sender's organisation ID to inform the MAH of the outcome of the quality control activity for each authorised medicinal product EV code.

- If no changes were performed by the EMA on a medicinal product entity submitted by the MAH, the operation result description will contain "*Product validated successfully as submitted*".
- If changes were performed by the EMA on a medicinal product entity submitted by the MAH, the operation result description will contain "*Entity updated successfully*". The list of changes made to each field will also be included.

The technical specifications of the XEVPRM acknowledgment message are described in Chapter 5: eXtended EudraVigilance Product Report Acknowledgement.

# 10. Document review & approval

***Reviewed by:*** Ilaria Del Seppia, Data Standardisation and Analytics

***Approved by:*** Peter Arlett, Head of Pharmacovigilance Department

# 11. References


A Guideline on the Summary of Product Characteristics (SmPC)

http://ec.europa.eu/health/files/eudralex/vol-2/c/smpc_guideline_rev2_en.pdf

Article 57 Guidance documents

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000336.jsp&mid=WC0b01ac05804d8b2b&jsenabled=true

Article 57 webpage (Training and Best Practice)

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000596.jsp&mid=WC0b01ac058079126e

Chapter 3.I. XEVPRM Technical Specifications

http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/03/WC500123679.pdf

Chapter 3.II: XEVPRM User Guidance:
http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/03/WC500123681.pdf

Chapter 5: eXtended EudraVigilance Product Report Acknowledgement

http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/03/WC500123669.doc

Legal Notice Legal Notice on the Implementation of Article 57(2) of Regulation (EC) No. 726/2004

http://www.ema.europa.eu/docs/en_GB/document_library/Other/2011/07/WC500108212.pdf

Regulation (EU) No 1235/2010

http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2010:348:0001:0016:EN:PDF

XEVMPD training

http://eudravigilance.ema.europa.eu/human/training3.asp

XEVMPD e-learning

http://eudravigilance.ema.europa.eu/human/training7.asp

# Annex I – Data fields subject to validation and high level validation process summary

The table below identifies the Article 57 data fields which are subject to validation and amendment by the Agency through the data validation process. The intended use of the data fields and the validation process applied by the Agency to each validated data filed is identified.

The data field summary identified in the table below is for quick reference only and does not supersede the guidance provided by Chapter 3.II: XEVPRM User Guidance.

Key


**Full Validation (PPI):** Submitted data validated against product information, usually the SmPC


**Full Validation (other):** Submitted data validated against a data source (Agency or other)


**Logical Validation:** Rational assessment of the validity of the submitted data based on expert knowledge and a sense check of relevant other fields within the database


**Not Validated:** Data field not subject to validation by the Agency because:

i. no data available against which validation can be undertaken by the Agency; or

ii. data is outside the scope of prioritised business areas;

iii. validation is not applicable to this field (identifiers generated automatically by the system).

| Art57 data field ref. code | Art57 data field name | Data field summary | Intended use of Art 57 data field | How are the data fields validated? | | Data field corrected by the EMA? |
|---|---|---|---|---|---|---|
| AP.2 | **Product EV Code** | **Ref: Chapter 3.II (1.2.2)**<br>EudraVigilance (EV) Code of the authorised medicinal product must be specified if the operation type is NOT an 'Insert' (1); i.e. if maintenance related operations are performed on an authorised medicinal product entity which was successfully inserted in the XEVMPD, the EV Code of the AMP entity must be referenced in this data field. | |  | Validation not applicable (identifier) | Not applicable |
| AP.12.13 | **Legal Basis** | **Ref: Chapter 3.II (1.2.12.13)**<br>The description of the legal basis for the marketing authorisation must be specified based on the available values detailed in Chapter 3.II, relating to the application type. | • Data analysis<br>• Regulatory actions and legal obligation |  | Validation using expert knowledge and sense check against other data fields | No |
| AP.12.MPT.1 | **Product Type** | **Ref: Chapter 3.II (1.2.12.14)**<br>The description of the type(s) of the medicinal product must be specified based on the available values as specified in Chapter 3.II. If multiple values apply to the same AMP, then multiple values must be selected. | • Data analysis<br>• Regulatory actions and legal obligation |  | Validation using expert knowledge and sense check against other data fields | No |
| AP.APF.1 | **Authorised Pharmaceutical Form** | **Ref: Chapter 3.II (1.2.14) & SmPC (Section 3)**<br>The authorised pharmaceutical form(s) must be specified as indicated in the section 3. of the SmPC. | • Data analysis<br>• Regulatory actions and legal obligation<br>• Communication with stakeholders |  | Validation against product information (SmPC Section 3) | Yes |

| Art57 data field ref. code | Art57 data field name | Data field summary | Intended use of Art 57 data field | How are the data fields validated? | | Data field corrected by the EMA? |
|---|---|---|---|---|---|---|
| AP.4 | **MAH Code** | **Ref: Chapter 3.II (1.2.4) & SmPC (Section 7)**<br>MAH EV Code corresponding to the legal entity of the medicinal product in a given country as indicated in section 7. SmPC must be specified. | | None | Validation not applicable (identifier) | Not applicable |
| O.2 | **Organisation Name** | **Ref: Chapter 3.II (1.6.2) & SmPC (Section 7)**<br>The name of the MAH organisation (legal entity) of the medicinal product must be specified as indicated in section 7. of the SmPC. | • Data analysis<br>• Regulatory actions and legal obligation<br>• Communication with stakeholders | Full (PPI) | Validation against product information (SmPC Section 7) | Yes |
| O.4 | **(MAH) EV Code** | **Ref: Chapter 3.II (1.6.4)**<br>EudraVigilance (EV) Code of the MAH organisation must be specified if the operation type is NOT an 'Insert'; i.e. if maintenance related operations are performed on an MAH organisation entity successfully inserted in the XEVMPD, the EV Code of the MAH organisation entity must be referenced in this field. | | None | Validation not applicable (identifier) | Not applicable |
| O.6 | **(MAH) Address** | **Ref: Chapter 3.II (1.6.6) & SmPC (Section 7)**<br>The address of the MAH (legal entity) must be specified as stated in section 7. of the SmPC. | • Data analysis<br>• Regulatory actions and legal obligation<br>• Communication with stakeholders | Full (PPI) | Validation against product information (SmPC Section 7) | Yes |

| Art57 data field ref. code | Art57 data field name | Data field summary | Intended use of Art 57 data field | How are the data fields validated? | | Data field corrected by the EMA? |
|---|---|---|---|---|---|---|
| O.7 | **(MAH) City** | **Ref: Chapter 3.II (1.6.7) & SmPC (Section 7)**<br>The city of the MAH must be specified as stated in section 7. of the SmPC. | • Data analysis<br>• Regulatory actions and legal obligation<br>• Communication with stakeholders | Full (PPI) | Validation against product information (SmPC Section 7) | Yes |
| O.8 | **(MAH) State (region)** | **Ref: Chapter 3.II (1.6.8) & SmPC (Section 7)**<br>The state (region) of the MAH may be specified as stated in section 7. of the SmPC. | • Outside the scope of the prioritised business areas | Full (PPI) | Validation against product information (SmPC Section 7) | Yes |
| O.9 | **(MAH) Postcode** | **Ref: Chapter 3.II (1.6.9) & SmPC (Section 7)**<br>The postcode of the MAH must be specified as stated in section 7. of the SmPC. | • Data analysis<br>• Regulatory actions and legal obligation<br>• Communication with stakeholders | Full (PPI) | Validation against product information (SmPC Section 7) | Yes |
| O.10 | **(MAH) Country Code** | **Ref: Chapter 3.II (1.6.10) & SmPC (Section 7) & ISO-3166-1 standard**<br>The country code of the MAH must be specified as stated in section 7. of the SmPC.<br>The country code is to be specified using the ISO-3166-1 standard. | • Data analysis<br>• Regulatory actions and legal obligation<br>• Communication with stakeholders | Full (PPI) | Validation against product information (SmPC Section 7) | Yes |

| Art57 data field ref. code | Art57 data field name | Data field summary | Intended use of Art 57 data field | How are the data fields validated? | | Data field corrected by the EMA? |
|---|---|---|---|---|---|---|
| O.19 | **(MAH) SME Status** | **Ref: Chapter 3.II (1.6.15)**<br>The SME status applicable to the MAH organisation must be selected.<br>The following values are available:<br>- N/A (1) – to be used by non-SMEs<br>- Micro (2)<br>- Small (3)<br>- Medium (4) | | None | Data is outside the scope of prioritised business areas | Not applicable |
| O.20 | **(MAH) SME Number** | **Ref: Chapter 3.II (1.6.16)**<br>The SME number may be provided if available. | | None | Outside the scope of the prioritised business areas | Not applicable |
| AP.5 | **QPPV Code** | **Ref: Chapter 3.II (1.2.5)**<br>The QPPV code of the QPPV responsible for the authorised medicinal product must be specified. | | None | Validation not applicable (identifier) | Not applicable |
| AP.6 | **MFL details** | **Ref: Chapter 3.II (1.2.6)**<br>The Pharmacovigilance System Master File Location (PSMFL) Code of the place where the PSMF for the authorised medicinal product is located must be specified if the PSMFL information was submitted in the XEVMPD and the PSMFL Code is available. | • Communication with stakeholders | Logical | Validation by checking dialling code correct, number of required digits present | No |

| Art57 data field ref. code | Art57 data field name | Data field summary | Intended use of Art 57 data field | How are the data fields validated? | | Data field corrected by the EMA? |
|---|---|---|---|---|---|---|
| AP.7 | **PhV enquiry email** | **Ref: Chapter 3.II (1.2.7)**<br>The email address where enquiries related to Pharmacovigilance can be submitted must be specified. | • Communication with stakeholders |  | Validation by checking that the correct format of the e-mail address applies | No |
| AP.8 | **PhV enquiry phone** | **Ref: Chapter 3.II (1.2.8)**<br>The phone number where enquiries related to Pharmacovigilance can be directed must be specified. It may be the same as the phone number of the QPPV. | • Communication with stakeholders |  | Validation by checking dialling code correct, number of required digits present | No |
| AP.11 | **Info date** | **Ref: Chapter 3.II (1.2.11)**<br>The date when the lifting of suspension of a marketing authorisation becomes effective must be specified when "Authorisation Status" changes from "Valid - Suspended" to any "Valid" status. | • Outside the scope of the prioritised business areas |  | Validation through sense check of chronology of suspension date and lifting of suspension date | No |
| AP.12.1 | **Authorisation Country** | **Ref: Chapter 3.II (1.2.12.1) & ISO-3166-1 standard**<br>The country code of the country of authorisation must be specified. The country code is to be specified using the ISO-3166-1 standard. The official list of ISO 3166-1 country codes is maintained by the International Organization for Standardization. | • Data analysis<br>• Regulatory actions and legal obligation<br>• Communication with stakeholders |  | Validation against product information (SmPC – language check, check of authorisation number format - specific to country) | No |

| Art57 data field ref. code | Art57 data field name | Data field summary | Intended use of Art 57 data field | How are the data fields validated? | | Data field corrected by the EMA? |
|---|---|---|---|---|---|---|
| AP.12.2 | **Authorisation Procedure** | **Ref: Chapter 3.II (1.2.12.2)**<br>The procedure through which the medicinal product was authorised must be specified. List of available authorisation procedure values can be found in the XEVMPD look-up table and in the Controlled Vocabulary (CV) lists published on the Agency's website. | • Data analysis<br>• Regulatory actions and legal obligation<br>• Communication with stakeholders | Logical | Validation through sense check against authorisation country and MRP number | No |
| AP.12.3 | **Authorisation Status** | **Ref: Chapter 3.II (1.2.12.3)**<br>The status of the authorisation of a medicinal product must be specified. The information stated in this field does not refer to the marketing status (i.e. marketed/not marketed). List of available authorisation status values can be found in the XEVMPD look-up table and in the Controlled Vocabulary (CV) lists published on the Agency's website. | • Regulatory actions and legal obligation<br>• Communication with stakeholders | Logical | Validation through sense check against authorisation country and MRP number | No |
| AP.12.4 | **Authorisation Number** | **Ref: Chapter 3.II (1.2.12.4) & SmPC (Section 8)**<br>Marketing authorisation number assigned by the Competent Authority and as stated in section 8 of the SmPC must be specified. Only one number must be stated in this field. If multiple authorisation numbers are stated in the SmPC, multiple product entities should be submitted in the XEVMPD. | • Data analysis<br>• Regulatory actions and legal obligation<br>• Communication with stakeholders | Full (PPI) | Validation of entry against product information (SmPC Section 8) | Yes |

| Art57 data field ref. code | Art57 data field name | Data field summary | Intended use of Art 57 data field | How are the data fields validated? | | Data field corrected by the EMA? |
|---|---|---|---|---|---|---|
| AP.12.5 | **Authorisation /Renewal Date** | **Ref: Chapter 3.II (1.2.12.5) & SmPC (Section 9)** 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 of the SmPC. The authorisation/ renewal date is to be specified consisting of year, month and day or year and month. | • Regulatory actions and legal obligation<br>• Communication with stakeholders | Full (PPI) | Validation of entry against product information (SmPC Section 9) | Yes |
| AP.12.7 | **MRP Number** | **Ref: Chapter 3.II (1.2.12.7)** MRP/DCP/EMEA Procedure Number must be specified depending on the applicable authorisation procedure. The format of the MRP/DCP number should be the same as in the SmPC (if included) without “MR”, “DC” etc. or as stated in the MR Index on the HMA website, which is a combination of only four sections (CC/D/nnnn/sss). | • Data analysis<br>• Regulatory actions and legal obligation<br>• Communication with stakeholders | Full (other) | Validation against HMA database | Yes |
| AP.12.8 | **EU Number** | **Ref: Chapter 3.II (1.2.12.8) & SmPC (Section 8)** The marketing authorisation number as assigned by the EU Commission and as stated in section 8. of the SmPC must be specified. | • Data analysis<br>• Regulatory actions and legal obligation<br>• Communication with stakeholders | Full (PPI) | Validation against product information (SmPC Section 8) | Yes |
| AP.12.9 | **Orphan Drug** | **Ref: Chapter 3.II (1.2.12.9)** The value indicating whether the AMP is considered an orphan drug medicine must be specified. The disease (orphan) designation of a medicinal product from the European Medicines Agency's Committee on Orphan | • Outside the scope of the prioritised business areas | Full (other) | Full validation against EMA database (orphan drugs database) | Yes |

| Art57 data field ref. code | Art57 data field name | Data field summary | Intended use of Art 57 data field | How are the data fields validated? | | Data field corrected by the EMA? |
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| | | Medicinal Products (COMP) must be specified unless the operation type is 'Nullification (4)' or 'Invalidate MA (6)' | | | | |
| AP.12.10 | **Additional Monitoring** | **Ref: Chapter 3.II (1.2.12.10)& SmPC**<br>The value indicating whether the AMP is subject to additional monitoring must be specified. Indication for additional monitoring (black triangle/symbol) for a specific AMP can be found in the SmPC of the authorised medicinal product. | | None | Outside the scope of the prioritised business areas | Not applicable |
| AP.12.12 | **Invalidation/ Withdrawn Date** | **Ref: Chapter 3.II (1.2.12.12)**<br>The date as of when the "Authorisation status" “Not valid” or “Valid - Suspended" becomes effective must be specified depending on the applicable authorisation status. | • Regulatory actions and legal obligation | Logical | Validation through sense check of timelines – for example, withdrawals to occur after authorisation. Check against supporting documentation regarding withdraws. | No |
| AP.13.1 | **Product Name** | **Ref: Chapter 3.II (1.2.13.1) & SmPC (Section 1)**<br>The medicinal product name stated in Section 1. of the SmPC must be specified. | • Data analysis<br>• Regulatory actions and legal obligation<br>• Communication with stakeholders | Full (PPI) | Validation against product information (SmPC Section 1) | Yes |
| AP.13.2 | **Product Short Name** | **Ref: Chapter 3.II (1.2.13.2) & SmPC (Section 1)**<br>If included in the medicinal product name stated in | • Data analysis<br>• Regulatory actions and legal | Full (PPI) | Validation against product information | Yes |

| Art57 data field ref. code | Art57 data field name | Data field summary | Intended use of Art 57 data field | How are the data fields validated? | | Data field corrected by the EMA? |
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| | | Section 1 of the SmPC, the invented (trade) name part with any other designation except the strength/ pharmaceutical form must be specified. | • obligation<br>• Communication with stakeholders | | (SmPC Section 1) | |
| AP.13.3 | **Product Generic Name** | **Ref: Chapter 3.II (1.2.13.3) & SmPC (Section 1)** If included in the medicinal product name stated in Section 1 of the SmPC, the invented (trade) name part with any other designation except the strength/pharmaceutical form must be specified. | • Data analysis<br>• Regulatory actions and legal obligation<br>• Communication with stakeholders | Full (PPI) | Validation against product information (SmPC Section 1) | Yes |
| AP.13.4 | **Product Company Name** | **Ref: Chapter 3.II (1.2.13.4) & SmPC (Section 1)** If included in the medicinal product name stated in Section 1. of the SmPC, the Company name part of the medicinal product name without any other designations such as trade mark, strength or pharmaceutical form must be specified. | • Data analysis<br>• Regulatory actions and legal obligation<br>• Communication with stakeholders | Full (PPI) | Validation against product information (SmPC Section 1) | Yes |
| AP.13.5 | **Product Strength Name** | **Ref: Chapter 3.II (1.2.13.5) & SmPC (Section 1)** If included in the medicinal product name stated in Section 1. of the SmPC, the strength part of the medicinal product name without any other designations must be specified. | • Data analysis | Full (PPI) | Validation against product information (SmPC Section 1) | Yes |
| AP.13.6 | **Product Form Name** | **Ref: Chapter 3.II (1.2.13.6) & SmPC (Section 1)** If included in the medicinal product name stated in Section 1. of the SmPC, the pharmaceutical form name part of the medicinal product name without any other designations must be specified. | • Data analysis | Full (PPI) | Validation against product information (SmPC Section 1) | Yes |

| Art57 data field ref. code | Art57 data field name | Data field summary | Intended use of Art 57 data field | How are the data fields validated? | | Data field corrected by the EMA? |
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| AP.13.7 | **Package Description** | **Ref: Chapter 3.II (1.2.15) & SmPC (Section 6.5)**<br>A brief package description of the pack size(s) corresponding to the referenced authorisation number as stated in section 6.5 of the SmPC may be specified in the language of the SmPC. An English text is also acceptable. | • Outside the scope of the prioritised business areas until ISO IDMP implementation (2016) | Full (PPI) | Validation against product information (SmPC Section 6.5) | Yes |
| AP.14 | **Comments** | **Ref: Chapter 3.II (1.2.16) & SmPC (Section 4.1, 4.2)**<br>The text in English “Medicinal product authorised for the treatment in children” must be stated if an indication for paediatric population (children under the age of 18) is stated in Section 4.1 of the SmPC and/or a posology is stated for any subset of the paediatric population in Section 4.2. of the SmPC. | • Data analysis<br>• Regulatory actions and legal obligation<br>• Communication with stakeholders | Full (PPI) | Validation against product information (SmPC Section 4.1, 4.2) | Yes |
| PP.1 | **Pharmaceutical Form** | **Ref: Chapter 3.II (1.2.17.1) & SmPC (Section 3)**<br>The administrable pharmaceutical form(s) must be specified in accordance with Section 3. of the SmPC. The pharmaceutical form stated in section 3. of the SmPC may differ from the standard term included in the EDQM standard term list. In such cases, the EDQM standard term available in the XEVMPD must be selected. | • Data analysis<br>• Regulatory actions and legal obligation<br>• Communication with stakeholders | Full (PPI) | Validation against product information (SmPC Section 3) | Yes |

| Art57 data field ref. code | Art57 data field name | Data field summary | Intended use of Art 57 data field | How are the data fields validated? | | Data field corrected by the EMA? |
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| PP.AR.1 | **Administration Route** | **Ref: Chapter 3.II(1.2.17.2) & SmPC (Section 4.2)**<br>The route of administration of the pharmaceutical form must be specified in accordance with Section 4.2. of the SmPC. Administration route section describes the route(s) of administration i.e. the path by which the medicinal product is taken into or makes contact with the body. | • Regulatory actions and legal obligation<br>• Communication with stakeholders | Full (PPI) | Validation against product information (SmPC Section 4.2) | Yes |
| PP.ACT.1 | **Active Substance Code** | **Ref: Chapter 3.II (1.2.17.4) & SmPC (Section 2)**<br>The EV Code(s) of the substance(s) indicated as the active ingredient(s) of the medicinal product according to the description provided in section 2. of the SmPC must be specified. The substance name must be specified in line with the description of the ingredients present in the medicinal product as described in the SmPC of the country of authorisation | | None | Validation not applicable (identifier) | Not applicable |
| PP.ACT.2-14 | **Active Substance and Strength** | **Ref: Chapter 3.II (1.2.17.5) & SmPC (Section 2)**<br>The strength of the substance name specified in the "Active ingredient substance code" must be specified in accordance with section 2. of the SmPC.<br>Strength must be entered in the XEVMPD in accordance with the ISO IDMP standards based on a numerator and denominator. | • Data analysis<br>• Regulatory actions and legal obligation<br>• Communication with stakeholders | Full (PPI) | Validation against product information (SmPC Section 2) | Yes |

| Art57 data field ref. code | Art57 data field name | Data field summary | Intended use of Art 57 data field | How are the data fields validated? | | Data field corrected by the EMA? |
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| PP.ADJ.1 | **Adjuvant Substance Code** | **Ref: Chapter 3.II (1.2.17.10) & SmPC (Section 2 or 6)**<br>The EV Code(s) of the substance(s) indicated as adjuvant(s) of the medicinal product according to the description provided in section 2 (or section 6) of the corresponding SmPC must be specified. | • Data analysis<br>• Regulatory actions and legal obligation<br>• Communication with stakeholders | Full (PPI) | Validation against product information (SmPC Section 2) | Yes |
| PP.ADJ.2-14 | **Adjuvant Substance Strength** | **Ref: Chapter 3.II (1.2.17.11) & SmPC (Section 6.1)**<br>The strength of the substance stated as the adjuvant of the pharmaceutical product in section 2. of the corresponding SmPC must be specified. Whenever possible, the substance strength should be expressed as a unit of measurement. | • Data analysis<br>• Regulatory actions and legal obligation<br>• Communication with stakeholders | Full (PPI) | Validation against product information (SmPC Section 2) | Yes |
| PP.EXC.1 | **Excipient Substance Code** | **Ref: Chapter 3.II(1.2.17.8) & SmPC (Section 6.1)**<br>The EV Code(s) of the substance(s) indicated as excipient(s) of the medicinal product according to the description provided in section 6.1. of the corresponding SmPC must be specified. The substance name must be specified in line with the description of the ingredients present in the medicinal product as described in the SmPC of the country of authorisation | | None | Validation not applicable (identifier) | Not applicable |
| PP.EXC.2-14 | **Excipients and strength** | **Ref: Chapter 3.II (1.2.17.9) & SmPC (Section 6.1)**<br>It is optional to describe the strength(s) of excipient(s). If this information is provided, the | • Outside the scope of the prioritised business areas | Full (PPI) | Validation against product information (SmPC Section 6.1) | Yes |

| Art57 data field ref. code | Art57 data field name | Data field summary | Intended use of Art 57 data field | How are the data fields validated? | | Data field corrected by the EMA? |
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| | | strength(s) of the excipient(s) as listed in section 6.1 of the SmPC must be specified in the pharmaceutical product. | | | | |
| PP.MD.1 | **Medical Device Code** | **Ref: Chapter 3.II (1.2.17.12)**<br>The EV code of a medical device where it forms an integral part of the medicinal product must be specified. Medical device description is currently only required for Advanced Therapy Medicinal Products (ATMPs), where applicable. | • Regulatory actions and legal obligation<br>• Communication with stakeholders | Full (PPI) | No data currently submitted for validation | Yes |
| AP.ATC.1 | **ATC Code** | **Ref: Chapter 3.II (1.2.18) & SmPC (Section 5.1)**<br>The ATC code as described in Section 5.1 of the SmPC must be specified. A “standard” ATC code must be specified whenever possible. MAHs may reference deprecated ATC Codes in Authorised Medicinal Products to facilitate the Article 57(2) electronic submission of information on medicines. | • Data analysis<br>• Regulatory actions and legal obligation<br>• Communication with stakeholders | Full (PPI) | Validation against product information (SmPC Section 5.1) | Yes |
| AP.IND.1 | **MedDRA Version** | **Ref: Chapter 3.II (1.2.19.1)**<br>The indication(s) is/are to be coded using MedDRA in its latest version where applicable | | None | No data available against which validation can be undertaken | Not applicable |
| AP.IND.2 | **MedDRA Level** | **Ref: Chapter 3.II (1.2.19.2)**<br>Low Level Terms (LLT) must be specified. | | None | No data available against which validation can be undertaken | Not applicable |
| AP.IND.3 | **Indications (MedDRA)** | **Ref: Chapter 3.II (1.2.19.3)**<br>The indication(s) is/are to be coded using the English term and corresponding code. Where a specific | • Data analysis<br>• Communication with stakeholders | Full (PPI) | Validation against product information (SmPC Section | Yes |

| Art57 data field ref. code | Art57 data field name | Data field summary | Intended use of Art 57 data field | How are the data fields validated? | | Data field corrected by the EMA? |
|---|---|---|---|---|---|---|
| | | language is not supported in MedDRA, the MedDRA Code associated with the English equivalent term should be used. Multiple terms can be used to code the medical concepts of indication(s), the signs, symptoms or intended effects. It is not necessary to update medicinal product entries when a new MedDRA version is released. If a new MedDRA version is available, the latest current version should be used to codify the indications. Efforts should be made to capture the most granular and comprehensive level of information available in MedDRA; where the stage or type of a disease is available, this should be captured as well. | | | 4.1)<br>It is noted that there is scope for interpretation and the Agency is in the process of creating a detailed guide for further clarification. | |
| AP.PEV.1 | **Previous EV Code** | **Ref: Chapter 3.II (1.2.20)**<br>The EV Code of the development product may be specified if the authorised product was submitted to the XEVMPD in its development form. The EV Code of an authorised product must be specified in the context of Transfer/Renewal of Marketing Authorisation as applicable. | • Data analysis<br>• Regulatory actions and legal obligation<br>• Communication with stakeholders |  | Validation through sense check against previous and current EV codes | No |
| AP.PPI.1 | **Attachment EV Code** | **Ref: Chapter 3.II (1.2.21.1)**<br>The EV Code of the attachment referring to the authorised medicinal product must be specified. | |  | Validation not applicable (identifier) | Not applicable |

| Art57 data field ref. code | Art57 data field name | Data field summary | Intended use of Art 57 data field | How are the data fields validated? | | Data field corrected by the EMA? |
|---|---|---|---|---|---|---|
| AP.PPI.2 | **Attachment Validity Declaration** | **Ref: Chapter 3.II (1.2.21.2)**<br>Validity confirmation that the referenced attachment is the latest version of the documentation must be provided when performing an update or insert of an authorised product where a referenced PPI attachment was previously loaded in the XEVMPD. | |  | No data available against which validation can be undertaken | Not applicable |

# Annex II - Use of AMP versions from Art57 database

The table below defines which version of the data is used by the various processes relying on the Article 57 database.

Key

**Latest Version:** Most recent data available as recorded in the Article 57 database

| Art57 Business Use | AMP version used from Art57 database |
|---|---|
| Performance of data analysis: | |
| • EudraVigilance Data Analysis System (EVDAS) | All versions |
| • Signal Management | Latest EMA version |
| • Establish a complete list of medicinal product and active substance information to support the coding of such information reported in Individual Case Safety Reports (ICSRs) | Latest EMA version |
| Facilitate medicines regulation and fulfil regulatory actions and legal obligations: | |
| • Referrals | Latest version (MAH or EMA) |
| • PSUR repository | Latest version (MAH or EMA) |
| • PSUR single assessment | Latest version (MAH or EMA) |
| • Medical Literature Monitoring | Latest version (MAH or EMA) |
| • Calculation of pharmacovigilance fees (Annual and Procedural) | Latest version (MAH or EMA) |
| • Art57 Publication Dashboard Report (notifications of QPPV/MFL to NCAs) – In development | Latest version (MAH or EMA) |
| Communicate effectively with Agency stakeholders | |
| • Targeted Pharmacovigilance Risk Assessment Committee (PRAC) communications | Latest version (MAH or EMA) |