4 January 2021
EMA/175299/2015 Rev.5

Pharmacovigilance Fees

Questions & Answers (Q&As)

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Table of Contents

1. Pharmacovigilance Fees payable to the European Medicines Agency under Regulation (EU) No 658/2014

1.1. Which fees are levied by Regulation (EU) No 658/2014?

The European Medicines Agency (EMA) charges two types of fees for pharmacovigilance activities under Regulation (EU) 658/2014:

1) Procedure-based fees for:

- the EU single assessment of periodic safety update reports (PSURs);
- post-authorisation safety studies (PASS) protocols and study results;
- pharmacovigilance-related referrals.

2) An annual fee relating to the pharmacovigilance activities of the Agency with respect to:

- information technology systems (especially the maintenance of the Eudravigilance database);
- the monitoring of selected medical literature.

This type of fee is only applicable to nationally authorised medicines, as annual fees related to centrally authorised medicines are already covered by Regulation (EC) No 297/95.

Reference:
Regulation (EU) 658/2014
Regulation (EC) No 297/95

1.2. Which medicinal products are out of scope of Regulation (EU) No 658/2014?

There are various types of medicinal products which are excluded from the scope of the pharmacovigilance fee regulation including:

- Homeopathic and herbal medicinal products registered, respectively, under Articles 14 and 16a of Directive 2001/83/EC;
- Medicinal products authorised to be placed on the market in the absence of a marketing authorisation or of a pending application for a medicinal product authorised in another Member State, as per Article 126a of Directive 2001/83/EC;
- Medicinal products for human use intended exclusively for marketing outside the European Union authorised under Article 58 of Regulation (EC) No 726/2004;
- Medicinal products subject to parallel distribution or parallel import as the obligation to follow the pharmacovigilance fees legislation lies on the marketing authorisation holder not the distributor.

1.3. What is a chargeable unit? How will they be determined?

As per Article 2(1) of the Regulation (EU) No 658/2014, a 'chargeable unit' means a unit defined by a unique combination of the following dataset:

- name of the medicinal product, as defined in point 20 of Article 1 of Directive 2001/83/EC;
- marketing-authorisation holder;
- the Member State in which the marketing authorisation is valid;

- active substance or a combination of active substances;
- pharmaceutical form.

Any variation in one of the fields will result in an additional chargeable unit. See examples in the table below (in this example, the total amount of chargeable units for the active substance 'Y' corresponds to the four chargeable units for marketing-authorisation holder 'Z'):

Name of the medicinal product	Marketing authorisation holder (MAH)	Member State of Authorisation	Active Substance (AS)	Pharmaceutical Form	Chargeable Unit (C.U.) count	Comment
Example®	MAH Z	Ireland	AS Y	Orodispersible tablet	1	
Example®	MAH Z	Ireland	AS Y	Film-coated tablet	1	Compared to the above, this is a new C.U. due to the different pharmaceutical form.
Example® Slow Release	MAH Z	Ireland	AS Y	Film-coated tablet	1	Compared to the above, this is a new C.U. due to the different name of the medicinal product.
Example® Slow Release	MAH Z	Belgium	AS Y	Film-coated tablet	1	Compared to the above, this is a new C.U. due to the different Member State.

More information:

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

1.4. What are chargeable units used for?

The chargeable unit is the basis for the calculation of pharmacovigilance fees for the:

- single assessment of periodic safety update reports (PSURs), where more than one marketing authorisation holder (MAH) is involved;
- the assessment of pharmacovigilance-related referrals, where more than one marketing authorisation holder (MAH) is involved;
- annual fee for nationally authorised products which relates to information technology and literature monitoring.

More information:

Explanatory note on pharmacovigilance fees payable to the European Medicines Agency

1.5. Will pharmacovigilance fees apply to medicinal products authorised in United Kingdom?

Fee calculations for nationally authorised products in pharmacovigilance procedures are based on information recorded in Article 57 database. From 1 January 2021 national marketing authorisations

with respect to Northern Ireland that are granted to marketing authorisation holders in EU/EEA or Northern Ireland and are correctly reflected in Art. 57 database (i.e. with 'United Kingdom (Northern Ireland)' as country of authorisation) will be included in the fee calculations for respective EMA procedures.

The marketing authorisation holders are advised that the advice note listing the data applicable for the calculation of the fee will be sent for such products only to the qualified persons for pharmacovigilance (QPPVs) that are established in EU/EEA or Northern Ireland, in line with the applicable requirements.

More information:

Brexit-related guidance for companies

1.6. Will pharmacovigilance fees apply to medicinal products authorised in Iceland, Liechtenstein and Norway?

Norway, Iceland and Liechtenstein form the EEA with the 27 Member States of the European Union. These countries have, through the EEA agreement, adopted the complete Union acquis on medicinal products and are consequently parties to the European Union procedures.

Regulation (EU) No 658/2014 has been incorporated into the EEA Agreement, therefore making the pharmacovigilance fee regulation applicable to all EEA countries.

However, medicinal products authorised in Liechtenstein are not subject to pharmacovigilance fees due to its specific administrative status.

More information:

Notice to Applicants – Volume 2A Procedures for marketing authorisation: Chapter 1 Marketing Authorisation

Decision of the EEA Joint Committee No 265/2014 of 12 December 2014

1.7. How many chargeable units will be calculated for centrally authorised products (CAPs)?

Following the incorporation of Regulation (EU) No 658/2014 into the EEA Agreement, for medicinal products which have 'EU' as authorisation country code in Article 57 database, a 'new' chargeable unit will be generated for 30 distinct authorisation country codes (corresponding to the 27 EU Member States plus Norway and Iceland plus United Kingdom with respect to Northern Ireland), resulting in 30 chargeable units for medicinal products authorised according to the centralised procedure.

Liechtenstein will not be taken into account due to its specific administrative status.

More information:

Decision of the EEA Joint Committee No 265/2014 of 12 December 2014

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

1.8. Will pharmacovigilance fees apply to different strengths of a medicinal product?

As per the definition of a chargeable unit in Article 2(1) of Regulation (EU) No 658/2014, a chargeable unit is independent of the strength.

Therefore, medicinal products which have the same elements as per the definition of a chargeable unit and differ only by strength will be considered as a single chargeable unit for the calculation of the pharmacovigilance fees. See the example below:

Name of the medicinal product	Marketing authorisation holder (MAH)	Member State of Authorisation	Active Substance (AS)	Pharmaceutical Form	Strength
Example®	MAH Z	Greece	AS Y	Film-coated tablet	10mg
Example®	MAH Z	Greece	AS Y	Film-coated tablet	15mg
Example®	MAH Z	Greece	AS Y	Film-coated tablet	20mg

1.9. The marketing authorisation of a product has been suspended. Will it be subject to a pharmacovigilance fee?

Suspension of a marketing authorisation does not exclude a medicinal product from the scope of Regulation (EU) No 658/2014 as the marketing authorisation is still legally valid.

Only medicinal products whose marketing authorisation status is declared as below in Article 57 database (as per relevant EudraVigilance code(s)) will not be subject to a pharmacovigilance fee:

- Withdrawn by the Marketing Authorisation Holder;
- Revoked by a Competent Authority;
- Not Renewed by Competent Authority;
- Not Submitted for Renewal by the Marketing Authorisation Holder;
- Expired due to Sunset Clause;
- Superseded by Marketing Authorisation Renewal/Variation;
- Superseded by a Marketing Authorisation Transfer.

1.10. Will I, as a marketing authorisation holder, have the opportunity to review the information of products prior to invoicing?

To support marketing authorisation holders, an advice note will be generated and sent out to the designated marketing-authorisation holder's Qualified Person for Pharmacovigilance (QPPV) prior to issuing an invoice for a periodic safety update report (PSUR) procedure (i.e. prior to the start of the procedure) and an annual fee. An advice note will be sent after the start of the procedure for pharmacovigilance-related referrals.

Advice notes are not generated for PASS procedures as the calculation of the pharmacovigilance fee payable by each marketing authorisation holder involved in the procedure is not based on the principle of chargeable units.

The advice note provides information on the chargeable units that have been identified for validation at a given point in time within the 'Article 57 database'.

In order to have a reliable and complete list of medicinal products and related chargeable units, the QPPV is requested to review (and, if necessary, amend or add) the data directly in the 'Article 57 database' for the relevant product(s) authorised for each marketing-authorisation holder.

This should be performed in liaison with the marketing-authorisation holder at the earliest opportunity and no later than:

- by the submission date as per the EU reference dates (EURD) list for PSUR(s);
- 10 calendar days from the date of the advice note for pharmacovigilance-related referrals
- by 30 June of the respective year; concerning the annual fee for information technology systems and literature monitoring

In absence of any action by the given deadline, the Agency will regard the information in the 'Article 57 database' as agreed by the marketing-authorisation holder and consistent with the marketing-authorisation holder's obligations as defined in Article 57 (2) of Regulation (EC) No 726/2004.

More information about data submission in Article 57 database:

How to submit information on authorised medicines to the EMA

Guidance documents related to data submission for authorised medicines

1.11. To whom will the advice note be sent? Is it possible to send the advice note to another (additional) contact point?

The advice note will always be sent to the designated Qualified Person for Pharmacovigilance (QPPV) as stated in the 'Article 57 database' for the respective product(s).

This is an automated process; therefore, the Agency is not able to send the advice note to any additional e-mail address or any other contact point other than the QPPV provided in 'Article 57 database' for the respective product entry.

Please note that changing the QPPV (i.e.: different person taking the respective role) in Eudravigilance registration system does not lead to an automatic update of the respective authorised medicinal product entries in the Article 57 database. A dedicated update of product entries must be made to amend the QPPV referenced in each individual entry. However, changes of details for a particular QPPV (e.g.: amendments of contact details) will be automatically updated without any other further changes required at product level.

1.12. What has happened if I did not receive an advice note?

The advice note is generated through an automated process based on information recorded in 'Article 57 database' on a relevant date for the procedure concerned. There are several reasons why an advice note might not have been generated, for example:

- the QPPV details present in 'Article 57 database' for the medicinal product are incorrect, therefore, the advice note might have been sent out to a different QPPV,
- the concerned medicinal product entries are incorrect and/or incomplete which may have excluded the products from the respective procedure (e.g. wrong legal basis),
- the concerned medicinal product entries were not present in 'Article 57 database' on the date of creation of the advice note.

Please note that the advice note is provided as an additional support to the marketing authorisation holder; the non-receipt of an advice note does not exempt from the receipt of an invoice or the proactive review of data in Article 57 database.

We would like to remind that marketing authorisation holders are obliged to maintain the submitted medicinal product information in Article 57 database and notify the EMA of any newly authorised medicines or variations to the terms of the marketing authorisation according to the requirements introduced by Article 57(2) of Regulation No 726/2004.

2. Single assessment of periodic safety update reports (PSURs)

2.1. What fee applies to the assessment of periodic safety update reports (PSURs)?

For the PSUR assessment involving only one marketing-authorisation holder the total amount of the fee will be levied on that marketing authorisation holder.

For the PSUR assessment, under an EU PSUR single assessment procedure, referred also as periodic safety update single assessment (PSUSA), involving more than one marketing-authorisation holder, the total amount of the fee will be divided among all the marketing-authorisation holders concerned proportionately to the number of chargeable units.

The total amount of chargeable units involved in a PSUR procedure will be identified from the 'Article 57 database'. An advice note will be generated at the data lock point (DLP) date and sent accordingly for review to the relevant Qualified Person for Pharmacovigilance (QPPV), prior to the start of a PSUSA procedure, in order to ensure the accurate identification of the chargeable units prior to issuing an invoice at the start of the procedure.

More information:

Regulation (EU) 658/2014
EU reference dates (EURD) list
Post-authorisation procedural guidance on periodic safety update reports
Explanatory note on pharmacovigilance fees payable to the EMA

2.2. Are medicinal products authorised under Articles 10(1) [generics], 10a [well established use], 14 [homeopathic] or 16a [herbal] of Directive 2001/83/EC subject to a fee for the assessment of PSURs?

Medicinal products authorised under Articles 10(1) and 10a or registered under Articles 14 or 16a of Directive 2001/83/EC are in principle exempted from routine submission of PSURs, in accordance with Article 107b(3) of Directive 2001/83/EC.

However, if the obligation to submit a PSUR is required by the EURD list under section "*Are PSURs required for products referred to in Articles 10(1), 10a, 14, 16a of Directive 2001/83/EC*: YES"; these medicinal products will be in the scope of the PSUR assessment. Medicinal products authorised under Articles 10(1) and 10a of Directive 2001/83/EC will be subject to pharmacovigilance fees, while medicinal products registered under Articles 14 and 16a of Directive 2001/83/EC will be exempted from pharmacovigilance fees, in accordance with Article 1(2) of Regulation (EU) No 658/2014.

More information:

Regulation (EU) 658/2014
Directive 2001/83/EC

EU reference dates (EURD) list
Post-authorisation procedural guidance on periodic safety update reports
Explanatory note on pharmacovigilance fees payable to the EMA

2.3. Are medicinal products authorised under Article 10(3) [hybrids] of Directive 2001/83/EC subject to a fee for the assessment of PSURs?

Medicinal products authorised under Article 10(3) of Directive 2001/83/EC are not exempted from the obligation to submit PSURs and therefore are subject to a pharmacovigilance fee for the assessment of PSUR.

More information:

Post-authorisation procedural guidance on periodic safety update reports

2.4. Is it possible to estimate the fee to be paid by a marketing authorisation holder involved in an EU PSUR single assessment prior to the invoice?

When the PSUR procedure involves more than one marketing-authorisation holder, the total amount of the fee will be divided among all the marketing-authorisation holders concerned proportionately to the number of chargeable units.

The share payable by each marketing authorisation holder will be calculated by the Agency. In this respect, an advice note will be generated at the data lock point (DLP) date and sent accordingly to the relevant QPPVs, for review, in order to ensure the accurate identification of the chargeable units for the products involved in the procedure.

It is therefore difficult to provide an estimate of all chargeable units and corresponding fee that will apply prior to invoicing considering possible reductions that may apply and changes that may occur between the time the advice note is sent and the submission date.

2.5. There is an on-going transfer for the marketing authorisation of our product, who will have to pay for the PSUR assessment?

If a marketing-authorisation for a product has officially been transferred (relevant legal act by the competent authority), the product information in 'Article 57 database' should be updated accordingly.

Therefore, the Agency needs to be notified of the transfer of the marketing authorisation using the eXtended EudraVigilance Product Report Message (XEVPRM) format.

The invoice will be issued to the marketing authorisation holder identified in 'Article 57 database' at the start date of the procedure.

2.6. My product is not marketed. Will I be subject to a pharmacovigilance fee for the assessment of PSUR?

The marketing-authorisation holders which are subject to a fee for assessment of PSURs will be established on the basis of the obligation to submit the PSUR(s). The obligation itself depends on the authorisation status of the medicinal product, regardless of its marketing status.

Any marketing authorisation holder required to submit a PSUR will be subject to a pharmacovigilance fee whether the medicinal product is marketed or not.

2.7. Our marketing authorisation has been withdrawn. Will I have to pay a fee?

If a marketing authorisation for a product has officially been withdrawn (relevant legal act by the competent authority), the product information in 'Article 57 database' should be updated accordingly. If such update is done at the latest by start of procedure, the product will not be subject to a fee, even if the PSUR for this product was submitted according to the deadline provided in the EURD list.

Please note that marketing-authorisation holders are obliged to maintain their medicinal product data in 'Article 57 database' up-to-date according to the requirements introduced by Article 57(2) of the Regulation No 726/2004. Therefore, the Agency needs to be notified of the withdrawal of the marketing authorisation using the eXtended EudraVigilance Product Report Message (XEVPRM) format.

2.8. Our product is a nationally authorised product, whose active substance /combination of active substances are not included in the EURD list; will we be required to submit a PSUR at European level and be subject to a fee?

For nationally authorised medicinal products, containing substances or combination of active substances not included in the EURD list, and for which no EU periodic safety update single assessment procedure (PSUSA) procedure has been established, the assessment of the PSUR will remain at national level. In such a case, marketing-authorisation holders are not required to submit a PSUR to the EMA and consequently, these products will not be subject to a fee for assessment of PSURs by the Pharmacovigilance Risk Assessment Committee (PRAC).

3. Assessment of imposed, non-interventional post-authorisation safety studies (PASS)

3.1. What fee applies for the assessment of post authorisation safety studies (PASS)?

As per Part II of the Annex of the Regulation EU No 658/2014, the fee for the assessment of PASS shall be paid in two instalments:

- First instalment for the assessment of the draft protocol
- Second instalment for the assessment of the final study report by the Pharmacovigilance Risk Assessment Committee (PRAC)

More information:

Regulation (EU) 658/2014

Post-authorisation procedural guidance on post-authorisation safety studies

Explanatory note on pharmacovigilance fees payable to the EMA

3.2. What type of post-authorisation safety studies are subject to a pharmacovigilance fee?

For centrally authorised products or nationally authorised products, the assessment of non-interventional post-authorisation safety study protocols and final study results imposed as a condition to the marketing authorisation (either at the time of the approval of the marketing authorisation or

post-authorisation) and when conducted in more than one Member State will be carried out by the PRAC according to Articles 107n to Article 107q of Directive 2001/83/EC.

For the assessment of the draft protocol and the final results of these studies, the Agency levies a fee. The Agency does not levy a fee for the assessment of significant protocol amendments as defined in Article 107o of Directive 2001/83/EC.

3.3. Will a fee apply when a marketing authorisation holder submits an amendment to the draft protocol or interim study reports?

As per Article 5(4) of Regulation EU No 658/2014, the Agency shall levy a fee for the assessment of the draft protocol and one for the assessment of the final study report.

An additional fee will not be applicable when amendments are made to the draft protocol or for the submission of interim study reports.

3.4. How will the fee be calculated when several study reports are submitted within one study? Will each study report incur a separate fee?

As per Part II of the Annex of the Regulation EU No 658/2014, the fee for the assessment of a post authorisation safety study shall be paid in two instalments:

- First instalment for the assessment of the draft protocol
- Second instalment for the assessment of the final study report by the Pharmacovigilance Risk Assessment Committee (PRAC).

In principle, a PASS protocol should involve a single study report and therefore, would trigger a single fee.

However, in cases whereby several study reports are submitted, the different study reports may be subject to a separate fee, depending on the nature of the study and the description of the protocol.

3.5. For example (indicative), if a single study protocol covers more than one study (i.e. different investigators, methodology, registration numbers, etc.); a separate fee shall be levied for each study report. However, if there are several outcomes (e.g. interim report) within a single study, only one fee will be applicable How is the fee calculated when several marketing authorisation holders are involved?

Where the obligation to conduct a post-authorisation safety study is imposed on more than one marketing-authorisation holder, the same concerns apply to more than one medicinal product and the marketing-authorisation holders concerned conduct a joint post-authorisation study, the amount payable by the marketing-authorisation holder shall be levied by evenly dividing the total amount of the fee among those marketing-authorisation holders as laid down in point 2 in Part II of the Annex of Regulation (EU) No 658/2014.

3.6. How will the fee be calculated when a marketing authorisation holder joins/leaves the consortium following the date of the first submission of a joint post-authorisation safety study?

As per Part II of the Annex of the Regulation EU No 658/2014, the fee for the assessment of PASS shall be paid in two instalments:

- First instalment for the assessment of the draft protocol
- Second instalment for the assessment of the final study report by the Pharmacovigilance Risk Assessment Committee (PRAC)

The first submission of the joint post-authorisation safety study protocol will be considered the determining basis for fee calculating purposes for the draft protocol.

If additional marketing authorisation holder(s) join the consortium following the first submission and invoicing, the amount payable by each marketing authorisation holder will not be recalculated by the Agency, although new participant(s) will be included in the procedure. However, if the participants in the consortium wish, they can arrange an internal agreement to re-divide further the share of the applicable fee.

Similarly, in case one or more marketing authorisation holders leave the consortium following the first submission, they will be liable to pay their shared part of the fee as invoiced. Moreover, no reimbursement will be issued for the already paid invoices.

Moreover, in case of resubmission of a separate protocol (single or joint), a separate procedure and consequently a new fee or share of the fee will be calculated.

Of note, the second instalment of the fee, related to the final study report, will be invoiced based on the updated consortium, if any changes have occurred. As such, changes in number of marketing authorisation holders will be taken into account for the final payment.

3.7. How will the fee be divided for mutual recognition procedure (MRP) or decentralised procedure (DCP) products?

If MRP/DCP products are involved, the fee will be divided between the different marketing-authorisation holders in the different Member States.

3.8. There is an on-going transfer for the marketing authorisation of our product, who will have to pay for the PASS assessment?

If a marketing authorisation for a product has officially been transferred (relevant legal act by the competent authority), the product information in 'Article 57 database' should be updated accordingly.

Therefore, the Agency needs to be notified of the transfer of the marketing authorisation using the eXtended EudraVigilance Product Report Message (XEVPRM) format.

The invoice will be issued to the identified marketing-authorisation holder at the start of the procedure.

4. Assessment of pharmacovigilance-related referrals

4.1. What fee applies for pharmacovigilance-related referrals?

As per Part III of the Annex of the Regulation EU No 658/2014, the fee for the assessment of pharmacovigilance-related referrals shall be:

- A baseline fee where one or two active substances and/or combination of active substances are included in the assessment.
- An additional fee per each additional active substance or combination of active substances as of the third active substance or combination of substances.

The fee shall not exceed the ceiling set, irrespective of the number of active substances and/or combination of substances.

More information:
Regulation (EU) 658/2014
Explanatory note on pharmacovigilance fees payable to the EMA
Procedural guidance on referrals

4.2. What type of referral is considered to be pharmacovigilance-related?

The Agency shall levy a fee for the referral procedures initiated as a result of the evaluation of pharmacovigilance data under the second subparagraph of Article 31(1), Article 31(2) and Articles 107i to 107k of Directive 2001/83/EC or under Article 20(8) of Regulation (EC) No 726/2004.

4.3. How is the fee divided when several marketing-authorisation holders are involved in the procedure?

The Agency shall calculate the proportion of chargeable units held by each marketing-authorisation holder concerned out of the total number of chargeable units held by all marketing-authorisation holders involved in the procedure.

More information:

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

4.4. We are the only marketing authorisation holder involved in a referral of one active substance/one combination of active substances; will any fee reduction apply?

According to Article 6(5) of Regulation (EU) No 658/2014, a fee reduction applies in the case of the assessment of a pharmacovigilance-related referral involving only one substance or one combination of substances and one marketing-authorisation holder.

The amount shall be two thirds of the applicable fee.

5. Annual fee for information technology systems and literature monitoring

5.1. What does the pharmacovigilance annual fee refer to?

As per Article 7 of the Regulation (EU) No 658/2014, the Agency will levy an annual fee for the conduct of pharmacovigilance activities relating to information technology systems, in particular the maintenance of the Eudravigilance database and for the monitoring of selected medical literature.

The pharmacovigilance annual fee is only applicable to nationally authorised medicinal products as annual fees related to centrally authorised products are already covered by Regulation (EC) No 297/95.

The amount of the annual fee shall be calculated on the basis of chargeable units. A fixed fee shall apply per chargeable unit.

More information:

Explanatory note on pharmacovigilance fees payable to the EMA

5.2. Our marketing authorisation will be withdrawn/transferred after the 1 July. Will we have to pay the full amount of pharmacovigilance annual fee?

The Agency shall levy once a year a pharmacovigilance annual fee to nationally authorised products on the 1 July of every year.

The fee will cover the period from 1 January to 31 December. There are no pro-rata calculations.

5.3. Our marketing authorisation was withdrawn prior to 1 July; will we be subject to a pharmacovigilance annual fee?

Changes to the product information should be made in 'Article 57 database' as necessary to reflect the current situation of the marketing authorisation. The data used to issue an invoice for the annual fee will be based on the information held in the 'Article 57 database' on 1 July.

If the marketing authorisation of the product is withdrawn and 'Article 57 database' updated accordingly before that date, the marketing authorisation will not be subject to an annual fee.

5.4. There is an on-going transfer for the marketing authorisation of our product; who will have to pay for the pharmacovigilance annual fee?

If a marketing authorisation for a product has officially been transferred (relevant legal act by the competent authority), the product information in 'Article 57 database' should be updated accordingly.

Therefore, the Agency needs to be notified of the transfer of the marketing authorisation using the eXtended EudraVigilance Product Report Message (XEVPRM) format. Marketing-authorisation holders are required to update the information at the latest, by the 30 June.

The invoice will be issued to the marketing authorisation holder identified in Article 57 database on the 1 July.

6. Fee reductions and exemptions

6.1. What fee reductions and exemptions apply to the pharmacovigilance fees?

The below table details the various fee reductions and exemptions applicable per pharmacovigilance fee type:

Type of procedure/service	Micro enterprises	Small and medium-sized enterprises	Generics, well-established use, homeopathic and herbal products
Single assessments of PSURs	Exempt	60% of the applicable fee or share of fee	Full fee/ share of the fee
Assessment of imposed PASS (conducted in more than one member state)	Exempt	60% of the applicable fee or share of fee	Full fee / share of the fee

Assessment of Pharmacovigilance Referrals	Exempt	60% of the applicable fee or share of fee	Full fee / share of the fee
Annual Service (information technology and monitoring of selected medical literature)	Exempt	60% of the applicable fee	80% of the amount applicable to the chargeable units concerned

More information:

Explanatory note on pharmacovigilance fees payable to the European Medicines Agency

6.2. My product is a generic, how can I ensure that the fee reduction is applied for annual fees?

All holders of marketing authorisations for medicines in the European Union (EU) and the European Economic Area (EAA) must submit information to the European Medicines Agency (EMA) on authorised medicines and keep this information up-to-date; this includes the provision of the correct legal basis of the application at the time when the marketing authorisation was initially granted.

6.3. We are a micro-, small- or medium-sized enterprise (SME), holder of a marketing authorisation for a generic product. What fee reduction will apply for the pharmacovigilance annual fee?

As per Article 7(5) of Regulation (EU) No 658/2014, only the fee reduction in regards to the SME status will apply.

6.4. How do I claim pharmacovigilance fee incentives as a SME?

Unless the marketing authorisation holder claiming to be a micro, small or medium sized enterprise has already provided a declaration to the Agency, such declarations should ideally be made prior to an invoice being issued by the Agency or, at the latest, 30 calendar days from the date of the invoice.

The Agency shall apply the exemption/reduction on the basis of that declaration and may request from companies, in accordance with standard operating procedures, evidence that they meet the definition of micro, small and medium-sized enterprises of Commission Recommendation 2003/361/EC (see SME office webpage).

Marketing authorisation holders who already hold a valid Agency's SME status are advised to check the expiry date and provide an updated declaration, if necessary, to ensure that the incentives remain applicable at the time of fee determination.

Where a marketing authorisation holder claiming, or having claimed, a fee reduction or exemption fails to demonstrate that it is entitled to a reduction or exemption, the full applicable amount will be increased by 10% in accordance with Article 8(5) of the Regulation.

Accordingly, an increased invoice is triggered in instances where:

- an SME status application or renewal thereof is withdrawn by the marketing authorisation holder or closed by the Agency due to lack of response, or

- a marketing authorisation holder claiming to be a micro enterprise is qualified as a small or medium-sized enterprise.

Information on the SME definition and registration as a SME at the EMA is available on the webpage: "Applying for SME status".

Companies are advised to contact the SME office for queries relating to the SME definition and declaration form, before formally making a declaration to the Agency: sme@ema.europa.eu.

6.5. Can I still benefit from a fee reduction/exemption after the invoice has been issued?

Any marketing-authorisation holder claiming to be a micro- or small- and medium-sized enterprise entitled to a fee reduction/exemption can make a declaration to that effect to the Agency within 30 calendar days from the date of the invoice from the Agency.

The Agency will apply the relevant fee reduction or exemption on the basis of that declaration.

Please note that if the declaration is submitted after the deadline, the marketing authorisation holder will only benefit from a fee reduction or exemption from the next invoice issued to them.

7. Information in Article 57 database and pharmacovigilance fees

7.1. My product is authorised in a multilingual country, why are some ev codes missing from the advice note?

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;
- Mutual Recognition Procedure number;
- EU Number;
- derived active substance/or combination of active substances;
- derived Pharmaceutical Form;
- 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.

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.

More information:

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

7.2. My medicinal product was authorised a few days before the DLP date. Am I subject to the obligation of PSUR submission and a pharmacovigilance fee?

Marketing authorisation holders are required to submit PSURs once a medicinal product is authorised in the EU. As such, any marketing authorisation granted before the data lock point date is subject to the obligation to submit a PSUR and the subsequent pharmacovigilance fee.

Marketing authorisations granted on or after the data lock point date will be subject to the next reporting period.

7.3. The update of Article 57 database was performed prior to receiving the invoice, however the updates were not taken into account.

The pharmacovigilance fees are calculated based on information recorded in Article 57 database on a specific date such as:

- On the start date for procedure-based fees;
- 1 July for the pharmacovigilance annual fee.

Therefore, any changes performed after the abovementioned dates will not be taken into account for the current activity; however, it will be taken into account for future procedures.

More information:

Regulation (EU) 658/2014

7.4. How can an authorised medicinal product (AMP) entity be nullified in Article 57 database?

When an AMP has been submitted by mistake or identified as a duplicate, such entities must be nullified by using the operation type "Nullification" (4). The reason for nullification must be specified in the data element "Comment" (AP.14) before sending the XEVPRM.

Nullification by the marketing authorisation holder is not allowed on AMP entities which are flagged as "Valid" in the XEVMPD following a quality control check by the Agency. Only the EMA can nullify such AMP entities.

Therefore, a request for nullification should be submitted via the EMA Service Desk portal in accordance with the guidance provided in paragraph on "Nullification of duplicated/obsolete XEVMPD entities" of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance.

Marketing authorisation holders should specify in their nullification request the:

- EudraVigilance code(s) of the authorised medicinal product;
- the organisation's name;
- EudraVigilance registration ID;
- reason for nullification should be included in the request.

If an amendment of more than 10 entities is requested, the EV Codes should be provided in an Excel spreadsheet.

In order to ensure the nullification of the EV Codes requested before the generation of the invoice, the requests should be submitted **at least 15 calendar days before the planned invoice date (e.g. for annual fees by 15 June)**.

More information:

Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance

7.5. In the context of the pharmacovigilance annual fee, what is the deadline to request a nullification of an authorised medicinal product (AMP) entry in Article 57 database by the EMA?

The pharmacovigilance annual fee is calculated based on information recorded in Article 57 database on 1 July. Marketing authorisation holders are advised to amend the product information in Article 57 database by 30 June. In exceptional cases where modifications need to be performed by the EMA on behalf of the marketing authorisation holder, e.g. if the marketing authorisation holder is unable to nullify duplicated entries or entries provided erroneously because they have been validated by the EMA; such requests should be submitted via the EMA Service Desk portal as soon as possible and at least 10 calendar days, i.e. 20 June, before the planned invoice date, to ensure that all the necessary actions are performed before the generation of the invoice.

More information:

Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance

8. Payment modalities

8.1. When are pharmacovigilance fees due?

Procedure-based fees are due on the procedure start date.

The **annual fee** is due on 1 July of every year.

The fees must be paid to EMA within 30 calendar days from the date of the invoice.

8.2. To whom will the invoice be issued?

The Agency will issue an invoice to the marketing authorisation holder's address i.e. the address of the legal entity held on the Agency's file.

Marketing authorisation holders are reminded about the obligation to submit and maintain updated information to the database as referred to in Article 57(2) of Regulation (EC) No 726/2004.

8.3. We are a group of companies with a centralised payment system; can you send all invoices to a unique address?

Marketing authorisation holders requiring their invoices issued to a billing address different from the one of the legal entities must provide such address - at least five working days before the fee due date indicated above - to the accounts receivable's service: accountsreceivable@ema.europa.eu.

The Agency will not be able to process any change the billing addresses retrospectively on invoices which have already been issued.

Please note that the billing address will be associated to the legal entity. As such it will be applicable to all pharmacovigilance and general fees invoices issued to the concerned legal entity.

8.4. Can I have a purchase order quoted on the invoice?

Marketing authorisation holders requiring a purchase order number or similar references on their invoice are encouraged to issue a standing (blanket) purchase order covering all marketing authorisation and/or pharmacovigilance fees levied by the Agency for a given period and to provide such reference - before the fee due date indicated above - to the Agency's accounts receivable service at accountsreceivable@ema.europa.eu.

8.5. When will I receive the invoice?

Invoices will be issued:

- within 30 days from the start of the procedure for post-authorisation safety studies (PASS)/periodic safety update reports (PSURs) and pharmacovigilance-related referrals; and
- by 31 July of each year for pharmacovigilance annual fees.

8.6. Can I receive the invoice by email?

The Agency has implemented an **online invoicing portal** to enable customers to:

- get instant access to their account;
- view and print-out invoices;
- view their detailed chargeable units line listing for pharmacovigilance fees;
- raise invoice queries;
- search through archived invoices;
- view payments made.

The Agency sends all invoices by email only (to the email address provided by the marketing authorisation holder), unless such settings are changed via the invoicing portal.

Additional information on invoicing and how to register with the EMA invoicing portal, see How to pay.

8.7. How do I get a copy of the invoice?

Your invoices will be stored in the invoice portal for up to five years. Invoice copies can be obtained from the invoicing portal.

Additional information on invoicing and how to register with the EMA invoicing portal, see How to pay.

8.8. How should the payment of the invoice be made?

Payments must be made by the **payable date** indicated on the invoice in EUR by bank transfer.

Payments must be made net of all bank charges, withholding taxes and any other deductions. Payment of Agency invoices is subject to its terms and conditions.

For more information, see How to pay

8.9. How do I raise a query on the invoice?

Any query arising on the invoice must be notified to Agency within 30 calendar days from the date of the invoice via the online invoicing portal.

Please note that raising a query does not suspend the payment period and the invoice still needs to be paid by its due date. If the query leads to a correction of the invoice, any amount overpaid will be reimbursed by Agency or offset against a future invoice.