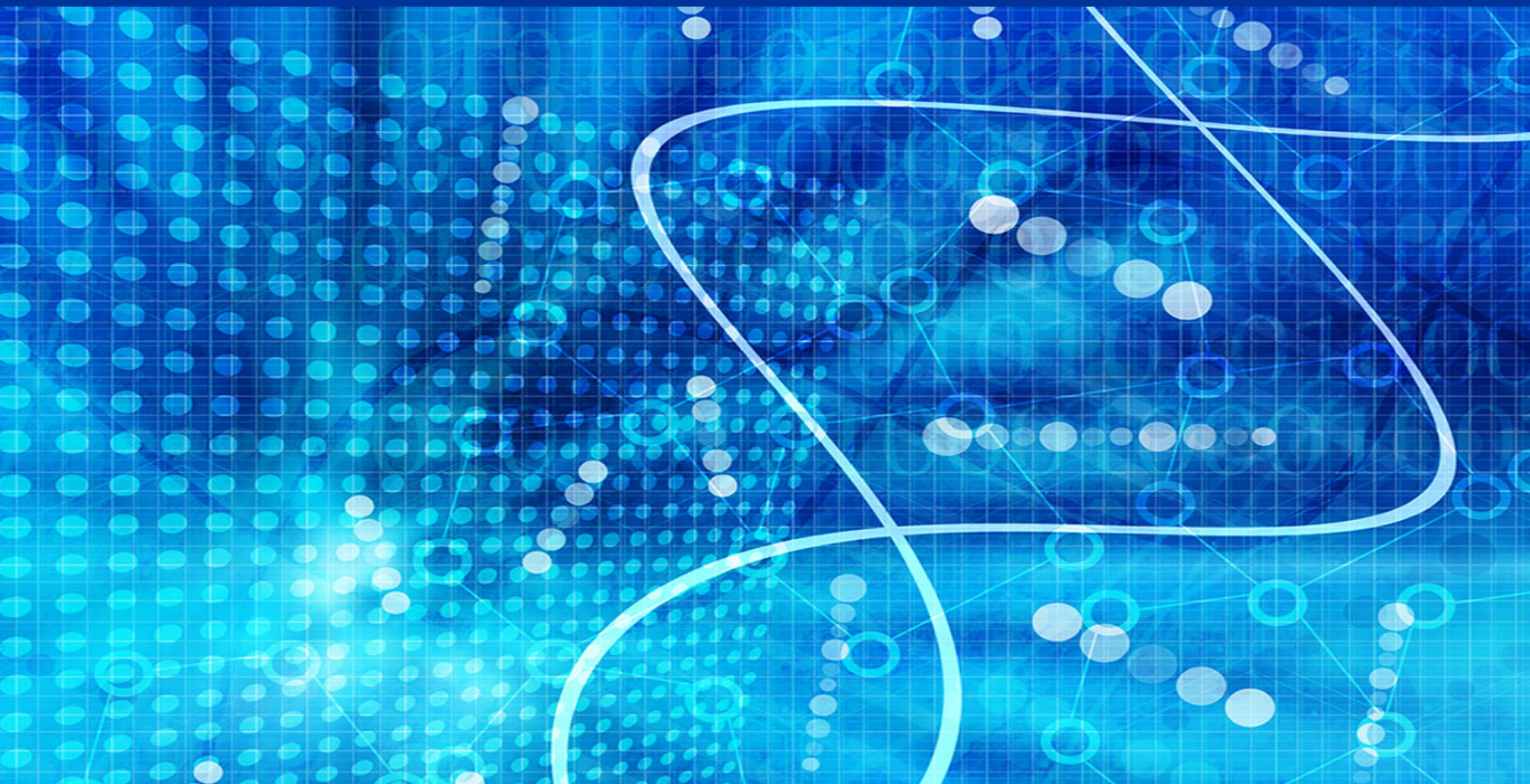




EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

# **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*<sup>1</sup>.

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*<sup>2</sup> and its implementing rules. For information on these fees, please see the [explanatory note on general 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.

**Changes introduced in this version (3 October 2022)**

- Increase in the level of fees (other than pharmacovigilance annual fees) to adjust for an inflation rate of +0.3% (related to 2020) and +5.3% (related to 2021) and rounding off to the nearest EUR 10.
- Increase in the level of pharmacovigilance annual fees to adjust for an inflation rate of +0.3% (related to 2020) and +5.3% (related to 2021), with no rounding.

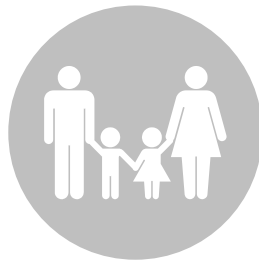
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<sup>1</sup> Official Journal L189, 27.06.2014, p. 112.

<sup>2</sup> Official Journal L35, 15.02.1995, p. 1

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Medicinal products for human use

# 1. Scope of Regulation (EU) No 658/2014

Regulation (EU) No 658/2014 provides for the European Medicines Agency, hereafter referred to as the 'Agency', to fund certain pharmacovigilance activities from fees charged to marketing authorisation holders. These activities include:

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

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').

<b>1</b>	<p><i>Procedure-based fees:</i></p> <ul style="list-style-type: none"> <li>• fee for the EU single assessment of periodic safety update reports (PSURs);</li> <li>• fee for post-authorisation safety studies (PASSs) protocols and study results; and</li> <li>• fee for pharmacovigilance-related referrals.</li> </ul>
<b>2</b>	<p><i>An annual fee</i> relating to the pharmacovigilance activities of EMA with respect to:</p> <ul style="list-style-type: none"> <li>• information technology systems (especially the maintenance of the Eudravigilance database); and</li> <li>• the monitoring of selected medical literature.</li> </ul> <p>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.</p>

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).

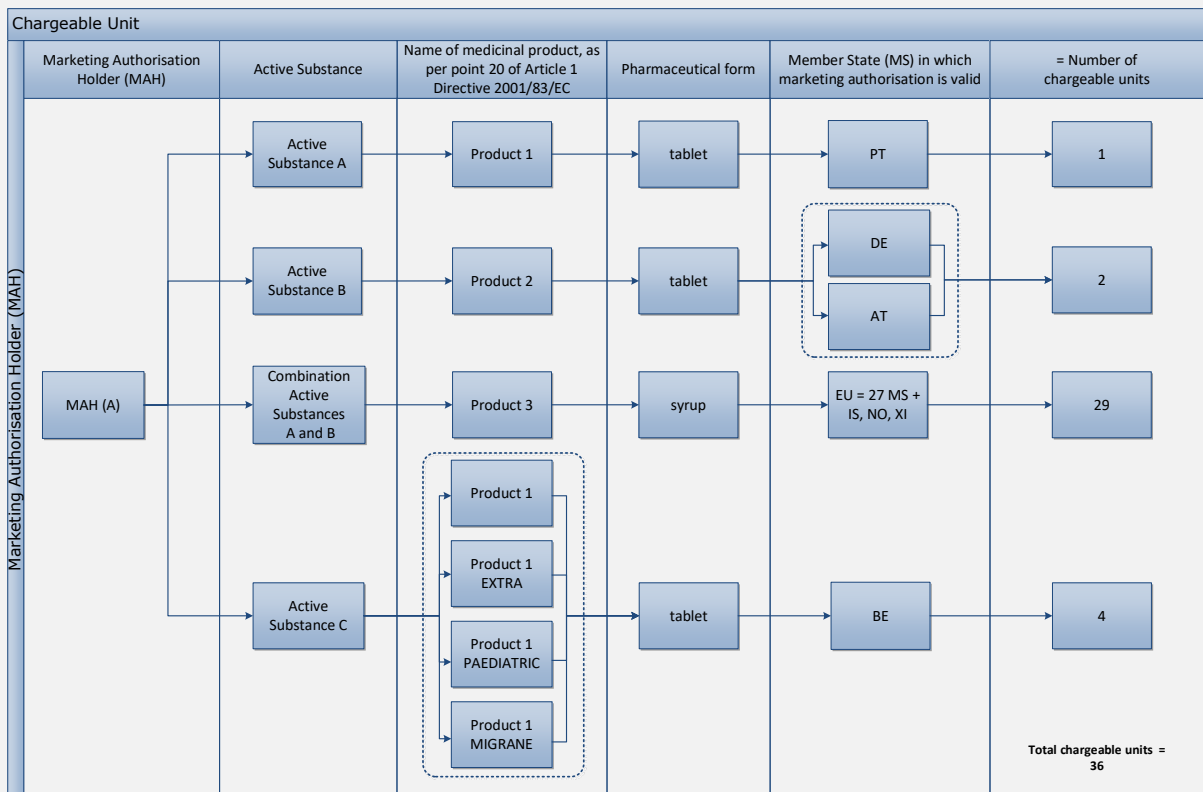
Medicinal products authorised to be placed on the market in the absence of a marketing authorisation or of a pending application for a medicinal product authorised in another Member State, as per Article 126a of Directive 2001/83/EC, are also excluded from the scope of the pharmacovigilance fee Regulation.

## 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:



**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.

Enterprise category	Headcount: Annual Work Unit (AWU)	Annual turnover	Annual balance sheet total
Medium-sized	<250	≤ € 50 million	≤ € 43 million
Small	<50	≤ € 10 million	≤ € 10million
Micro	<10	≤ € 2 million	≤€ 2million

**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

Type of procedure / service	Standard Fee	Micro enterprises	Small and medium-sized enterprises	Generics, well-established use, authorised homeopathic and herbal products
<b>Single assessments of PSURs</b>	<ul style="list-style-type: none"> <li>• <b>EUR 21 940</b> per procedure;</li> <li>• Due at the date of start of procedure;</li> <li>• 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).</li> </ul>	Exempt	60% of the applicable fee or share of fee	Full fee / share of the fee
<b>Assessment of imposed PASS (conducted in more than one member state)</b>	<ul style="list-style-type: none"> <li>• <b>EUR 48 370</b> per procedure to be paid in two instalments: <ul style="list-style-type: none"> <li>○ EUR 19 350 due at the start of the procedure for the assessment of the draft protocol;</li> <li>○ EUR 29 020 due at the start of the procedure for the assessment of the final study report;</li> </ul> </li> <li>• Can be levied on one MAH or more MAHs (joint PASS, even division of the fee).</li> </ul>	Exempt	60% of the applicable fee or share of fee	Full fee / share of the fee
<b>Assessment of Pharmacovigilance Referrals</b>	<ul style="list-style-type: none"> <li>• <b>EUR 201 450</b> if the referral only concerns 1 or 2 active substances and/or combinations;</li> <li>• Fee increased by EUR 43 670 for every additional active substances or combination, <b>up to maximum fee of EUR 332 460</b>;</li> <li>• Due at the date of start of procedure;</li> <li>• 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.</li> </ul>	Exempt	60% of the applicable fee or share of fee	Full fee / share of the fee
<b>Annual Service (pharmacovigilance information technology and monitoring of selected medical literature)</b>	<ul style="list-style-type: none"> <li>• <b>EUR 75</b> per chargeable unit;</li> <li>• Due on 1<sup>st</sup> July every year.</li> </ul>	Exempt	60% of the applicable fee	80% of the amount applicable to the chargeable units concerned



## 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 21 940) 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.



#### 21 940 EURO

Total fee

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.



#### 100%

For micro enterprises

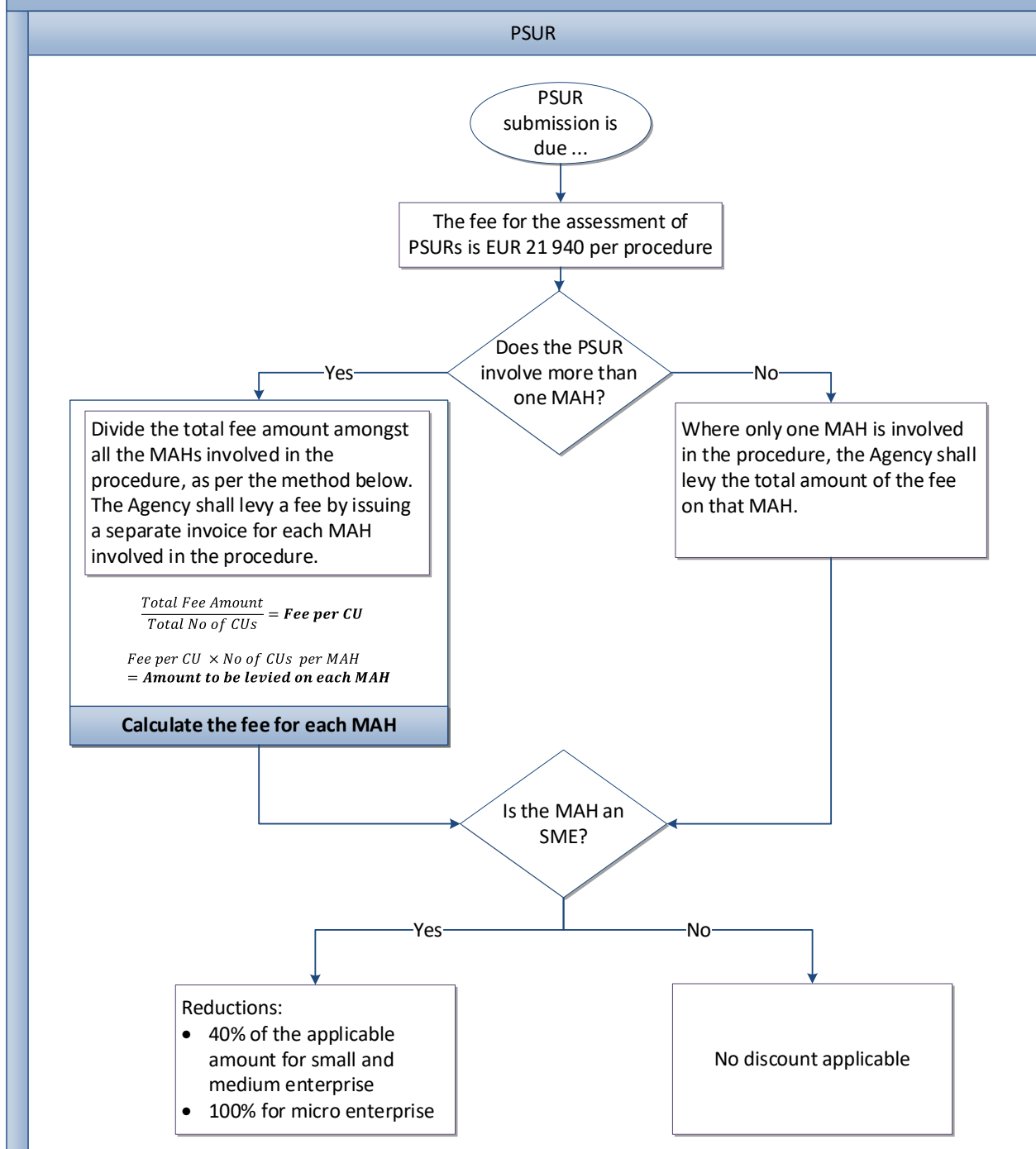
#### 40%

For small and medium-sized enterprises

Fee  
exemptions  
and reductions

**See section 6 for further information on fee exemptions and reductions.**

Fees payable for Single Assessment of PSUR (referred to as PSUR)



## 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 holder is charged for the assessment of an imposed, non-interventional post-authorisation safety study.

The fee is EUR 48 370 paid in two parts:

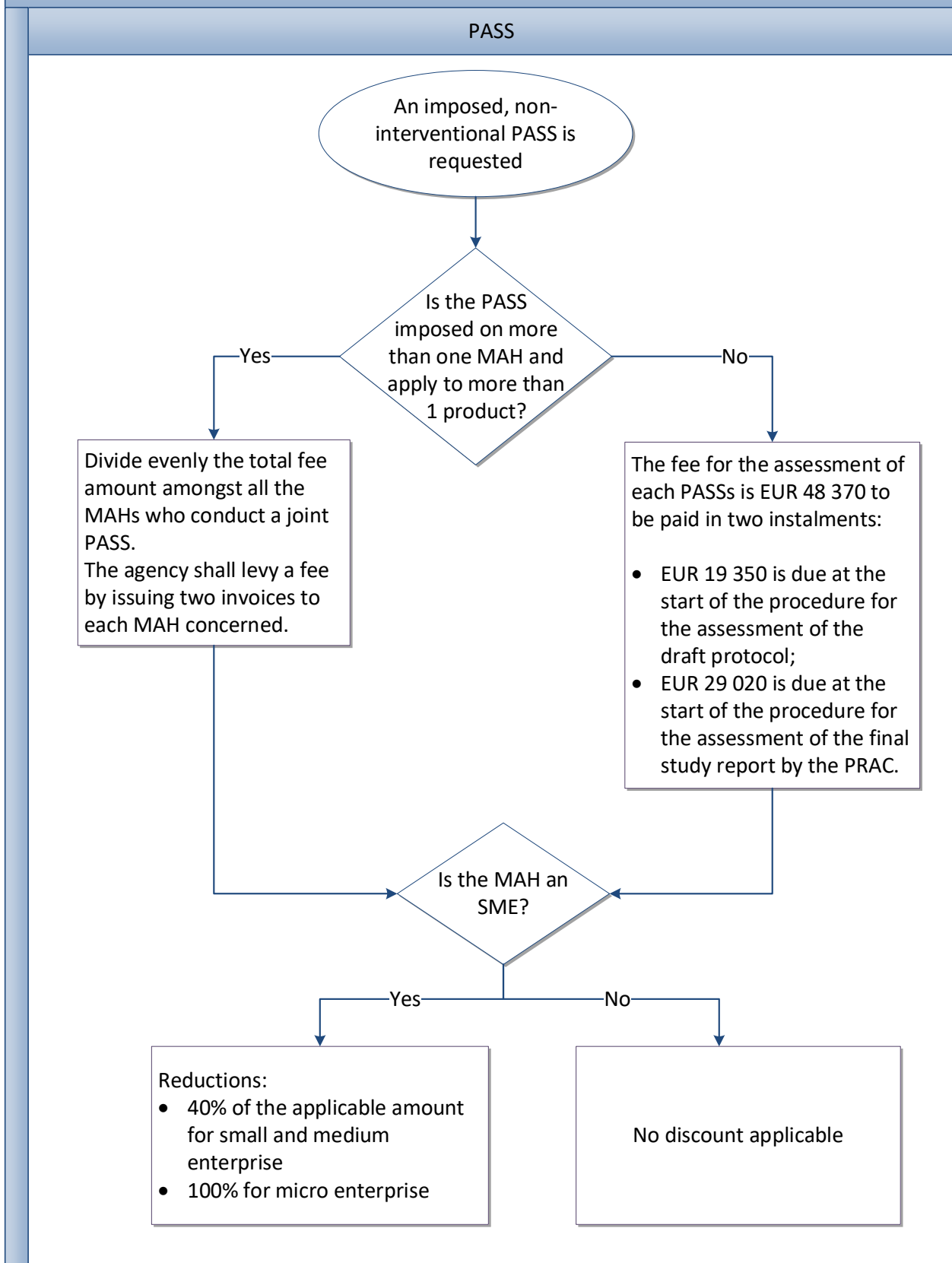
- EUR 19 350 for the assessment of the draft protocol; and
- EUR 29 020 for the assessment of the final study report.

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 involved.

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

	<b>48 370 EURO</b>
Total fee	Per procedure for the assessment of post authorisation safety studies that are conducted in more than one Member State. The fee is to be paid in two instalments:
	<b>-&gt; 19 350 EURO</b>
Part I	Per procedure for the assessment of the draft protocol;
	<b>-&gt; 29 020 EURO</b>
Part II	Per procedure for the assessment of the final study report by the Pharmacovigilance Risk Assessment Committee.
	<b>100%</b>
Fee exemptions and reductions	For micro enterprises
	<b>40%</b>
	For small and medium-sized enterprises
<b>See section 6 for further information on fee exemptions and reductions.</b>	

Fees payable for assessment of PASS



### 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 201 450 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 43 670 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 332 460 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.



**201 450 EURO**

Basic fee

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.



**+ 43 670 EURO**

Additional fee

Per additional active substance or combination of substances as of the third active substance or combination of substances.

**The maximum total fee amount is EUR 332 460, irrespective of the number of active substances and/or combination of substances.**



**134 300 EURO (2/3 of basic fee)**

Reduced fee

For a referral procedure with only one active substance and/or combination of active substances and one marketing authorisation holders involved in the referral procedure.



**100%**

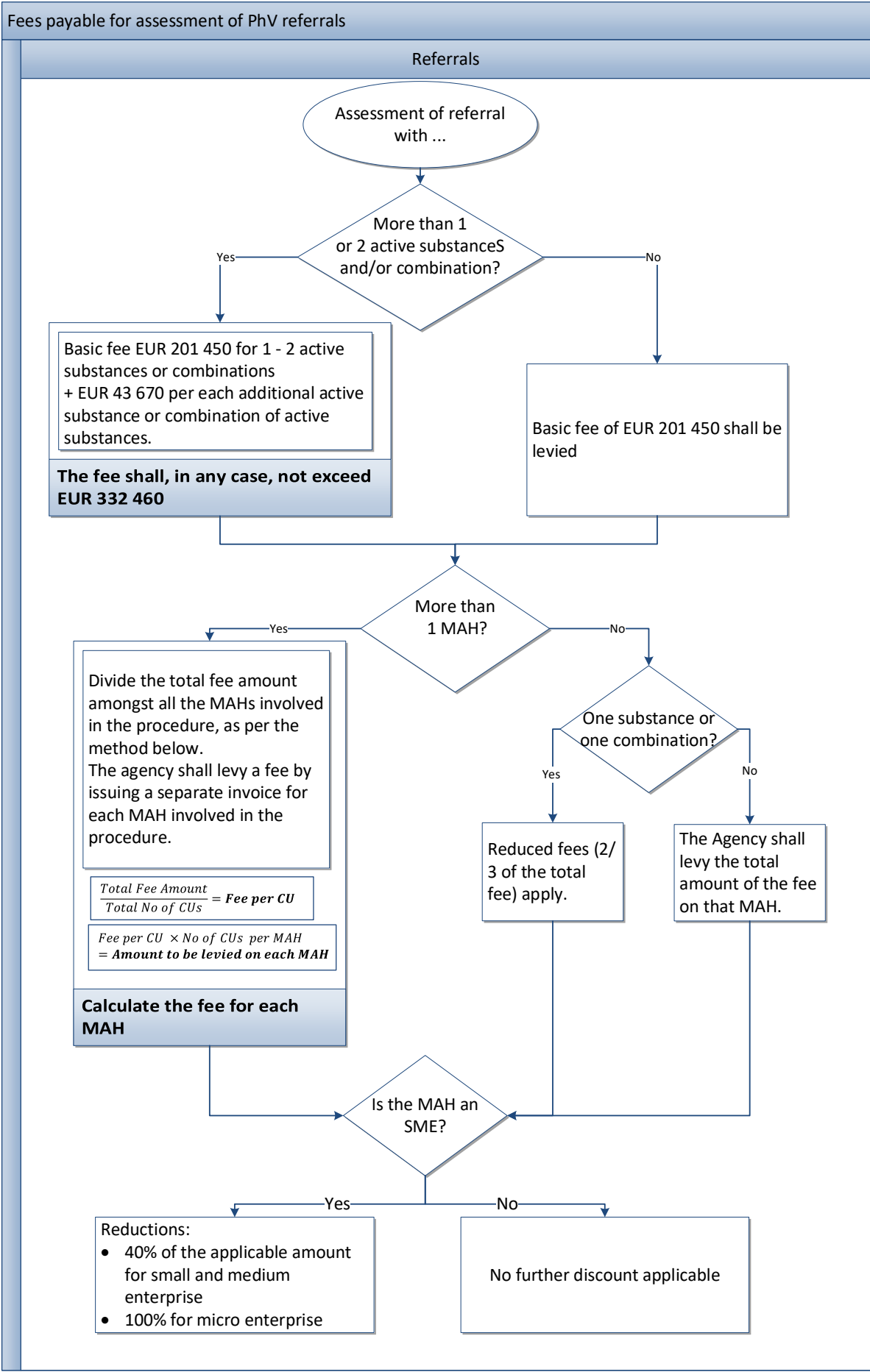
For micro enterprises

**40%**

Fee exemptions and reductions

For small and medium-sized enterprises

**See section 6 for further information on fee exemptions and reductions.**



## 5. Annual pharmacovigilance fee for information technology systems and literature monitoring

The Agency levies 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 75 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 1<sup>st</sup> of July of each year. The amount will cover the period from 1 January to 31 December of the year concerned.



**75 EURO**

Per chargeable unit per year.

Basic fee



**100%**

For micro enterprises

**40%**

For small and medium-sized enterprises

**20%**

For Marketing Authorisation Holders of

- generic medicinal products or
- well-established use medicinal products
- authorised homeopathic medicinal products (excluding homeopathic medicinal products registered through the simplified procedure) or
- authorised herbal medicinal products (excluding herbal medicinal products registered through the simplified procedure)

for the chargeable units corresponding to those products.

**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:

	<p>Medicinal products which are subject to a fee will be identified based on information recorded in the Article 57 database taking into account the scope of the procedure.</p>
<p>Verification of the products subject to a fee</p>	<p>As a support to marketing authorisation holders, an advice note will be sent to the relevant marketing authorisation holder's QPPVs prior to issuing an invoice for a PSUR procedure and an annual fee. An advice note will be sent after the start of the procedure for pharmacovigilance-related referrals.</p>
	<p>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.</p>
	<p>This will inform marketing authorisation holders of the medicinal products that have been identified according to the Article 57 database. 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.</p>
	<p>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.</p>

	<ul style="list-style-type: none"> <li><i>Payment of fees</i></li> </ul>
<p>Financial matters</p>	<p>The Agency will levy the fee by issuing an invoice to each marketing authorisation holder concerned.</p>
	<p>Payment of the fees shall be made only after the marketing authorisation holder has received an invoice issued by the Agency, by means of a transfer to the bank account of the Agency. Any bank charges related to that payment shall be borne by the marketing authorisation holder.</p>
	<p>Fees shall be paid to the Agency in euro within 30 calendar days from the date of the invoice. 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.</p>
	<p>Additional information on how to make a payment can be found on the 'How to Pay' section of the Agency's <a href="#">website</a>.</p>
	<ul style="list-style-type: none"> <li><i>Refund of fees paid in excess</i></li> </ul>
	<p>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.</p>



### Fee exemptions and reductions

- *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).

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

Micro enterprises are exempt from the payment of fees related to pharmacovigilance activities under Regulation 658/2014.

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

Any marketing authorisation holder claiming to be a micro, 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 in the section "Applying for SME status" of the [SME office webpage](#).

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, taking into account the headcount, turnover/balance sheet total thresholds, and if applicable the global ownership structure of the company, its partner entities or subsidiaries.

Marketing authorisation holders who already hold a valid SME status with the Agency are advised to check the expiry date and provide an updated declaration if necessary (see section "Applying for SME status" of the [SME office webpage](#)) to ensure that the incentives remain applicable at the time of fee determination.

The Agency may at any time request from marketing authorisation holders evidence that the conditions for a fee exemption or reduction and the definition of micro, small and medium-sized enterprises as laid down in Commission Recommendation 2003/361/EC are fulfilled (see [SME office webpage](#)).





Where a marketing authorisation holder claiming, or having claimed, a fee exemption or reduction fails to demonstrate that it is entitled to an exemption or a reduction, the full applicable amount will be increased by 10% in accordance with Article 8 (5) of the Regulation 658/2014.

Accordingly, an increased invoice is triggered in instances where:

- ✓ a 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.

Marketing authorisation holders 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.

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