Explanatory note on pharmacovigilance fees payable to the European Medicines Agency
The fees, fee exemptions and definitions described in this Explanatory Note apply as of 26 August 2014 and are based on Regulation (EU) No 658/2014 of the European Parliament and of the Council of 15.05.2014 on fees payable to the European Medicines Agency for the conduct of pharmacovigilance activities in respect of medicinal products for human use\(^1\).

This Explanatory Note does not include any fees or charges derived from the Council Regulation (EC) No 297/95 of 10.02.1995 on fees payable to the European Medicines Agency\(^2\) and its implementing rules. For information on these fees, please see Explanatory Note on fees payable to the European Medicines Agency.

**Disclaimer:**

This Explanatory Note is meant as a guidance note only. In case of discrepancies between the text and amounts of fees payable to the Agency quoted in the Explanatory Note and the provisions of the Pharmacovigilance fee Regulation (EU) No 658/2014, the latter document prevails.

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\(^1\) Official Journal L189, 27.06.2014, p. 112.

\(^2\) Official Journal L35, 15.02.1995, p. 1
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Medicinal products for human use

Directive 2010/84/EU introduced new pharmacovigilance activities to be carried out by the European Medicines Agency, hereafter referred to as the ‘Agency’, including:

- pharmacovigilance procedures carried out at Union level;
- the monitoring of literature cases; and
- the improved use of information technology tools.

The Directive also stipulates that the Agency should be able to fund these new activities from the fees charged to marketing authorisation holders.

This explanatory note concerns the fees related to pharmacovigilance activities (and the rules of payments) that apply to medicinal products for human use authorised in the Union under Regulation (EC) No 726/2004 and Directive 2001/83/EC. Please note that the fees covered in this Regulation apply without prejudice to the fees laid down in Regulation (EC) No 297/95.

Two types of fees are covered by Regulation (EU) No 658/2014, (the ‘Pharmacovigilance Fee Regulation’).

**Procedure-based fees:**

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

The fees for procedure-based activities apply from 26 August 2014.

**An annual fee relating to the pharmacovigilance activities of EMA with respect to:**

- information technology systems (especially the maintenance of the Eudravigilance database); and
- 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 fee Regulation (EC) No 297/95.

The pharmacovigilance annual fee shall apply from 1 July 2015.

In accordance with the policy of the Union to support small and medium-sized enterprises reduced fees apply to small and medium-sized enterprises whilst micro enterprises are entitled to a fee exemption.

A reduced annual fee will apply to medicinal products which have been authorised as generics, well-established use, homeopathic and herbal.

Homeopathic and herbal medicinal products which satisfy all the conditions for simplified registration, as per Article 14 and 16a of Directive 2001/83/EC are excluded from the scope of the Pharmacovigilance Fee Regulation (the pharmacovigilance activities for these medicinal products are already carried out by the Member States).

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, are also excluded from the scope of the pharmacovigilance fee Regulation.
2. Definitions

**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.

---

**Example:**

<table>
<thead>
<tr>
<th>Chargeable Unit</th>
<th>Marketing Authorisation Holder (MAH)</th>
<th>Active Substance</th>
<th>Name of medicinal product, as per point 20 of Article 1 Directive 2001/83/EC</th>
<th>Pharmaceutical form</th>
<th>Member State (MS) in which marketing authorisation is valid</th>
<th>Number of chargeable units</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAH (A)</td>
<td></td>
<td>Active Substance A</td>
<td>Product 1</td>
<td>tablet</td>
<td>PT</td>
<td>1</td>
</tr>
<tr>
<td>MAH (A)</td>
<td></td>
<td>Active Substance B</td>
<td>Product 2</td>
<td>tablet</td>
<td>DE, AT</td>
<td>2</td>
</tr>
<tr>
<td>MAH (A)</td>
<td></td>
<td>Combination Active Substances A and B</td>
<td>Product 3</td>
<td>syrup</td>
<td>EU (28 MS)</td>
<td>28</td>
</tr>
<tr>
<td>MAH (A)</td>
<td></td>
<td>Active Substance C</td>
<td>Product 1</td>
<td>tablet</td>
<td>BE</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Product 1 EXTRA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Product 1 PAEDIATRIC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Product 1 MIGRANE</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total chargeable units = 35
**Micro enterprise:** enterprise which employs fewer than 10 persons and whose annual turnover or annual balance sheet total does not exceed 2 million euro.

**Small enterprise:** enterprise which employs fewer than 50 persons and whose annual turnover or annual balance sheet total does not exceed 10 million euro.

**Medium enterprise:** enterprise which employs fewer than 250 persons and whose annual turnover does not exceed EUR 50 million or whose annual balance-sheet total does not exceed EUR 43 million.

**Article 57 database:** refers to Article 57 of Regulation (EC) No 726/2004 which defines the database on medicinal products - this includes all medicinal products authorised on the market within the Union, as submitted and updated by marketing authorisation holders.
### 3. Summary of Pharmacovigilance fees

<table>
<thead>
<tr>
<th>Type of procedure / service</th>
<th>Standard Fee</th>
<th>Micro enterprises</th>
<th>Small and medium-sized enterprises</th>
<th>Generics, well-established use, authorised homeopathic and herbal products</th>
</tr>
</thead>
</table>
| **Single assessments of PSURs** | • **EUR 19 500** per procedure;  
  • Due at the date of start of procedure;  
  • Can be levied on one or more MAHs (if two or more, the fee is shared according to the proportion of chargeable units held by each MAH for products involved in the procedure). | Exempt | 60% of the applicable fee or share of fee | Full fee* |
| **Assessment of imposed PASS (conducted in more than one member state)** | • **EUR 43 000** per procedure to be paid in two instalments:  
  - EUR 17 200 due at the start of the procedure for the assessment of the draft protocol;  
  - EUR 25 800 due at the start of the procedure for the assessment of the final study report;  
  • Can be levied on one MAH or more MAHs (joint PASS, even division of the fee). | Exempt | 60% of the applicable fee or share of fee | Full fee / share of the fee |
| **Assessment of Pharmacovigilance Referrals** | • **EUR 179 000** if the referral only concerns 1 or 2 active substances and/or combinations;  
  • Fee increased by EUR 38 800 for every additional active substances or combination, **up to maximum fee of EUR 295 400**;  
  • Due at the date of start of procedure;  
  • If levied on one MAH, the fee is reduced to two thirds; if levied on two or more MAHs, fee is shared according to the proportion of chargeable units held by each MAH. | Exempt | 60% of the applicable fee or share of fee | Full fee |
| **Annual Service (pharmacovigilance information technology and monitoring of selected medical literature)** | • **EUR 67** per chargeable unit;  
  • Due on 1st July every year as of 1st July 2015. | Exempt | 60% of the applicable fee | 80% of the amount applicable to the chargeable units concerned |

*A full fee applies to generics, well-established use, homeopathic and herbal products when they are within the scope of the procedure, as specified in the EURD list.*
4. Fees for Union-wide Pharmacovigilance procedures

4.1 Single Assessment of periodic safety update report (PSUR)

Periodic Safety Update Reports, PSURs, shall be submitted with known frequencies. The frequency of these reports can be found in the 'List of Union reference dates and frequency of submission of PSURs', also known as the EURD list. The EURD list consists of a list of active substances and combinations of active substances for which PSURs shall be submitted in accordance with the EU reference dates and frequencies.

Assessments for active substances and/or a combination of active substances included in the EURD list which fall under the obligation to submit a PSUR are subject to a fee under the Pharmacovigilance Fee Regulation.

Where the assessment involves only one marketing authorisation holder, the entire amount of the fee (EUR 19 500) shall be levied on the marketing authorisation holder. Where the assessment involves more than one marketing authorisation holder, the fee shall be divided amongst all concerned marketing authorisation holders based on the proportion of chargeable units held by each marketing authorisation holder.

<table>
<thead>
<tr>
<th>Total fee</th>
<th>19 500 EURO</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Per procedure for the assessment of periodic safety update reports shared by all marketing authorisation holders based on the proportion of chargeable units within the assessment.</td>
</tr>
</tbody>
</table>

| Fee exemptions and reductions | 100% | For micro enterprises | 40% | For small and medium sized enterprises |

See section 6 for further information on fee exemptions and reductions.
Fees payable for Single Assessment of tSUR (referred to as tSUR)

The fee for the assessment of PSURs is EUR 19,500 per procedure.

Does the tSUR submission involve more than one MAH?

- Yes: Divide the total fee amount amongst all the MAHs involved in the procedure, as per the method below. The Agency shall levy a fee by issuing a separate invoice for each MAH involved in the procedure.
  
  \[
  \text{Total Fee Amount} = \frac{\text{Fee per CU}}{\text{Total No of CUs}}
  \]
  
  \[
  \text{Fee per CU} = \frac{\text{No of CUs per MAH}}{\text{Amount to be levied on each MAH}}
  \]

- No: Where only one MAH is involved in the procedure, the Agency shall levy the total amount of the fee on that MAH.

Is the MAH an SME?

- Yes: Reductions:
  - 40% of the applicable amount for small and medium enterprise
  - 100% for micro enterprise

- No: No discount applicable
4.2 Assessment of post-authorisation safety studies (PASS)

The Agency levies a fee for the assessment carried out under Articles 107n to Article 107q of Directive 2001/83/EC and Article 28b of Regulation (EC) No 726/2004 of post-authorisation safety studies referred to in point (b) of Article 21a and point (a) of Article 22a (1) of Directive 2001/83/EC, and in point (cb) of Article 9(4) and point (a) of Article 10a (1) of Regulation (EC) No 726/2004 that are conducted in more than one Member State.

As per the provisions of the above mentioned legislation, the marketing authorisation holders is charged for the assessment of an imposed, non-interventional post-authorisation safety study.

The fee is EUR 43 000 paid in two parts:

- EUR 17 200 for the assessment of the draft protocol; and
- EUR 25 800 for the assessment of the final study report.

When several marketing authorisation holders have the obligation to conduct a joint post-authorisation safety study, the amount of the fee shall be divided equally amongst the marketing authorisation holders.

Furthermore, in order to avoid additional charges, marketing authorisation holders who have paid a fee for the assessment of a post-authorisation safety study will be exempted from any additional fee by the Agency or a national competent authority for the submission of these studies.
Fees payable for assessment of PASS

**PASS**

An imposed, non-interventional PASS is requested

Is the PASS imposed on more than one MAH and apply to more than 1 product?

Yes

Divide evenly the total fee amount amongst all the MAHs who conduct a joint PASS. The agency shall levy a fee by issuing two invoices to each MAH concerned.

No

The fee for the assessment of each PASSs is EUR 43 000 to be paid in two instalments:

- EUR 17 200 is due at the start of the procedure for the assessment of the draft protocol;
- EUR 25 800 is due at the start of the procedure for the assessment of the final study report by the PRAC.

Is the MAH an SME?

Yes

Reductions:

- 40% of the applicable amount for small and medium enterprise
- 100% for micro enterprise

No

No discount applicable
4.3 Pharmacovigilance-related referral procedures

The Pharmacovigilance Fee Regulation covers the assessment of referrals initiated as a consequence of concerns arising from the evaluation of pharmacovigilance activities data.

The fee amounts to EUR 179 000 per assessment of referrals procedure conducted on one or two active substances and/or on a combination of substances included in the same assessment. The fee is increased by EUR 38 000 for each additional active substance or combinations of active substances as of the third active substance or combination of substances.

Nevertheless, the fee cannot exceed EUR 295 400 irrespective of the number of active substances and/or combinations of active substances.

Where two or more marketing authorisation holders are involved in the procedure, the amount payable by each marketing authorisation holder shall be calculated by dividing the total amount of the fee among the marketing authorisation holders proportionately to the number of chargeable units.

<table>
<thead>
<tr>
<th>Fee Type</th>
<th>Amount</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basic fee</td>
<td>179 000 EUR</td>
<td>Per assessment of the referral procedure for one or two active substances and/or combination of substances included in the assessment, if two or more marketing authorisation holders are involved in the referral procedure.</td>
</tr>
<tr>
<td>Additional fee</td>
<td>+ 38 800 EUR</td>
<td>Per additional active substance or combination of substances as of the third active substance or combination of substances,</td>
</tr>
<tr>
<td>Reduced fee</td>
<td>119 333 EUR (2/3 of basic fee)</td>
<td>Per assessment of the referral procedure for one active substance and/or combination of active substances included in the assessment, if only one marketing authorisation holders is involved in the referral procedure.</td>
</tr>
</tbody>
</table>

The maximum total fee amount is EUR 295 400, irrespective of the number of active substances and/or combination of substances.

<table>
<thead>
<tr>
<th>Fee exemptions and reductions</th>
<th>Amount</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>For micro enterprises</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>For small- and medium sized enterprises</td>
<td>40%</td>
<td></td>
</tr>
</tbody>
</table>

See section 6 for further information on fee exemptions and reductions.
Fees payable for assessment of PhV referrals

**Referrals**

Assessment of referral with ...

More than 1 or 2 active substances and/or combination?

Yes

Basic fee EUR 179 000 for 1 - 2 active substances or combinations + EUR 38 800 per each additional active substance or combination of active substances.

The fee shall, in any case, not exceed EUR 295 400

No

Basic fee of EUR 179 000 shall be levied

More than 1 MAH?

Yes

Divide the total fee amount amongst all the MAHs involved in the procedure, as per the method below.

The agency shall levy a fee by issuing a separate invoice for each MAH involved in the procedure.

\[ \frac{\text{Total Fee Amount}}{\text{Total No of MAHs}} = \text{Fee per CU} \]

\[ \text{Fee per CU} \times \text{No of CUs per MAH} = \text{Amount to be levied on each MAH} \]

Calculate the fee for each MAH

No

One substance or one combination?

Yes

Reduced fees (2/3 of the total fee) apply.

No

The Agency shall levy the total amount of the fee on that MAH.

Is the MAH an SME?

Yes

Reductions:

- 40% of the applicable amount for small and medium enterprise
- 100% for micro enterprise

No further discount applicable

No
5. Annual pharmacovigilance fee for information technology systems and literature monitoring (levied from 1 July 2015)

The Agency will levy an annual fee for its pharmacovigilance activities relating to information technology systems, in particular the maintenance of the Eudravigilance database, and for the monitoring of selected medical literature.

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

The amount of the annual fee is EUR 67 per chargeable unit.

The total amount payable for each marketing authorisation holder will be calculated by the Agency based on the information recorded in Article 57 on the 1st of July of each year. The amount will cover the period from 1 January to 31 December of the year concerned.

<table>
<thead>
<tr>
<th>Basic fee</th>
<th>67 EURO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Per chargeable unit per year.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Fee exemptions and reductions</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>For micro enterprises</td>
<td></td>
</tr>
<tr>
<td>40%</td>
<td></td>
</tr>
<tr>
<td>For small- and medium sized enterprises</td>
<td></td>
</tr>
<tr>
<td>20%</td>
<td></td>
</tr>
<tr>
<td>For Marketing Authorisation Holders of</td>
<td></td>
</tr>
<tr>
<td>- generic medicinal products or</td>
<td></td>
</tr>
<tr>
<td>- well-established use medicinal products</td>
<td></td>
</tr>
<tr>
<td>- authorised homeopathic medicinal products or</td>
<td></td>
</tr>
<tr>
<td>- authorised herbal medicinal products</td>
<td></td>
</tr>
<tr>
<td>for the chargeable units corresponding to those products.</td>
<td></td>
</tr>
</tbody>
</table>

**Note:** Where the marketing authorisation holder of a product authorised as a generic, well-established use, homeopathic or herbal medicinal products is also a small or medium-sized enterprise, only the reduction for small- and medium sized enterprises will apply (40%).

See section 6 for further information on fee exemptions and reductions.
Fee determination and payment
6. Fee determination and payment

The table below outlines further details regarding the pharmacovigilance fees payable:

<table>
<thead>
<tr>
<th>Verification of the products subject to a fee</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medicinal products which are subject to a fee will be identified from those who are subject to the obligation to submit information to the Article 57 database.</td>
</tr>
<tr>
<td>As a support to marketing authorisation holders, an advice note will be sent to the relevant marketing authorisation holder’s QPPVs prior to the start of a PSUR, referral and prior to the date when the annual fee is due. This will inform marketing authorisation holders of the medicinal products that have been identified for validation within Article 57. Marketing authorisation holders are reminded about the obligation to submit and maintain updated information to the database as referred to in point (i) of the second subparagraph of Article 57(1) of Regulation (EC) No 726/2004.</td>
</tr>
<tr>
<td>Please note that the advice note is not a pro-forma invoice. The advice note is an extract of the content of the Article 57 database at a given point in time which is sent by the Agency to facilitate the checking of product information by the QPPV.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Financial matters</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fee due date</strong></td>
</tr>
<tr>
<td>Procedure based fees shall be due at the date of the start of the procedure. The annual fee shall be due on 1 July of every year in respect of that calendar year.</td>
</tr>
<tr>
<td><strong>Invoices</strong></td>
</tr>
<tr>
<td>The Agency will issue an invoice to the marketing authorisation holder’s billing address held on the Agency’s file. The invoice will contain details of the chargeable units as determined for each marketing authorisation holder, the fee amount to be paid as calculated on the basis of the chargeable units and information on how to make the payment.</td>
</tr>
<tr>
<td>Marketing authorisation holders being levied a fee by the Agency for the first time will be requested to provide the contact details of the person responsible for financial matters (e.g. to allow grouping of invoice payments for companies belonging to the same mother company) by contacting the Agency’s Accounts Receivable service: <a href="mailto:accountsreceivable@ema.europa.eu">accountsreceivable@ema.europa.eu</a>.</td>
</tr>
<tr>
<td><strong>Payments</strong></td>
</tr>
<tr>
<td>Payments must be made by the due date indicated on the invoice, net of all bank charges, withholding taxes and any other deductions, in Euro and by means of a transfer to the Agency’s bank account.</td>
</tr>
<tr>
<td>Payments should make clear reference to the invoice reference number. Alternatively, in the case of single remittance for multiple invoices, a remittance advice must be sent to the Agency, by email to <a href="mailto:accountsreceivable@ema.europa.eu">accountsreceivable@ema.europa.eu</a>.</td>
</tr>
<tr>
<td>The date on which the full amount of the payment has been received on the Agency’s bank account will be considered the date on which the payment has been made.</td>
</tr>
</tbody>
</table>
Additional information on ‘How to Pay’ can be found on the Agency’s website.

- **Refund of fees paid in excess**

  Any amount paid in excess shall be refunded by the Agency to the marketing authorisation holder, unless otherwise explicitly agreed with the marketing authorisation holder e.g. agreement to offset the excess amount against a fee which may become due in the future. Amounts below EUR 100 shall not be refunded unless the marketing authorisation holder expressly requests a refund.

### Fee reductions

- **Small and medium-sized enterprises**

  In accordance with the policy of the Union to support small and medium-sized enterprises, reduced fees will apply to such enterprises within the meaning of Commission Recommendation 2003/631/EC.

  The fee reduction will be applied on the basis of a declaration of the marketing authorisation holder claiming to be entitled to such a fee reduction.

  Any marketing authorisation holder claiming to be a small or medium-sized enterprise should make a declaration to that effect to the Agency, at the latest, within 30 calendar days from the date of the invoice. The declaration form is available on the section “How to apply” of the SME office webpage. The Agency shall apply the fee reduction on the basis of that declaration.

  Small and medium-sized enterprises shall pay 60% of the applicable amount.

  Companies wishing to benefit from one of the incentives should satisfy the criteria laid down in the SME Regulation. They must:

  ✓ be established in the European Economic Area (EEA);
  ✓ meet the definition of an SME.

  **Note: Marketing authorisation holders who already have a valid SME status with the Agency will not be required to make an additional declaration.**

- **Generics, well-established use, homeopathic and herbal medicinal products**

  Generic medicinal products, medicinal products authorised under the provisions relating to well-established medicinal use, authorised homeopathic medicinal products and authorised herbal medicinal products are subject to a reduced annual fee.

  The fee for those products shall be 80% of the applicable amount for annual fees.

  Where a marketing authorisation holder of a product authorised as a generic, well-established use, homeopathic or herbal medicinal products is a small or medium-sized enterprise, the amount of the fee to be levied shall be 60% of the applicable amount (reductions are not cumulative).

### Fee exemptions

- **Micro enterprises** are exempted from the payment of fees related to pharmacovigilance activities under Regulation 658/2014.
Any marketing authorisation holder claiming to be a micro enterprise should make a declaration to the Agency, at the latest, within 30 calendar days from the date of the invoice. The declaration form is available on the section “How to apply” of the SME office webpage. The Agency shall apply the fee reduction on the basis of that declaration.

If a marketing authorisation holder wrongly claims a fee reduction or fee exemption, the applicable fee amount will be increased by 10%.