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Calculating 'chargeable units' for pharmacovigilance fees as specified in Regulation (EU) No 658/2014

Guidance on how 'chargeable units' are derived from medicinal product information held within the 'Article 57' database

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Table of Contents

Disclaimer:

- All examples used in this document are fictitious and used for illustrative purposes only. Any resemblance to real medicinal products, marketing authorisation holders or individuals is purely coincidental and unintended.

1. Purpose

The purpose of this document is to describe the method used by the European Medicines Agency, hereafter referred to as 'the Agency', to determine the number of 'chargeable units' applicable to each marketing authorisation holder for the purpose of levying pharmacovigilance fees. The pharmacovigilance fees referred to in this document relate to the fees laid down in Regulation (EU) No 658/2014 which enables the Agency to collect fees for the conduct of pharmacovigilance activities as assigned to it by the 2010 Pharmacovigilance Legislation that became applicable in July 2012.

This document specifically focuses on the relevant fields in the 'Article 57' database[1] that are used for the calculation of the 'chargeable unit' and why certain products are excluded/included from the scope of the calculation. It will also explain how data that does not conform to the detailed guidance on the electronic submission of information on medicinal products for human use by marketing authorisation holders to the European Medicines Agency in accordance with Article 57(2), second subparagraph of Regulation (EC) No 726/2004 is handled in order to produce a 'chargeable unit'. Each data component within the dataset which defines a 'chargeable unit' will therefore be explained in detail regarding how it is derived from the 'Article 57' database.

This document will also provide information on the additional 'Article 57' fields used for broader pharmacovigilance fees purposes such as for the production of advice notes and for invoicing purposes.

2. Intended audience

The intended audience for this document are:

- Marketing authorisation holders (MAHs)
- Qualified Persons for Pharmacovigilance (QPPVs)
- Any other users of the 'Article 57' database

3. Scope

This document will provide information on how 'chargeable units', as defined in Regulation (EU) No 658/2014, are derived from medicinal product information held in the 'Article 57' database. It will not explain the product selection process used for procedure-based fees and the calculation of the fee, such as e.g. for referral procedures, as this is determined separately in accordance with the scope and legal requirements of the regulatory procedure concerned. It will also not explain how these 'chargeable units', once determined, are then translated into the fee amounts seen on pharmacovigilance fees-related invoices. Therefore, fee levels and the application of fee reductions or exemptions are out-of-scope for this document. The Agency has already published an explanatory note on pharmacovigilance fees payable to the Agency for its monitoring of the safety of medicines authorised in the European Union (EU). It describes:

- Each of the types of pharmacovigilance fees to be levied;
- The fee amounts per fee type;
- Applicable fee exemptions and reductions; and
- Explains how the Agency charges and collects fees from marketing authorisation holders.

[1] The 'Article 57' database is the database maintained at the European Medicines Agency established under the Article 57(2) of Regulation (EC) No 726/2004 where marketing authorisation holders are required to submit information to the Agency using the electronic format referred to as Article 57 format or eXtended EudraVigilance Product Report Message (XEVPRM) format.

4. Definition of a 'chargeable unit'

As provided for in Article 2 of Regulation (EU) No 658/2014, a 'chargeable unit' means a unit defined by a unique combination of the following dataset derived from information on all medicinal products authorised in the Union held by the Agency, and consistent with the obligation of marketing authorisation holders referred to in points (b) and (c) of Article 57(2) of Regulation (EC) No 726/2004 to submit such information to the database referred to in point (l) of the second subparagraph of Article 57(1) of that Regulation:

(a) name of the medicinal product, as defined in point 20 of Article 1 of Directive 2001/83/EC;

(b) marketing authorisation holder;

(c) the Member State in which the marketing authorisation is valid;

(d) active substance or a combination of active substances; and

(e) pharmaceutical form.

Point (d) of the first subparagraph is not applicable in the case of authorised homeopathic medicinal products or authorised herbal medicinal products, as defined, respectively, in points 5 and 30 of Article 1 of Directive 2001/83/EC.

Figure 1. Illustration of the unique combination of the following dataset which is used to derive a 'chargeable unit'

Each of these elements will be explored in greater detail to provide readers with an opportunity to understand how this information is obtained from the 'Article 57' database and how it is used to derive a 'chargeable unit'.

4.1. Name of the medicinal product, as defined in point 20 of Article 1 of Directive 2001/83/EC

Directive 2001/83/EC, in Article 1, point 20, refers to the name of the medicinal product as "The name, which may be either an invented name not liable to confusion with the common name, or a common or scientific name accompanied by a trade mark or the name of the marketing authorisation holder."

In terms of the 'Article 57' database, the production of the 'chargeable unit' product name, as shown in the advice notes and invoices, is derived using the following data elements:

Table 1. 'Article 57' data elements used to derive the 'Name of the medicinal product'

'Article 57' data elements reference code	'Article 57' data elements reference name	Reference to detailed guidance – chapter 3.II: XEVPRM User guidance
AP.13.1	Productname	Field should specify the Full presentation name as indicated in 1.2.13.1.
AP.13.2	Productshortname	Field should specify the Product Short Name as indicated in 1.2.13.2.
AP.13.3	Productgenericname	Field should specify the Product INN/Common Name as indicated in 1.2.13.3
AP.13.4	Productcompanyname	Field should specify the Product Company Name as indicated in 1.2.13.4

NOTE: If the full product name (i.e. AP.13.1) does not contain the company name, this information will not be derived into the final 'chargeable unit' product name. This is specifically applicable to generic products where the 'Article 57' requirement demands the provision of the generic company name where the product INN/Common Name is only available in the full presentation name (i.e. Business Rules: AP.13.4.BR. from *Article 57 Detailed Guidance Chapter 3.I*) .

4.1.1. Example 1: product name is an invented name

Productname (Full presentation name) = **ProductABC 200 mg capsules**

Productshortname = **ProductABC**

Productgenericname = (i.e.Product INN/Common Name) **= N/A**

Productcompanyname = **N/A**

Name of medicinal product used for 'Chargeable Unit' = ProductABC

4.1.2. Example 2: product name is a common or scientific name accompanied by a trade mark or the name of the marketing authorisation holder

Productname (Full presentation name) = **Ibuprofen PharmaZ 200 mg capsules**

Productshortname = **N/A**

Productgenericname (i.e.Product INN/Common Name) = **Ibuprofen**

Productcompanyname = **PharmaZ**

Name of medicinal product used for 'Chargeable Unit' = Ibuprofen PharmaZ

4.1.3. Key Considerations regarding the Medicinal Product Name

- The product presentation name elements should correspond to the name of the medicinal product as granted by the NCA/EC at time of authorisation and as stated in section 1 of the SmPC.

- Guidance on the correct procedure and principles to handle product names in the XEVMPD can be found in the 'EMA splitting of the Full Presentation Name of the medicinal product best practice' document.

4.2. Marketing Authorisation Holder

The 'Marketing Authorisation Holder' relates to the holder of the marketing authorisation, as granted by the NCA/EC, for the medicinal product concerned.

In terms of the 'Article 57' database, the following data elements are taken into consideration when producing the 'chargeable unit' Marketing Authorisation Holder as shown in the advice notes and invoices:

Table 2. 'Article 57' data elements used to derive the 'Marketing Authorisation Holder'

'Article 57' data elements reference code	'Article 57' data elements reference name	Reference to detailed guidance – chapter 3.II: XEVPRM User guidance
O.2	Name_org	Field should specify the MAH name as indicated in 1.6.2. Organisation name.
O.4	(MAH) ev_code	1.6.4. EV Code

Although both the Name_org and (MAH) ev_code are used in the 'chargeable unit', the data element used to determine the 'Marketing Authorisation Holder' component of the 'chargeable unit' is the (MAH) ev_code and **not** the Name_org. This is because the (MAH) ev_code represents the legal entity of the medicinal product in a given country as indicated in section 7. Marketing Authorisation Holder of the SmPC.

4.2.1. How these data elements are used to derive the 'Marketing Authorisation Holder'

All distinct (MAH) ev_codes which are associated with medicinal products that are subject to a pharmacovigilance fee are selected. These (MAH) ev_codes are then used to obtain detailed marketing authorisation holder information from the 'Article 57' database such as the marketing authorisation holder's name (using the Name_org field from the 'Article 57' database). This name is then used as the 'Marketing Authorisation Holder' component in the 'chargeable unit' that appears in advice notes and invoices.

4.2.2. Key Considerations regarding the 'Marketing Authorisation Holder'

- The Organisation controlled vocabulary should be de-duplicated and the marketing authorisation holder name should be consistently populated in the controlled vocabulary and referenced in the relevant products as applicable.
- Furthermore, marketing authorisation holders should reconcile and dismiss (i.e. nullify) the not-used marketing authorisation holder name and address in the XEVMPD Organisation controlled vocabulary (applicable to marketing authorisations holders that have previously submitted a variation).
- These steps will prevent the generation of duplicate 'chargeable units' and the duplication of invoices.

4.3. Member State in which the marketing authorisation is valid and Authorisation Procedure

Table 3. 'Article 57' data elements used to derive the 'Member State in which the marketing authorisation is valid'

'Article 57' data elements reference code	'Article 57' data elements reference name	Reference to detailed guidance – chapter 3.II: XEVPRM User guidance
AP.12.1	Authorisationcountrycode	Field should specify the Authorisation Country Code as indicated in 1.2.12.1.
AP.12.2	AuthorisationProcedure	Field should specify the Authorisation Procedure as indicated in 1.2.12.2.

4.3.1. How will these data elements be used to determine the 'Member State in which the marketing authorisation is valid'

The 'chargeable unit' will use the Authorisation Country Code, as held in the 'Article 57' database, as the 'Member State in which the marketing authorisation is valid'.

For medicinal products where the value in that field = EU and/or the Authorisation Procedure = 1 (EU authorisation procedures - Centralised Procedure), a new 'chargeable unit' will be generated for each distinct Authorisation Country Code, reflecting the fact that marketing authorisations granted for such products are valid throughout the EU, Iceland and Norway.

4.3.2. Example 1: How different authorisation country codes generate new 'chargeable units'

Table 4. Example 'chargeable units' with varying Member States in which the marketing authorisation is valid

Medicinal Product Name	Marketing Authorisation Holder	Member State where marketing authorisation is valid	Active Substance Names	Pharmaceutical Form
EXAMPLE	MAH Z	FR	FENTANYL	SUBLINGUAL TABLET
EXAMPLE	MAH Z	IS	FENTANYL	SUBLINGUAL TABLET
EXAMPLE	MAH Z	SI	FENTANYL	SUBLINGUAL TABLET
EXAMPLE	MAH Z	DK	FENTANYL	SUBLINGUAL TABLET
EXAMPLE	MAH Z	ES	FENTANYL	SUBLINGUAL TABLET
EXAMPLE	MAH Z	DE	FENTANYL	SUBLINGUAL TABLET
EXAMPLE	MAH Z	IT	FENTANYL	SUBLINGUAL TABLET
EXAMPLE	MAH Z	SE	FENTANYL	SUBLINGUAL TABLET

8 'chargeable units' have been generated due to the variation in the field for 'Member State where the marketing authorisation is valid'. One 'chargeable unit' per 'Member State where the marketing authorisation is valid' has been produced.

4.3.3. Key Considerations regarding the 'Member State in which the marketing authorisation is valid' and the 'Authorisation Procedure'

- If the authorisation procedure (i.e. centrally authorised procedure, nationally authorised procedure, mutual recognition procedure) and the corresponding Authorisation Country Code has been incorrectly inputted into the 'Article 57' database, the number of 'chargeable units' calculated may be wrong and the marketing authorisation holder could be incorrectly invoiced. It is therefore important to follow the business rules guidance (AP.12.1.BR.2) provided on assigning Authorisation Country Codes and Authorisation Procedure in the 'Article 57' database.
- Of note, for centrally authorised products where the Authorisation Country Code has been correctly set to 'EU' and/or the Authorisation Procedure is set to 1 (EU authorisation procedures - Centralised Procedure), this product will be split into 30 'chargeable units', one per EU member state, Iceland and Norway. There should be in total 30 'chargeable' units for the product including the products in Iceland and Norway.
- If medicinal product ev_codes for Iceland or Norway are not present in the 'Article 57' database for centrally authorised medicinal products, the corresponding 'chargeable units' will be generated by the 'chargeable unit' algorithm. However, in order to avoid the creation of duplicate 'chargeable units' due to the presence of medicinal product ev_codes for Iceland and Norway, the 'chargeable unit' algorithm de-duplicates these products to ensure that marketing authorisation holders are not incorrectly charged.
- In order to de-duplicate, centrally authorised medicinal products that generate the same 'chargeable unit' are identified by comparing the following data elements: Organisation EV Code, Derived Active Substance/or combination of Active Substances, Derived Pharmaceutical Form and derived Medicinal Product Name.

4.3.4. Example 2: Splitting of 'chargeable units' where authorisation country code = 'EU'

Table 5. Example of 'chargeable units' split into 30 EU member states, Iceland and Norway

Medicinal Product Name	Marketing Authorisation Holder	Member State where marketing authorisation is valid	Active Substance Names	Pharmaceutical Form
EXAMPLE	MAH Z	EU	PARACETAMOL	FILM-COATED TABLET

X 30 Member States, Iceland and Norway

Medicinal Product Name	Marketing Authorisation Holder	Member State where marketing authorisation is valid	Active Substance Names	Pharmaceutical Form
EXAMPLE	MAH Z	IT	PARACETAMOL	FILM-COATED TABLET
EXAMPLE	MAH Z	FR	PARACETAMOL	FILM-COATED TABLET
EXAMPLE	MAH Z	DE	PARACETAMOL	FILM-COATED TABLET
		…Repeat line for all 30 EU Member States, Iceland and Norway		

As **Authorisation Country Code = EU and/or Authorisation Procedure = 1**, 30 'chargeable units' will be generated from this medicinal product entry in the 'Article 57' database. In order to avoid the creation of duplicate 'chargeable units' due to the presence of medicinal product ev_codes for Iceland and Norway, the 'chargeable unit' algorithm will de-duplicate these products.

4.4. Active substance or a combination of active substances

Table 6. 'Article 57' data elements used to derive the 'Active substance/combination of active substances'

'Article 57' data elements reference code	'Article 57' data elements reference name	Reference to detailed guidance – chapter 3.II: XEVPRM User guidance
PP.ACT.1	Substancecode	Field should specify the Active Ingredient as indicated in 1.2.17.4.

4.4.1. How will this data element be used to determine the 'Active substance/combination of active substances'

- The 'chargeable unit' algorithm uses the 'Substancecode' field as referenced in a medicinal product. The 'Substance Preferred Name' is then derived based on the 'Substancecodes' present in the 'chargeable unit'. The 'Substance Preferred Name' is obtained from the published list of substances that can be found within the EudraVigilance eXtended Medicinal Product Dictionary (XEVMPD) substances excel file.

Figure 2. Example of common substance EV code but variation in the substance name

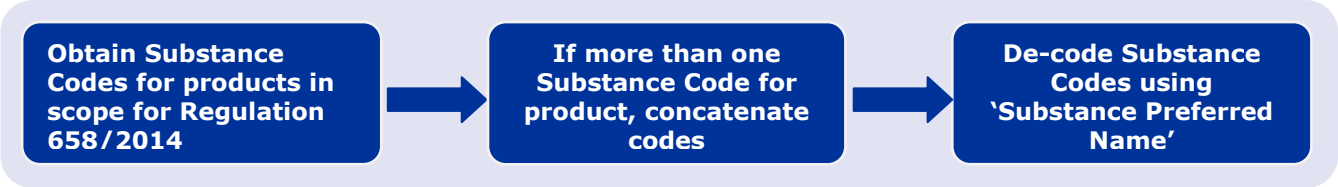
xEVMPD Code	Substance Name	Language	Name Type
SUB09611MIG	**PARACETAMOL**	**N/A**	**Substance Preferred Name**
SUB09611MIG	ACETAMINOPHEN	N/A	Substance Alias
SUB09611MIG	ПАРАЦЕТАМОЛ	BG	Substance Translation
SUB09611MIG	PARACETAMOLUM	CS	Substance Translation
SUB09611MIG	PARACETAMOL	CS	Substance Translation
SUB09611MIG	PARACETAMOL	DA	Substance Translation
SUB09611MIG	PARACETAMOL	DE	Substance Translation
SUB09611MIG	ΠΑΡΑΚΕΤΑΜΌΛΗ	EL	Substance Translation
SUB09611MIG	PARACETAMOL	ES	Substance Translation
SUB09611MIG	PARATSETAMOOLI	ET	Substance Translation
SUB09611MIG	PARATSETAMOOL	ET	Substance Translation
SUB09611MIG	PARASETAMOLIA	FI	Substance Translation
SUB09611MIG	PARASETAMOLI	FI	Substance Translation
SUB09611MIG	PARACÉTAMOL	FR	Substance Translation
SUB09611MIG	PARACETAMOL	FR	Substance Translation
SUB09611MIG	PARAICÉITAMÓL	GA	Substance Translation
SUB09611MIG	PARACETAMOL	HR	Substance Translation
SUB09611MIG	PARACETAMOL	HU	Substance Translation
SUB09611MIG	PARASETAMÓLI	IS	Substance Translation
SUB09611MIG	PARACETAMOLO	IT	Substance Translation
SUB09611MIG	ACETAMINOFENE	IT	Substance Translation
SUB09611MIG	PARACETAMOLUM	LA	Substance Translation
SUB09611MIG	PARACETAMOLIS	LT	Substance Translation

- If the medicinal product contains multiple active ingredients (as identified by the medicinal product having multiple Substancecodes), these substances are concatenated and appear in one 'chargeable unit'. The same string of concatenated substances is regarded/treated as the same "combination of active substances".

- Furthermore, for products with the following Medicinal Product Types:
  - 1. Authorised homeopathic medicinal products,
  - 2. Authorised herbal medicinal product,

  the 'active substance' component of the 'chargeable unit' is not applicable and will appear blank in the 'chargeable unit' line listing.

Figure 3. How the European Medicines Agency derives the 'Active substance/combination of active substances'



4.4.2. Key Considerations regarding the 'Active substance(s)'

- To facilitate the correct generation of 'chargeable units' based on the 'active substance or combination of active substances' data element, please follow the substance name guidelines as defined in the 'EMA Substance names best practice' document.

4.4.3. Example: Highlighting concatenation of substances found in 1 medicinal product; multiple medicinal products forming 1 'chargeable unit' and a blank 'active substance' due to medicinal product type

Table 7. Example 'chargeable unit'

Product EV Code	Medicinal Product Name	Marketing Authorisation Holder	Member State where marketing authorisation is valid	Active Substance Names	Substance Code	Pharmaceutical Form	Medicinal Product Type
PRD00001	EXAMPLE	MAH Z	GR	• CAFFEINE • PARACETAMOL	• SUB13146MIG • SUB09611MIG	FILM-COATED TABLET	Other
PRD00005| PRD00006| PRD00007| PRD00008	PRODUCT XYZ	MAH X	LT	• AMOXICILLIN • CLAVULANIC ACID	• SUB05481MIG • SUB06642MIG	PROLONGED-RELEASE TABLET	Other
PRD00009	EXAMPLE HOMEOPHARMA	MAH Y	DE			ORAL DROPS	Authorised Homeopathic medicinal product

One product with a **combination of active substances.**

Multiple products (for instance, that differ due to strength) forming **one 'chargeable unit'** with the same combination of active substances.

No active substance names or substance codes since this is an **authorised homeopathic medicinal product**

4.5. Pharmaceutical Form

For the purposes of the determining the 'pharmaceutical form' to be used in the calculation of the 'chargeable unit', the Agency uses the 'authorised pharmaceutical form' field.

Table 8. 'Article 57' data elements used to derive the 'Pharmaceutical Form'

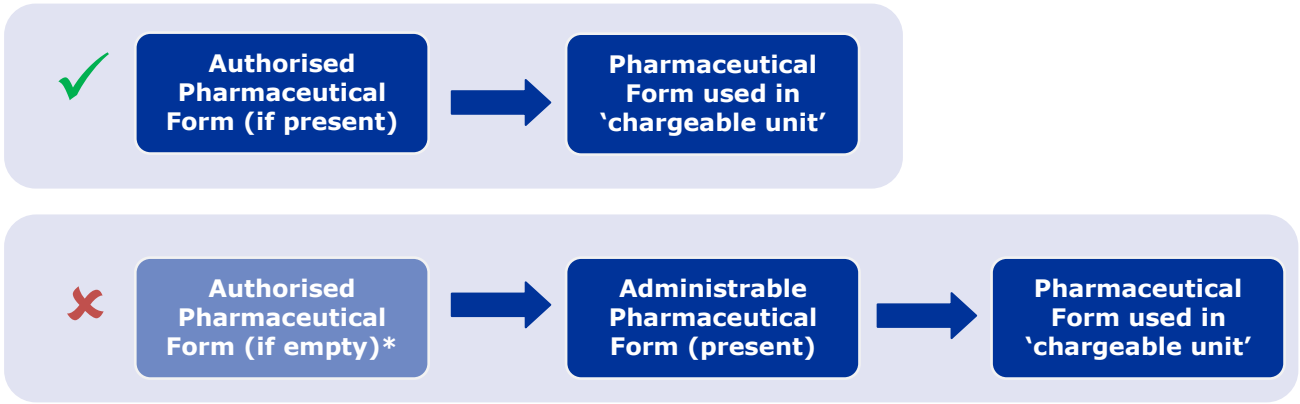
'Article 57' data elements reference code	'Article 57' data elements reference name	Reference to detailed guidance – chapter 3.II: XEVPRM User guidance
AP.APF.1	Authpharmformcode	Field should specify the Authorised pharmaceutical form(s) of the medicinal product as indicated in 1.2.14 Authorised Pharmaceutical Form.

4.5.1. How these data elements are used to derive the 'Pharmaceutical Form'

As of the 16th June 2014, marketing authorisation holders have been requested to submit medicinal product information in the new submission format where the 'Authorised Pharmaceutical Form', as indicated in section 3. Pharmaceutical Form of the authorised SmPC, is a mandatory field. Therefore, this is the field that is used in the 'chargeable unit' calculation to obtain the 'Pharmaceutical form'. The 'chargeable unit' algorithm uses the xEVMPD codes for Pharmaceutical Dose Forms and then derives the 'Authorised Pharmaceutical Form' value based on the published controlled vocabulary on XEVMPD Pharmaceutical Dose Forms.

However, in the event that the company did not comply with the 16th June 2014 requirements, and no 'Authorised Pharmaceutical Form' has been provided, the 'Administrable Pharmaceutical Form' will be used as the 'Pharmaceutical form' in the 'chargeable unit' calculation.

Figure 4. Deriving the 'pharmaceutical form'



* this will apply to marketing authorisation holders who have not yet re-submitted their medicinal production information in line with the 'Article 57' schema in use as of June 2014.

5. Filters for exemptions

As per the conditions set out in Regulation (EU) No 658/2014, a number of medicinal products are excluded from the scope of the Regulation. Therefore, in order to ensure that 'chargeable units' for these products are not created, a set of filters is applied to the products found within the 'Article 57' database to ensure that only those products which are subject to a pharmacovigilance fee are used to derive the resulting 'chargeable units'.

Table 9. 'Article 57' data elements used to determine if medicinal products should be excluded from the 'chargeable unit' calculation

'Article 57' data elements reference code	'Article 57' data elements reference name	Reference to detailed guidance – chapter 3.II: XEVPRM User guidance
AP.12.13	Legalbasis	Field should specify the Legal Basis as indicated in 1.2.12.13. Legal Basis.
AP.12.MPT.1	Producttypecode	Field should specify the Medicinal Product Type as indicated in 1.2.12.14 Medicinal Product.
AP.12.2	Authorisationprocedure	Field should specify the Authorisation Procedure as indicated in 1.2.12.2. Authorisation Procedure.
AP.12.3	Authorisationstatus	Field should specify the Authorisation Status as indicated in 1.2.12.3. Authorisation Status.

5.1. Relevant XEVMPD controlled vocabulary

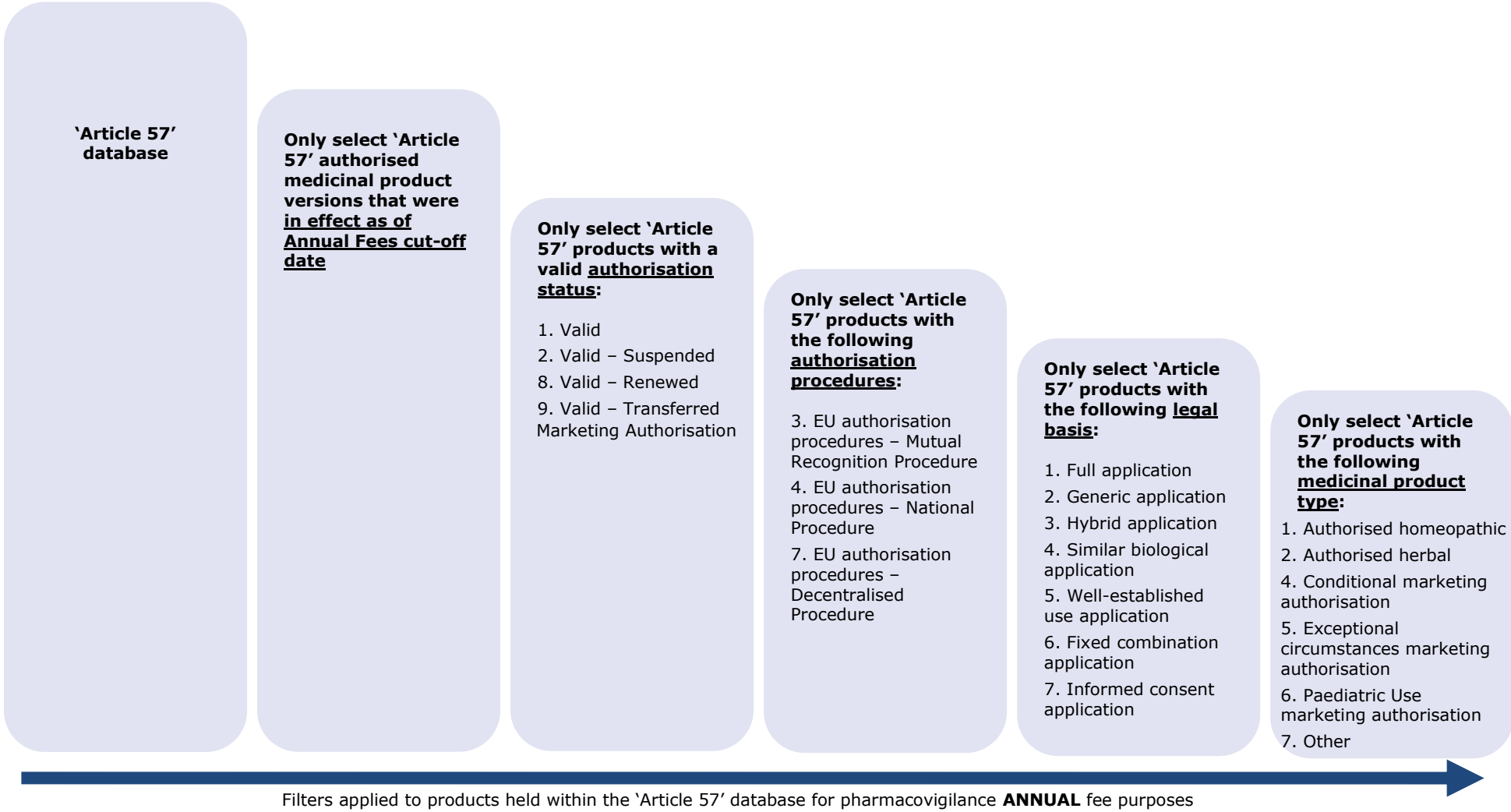
- AP12.13 Legal Basis:
  - http://www.ema.europa.eu/docs/en_GB/document_library/Other/2014/01/WC500160461.xls
- AP.12.MPT.1 Medicinal Product Type:
  - http://www.ema.europa.eu/docs/en_GB/document_library/Other/2014/01/WC500160462.xls
- AP.12.2 Authorisation Procedures:
  - http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/03/WC500123643.xls
- AP.12.3 Authorisation Status:
  - http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/03/WC500123644.xls

5.2. Key Considerations regarding the correct application of product filters

- For products that do not have a **legal basis** specified (this will apply to marketing authorisation holders who have not submitted in the new xEVMPD format), a legal basis of 1. Full application (Article 8(3) of Directive No 2001/83/EC) will be assigned to the medicinal product.
- For products that do not have a **medicinal product type** specified (this will also apply to marketing authorisation holders who have not submitted in the new xEVMPD format), a 'default' medicinal product type which is not exempt from the Regulation, and does not entitle the marketing authorisation holder to a fee discount, will be selected.
- To assign the correct applicable legal basis value and medicinal product type, marketing authorisation holders should amend their medicinal product entity in the 'Article 57' database at their earliest opportunity.

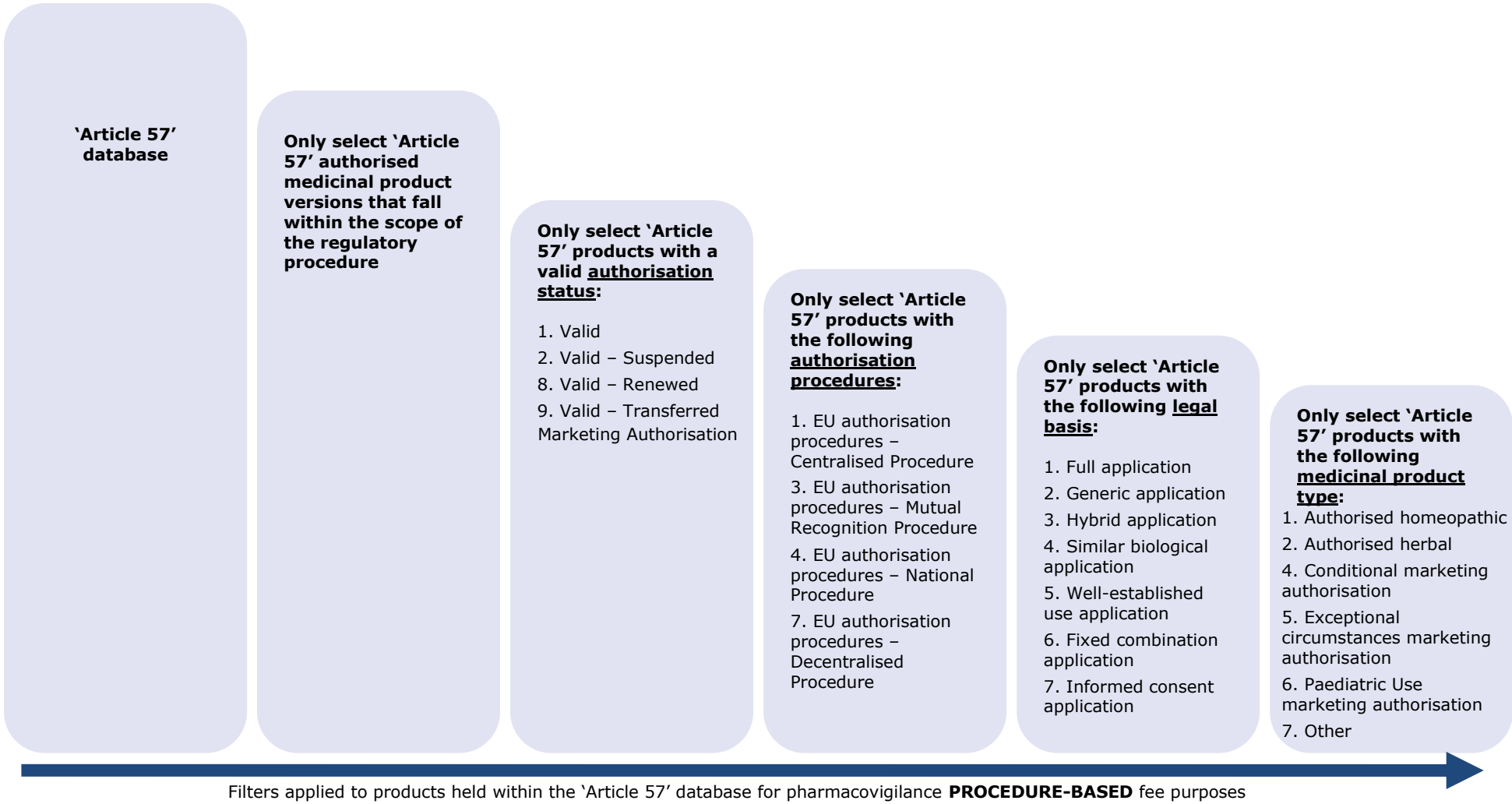
5.3. Summary diagram of filters applied to 'Article 57' medicinal product data to ensure that only those products subject to a pharmacovigilance fee are included in the scope of the 'chargeable unit' calculation (1)

Figure 5. Filters applied to data held in the 'Article 57' database for pharmacovigilance **ANNUAL** fees purposes



5.4. Summary diagram of filters applied to 'Article 57' medicinal product data to ensure that only those products subject to a pharmacovigilance fee are included in the scope of the 'chargeable unit' calculation (2)

Figure 6. Filters applied to data held in the 'Article 57' database for pharmacovigilance **PROCEDURE-BASED** fees purposes



6. Products authorised in Member States with more than one official language

In Member States with more than one official language where medicinal product information is available in more than one language and the corresponding SmPC/package leaflet/other similar text as authorised by the Authorising Body is therefore available in such language(s) (e.g. Belgium, Finland and Luxembourg), the medicinal product should be submitted in the XEVMPD for each of the available language(s).

In order to avoid the creation of duplicate 'chargeable units' due to multiple national language submissions, the 'chargeable unit' algorithm will de-duplicate these products to ensure that marketing authorisation holders are not incorrectly charged.

Table 10. 'Article 57' data elements used to de-duplicate products submitted due to multiple national languages

'Article 57' data elements reference code	'Article 57' data elements reference name	Reference to detailed guidance – chapter 3.II: XEVPRM User guidance
AP.12.1	Authorisationcountrycode	Field should specify the Authorisation Country Code as indicated in 1.2.12.1.
O.4	(MAH) ev_code	Field should specify the MAH EV Code as indicated in 1.6.4.
AP.12.4	Authorisationnumber	Field should specify the Authorisation number as indicated in 1.2.12.4.
AP.12.7	Mrpnumber	Field should specify the MRP, DCP or EMEA number as indicated in 1.2.12.7.
AP.12.8	EUnumber	Field should specify the EU number as indicated in 1.2.12.8.

Table 11. Additional data elements from the 'chargeable unit' algorithm used to de-duplicate products submitted in the XEVMPD for each of the available official languages of the Member State

Referenced section	'Chargeable Unit' algorithm terminology	Brief Explanation
4.4	Derived Active Substance or combination of active substances	List of active substances present in the medicinal product based on substance EV codes.
4.5	Derived Pharmaceutical form	Authorised pharmaceutical form or administrable pharmaceutical form if authorised pharmaceutical form is not available.
4.1	Derived Medicinal Product Name	Unique combination of some, or all, of the following fields: Full Presentation Name, Product Short Name, Product INN/Common Name, Product Company Name.

6.1.1. How these data elements are used to identify duplicate products due to multiple national language submissions

The 'chargeable unit' algorithm needs to identify products that should generate the same 'chargeable unit' medicinal product name but differ because of multiple national language submissions. This is done by comparing the following data elements: Authorisation Country Code, Organisation EV Code, Authorisation Number, MRP Number, EU Number, Derived Active Substance/or combination of Active Substances, derived Pharmaceutical Form and derived Medicinal Product Name. If all these data elements are the same, **except for derived Medicinal Product Name,** and the Authorisation Country Code is one of the following: BE, FI or LU, the algorithm deduces that these products are duplicate products and only generates one 'chargeable unit' for these products, despite differences in the derived Medicinal Product Name.

6.1.2. Key Considerations regarding products authorised in Member States with more than one official language

- Within the advice note and invoice line listings, **only one product EV code** will be listed for these 'chargeable units' with multiple national language submissions.
- The other product EV code(s) are discarded since they do not reflect a different medicinal product (unlike the other entries in the chargeable unit line listing where each product EV code corresponds to a different medicinal product).
- If one or more of the 'chargeable unit' data elements for a product that has been submitted for each of the available official languages needs to be amended, please update this data element in **all the product EV codes** that relate to this 'chargeable unit'. The product should have been submitted in the XEVMPD for each of the national language(s) and therefore there should be more than one product EV code connected to this 'chargeable unit'. Failure to do so may result in additional 'chargeable units' being created due to a variation in the 'chargeable unit' information.

6.1.3. Example 1: Multiple national language submission for products authorised in Belgium generating only one 'chargeable unit'

EV Code	Derived Medicinal Product Name	Official Language	Authorisation Country	Authorisation Procedure	MRP/DCP /EMEA Number	EU Number	Derived Pharmaceutical Form	Derived Active Substance(s)	(MAH) ev_code
PRD00010	XYZ® 300 Mikrogramm Tabletten	German	Belgium	EU authorisation procedures - Mutual Recognition Procedure	BE-A-0000-XXX		FILM-COATED TABLET	CAFFEINE PARACETAMOL	ORG12345 (MAH Z)
PRD00011	XYZ® 300 microgram tabletten	Dutch	Belgium	EU authorisation procedures - Mutual Recognition Procedure	BE-A-0000-XXX		FILM-COATED TABLET	CAFFEINE PARACETAMOL	ORG12345 (MAH Z)
PRD00012	XYZ® 300 microgrammes comprimé	French	Belgium	EU authorisation procedures - Mutual Recognition Procedure	BE-A-0000-XXX		FILM-COATED TABLET	CAFFEINE PARACETAMOL	ORG12345 (MAH Z)

Medicinal Product Name	Marketing Authorisation Holder	Member State where marketing authorisation is valid	Active Substance Names	Pharmaceutical Form
XYZ® 300 MIKROGRAMM TABLETTEN	MAH Z	BE	CAFFEINE PARACETAMOL	FILM-COATED TABLET

The above multi-language product submission forms **one 'chargeable unit'** as the Organisation EV Code, Authorisation Number, MRP Number, EU Number, Derived Active Substance/or combination of Active Substances, derived Pharmaceutical Form are all the same and the Authorisation Country = BE. The only variation in these medicinal products is the derived medicinal product name and this is due to the multiple national language submission requirements. This step will ensure that marketing authorisation holders are not charged more than once for the same product despite differences in the derived medicinal product name.

7. Creating distinct 'chargeable units'

Once the 'chargeable unit' algorithm has derived the necessary product information to create a 'chargeable unit' and excluded medicinal products that are not subject to a pharmacovigilance fee, a list of 'chargeable units' will be generated per marketing authorisation holder.

The way the algorithm accomplishes this is by reviewing a table of products (with the associated 'chargeable unit' data elements) and it then selects only those distinct products. A product is distinct if at least one of the following data elements is distinct from other chargeable products:

- Derived Product Name
- Organisation EV code
- Member State Country code
- Derived Active Ingredient(s)
- Derived Pharmaceutical form

7.1. Example 1: One 'chargeable unit' for multiple medicinal products

Table 12. Example medicinal products output used to identify distinct 'chargeable units'

EV Code	Derived Product Name	Organisation EV code	Member State Country Code	Derived Active Ingredient(s)	Derived Pharmaceutical Form
PRD00010	XYZ®	ORG123456	PT	CAFFEINE PARACETAMOL	FILM-COATED TABLET
PRD00011	XYZ®	ORG123456	PT	CAFFEINE PARACETAMOL	FILM-COATED TABLET
PRD00012	XYZ®	ORG123456	PT	CAFFEINE PARACETAMOL	FILM-COATED TABLET
PRD00013	XYZ®	ORG123456	PT	CAFFEINE PARACETAMOL	FILM-COATED TABLET

EV Code(s)	Medicinal Product Name	Marketing Authorisation Holder	Member State in which the marketing authorisation is valid	Active substance or a combination of active substances	Pharmaceutical form
PRD00010|PRD00011|PRD00012|PRD00013|	XYZ®	MAH Z	PT	CAFFEINE PARACETAMOL	FILM-COATED TABLET

As **none of the 'chargeable unit' data elements are distinct** (for example, because these products only differ due to their strengths), all these medicinal products are considered to be **one 'chargeable unit'**.

7.2. Example 2: Multiple 'chargeable units' since 'chargeable unit' data elements vary

Table 13. Example of distinct 'chargeable units' due to variations in the data elements used to derive a 'chargeable unit'

Medicinal Product Name	Marketing Authorisation Holder	Member State in which the marketing authorisation is valid	Active substance or a combination of active substances	Pharmaceutical form
EXAMPLE	MAH Z	GR	PARACETAMOL	FILM-COATED TABLET
EXAMPLE	MAH Z	GR	PARACETAMOL	**ORODISPERSIBLE TABLET**
EXAMPLE FAST	MAH Z	GR	PARACETAMOL	ORODISPERSIBLE TABLET
EXAMPLE FAST	MAH Z	**IT**	PARACETAMOL	ORODISPERSIBLE TABLET

This example contains **4 'chargeable units'** due to variations in the data elements used to derive a 'chargeable unit':

- The second 'chargeable unit' differs from the first due to variation in the pharmaceutical form:
  - **Film-coated tablet vs. Orodispersible tablet**
- The third 'chargeable unit' has a different medicinal product name:
  - **Example vs. Example Fast**
- The last 'chargeable unit' is authorised in a different Member State:
  - **Greece vs. Italy**

8. Additional 'Article 57' data elements used for pharmacovigilance fees purposes but not used for calculating the 'chargeable units'

The 'Article 57' database is not only used to provide medicinal product information for the purpose of calculating the 'chargeable units', it is also used for other pharmacovigilance fees-related purposes.

Table 14. Additional 'Article 57' data elements used to for pharmacovigilance fees purposes

'Article 57' data elements reference code	'Article 57' data elements reference name	Reference to detailed guidance – chapter 3.II: XEVPRM User guidance
O.2	Name_org	Field should specify the MAH name as indicated in 1.6.2. Organisation name.
O.6	Address	Field should specify the address as indicated in 1.6.6. Address.
O.7	City	Field should specify the city as indicated in 1.6.7. City.
O.8	State(region)	1.6.8. State (O.8)
O.9	Postcode	Field should specify the postcode as indicated in 1.6.9. Postcode
O.10	Countrycode	Field should specify the country code as indicated in 1.6.10. Country Code
O.19	SME_status	Field should specify the SME status as indicated in 1.6.15. SME Status.
AP.5	QPPVcode	Field should specify the QPPV code as indicated in 1.2.5. Qualified Person responsible for Pharmacovigilance (QPPV) code.

8.1. How are these 'Article 57' data elements used for pharmacovigilance fees purposes?

a) Details of the marketing authorisation holder:

The details of the marketing authorisation holder (name, address, city, state (region), postcode and country code) are used in the appendix of the advice note to separate the 'chargeable units' line listings by marketing authorisation holder.

Furthermore, in the **absence of any specific billing address information for a marketing authorisation holder**, the invoice for pharmacovigilance fees will be sent to the marketing authorisation holder using the organisation details provided in the 'Article 57' database.

Therefore, marketing authorisation holders being levied a fee by the Agency for the first time are encouraged to **provide the contact details of the person responsible for financial matters** (who can cover more than one marketing authorisation holder, to allow payment of a group of invoices) at the earliest opportunity by contacting the Agency's Accounts Receivable service.

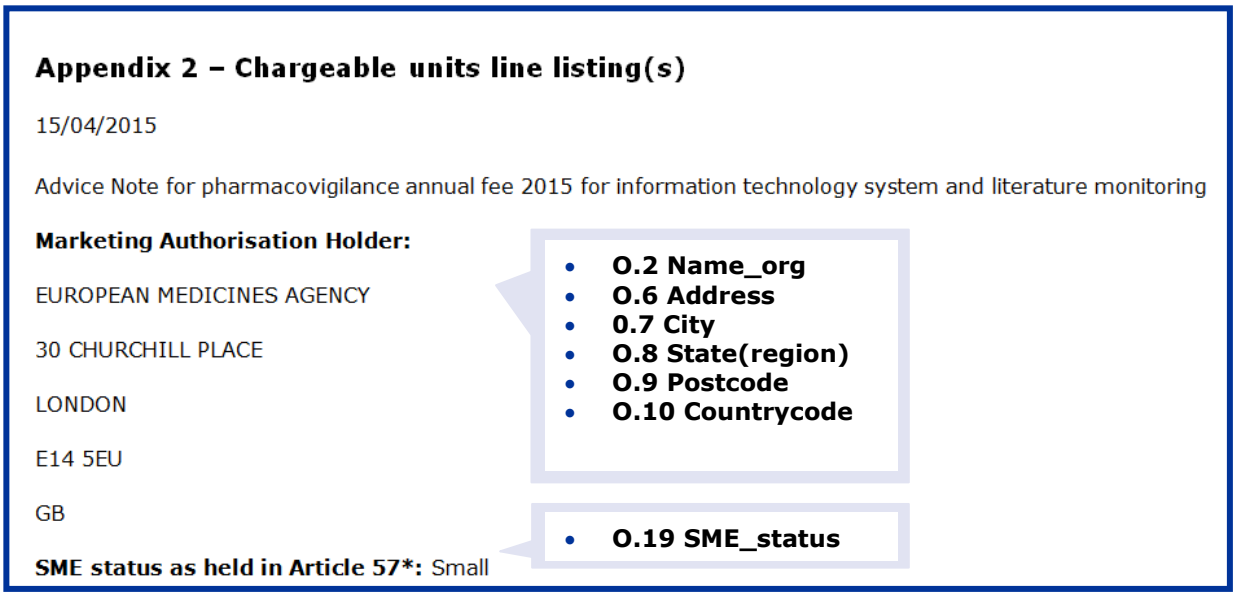
b) SME status

Marketing authorisation holders who are a micro-, small- or medium-sized enterprise (SME) are entitled to either a fee reduction or fee exemption provided that they have formally submitted a declaration to that effect to the Agency.

The SME status held within the 'Article 57' database is used by the Agency to check the number of marketing authorisation holders who have claimed to be an SME but have not yet submitted a formal declaration for SME status to the Agency.

The marketing authorisation holder's SME status, as held with the 'Article 57' database, can be found in Appendix 2 of the advice note.

Figure 7. Details of marketing authorisation holder used in the advice note

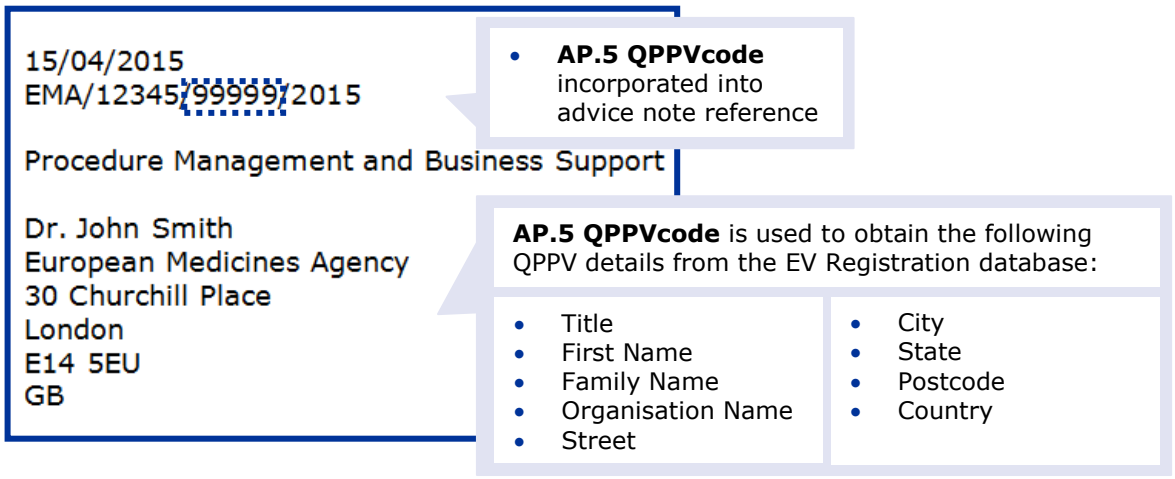


c) QPPV details

The QPPV code associated with each medicinal product in the 'Article 57' database is used in order to determine who to send the advice notes to, and where to send these advices notes (using the QPPV e-mail address maintained in the EudraVigilance database).

The advice note is addressed to the QPPV responsible for the medicinal products listed in the appendix of the advice note which the EMA has determined to be subject to a pharmacovigilance fee. Subsequently, as an **advice note is produced per QPPV and not per MAH**, one advice note may contain the 'chargeable unit' line listings for multiple MAHs if those products all have the same QPPV.

Figure 8. QPPV details used for advice note purposes



9. Reference material:

EU LEGISLATION:

- Regulation (EU) No 658/2014 of the European Parliament and of the Council of 15 May 2014 on fees payable to the European Medicines Agency for the conduct of pharmacovigilance activities in respect of medicinal products for human use:
  - http://ec.europa.eu/health/files/eudralex/vol-1/reg_2014_658/reg_2014_658_en.pdf
- Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency:
  - http://ec.europa.eu/health/files/eudralex/vol-1/reg_2004_726/reg_2004_726_en.pdf
- Directive 2001/83/EC of the European Parliament and of the Council 6 November 2001 on the community code relating to medicinal products for human use:
  - http://ec.europa.eu/health/files/eudralex/vol-1/dir_2001_83_consol_2012/dir_2001_83_cons_2012_en.pdf

EMA WEBPAGES:

- Pharmacovigilance fees payable to the European Medicines Agency webpage:
  - http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000632.jsp&mid=WC0b01ac058089678e
- Data submission for authorised medicines (Article 57) webpage:
  - http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000496.jsp&mid=WC0b01ac058078fbe0
- 2010 Pharmacovigilance Legislation webpage:
  - http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000491.jsp&mid=WC0b01ac058058f32d
- Micro-, small- and medium-sized-enterprise (SME) office webpage:
  - http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000059.jsp&mid=WC0b01ac05800240cc

GUIDANCE DOCUMENTS:

- Explanatory note on pharmacovigilance fees payable to the European Medicines Agency:
  - http://www.ema.europa.eu/docs/en_GB/document_library/Other/2015/03/WC500183456.pdf
- Detailed guidance on the electronic submission of information on medicinal products for human use by marketing authorisation holders to the European Medicines Agency in accordance with Article 57(2), second subparagraph of Regulation (EC) No 726/2004 - Chapter 3.I: XEVPRM Technical Specifications:
  - http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/03/WC500123679.pdf
- Detailed guidance on the electronic submission of information on medicinal products for human use by marketing authorisation holders to the European Medicines Agency in accordance with Article 57(2) of Regulation (EC) No. 726/2004 - Chapter 3.II: XEVPRM User Guidance:
  - http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/03/WC500123681.pdf
- EMA splitting of the Full Presentation Name of the medicinal product best practice - Procedure and principles to handle product name in the XEVMPD:
  - http://www.ema.europa.eu/docs/en_GB/document_library/Other/2014/06/WC500168583.pdf

- EMA Substance names best practice - Procedure and principles to handle substance name in the substance management system:
  - http://www.ema.europa.eu/docs/en_GB/document_library/Other/2014/06/WC500168582.pdf
- Declaration on the qualification of an enterprise as a micro, small or medium-sized enterprise (SME):
  - http://www.ema.europa.eu/docs/en_GB/document_library/Template_or_form/2012/12/WC500135919.pdf

XEVMPD CONTROLLED VOCABULARIES (CV):

- Substances:
  - http://www.ema.europa.eu/docs/en_GB/document_library/Other/2013/04/WC500142231.xlsx
- Legal Basis:
  - http://www.ema.europa.eu/docs/en_GB/document_library/Other/2014/01/WC500160461.xls
- Medicinal Product Type:
  - http://www.ema.europa.eu/docs/en_GB/document_library/Other/2014/01/WC500160462.xls
- Authorisation Procedures:
  - http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/03/WC500123643.xls
- Authorisation Status:
  - http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/03/WC500123644.xls