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*[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 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 (4 October 2023)

- Increase in the level of fees (other than pharmacovigilance annual fees) to adjust for an inflation rate of 10.4% (related to 2022) and rounding off to the nearest EUR 10.
- Increase in the level of pharmacovigilance annual fees to adjust for an inflation rate of 10.4% (related to 2022), with no rounding.

[1] Official Journal L189, 27.06.2014, p. 112.
[2] Official Journal L35, 15.02.1995, p. 1

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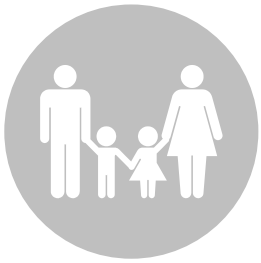


Medicinal products for human use

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').

1	*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.
2	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.

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

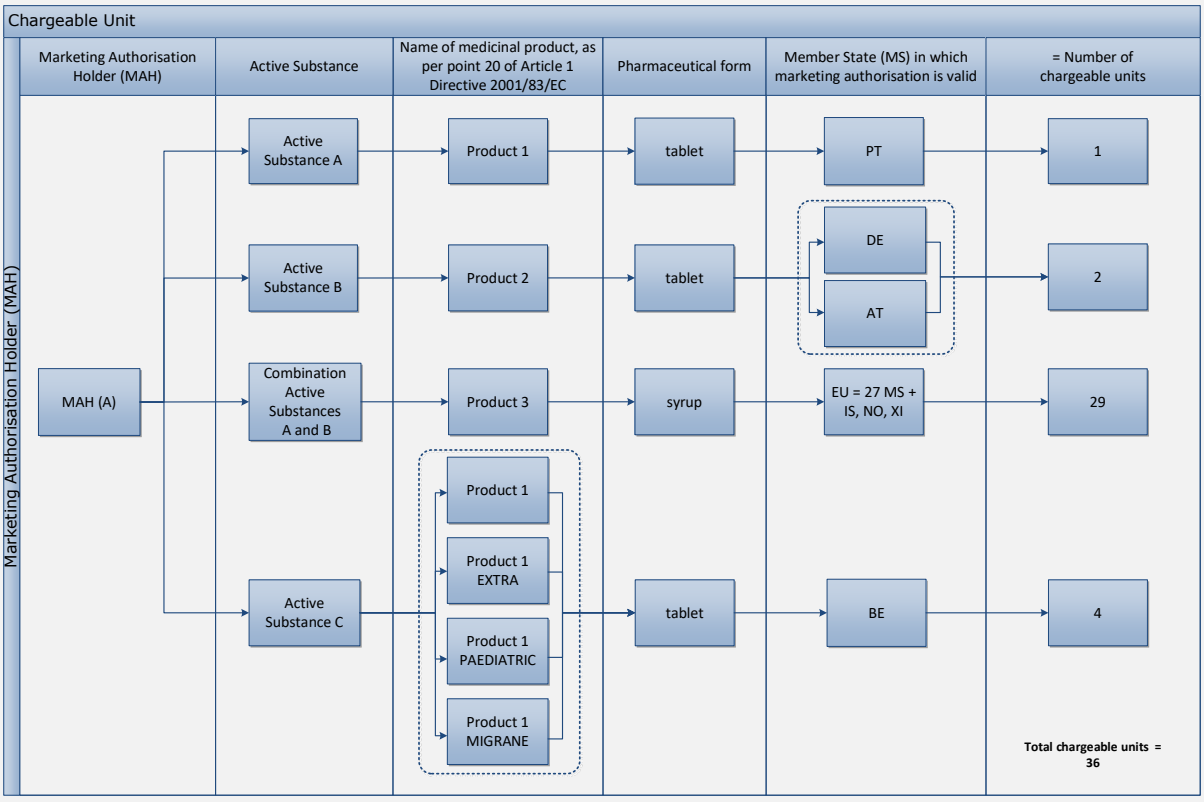
(b) marketing authorisation holder

(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	or	Annual balance sheet total
Medium-sized	<250	≤ € 50 million	or	≤ € 43 million
Small	<50	≤ € 10 million	or	≤ € 10million
Micro	<10	≤ € 2 million	or	≤€ 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
Single assessments of PSURs	• **EUR 24 220** 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 / share of the fee
Assessment of imposed PASS (conducted in more than one member state)	• **EUR 53 400** per procedure to be paid in two instalments: ○ EUR 21 360 due at the start of the procedure for the assessment of the draft protocol; ○ EUR 32 040 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 222 400** if the referral only concerns 1 or 2 active substances and/or combinations; • Fee increased by EUR 48 210 for every additional active substances or combination, **up to maximum fee of EUR 367 030**; • 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 / share of the fee
Annual Service (pharmacovigilance information technology and monitoring of selected medical literature)	• **EUR 83** per chargeable unit; • Due on 1st July every year.	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)

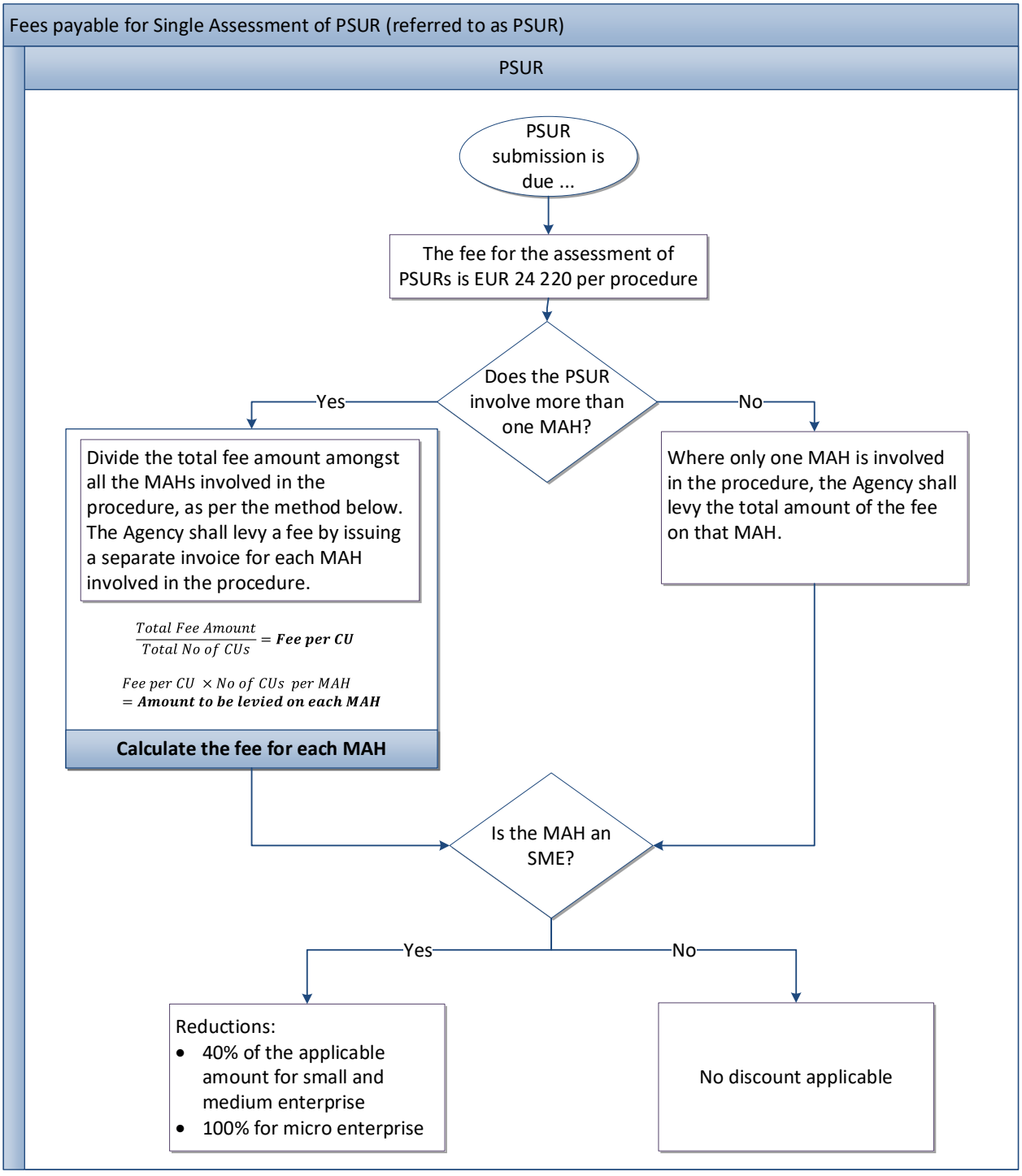
Periodic Safety Update Reports, PSURs, shall be submitted with known frequencies. The frequency of these reports can be found in the 'List of Union reference dates and frequency of submission of PSURs', also known as the EURD list. The EURD list consists of a list of active substances and combinations 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 24 220) 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.

Total fee	**24 220 EURO** 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.
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 PSUR (referred to as PSUR)
PSUR
PSUR submission is due ...
The fee for the assessment of PSURs is EUR 24 220 per procedure
Does the PSUR involve more than one MAH?
Yes
No
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.
Total Fee Amount / Total No of CUs = Fee per CU
Fee per CU × No of CUs per MAH = Amount to be levied on each MAH
Calculate the fee for each MAH
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
No
Reductions:
40% of the applicable amount for small and medium enterprise
100% for micro enterprise
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 holder is charged for the assessment of an imposed, non-interventional post-authorisation safety study.

The fee is EUR 53 400 paid in two parts:

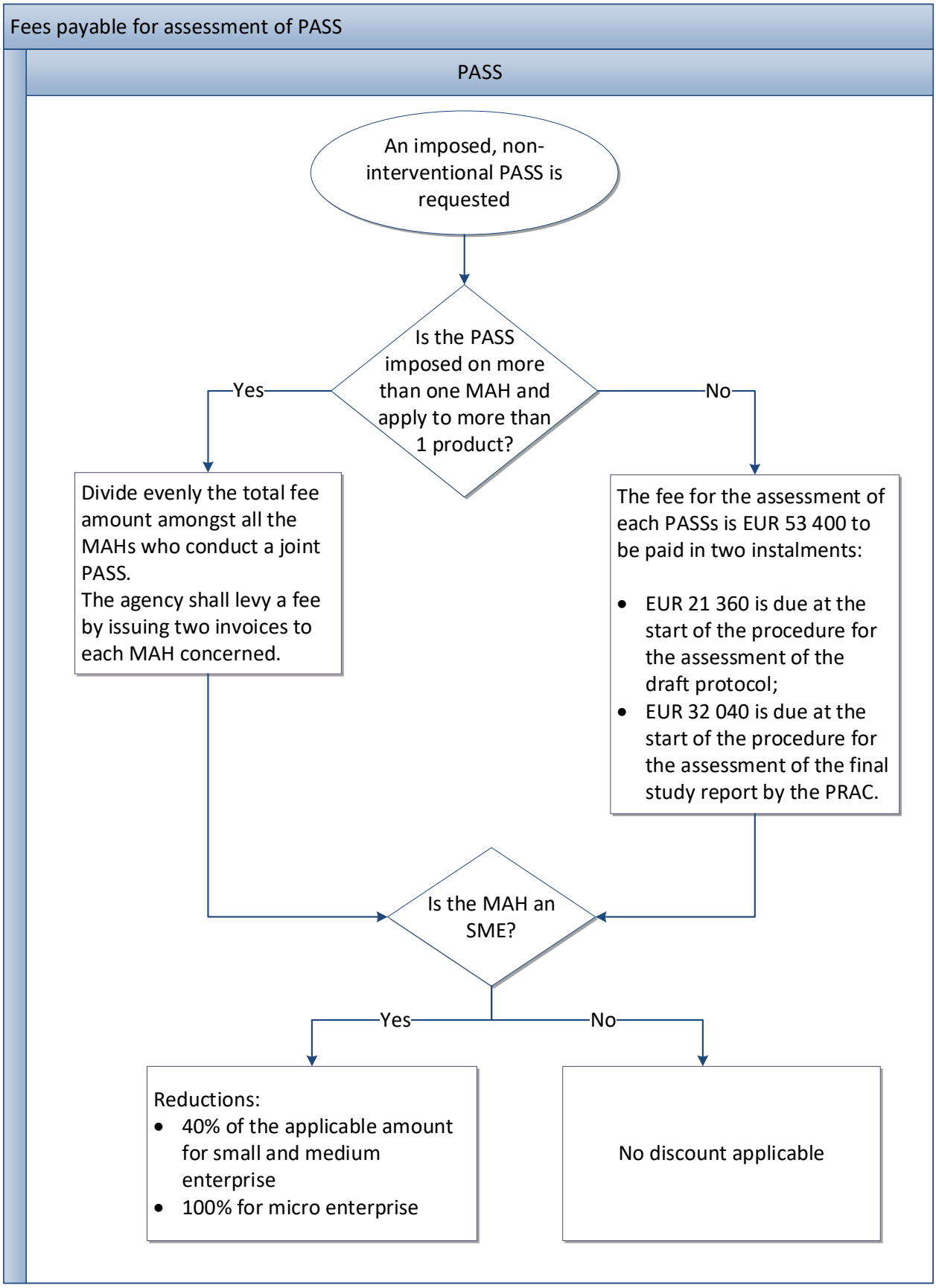
- EUR 21 360 for the assessment of the draft protocol; and
- EUR 32 040 for the assessment of the final study report.

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.

Total fee	**53 400 EURO** 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:
Part I	**-> 21 360 EURO** Per procedure for the assessment of the draft protocol;
Part II	**-> 32 040 EURO** Per procedure for the assessment of the final study report by the Pharmacovigilance Risk Assessment Committee.
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 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
No
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.
The fee for the assessment of each PASSs is EUR 53 400 to be paid in two instalments:
• EUR 21 360 is due at the start of the procedure for the assessment of the draft protocol;
• EUR 32 040 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
No
Reductions:
• 40% of the applicable amount for small and medium enterprise
• 100% for micro enterprise
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.

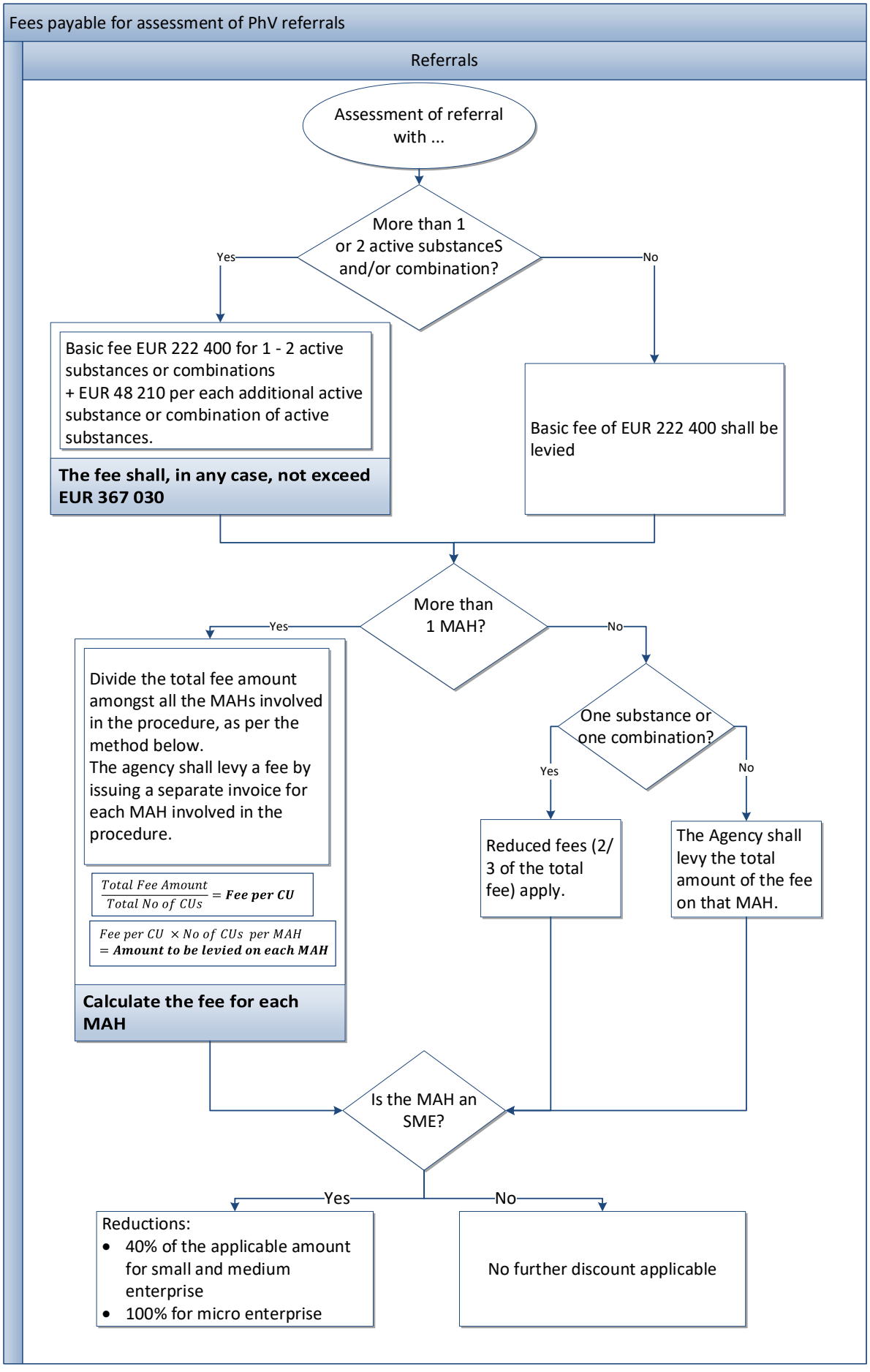
The fee amounts to EUR 222 400 per assessment of referrals procedure conducted on one or two active substances and/or on a combination of substances included in the same assessment. The fee is increased by EUR 48 210 for each additional active substance or combinations of active substances as of the third active substance or combination of substances.

Nevertheless, the fee cannot exceed EUR 367 030 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.

 Basic fee	**222 400 EURO** 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.
 Additional fee	**+ 48 210 EURO** 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 367 030, irrespective of the number of active substances and/or combination of substances.	
 Reduced fee	**148 260 EURO (2/3 of basic 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.

 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 assessment of PhV referrals
Referrals
Assessment of referral with ...
More than 1 or 2 active substanceS and/or combination?
Yes
No
Basic fee EUR 222 400 for 1 - 2 active substances or combinations
+ EUR 48 210 per each additional active substance or combination of active substances.
The fee shall, in any case, not exceed EUR 367 030
Basic fee of EUR 222 400 shall be levied
More than 1 MAH?
Yes
No
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.
Total Fee Amount / Total No of CUs = Fee per CU
Fee per CU × No of CUs per MAH = Amount to be levied on each MAH
Calculate the fee for each MAH
One substance or one combination?
Yes
No
Reduced fees (2/3 of the total fee) apply.
The Agency shall levy the total amount of the fee on that MAH.
Is the MAH an SME?
Yes
No
Reductions:
40% of the applicable amount for small and medium enterprise
100% for micro enterprise
No further discount applicable

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 83 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.

Basic fee

83 EURO

Per chargeable unit per year.

Fee exemptions and reductions

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:

Verification of the products subject to a fee

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.

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.

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.

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 (l) of the second subparagraph of Article 57(1) of Regulation (EC) No 726/2004.

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.

Financial matters

- *Payment of fees*

The Agency will levy the fee by issuing an invoice to each marketing authorisation holder concerned.

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.

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.

Additional information on how to make a payment can be found on the 'How to Pay' section of 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 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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