



**EUROPEAN COMMISSION**  
HEALTH AND CONSUMERS DIRECTORATE-GENERAL  
Health systems and products  
**Medicinal products – authorisations, EMA**

Brussels,  
D(2012)

## **INTRODUCTION OF FEES TO BE CHARGED BY THE EMA FOR PHARMACOVIGILANCE**

**CONCEPT PAPER SUBMITTED FOR PUBLIC CONSULTATION**

**Deadline for replies to this Public Consultation: 15 September 2012**

*This document does not represent an official position of the European Commission. It is a tool to explore the views of interested parties on a preliminary draft. The suggestions contained in this document do not prejudice the form and content of any future proposal by the European Commission.*

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## Glossary

ADR:	Adverse Drug Reaction
CAP:	Centrally Authorised Product
CMDh:	Coordination Group for Human Medicinal Products
EMA:	European Medicines Agency
EV:	EudraVigilance database (of ADRs)
MA:	Marketing Authorisation
MAH:	Marketing Authorisation Holder
MRP / DP:	Mutual Recognition Procedure / Decentralised Procedure
MS:	Member State
NAP:	Nationally Authorised Product
NCA:	National Competent Authority
PASS:	Post-Authorisation Safety Study
PRAC:	Pharmacovigilance Risk Assessment Committee at the EMA
PSUR:	Periodic Safety Update Report

## 1. INTRODUCTION

The European Medicines Agency ('EMA') is an EU body with its own legal personality. EMA is responsible for coordinating the scientific resources put at its disposal by the Member States for the evaluation, supervision and pharmacovigilance of medicinal products. It is amongst the few EU Agencies which are fee-earning. Under Article 67(3) of the Regulation (EU) No 726/2004 ('the Regulation'), EMA's revenue shall consist of an EU contribution and fees charged for undertakings for obtaining and maintaining EU marketing authorisations and for other services. Currently, approximately 85% of EMA's revenues derive from fees, and the remaining 15% from the EU budget.

The pharmaceutical legislation on pharmacovigilance has recently been revised through the adoption of Regulation (EU) No 1235/2010 of the European Parliament and of the Council amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 (hereinafter referred to as 'the Regulation') and Directive 2010/84/EU of the European Parliament and of the Council amending, as regards pharmacovigilance, Directive 2001/83/EC (hereinafter referred to as 'the Directive')<sup>1</sup>. Pharmacovigilance relates to the detection, assessment and prevention of adverse effects of medicinal products. The new legislation will strengthen the EU pharmacovigilance system and improve the protection of public health. The new legislation also provides that **industry is to be charged fees by EMA** for the conduct of pharmacovigilance activities, whereas the previous (2004) wording of Article 67(4) of the Regulation provides that these activities are to be publicly funded.

Only medicinal products which have been authorised in accordance with EU legislation either by the European Commission or by the national competent authorities ('NCAs') in the Member States ('MS') can be placed on the market in the EU. EU-wide marketing authorisations ('MA') are issued by the European Commission (on the basis of a scientific opinion of EMA) according to the centralised procedure. Hereinafter, such products are referred to as centrally authorised products ('CAPs'). A MA can also be issued by an NCA for its own territory (pure national marketing authorisation). As regards MAs in several MS, there are two procedures: (i) mutual recognition procedure where a medicinal product is first authorised in one MS under the national procedure, and in the case where subsequent applications for MAs are filed in other MS, the latter agree to recognise the validity of the first MA; and (ii) decentralised procedure where the MA applications are submitted simultaneously in different MS and for which one MS acts as reference MS (carrying out the scientific evaluation). Products authorised by the NCAs under any of the latter three procedures are hereinafter referred to jointly as 'non-centrally authorised products' ('non-CAPs').

Given that the new pharmacovigilance legislation provides a significantly greater role for EMA in the area of pharmacovigilance, i.e. irrespective of how the medicinal products have been authorised (therefore including both nationally and centrally authorised products), it is justified that EMA will **charge fees also where nationally authorised products (non-CAPs) are involved** (Article 67(3) of the Regulation). It should also be borne in mind that while the new pharmacovigilance legislation lays down certain obligations on the industry, the activity of the regulatory authorities in the area of pharmacovigilance (notably the detection of safety signals, assessment of these signals

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<sup>1</sup> OJ L 348 on 31 December 2010.

and regulatory follow-up) constitute a service to the industry. EMA will have certain functions in pharmacovigilance activities, due amongst other things to the creation of a new scientific committee at EMA, the Pharmacovigilance Risk Assessment Committee ('PRAC'). Additionally, coordination tasks or IT support tasks, such as the enhancement of the EudraVigilance ('EV') database, have been assigned to the Agency.

The Commission's proposal of 10 December 2008 to amend the pharmacovigilance legislation was accompanied by a Financial Statement<sup>2</sup> whereby all costs related to activities resulting from the legislative proposal are to be recouped through fees. This proposal was amended by the Council and the European Parliament during the legislative process, while the financial statement was not modified. This is important, as some additional tasks were entrusted to EMA that were not foreseen in the Financial Statement and these tasks are to be covered by fees. Even if the Financial Statement accompanying the legislative proposal on pharmacovigilance from 2008 is now outdated, it provides some insight into what types of fees for pharmacovigilance activities were foreseen. Indeed, it laid down the following 4 types of fees for the following activities: - referrals (estimation 20/year at 72,800€), - Periodic Safety Evaluation Reports ('PSURs') assessed (1000/year at 6,100€), - Post-authorisation Safety Studies ('PASSes') (study assessments 300/year at 6,100€) and – Risk management assessments (100/year at 12,100€). The final proposal for introduction of fees for pharmacovigilance will be accompanied by its own financial statement.

The pharmacovigilance legislation will become **applicable in July 2012** and therefore, it is urgent to enable EMA to charge fees for the fulfilment of its pharmacovigilance tasks. Fees payable to the EMA are laid down in Council Regulation (EC) No 297/95 ('Fees Regulation')<sup>3</sup>. These fees are normally subject to annual adjustments to the inflation rate under Article 12(5) of the Fees Regulation, and hence also the fees for pharmacovigilance should be subject to such adjustments. This Concept Paper deals with pharmacovigilance fees, and therefore the comments in this public consultation should relate to this topic only and not in general to the Fees Regulation. It should be noted that the Commission will proceed, after having put forward fees for pharmacovigilance, as a second step, with an overall revision of the Fees Regulation which will be preceded by another public consultation.

Given that the pharmacovigilance legislation only concerns medicinal products for human use, there can be no introduction of pharmacovigilance fees for veterinary products in this revision. A Commission proposal to amend in addition certain provisions of the pharmacovigilance legislation is currently going through the legislative process

Finally, it should be borne in mind that the existing legislation provides for various fee incentives for small and medium sized enterprises ('SMEs') for applicants and holders of MAs for CAPs. However, most of the fee incentives relate to the pre-authorisation stage and, for example, the SMEs currently pay the full annual fee to EMA. It is nevertheless

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<sup>2</sup> <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2008:0665:FIN:en:PDF> and

<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2008:0664:FIN:en:PDF>.

<sup>3</sup> OJ L 35, 15.2.1995 p.1.

important to ensure that any amendment to the current legal framework regarding the payment of fees by SMEs to EMA for pharmacovigilance does not undermine these incentives.

This Concept Paper will be disseminated as widely as possible to all stakeholders and EMA will also send it to all SMEs which are included in the SME register<sup>4</sup>.

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<sup>4</sup> <http://fmapps.emea.europa.eu/SME/>

## 2. LEGAL BASE

### 2.1. Fees Regulation

According to Article 70 of Regulation 726/2004, the structure and the level of fees are laid down in the Fees Regulation which was last modified in 2005. For the application of the Fees Regulation, there are Implementing Rules adopted by the Management Board of EMA. These rules provide, *inter alia*, that the national competent authorities in the Member States acting as rapporteurs or co-rapporteurs, i.e. carrying out the evaluation of medicinal products and the subsequent follow-up, are reimbursed by the EMA for their work. There is, however, some work that currently does not generate fees for EMA, and for which the rapporteurs/co-rapporteurs are not remunerated.

As regards pharmacovigilance activities, Article 67(4) of the Regulation lays down in its current wording that “Activities relating to pharmacovigilance (...) shall receive adequate public funding commensurate with the tasks conferred”. Consequently, the “Community contribution” (budget of the EU) referred to in Article 67(3) of the Regulation, is currently used, *inter alia*, for pharmacovigilance activities conducted by the Agency.

This situation will change in July 2012 when the new pharmacovigilance provisions become applicable as the amended Article 67 of the Regulation allows as of that date for pharmacovigilance activities to be covered by fees. Therefore, it is necessary to ensure that EMA will be able to charge fees for these activities. It should, however, be noted that certain post-authorisation activities are currently covered by the annual fee. Indeed, recital 4 of Council Regulation (EC) No 1905/2005 amending Regulation (EC) No 297/95 acknowledged this:

*‘Regulation (EC) No 726/2004 lays down provisions for new post-authorisation activities to be carried out by the Agency. These tasks include the recording of the actual marketing of medicinal products authorised in accordance with Community procedures, the maintenance of marketing authorisation dossiers and of the various databases managed by the Agency, as well as the continuous follow-up of the risk-benefit balance of authorised medicinal products. In addition, it is necessary to reduce the Agency’s dependence on fees related to new applications. The annual fee should therefore be increased by 10 % to accommodate those changes.’*

### 2.2. The new pharmacovigilance legislation

The relevant provision that will allow the pharmacovigilance activities of EMA to be subject to fees is Article 67 of the Regulation which reads as follows:

*‘The Agency’s revenue shall consist of a contribution from the Union and fees paid by undertakings for obtaining and maintaining Union marketing authorisations and for other services provided by the Agency, or by the coordination group as regards the fulfilment of its tasks in accordance with Articles 107c, 107e, 107g, 107k and 107q of Directive 2001/83/EC.’ (new Article 67(3))*

*‘Activities relating to pharmacovigilance, to the operation of communications networks and to market surveillance shall be under the permanent control of the Management Board in order to guarantee the independence of the Agency. This shall not preclude the Agency from charging fees to marketing authorisation holders for performing these*

*activities by the Agency on the condition that its independence is strictly guaranteed.’ (new Article 67(4))*

Moreover, the recitals of Regulation (EU) No 1235/2010 confirm that the legislator had the intention that fees will now become the major source of revenue for financing the pharmacovigilance activities of the Agency and the scientific assessment conducted by the Pharmacovigilance Risk Assessment Committee or the coordination group for human medicinal products (CMDh):

*(13) In order to protect public health, the pharmacovigilance activities of the Agency should be adequately funded. It should be ensured that adequate funding is possible for pharmacovigilance activities by empowering the Agency to charge fees to marketing authorisation holders. However, the management of those collected funds should be under the permanent control of the Management Board in order to guarantee the independence of the Agency.*

*(14) To ensure the highest levels of expertise and the functioning of the Pharmacovigilance Risk Assessment Committee, rapporteurs providing assessments for Union pharmacovigilance procedures, periodic safety update reports, post-authorisation safety study protocols and risk management systems should receive payment through the Agency.*

*(15) Therefore, the Agency should be empowered to charge fees in return for performing the activities of the coordination group within the Union system of pharmacovigilance, as provided for in Directive 2001/83/EC, and the rapporteurs within the coordination group should, in turn, be paid by the Agency.*

### **2.3. General principles in proposing fees for pharmacovigilance**

The objective of proposing fees for pharmacovigilance activities is to finance the new pharmacovigilance tasks that have been entrusted to EMA under the pharmacovigilance legislation. In proposing these fees, the following principles should be respected:

- Proportionality between the amount (level) of the fees and the nature of the work/tasks actually carried out by EMA as well as the regulatory network (i.e. EMA and the NCAs) and maintaining consistency between fees for existing, comparable tasks/work across various procedures.
- Transparency in order for marketing authorisation holders ('MAHs') to know to what tasks the fee corresponds to and to avoid that they are charged twice (by EMA and the Member States) for the same work.
- Equal treatment of MAHs, except for justified reasons (e.g. SMEs).
- Minimum additional administrative complexity of the fee structure by avoiding the introduction of additional fee levels.



### 3. PROPOSED FEES

Different/separate fees can be envisaged for each specific pharmacovigilance activity, notably for the various procedures involving assessments by PRAC. Indeed, 4 different types of fees for various assessment procedures involving PRAC were foreseen in the Financial Statement that accompanied the Commission's legal proposal. In addition, a pharmacovigilance service fee, charged on an yearly basis, is being considered in order to cover the new services and activities of EMA, such as literature monitoring, that benefit the industry but for which it is not possible (or very difficult) to identify individual addressees. Moreover, EMA will also have a number of tasks in the field of information technology, notably maintaining the EV on adverse drug reactions 'ADRs' which entail costs that need to be covered. The submission of ADR reports by both MAHs and NCAs exclusively to EV in the future represents a considerable simplification and reduction of administrative burden for the MAHs compared with the current system (where ADR reports are sent by MAHs to the NCAs and in some cases also to EV and where NCAs submit serious ADR reports to the other MS and EMA).

On the basis of the tasks of EMA (and PRAC) laid down in the pharmacovigilance legislation and taking into account the Financial Statement, as well as the current structure and level of fees established by the 'Fee Regulation', the different types of pharmacovigilance fees envisaged are explained below. These fees are charged irrespective of whether the products involved are centrally authorised or non-centrally authorised. The level of the proposed fees is based on current experience of EMA, which has benchmarked the proposed fees for pharmacovigilance against existing fees in the current Fee Regulation for similar type of work, in order to maintain proportionality and coherence.

#### 3.1. Fee for assessments of Periodic Safety Update Reports

Under the new Pharmacovigilance legislation, an EU-wide assessment ('single assessment') of Periodic Safety Update Reports ('PSURs') is to be performed at EU-level for medicinal products authorised in more than one MS and in the case of medicinal products that are subject to different MA containing the same active substance or the same combination of active substances and for which EU reference dates and frequency of submissions has been established (even though they are subject to different authorisations). Products for which a MA is granted under the provisions relating to generics, well-established use, homeopathic products or traditional use herbal products will not be required to submit PSURs unless there is a specific requirement. The single assessment of PSURs will be carried out by a MS (taking into account the reference MS, if applicable) appointed by the Coordination Group ('CMDh') or, if there is one or more CAPs involved, by a rapporteur appointed by the PRAC.

In line with the benchmarking approach, it is proposed to charge (a basic) fee of **maximum 80,300 €** for each assessment of a PSUR. This maximum amount is equal to the current fee for a Type II variation, based on the scope of the procedure, the extent of the data to be assessed and the workload involved both for PRAC rapporteurs and EMA. In common with the Type II variation, the assessment of the submitted PSUR is performed by the Rapporteur with the involvement of a scientific committee. The data to be assessed for a PSUR (summaries of data relevant to benefit-risk, scientific evaluation of the benefit-risk balance, volume of sales and Eudravigilance data) is comparable to the data being assessed in the context of a Type II variation.

A maximum fee of **80,300 €** is proposed for each assessment of a PSUR for products that have been authorised for 2 years or more whilst a lower fee of **40,150€** is proposed for products which have been authorised for less than 2 years. The assessment of PSURs is based on the cumulative data available at the time of submission. As a consequence, the workload in assessing PSURs for products which have been authorised for more than 2 years is considerably higher and therefore a higher fee is proposed for such assessment.

This fee should be charged for the assessment of the PSUR irrespective of the route of authorisation (centralised/decentralised/national) of the products concerned. This fee would be a new type of fee which does not currently exist.

### **Grouping**

As the MAH may not be the same for the same product in different MS, it should be possible for the MAHs of products which are part of the same single assessment procedure **to group for the purpose of paying a single fee** and of providing a single PSUR and any other documentation during the procedure. As the administrative workload increases the more MAHs there are in the group, it is proposed to add **an administrative fee of 500€** for each additional MAH in a group (without any limit of the number of MAHs). This administrative fee would be retained by EMA. It may be noted that grouping is currently possible under Article 4(2) of the Fees Regulation for certain referrals initiated by the applicant for a MA or the holder of an existing MA for the purpose of paying only one single referral fee. A proportion of the basic fee payable to EMA will serve to remunerate PRAC rapporteurs / co-rapporteurs.

### **Fee reductions for SMEs**

Fee reductions are foreseen for SMEs (see below point 3.5).

**Consultation item n°1: Do you agree with the proposed fee for single assessment of PSURs? If not, please explain and/or suggest alternative.**

**Consultation item n°2: Do you consider relevant the concept of grouping as proposed? If not, please explain and/or suggest alternative.**

### 3.2. Fee for assessment of Post-Authorisation Safety Studies

A Post-Authorisation Safety Study ('PASS') may be imposed as part of the initial MA or subsequently in the post-authorisation phase. The assessment of study protocols, amendments and reports submitted to PRAC will be performed by PRAC, except for studies which will be performed only in one MS and which have been requested in the post-authorisation phase, as they are assessed by the NCA concerned. For the assessment of each *final* study report for PASS, in line with the benchmarking approach, it is proposed to charge a fee of **80,300 €**. The amount is equal to the current fee for a Type II variation. Assessment of clinical study reports and the potential consequential changes to the marketing authorisation are equivalent to Type II variations in terms of the amount of data to be assessed and the workload involved. Therefore, a fee at the level of a Type II variation fee is proposed.

This would be a new type of fee which does not currently exist. No separate fee is proposed for the assessment of the PASS protocols and protocol amendments.

#### **Grouping**

According to the Pharmacovigilance legislation, MAHs should be encouraged to perform a joint PASS in case the same concern applies to more than one product. It is therefore also proposed that where MAHs have jointly performed the same PASS and provided a single final study report, the MAHs concerned by the procedures in Art 107q of the Directive **may be grouped for the purpose of paying one single PASS assessment fee** as there will also be only one assessment in such cases. In addition to the basic fee, it is proposed to charge an **administrative fee of 500€** for each of the second and subsequent MAHs that are grouped. This administrative fee would be retained by EMA. A proportion of the basic fee payable to EMA will serve to remunerate PRAC rapporteurs / co-rapporteurs.

#### **Fee reductions for SMEs**

Fee reductions are foreseen for SMEs (see below point 3.5).

**Consultation item n°3: Do you agree with the proposed fee for the assessment of PASSes? If not, please explain and/or suggest alternative.**

**Consultation item n°4: Do you consider relevant the concept of grouping as proposed? If not, please explain and/or suggest alternative.**

### 3.3. Fee for Assessment of Pharmacovigilance Referrals

For pharmacovigilance referrals following the Union procedure under Articles 107i/107j-k of the Directive involving the PRAC, it is proposed to charge a pharmacovigilance referral fee. Different levels of the pharmacovigilance referral fee are envisaged, depending on the workload involved, ranging from **80,300€** to a **maximum of 267,400€**. The ceiling of 267,400€ will apply when the workload is equivalent to a full benefit-risk assessment (see below). The referral fee would be charged per active substance or combination thereof, belonging to each applicant or MAH. **The fee would be subject to grouping and the cost per applicant or MAH may therefore be substantially lower** depending on the size of the group (see below).

The current referral fee cannot be used as a benchmark, as it concerns only one MAH with one issue to be addressed. The proposed **maximum** amount for pharmacovigilance referrals is equal to the current fee for an initial MA application in the centralised procedure. Pharmacovigilance referrals that entail full benefit-risk assessment are considered to be the exception; they are comparable to the assessment of the initial MA applications, based on the scope of the procedures, the extent of the data to be assessed and the workload involved both for PRAC rapporteurs and EMA. Thus, the maximum fee would only be charged where a full benefit-risk assessment is being performed. To illustrate this point, in the scope of a full safety and efficacy assessment in the context of a referral, all clinical and non-clinical data are submitted and include not only the initial data, but also all the data accumulated since the marketing authorisation was granted. In this way, although the assessment does not include all modules of an initial application, the data to be assessed and the work involved is comparable to an initial application.

On the other hand, the lowest fee of 80,300€ would be applicable to referral procedures which relate for example to the assessment of specific parts of the marketing authorisation, e.g. introduction of new contraindications. Such changes to the marketing authorisation are usually introduced via Type II variations and the fee for such referrals is therefore proposed to be equal to the current Type II variation fee. Both procedures involve the scientific assessment by a rapporteur of specific parts of a dossier and the involvement of a scientific committee.

Only the maximum and the minimum fee levels are presented in this concept paper because further reflections are necessary to define any intermediate fee levels for pharmacovigilance referrals, depending on the workload involved. Such other fee levels should also reflect the outcome of the ongoing revision of some of the provisions for referrals in the pharmacovigilance legislation.

This fee would be charged irrespective of the route of authorisation or products involved (i.e. for both non-CAPs and CAPs) as the work carried out by EMA and the rapporteurs is the same.

Currently, a referral fee is foreseen for specific non-pharmacovigilance referrals initiated by MAHs (Article 4(1) of the current Fees Regulation). For the pharmacovigilance referrals, it is proposed to charge a separate fee for the assessment of each active substance or combination of substances involved in the procedure. Indeed, each active substance or combination of substances requires the assessment of a different set of data, especially as additional products and MAHs are involved.

Pharmacovigilance referrals can be triggered under Article 31 and Article 107i of the Directive or under Article 20 of the Regulation. The ongoing revision of some of the provisions for referrals in the pharmacovigilance legislation may still lead to some additional changes. Some referrals triggered under Article 31 of the Directive or Article 20 of the Regulation may, however, be non-pharmacovigilance referrals. It is therefore proposed to charge the pharmacovigilance referral fee for all referrals relating to pharmacovigilance that follow the procedure under Article 107i/107j-k of the Directive involving the PRAC, irrespective of the article under which the referral was triggered.

### **Grouping**

As the applicant/MAH may not be the same for the same product in different MS, it should be possible for the applicants/MAHs of the same product **to group for the purpose of paying one single fee** and to provide common answers/clarifications during the procedure. It should also be possible to group for the purpose of the referral across different products with the same active substance or combination of substances as the workload will be less. EMA records show that the mean number of MAHs involved in a referral procedure was 116 in 2009, and 139 in 2010. Therefore, grouping will proportionally decrease the cost per applicant/MAH.

As the administrative workload increases with the number of applicants/MAHs in the group, it is proposed to charge an **administrative fee of 500€** for each additional applicant/MAH who is part of the group. This administrative fee would be retained by EMA. A proportion of the basic fee payable to EMA will serve to remunerate PRAC rapporteurs / co-rapporteurs.

### **Fee reductions for SMEs**

Fee reductions are foreseen for SMEs (see below point 3.5).

**Consultation item n°5: Do you agree with the proposed fee for the assessment of pharmacovigilance referrals? If not, please explain and/or suggest alternative.**

**Consultation item n°6: Do you agree with the concept of grouping as proposed? If not, please explain and/or suggest alternative.**

### 3.4. Pharmacovigilance Service Fee

#### 3.4.1. New Pharmacovigilance Service Fee

It is proposed to charge each MAH a pharmacovigilance service fee of **maximum 1,000 EUR** per year and per medicinal product, defined by the same active substance or combination of substances, registered on the list of products established under Article 57(2) of the Regulation.

#### Examples

##### *MAH 1*

Product	Active substance(s)	Number of pharmacovigilance service fees to be paid
A	S1	2
B	S2	
C	S1	

##### *MAH 2*

Product	Active substance(s)	Number of pharmacovigilance service fees to be paid
A	S1	3
B	S2	
C	S1+S2	

##### *MAH 3*

Product	Active substance(s)	Number of pharmacovigilance service fees to be paid
A	S1	5
B	S2	
C	S1+S2	
D	S1+S2+S3	
E	S2+S3	
F	S1+S2	

It may be noted that there is no existing suitable benchmark for this type of fee. This fee is intended to cover general activities related to the new pharmacovigilance tasks of the Agency, including operation of specific ICT tools. The EV database and the PSUR repository are important prerequisites for the conduct of the new pharmacovigilance activities of EMA for both CAPs and non-CAPs. These activities relating to both CAPs and non-CAPs include literature monitoring and monitoring the effectiveness of public health measures (e.g. risk management systems, through outsourced studies of their outcomes using longitudinal patient databases).

The proposed pharmacovigilance service fee would be charged yearly to MAHs of CAPs and non-CAPS.

#### *3.4.2. Current Annual Fee*

The Agency currently charges an annual fee for CAPs. This fee covers all authorised presentations of a given medicinal product. Of this annual fee, 30% is foreseen for EMA pharmacovigilance and inspection staff costs, as assigned to the EMA by the currently applicable legislation. This part of the current annual maintenance fee should continue to be charged as it covers the specific work that EMA currently undertakes on signal detection and risk management plans for CAPs. These tasks will remain unchanged under the new Pharmacovigilance legislation and this work is not covered by any of the proposed specific pharmacovigilance fees. Similar activity for NAPs will be undertaken by the NCAs. Furthermore, it should be noted that under the proposal for new pharmacovigilance fees, a separate variation fee will no longer be charged by the EMA for the implementation of changes to the MA of CAPs following the assessment of a PSUR or PASS Report (whereas MAHs with non-CAPs will still be required to submit requests for variations to the competent NCAs for which normally a fee is charged).

<p><b>Consultation item n°7: Do you agree with the proposed pharmacovigilance service fee? If not, please explain and/or suggest alternative.</b></p>
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### 3.5. Fee incentives for micro, small and medium-sized enterprises as regards pharmacovigilance

By derogation from the relevant provisions of the Fees Regulation, fee incentives for micro, small and medium-sized enterprises ('SMEs') that hold a MA for CAPs are laid down in the Commission Regulation (EC) No 2049/2005 ('SME Regulation')<sup>5</sup>. In addition to fee reductions, the SME Regulation also provides for administrative assistance by EMA to SMEs.

In the post-authorisation phase, SMEs with CAPs currently pay the full annual fee and the full variation fee. Fee incentives for SMEs are limited in this phase to a 90% reduction of the fees for inspections, scientific advice and scientific services.

Under Article 70(2) of the Regulation, the Commission shall adopt provisions establishing circumstances in which SMEs having CAPs may pay reduced fees, defer payments of the fee, or receive administrative assistance. The same logic should apply also for the SMEs with non-CAPs. Under the new pharmacovigilance legislation, EMA will be empowered to charge pharmacovigilance fees also for non-CAPs, and it is important to avoid discriminatory treatment of the SMEs on the basis of the route of authorisation of their respective products. Therefore, and in order to be consistent with the overall EU policy towards SMEs, it is proposed that reduced pharmacovigilance fees be charged to SMEs with non-CAPs.

Under the recently adopted policy in respect of micro-enterprises ("Small Business Act"), the Commission follows an approach whereby micro-enterprises are wherever possible exempt from EU legislation or whereby special regimes are introduced so as to minimise the regulatory burden on them<sup>6</sup>. Micro-enterprises are the smallest category of SME, with less than ten employees and a turnover or balance sheet total equal to or less than 2m EUR.<sup>7</sup>

It is therefore proposed that **micro-enterprises be exempt** from any pharmacovigilance fees. As indicated at the end of this document, SMEs and micro-enterprises that reply to this Public Consultation are specifically requested to indicate if they are an SME or a micro-enterprise.

While the number of SMEs with non-CAPs is currently not known, it is estimated that the majority of all MAHs of non-CAPs are SMEs. According to the limited information available, in the pharmaceutical sector only a limited number of NCAs seem to identify MAHs as SMEs within the meaning of the Commission Recommendation 2003/362/EC.

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<sup>5</sup> OJ L 329/4 of 16.12.2005.

<sup>6</sup> <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2008:0394:FIN:en:PDF>

<sup>7</sup> Article 2(3) of the Annex to Commission Recommendation 2003/361/EC.



### *3.5.1. Fee incentives for products involved in pharmacovigilance procedures at EU level*

As regards the procedures referred to above under point 3.1-3.3. (i.e. PSUR single assessments, PASS assessments and pharmacovigilance referral assessments), it is proposed that the SMEs - irrespective of whether they have CAPs or non-CAPs - be granted a 50% reduction of the proposed full fees. As regards PSURs, PASSes and pharmacovigilance referrals (procedures under points 3.1-3.3.), the 50% reduction would only apply when SMEs are not involved in a grouping, because the principle of grouping, as described above, implies a minimum 50% reduction (and more, when there are more than two MAHs in the group). The SME thus has a choice as to whether to group or not and in case it is not grouping, the SME will benefit from a 50% reduction of the fee. Grouping is, however, encouraged (and often it will be more advantageous for the SMEs depending on the number of MAHs involved). The EMA will facilitate the grouping of SMEs notably by identifying other MAHs with which the SMEs in question could group.

### *3.5.2. Pharmacovigilance Service Fee*

As mentioned above, the new pharmacovigilance services and activities of EMA that are proposed to be covered by the pharmacovigilance service fee concern literature monitoring and specific ICT tools. These services and activities also benefit SMEs. As the charging of the pharmacovigilance service fee is proposed on the basis of the active substance or combination of substances, SMEs will be charged proportionally less than bigger companies, holding a larger product portfolio. At the same time, this approach reduces the administrative burden for the SMEs as they will not need to provide proof of their eligibility for SME status in relation to the payment of the annual service fee.

As EMA will continue to carry out certain pharmacovigilance activities also for SMEs with CAPs (as for other MAHs with CAPs), such as signal detection and risk management plans, it is proposed not to change the current annual fee to SMEs. Similar activity is carried out by the NCAs for SMEs with non-CAPs for which an annual fee is often charged (without specific SME reductions).

**Consultation item n°8: Do you agree with the proposed approach for fee reductions for SMEs as regards the pharmacovigilance procedures at EU level (point 3.5.1)? If not, please explain why and provide suggestions how this could be improved.**

**Consultation item n°9: Do you agree with the proposed approach with regard to the pharmacovigilance service fee for SMEs (point 3.5.2)?**

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**Consultation item n°10: What other aspects would you like to raise? Do you have additional comments?**

The Commission invites comments on this consultation paper, and especially on the boxed “consultation items” by **15 September 2012** evening at the latest. Responses are sent preferably by email, **exclusively** to [SANCO-FEES-PHARMACOVIGILANCE@ec.europa.eu](mailto:SANCO-FEES-PHARMACOVIGILANCE@ec.europa.eu), or by post to Directorate General for Health and Consumers, Unit SANCO/D/5, BE-1049 Brussels. The subject of the email/letter should refer to "PC/12/05 – Public Consultation on pharmacovigilance fees".

Submitting parties should indicate whether they are stakeholder associations or private parties. In case of associations, please indicate clearly the type of stakeholder (patient representative, healthcare professional representative, etc.). In case of companies, please indicate whether the company falls within the EU definition of a small and medium enterprise (*Commission Recommendation of 6 May 2003 concerning the definition of micro, small and medium-sized enterprises (OJ L 124, 20.5.2003, p. 36–41)*). Especially, micro-enterprises that provide comments are requested to specify whether they fulfil the definition of a micro-enterprise.

Contributions will be made publicly available on the ‘Pharmaceuticals’ website of the Commission<sup>8</sup> once the consultation period is over. If you do not wish your contribution to be made public please indicate this clearly and specifically in the submitted documentation. In this case, only an indication of the contributor will be disclosed.

Professional organisations are invited to register in the Commission’s Register for Interest Representatives (<http://ec.europa.eu/transparency/regrin/>) set up in the framework of the European Transparency Initiative with a view to providing the Commission and the public with information about the objectives, funding and structures of interest representatives.

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<sup>8</sup> [http://ec.europa.eu/health/documents/new\\_en.htm](http://ec.europa.eu/health/documents/new_en.htm)