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Subject:	Proposal for a REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL on fees payable to the European Medicines Agency for the conduct of pharmacovigilance activities in respect of medicinal products for human use (Text with EEA relevance)

Delegations will find attached a report from the Commission, submitted under a covering letter from Mr Jordi AYET PUIGARNAU, Director to Mr Uwe CORSEPIUS, Secretary-General of the Council of the European Union.

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Proposal for a

REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

on fees payable to the European Medicines Agency for the conduct of pharmacovigilance activities in respect of medicinal products for human use

(Text with EEA relevance)

{SWD(2013) 234 final}
{SWD(2013) 235 final}

EXPLANATORY MEMORANDUM

1. CONTEXT OF THE PROPOSAL

The legal framework of pharmacovigilance for medicinal products for human use marketed within the EU is provided for in Regulation (EC) No 726/2004[1] ('the Regulation') and in Directive 2001/83/EC[2] ('the Directive'). The EU pharmacovigilance legislation for medicinal products for human use has been subject to a major review and an impact assessment that led to the adoption of a revised legislation[3] in 2010, which strengthens and rationalises the system for safety monitoring of medicines on the European market. This legislation is applicable as of July 2012. It provides for a number of EU-wide procedures to assess pharmacovigilance data which may lead to regulatory action. Some additional amendments to the pharmacovigilance legislation were introduced in 2012 following the 'Mediator' case[4].

Whilst streamlining the EU-wide post-authorisation safety assessment and monitoring of medicines, the revised pharmacovigilance legislation significantly widened the tasks of the European Medicines Agency ('the Agency') with regard to pharmacovigilance, irrespective of whether the medicinal products have been authorised via the 'centralised procedure' (in accordance with the Regulation) or via national procedures (in accordance with the Directive). The Agency has therefore acquired pharmacovigilance competences also for nationally authorised medicines, in addition to reinforced competences for centrally authorised medicines.

To finance these activities, the revised pharmacovigilance legislation provides for fees to be charged to marketing authorisation holders. These fees should be related to pharmacovigilance activities performed at the level of the EU, notably in the context of the EU-wide assessment procedures. These procedures include scientific assessment carried out by rapporteurs from the national competent authorities of the Member States. These fees are therefore not intended to cover the pharmacovigilance activities of the national competent authorities performed at national level. Member States may accordingly continue to charge fees for the activities performed at national level which should, however, not overlap with the fees laid down in this legal proposal.

Since the revised pharmacovigilance legislation only concerns medicinal products for human use, this proposal on fees for pharmacovigilance only covers these medicinal products.

2. RESULTS OF CONSULTATIONS WITH THE INTERESTED PARTIES AND IMPACT ASSESSMENTS

Public Consultation

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1 OJ L 136, 30.4.2004.

2 OJ L 311, 28.11.2001.

3 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 and Directive 2010/84/EU of the European Parliament and of the Council amending, as regards pharmacovigilance, Directive 2001/83/EC, OJ L 348 of 31.12.2010.

4 Directive 2012/26/EU, OJ L 299 of 27.10.2012, and Regulation (EU) No 1027/2012, OJ L 316 of 14.11.2012.

As part of the preparation of this legal proposal on fees for pharmacovigilance, DG SANCO, in close collaboration with the Agency, drafted a concept paper for public consultation. Given that the Union-wide pharmacovigilance procedures foreseen in the revised pharmacovigilance legislation are new procedures, the concept paper used existing procedures that were considered sufficiently similar as benchmarks for the new procedures. In addition, a pharmacovigilance service fee to be charged on an annual basis was considered in the paper, in order to cover those activities of the Agency that benefit industry in general, but for which it is virtually impossible to identify the individual addressee(s).

The Commission launched the public consultation on 18 June 2012 with a deadline for replies on 15 September 2012. In total, 85 replies were received (mainly from industry, but also from the Member States and other stakeholders). The summary of the replies to the public consultation was published on the website of DG SANCO on 29 November 2012. In general, the comments were rather negative, notably as regards the amounts proposed for the fees. They were considered to be too high and without sufficient justification as regards the workload and costs. Grouping of marketing authorisation holders, especially for submitting a single Periodic Safety Update Report, was considered by many as not applicable in practice. Many respondents questioned the benchmarks that were used and considered that pharmacovigilance fees should be rather based on estimations of the time spent and the associated cost of the assessment work. Several industry respondents flagged the risk of possible double charging of the Agency and the Member States, given that many of the competent authorities in the Member States currently charge fees for pharmacovigilance. Particular concerns were expressed by small and medium-sized enterprises, stating that despite the proposed fee reductions in the concept paper, the amounts were still too high. Also many responses from industry associations, representing products such as generic medicinal products, considered that the proposed fee levels would unfairly affect marketing authorisation holders with a large portfolio of products with well-established safety profiles.

Impact assessment

In line with the above-mentioned comments, the Impact Assessment report that accompanies this proposal considered several options, based on estimation of cost. This new approach is in line with the recommendations of the European Court of Auditors[5] and the European Parliament[6] to base the payment system for services provided by Member States' authorities on costs.

Consistent with the legal proposal on pharmacovigilance of 2008 and with the EU legislation on pharmacovigilance, all options of legislative action were based on the assumption that the total cost related to pharmacovigilance would be covered through fees. Regulation (EU) No 1235/2010 provides notably for a new wording of article 67(3) of Regulation (EC) No 726/2004: *'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.'* Recital 13 notably states that 'It should be ensured that adequate funding is possible for

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5 Report on the annual accounts of the European Medicines Agency for the financial year 2011, together with the Agency's replies (2012/C 388/20), OJ C 388/116, 15.12.2012

6 Resolution of the European Parliament of 23 October 2012 with observations forming an integral part of its Decision on discharge in respect of the implementation of the budget of the European Medicines Agency for the financial year 2010, OJ L 350, 20/12/2012 p. 0082 - 0087

pharmacovigilance activities by empowering the Agency to charge fees to marketing authorisation holders. ' and Recital 24 explains that the new legal provisions '*widen the tasks of the Agency with regard to pharmacovigilance, including the monitoring of literature cases, the improved use of information technology tools and the provision of more information to the general public. The Agency should be enabled to fund these activities from fees charged to marketing authorisation holders.'*

The selected option foresees two separate types of fees:

(1) Fees for procedures for the assessment of periodic safety update reports, post-authorisation safety studies and pharmacovigilance referrals.

(2) An annual flat fee to be charged to marketing authorisation holders having at least one medicinal product that is authorised in the EU and registered in the database provided for in Article 57(1)(l) of the Regulation. This annual flat fee would cover only the costs of the pharmacovigilance activities of the Agency other than those related to the above-mentioned procedures. Therefore, it is foreseen that the fee revenue from the annual flat fee be retained by the Agency.

Some fee reductions and fee waivers are foreseen in respect of the proposed fees:

- In line with the general EU policy to support small and medium-sized enterprises, reductions for medicinal products for which the marketing authorisation holder is a small or medium-sized enterprise would be granted for all types of fees. Micro enterprises would be exempted from all fees. The reduction rates for small and medium-sized enterprises are based on the comparisons of data of added values per employee in the sector, as a possible measure of profitability of companies. The proposed contribution of small and medium enterprises to the financing of pharmacovigilance was reduced accordingly, whereas micro-enterprises should be entirely exempt from the obligation to pay pharmacovigilance fees.

- Moreover, certain fee reductions reflect the risk-based approach of the pharmacovigilance legislation acknowledging the differences in the safety profile of new and more established medicinal products for which time has allowed to collect data. A reduction of the annual flat fee is therefore proposed for authorised generic, homeopathic and herbal medicinal products and for medicinal products authorised on grounds of well-established medical use. However, where these medicinal products are included in the Union-wide pharmacovigilance procedures, the full fees for procedures would apply. Registered homeopathic and herbal medicinal products would be exempted from all fees.

- Finally, as marketing authorisation holders for medicinal products authorised under the Regulation currently pay an annual fee to the Agency for maintenance of the authorisation including pharmacovigilance activities covered by the proposed fee, these marketing authorisations would be exempted from the annual flat fee in order to avoid double charging.

Marketing authorisation holders would be charged as follows:

- Marketing authorisation holders having at least one product involved in a Union-wide pharmacovigilance procedure would be charged a fee for procedures,

- Marketing authorisation holders in the EU[7], with the exceptions explained above, would be charged the annual flat fee.

Therefore, marketing authorisation holders that are not involved in any EU procedure would only pay the annual flat fee component, with the above-mentioned exceptions.

The criteria that were identified as the most decisive in analysing the impact of options were fairness, proportionality and transparency of the overall pharmacovigilance fee system, including the adequacy of the relation between the work carried out and the type and level of fee. Other important criteria considered within the analysis were the stability and the simplicity of the Agency pharmacovigilance fee-system.

Under the selected option, fees are proportionate to the workload and the costs, but cannot be entirely predictable by the inherent nature of the pharmacovigilance activities. In order to avoid extreme cases and to allow for a readable, applicable and usable legislative text, it is proposed that procedure-based fees generate an average fee revenue that is based on the average estimated cost of each procedure.

A combination of procedure-based fees and an annual flat fee has been considered to be the most transparent, cost-based, activity-based and proportionate way of setting the new fees, in order to cover the cost under the new pharmacovigilance legislation. This analysis was carried out in the light of a strong preference expressed by stakeholders for a policy approach based on fairness and transparency. With this approach, the products being part of a pharmacovigilance procedure at EU level will contribute to the financing of the cost of the procedure. This is also in line with the risk-based approach of the pharmacovigilance legislation. At the same time, the cost of general pharmacovigilance activities of the Agency, and only that part of its total pharmacovigilance cost, would be recouped through the annual flat fee charged to marketing authorisation holders who benefit overall from the EU pharmacovigilance system. These activities of the Agency relate notably to the information technology systems, safety data management and literature monitoring.

In order to have a fair system, it was considered necessary to identify a single, chargeable unit as there are different ways in the EU of assigning authorisation numbers to and counting medicinal products. To facilitate adverse reaction reporting and signal detection, it is necessary to describe medicinal products with maximum precision in order to take account of differences in strength, pharmaceutical forms, routes of administration etc. Therefore, the Agency has set up the structure of the database described in Article 57(2) of the Regulation to neutralise these differences by means of individual entries. These entries have been chosen as a chargeable unit.

Remuneration of Member States authorities acting as rapporteurs

In line with the above-mentioned recommendations of the European Court of Auditors and the European Parliament, it is proposed that rapporteurs from the national competent authorities of the Member States be remunerated according to a fixed scale based on estimations of cost. The amount of remuneration is based on the average procedure costs as estimated for each type of procedure. Where fee reductions apply, the remuneration of the Member States will be adjusted accordingly, including reductions for small and medium-sized enterprises which are in line with the policy of the Union to support small and medium-sized enterprises.

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[7] Registered in the database provided for in Article 57(1)(l) of the Regulation.

3. LEGAL ELEMENTS OF THE PROPOSAL

Subsidiarity principle

The Agency is a European decentralised Agency established under the Regulation and hence the decision on its funding and charging of fees is to be taken at the EU level. The new pharmacovigilance legislation provides a legal base for the Agency to charge fees for pharmacovigilance. Hence, only the Union can act to enable the Agency to charge fees for pharmacovigilance.

Only pharmacovigilance activities that are performed at EU level and involving the Agency are covered by this proposal. As regards pharmacovigilance activities remaining at national level, the EU is not competent and Member States may still continue charging national fees accordingly.

Proportionality principle

The proposal does not go beyond what is necessary to achieve the general objective pursued, i.e. to introduce fees in order to allow the proper implementation of the pharmacovigilance legislation that is applicable since July 2012.

Legal basis

The proposed Regulation is, like the EU pharmacovigilance legislation based on a dual legal basis: Article 114 and Article 168(4)(c) TFEU. The proposed Regulation is based on Article 114 TFEU as differences between national legislative, regulatory and administrative provisions on medicinal products tend to hinder intra-Union trade and therefore directly affect the operation of the internal market. This Regulation ensures the availability of the necessary financial resources to apply the stream-lined Union procedures for the assessment of serious safety issues for nationally authorised products, which have been introduced amongst other things to prevent or eliminate obstacles that could result from parallel procedures at national level. Thereby this Regulation contributes to the well-functioning of the internal market and the common post-marketing surveillance of medicinal products.

In addition, the proposed Regulation is based on Article 168(4)(c) TFEU as it aims at supporting the goal of setting high standards of quality and safety of medicinal products. According to Articles 168(4) and 4(2)(k) TFEU this Union competence is – like Article 114 TFEU - a shared competence which is exercised with the adoption of the proposed Regulation.

The proposed Regulation aims at setting high standards of quality and safety for medicinal products as it ensures the availability of sufficient financial resources to perform the pharmacovigilance activities that are necessary to guarantee that high standards are maintained once the product is authorised.

Article 168(4)(c) TFEU cannot serve as sole legal basis, but needs to be complemented with the legal basis of Article 114 TFEU as it, as set out above, pursues equally as object the establishment and functioning of the internal market, and the setting of high standards of quality and safety for medicinal products.

Choice of the legal instrument

Since the Treaty on the Functioning of the European Union became applicable, all legislative procedures are normally based on the previous 'co-decision procedure' involving both the Council and the European Parliament. Therefore, for legal certainty, it is proposed to create for pharmacovigilance fees a new Regulation of the Council and the European Parliament, which will be subject to the ordinary legislative procedure (Article 294 of the TFEU).

The adoption of a proposal for a Regulation on pharmacovigilance fees is aimed at allowing the Agency to have adequate funding in order to properly implement the already applicable pharmacovigilance legislation.

The existing Council Regulation (EC) No 297/95[8] of 10 February 1995 on fees payable to the Agency would continue to apply, whereas the proposed Regulation would apply to pharmacovigilance fees for activities laid down in the applicable pharmacovigilance legislation. The two legal instruments would be complementary.

4. BUDGETARY IMPLICATION

Consistent with the legal proposal on pharmacovigilance of 2008 and with the Pharmacovigilance legislation adopted in 2010, according to which the Agency should be enabled to fund pharmacovigilance activities from fees charged to marketing authorisation holders (see section on Impact Assessment), all options of legislative action, including the option which underpins this proposal, were based on the assumption that the costs related to pharmacovigilance would be covered through fees.

Therefore, no impact on the EU general budget is foreseen in the accompanying financial statement of this proposal.

5. OPTIONAL ELEMENTS

European Economic Area

The proposed act is of relevance to the EEA.

[8] OJ L 35, 15.2.1995, p. 1.

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on fees payable to the European Medicines Agency for the conduct of pharmacovigilance activities in respect of medicinal products for human use

(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty on the Functioning of the European Union, and in particular Article 114 and Article 168(4)(c) thereof

Having regard to the proposal from the European Commission,

After transmission of the draft legislative act to the national Parliaments,

Having regard to the opinion of the European Economic and Social Committee[9],

Having regard to the opinion of the Committee of the Regions[10],

Acting in accordance with the ordinary legislative procedure,

Whereas:

(1) The revenues of the European Medicines Agency (hereinafter 'the Agency') consist of a contribution from the Union and fees paid by undertakings for obtaining and maintaining Union marketing authorisations and for other services referred to in Article 67(3) of Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[11].

(2) The provisions on pharmacovigilance relating to medicinal products of human use laid down in Regulation (EC) No 726/2004 and Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use[12] were amended by Directive 2010/84/EU of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to

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9 OJ C , , p. .
10 OJ C , , p. .
11 OJ L 136, 30.4.2004, p. 1.
12 OJ L 311, 28.11.2001, p. 67.

medicinal products for human use[13], Regulation (EU) No 1235/2010 of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products[14], Directive 2012/26/EU of the European Parliament and of the Council of 25 October 2012 amending Directive 2001/83/EC as regards pharmacovigilance[15] and Regulation (EU) No 1027/2012 of the European Parliament and of the Council of 25 October 2012 amending Regulation (EC) No 726/2004 as regards pharmacovigilance[16]. Those amendments only cover medicinal products for human use. Those amendments provide for new pharmacovigilance tasks for the Agency including Union-wide pharmacovigilance procedures, the monitoring of literature cases, the improved information technology tools and the provision of more information to the general public. Furthermore, the pharmacovigilance legislation stipulates that the Agency should be enabled to fund those activities from fees charged to marketing authorisation holders. New categories of fees should therefore be created to cover the new and specific tasks of the Agency.

(3) In order to enable the Agency to charge fees for those new pharmacovigilance tasks, a Regulation should be adopted. The fees provided for in this Regulation should be applicable without prejudice to the fees laid down in Council Regulation (EC) No 297/95 of 10 February 1995 on fees payable to the Agency [17]as that Regulation covers fees for activities of the Agency in respect of medicinal products authorised under Regulation (EC) No 726/2004.

(4) This Regulation should be based on the double legal basis of Article 114 and Article 168(4)(c) of the Treaty on the Functioning of the European Union (TFEU). It aims at financing pharmacovigilance activities that contribute to achieving an internal market as regards medicinal products for human use, taking as a base a high level of protection of health. At the same time, the Regulation provides financial resources supporting the activities to address common safety concerns in order to maintain high standards of quality, safety and efficacy of medicinal products for human use. Both objectives are being pursued simultaneously and are inseparably linked, so that one is not secondary to another.

(5) The structure and amounts of the fees for pharmacovigilance collected by the Agency as well as the rules for payment should be established. The structure of the fees should be as simple as possible to apply in order to minimise the related administrative burden.

(6) In line with the Joint Statement of the European Parliament, the Council of the EU and the European Commission of 19 July 2012 on the Common Approach on decentralised agencies, for bodies for which the revenue is constituted by fees and charges in addition to the Union contribution, fees should be set at a level such as to avoid a

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13 OJ L 348, 31.12.2010, p.74.
14 OJ L 348, 31.12.2010, p.1.
15 OJ L 299, 27.10.2012, p.1.
16 OJ L 316, 14.11.2012, p.38.
17 OJ L 35, 15.2.1995, p. 1.

deficit or a significant accumulation of surplus and be revised when this is not the case. Therefore, the fees set out in this Regulation should be based on an evaluation of the Agency's estimations and forecasts as regards its workload and related costs and on the basis of an evaluation of the costs of the work carried out by the competent authorities of the Member States acting as rapporteurs in accordance with Articles 61(6), 62(1) of Regulation (EC) No 726/2004 and Articles 107e 107q and 107j of Directive 2001/83/EC.

(7) Fees referred to in this Regulation should be transparent, fair and proportionate to the work carried out.

(8) This Regulation should only refer to fees which are to be levied by the Agency, whereas the competence to decide on possible fees levied by the competent authorities of the Member States should remain with the Member States. Marketing authorisation holders should not be charged twice for the same pharmacovigilance activity. Member States should therefore not levy fees for the activities which are covered by this Regulation.

(9) For reasons of predictability and clarity, the amounts of the fees should be established in euro.

(10) Two different types of fees should be levied under this Regulation in order to take account of the diversity of tasks of the Agency and of the rapporteurs. Firstly, fees for the pharmacovigilance procedures carried out at Union level should be charged to those marketing authorisation holders whose medicinal products are part of the procedure. Those procedures relate to the assessment of periodic safety update reports, assessment of post-authorisation safety studies and assessments in the context of referrals initiated as a result of pharmacovigilance data. Secondly, an annual flat fee should be charged for other pharmacovigilance activities carried out by the Agency that benefit marketing authorisation holders overall. Those activities relate to information technology, notably maintenance of the 'Eudravigilance' database referred to in Article 24 of Regulation (EC) No 726/2004, signal detection and monitoring of selected medical literature.

(11) Marketing authorisation holders for medicinal products authorised under Regulation (EC) No 726/2004 already pay an annual fee to the Agency for the maintenance of their authorisations, which includes pharmacovigilance activities that are covered by the annual flat fee established by this Regulation. In order to avoid double charging for those pharmacovigilance activities of the Agency, the annual flat fee established by this Regulation should not be charged for marketing authorisations granted under Regulation (EC) No 726/2004.

(12) The work carried out at Union level in respect of the assessment of non-interventional post-authorisation safety studies imposed by an authority and of which the protocol has been endorsed by the Pharmacovigilance Risk Assessment Committee, involves the supervision of these studies, starting from the assessment of the draft protocol, and is not limited to the assessment of the final study reports. Therefore, the fee levied for this procedure in respect of studies that have been finalised should cover all the work relating to the study. In order to avoid double charging, marketing authorisation holders who are charged the fee for the assessment of non-interventional post-

authorisation safety studies imposed by an authority, should be exempted from any other fee charged by a competent authority for the submission of those studies.

(13) Rapporteurs rely for their assessment on the scientific evaluation and resources of national marketing authorisation bodies, whilst it is the responsibility of the Agency to coordinate the existing scientific resources put at its disposal by the Member States. In view of that and to ensure adequate resources for the scientific assessments relating to the Union-wide pharmacovigilance procedures, the Agency should remunerate the scientific assessment services provided by the rapporteurs appointed by Member States as members of the Pharmacovigilance Risk Assessment Committee referred to in Article 56(1)(aa) of Regulation (EC) No 726/2004 or, where relevant, by rapporteurs in the coordination group referred to in Article 27 of Directive 2001/83/EC. The level of remuneration for the work carried out by those rapporteurs should be based on average estimations of the workload involved and should be taken into account in setting the level of the fees for Union-wide pharmacovigilance procedures.

(14) Fees should be levied on a fair basis on all marketing authorisation holders. Therefore, a single chargeable unit should be established irrespective of the procedure under which the medicinal product has been authorised, either under Regulation (EC) No 726/2004 or under Directive 2001/83/EC and the way in which authorisation numbers are assigned by the Member States. The individual entries corresponding to authorisations in the database referred to in Article 57(1)(l) of Regulation (EC) No 726/2004 based on information from the list of all medicinal products for human use authorised in the Union referred to in Article 57(2) thereof meet this objective.

(15) In line with the policy of the Union to support small and medium-sized enterprises, reduced fees should apply to small and medium-sized enterprises within the meaning of Commission Recommendation 2003/361/EC of 6 May 2003 concerning the definition of micro, small and medium-sized enterprises[18]. Consistent with this policy, micro enterprises within the meaning of that Recommendation should be exempted from all fees under this Regulation.

(16) Generic medicinal products, medicinal products authorised under the provisions relating to well-established medicinal use, authorised homeopathic medicinal products and authorised herbal medicinal products should be subject to a reduced annual flat fee as those products generally have a well-established safety profile. However, in cases where these products are part of any of the Union-wide pharmacovigilance procedures, the full fee should be charged in view of the work involved. As the legislation on pharmacovigilance encourages the conduct of joint post authorisation safety studies, marketing authorisation holders should share the applicable fee in case a joint study is submitted.

(17) Homeopathic and herbal medicinal products registered in accordance with Article 14 and Article 16a of Directive 2001/83/EC should be excluded from this Regulation as the pharmacovigilance activities for these products are carried out by the Member States.

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[18] OJ L 124, 20.5.2003, p.36.

(18) In order to avoid disproportionate administrative workload for the Agency, reductions and exemptions provided for in this Regulation should apply on the basis of a declaration of the marketing authorisation holder that claims to be entitled to the reduction or the exemption. The submission of incorrect information should therefore be discouraged through an increase of the applicable amount of the fee.

(19) For reasons of consistency, deadlines for the payment of fees levied under this Regulation should be established taking due account of the deadlines of the procedures relating to pharmacovigilance provided for in Regulation (EC) No 726/2004 and Directive 2001/83/EC.

(20) Fees provided for under this Regulation should be adapted when appropriate to take account of inflation and, for that purpose, the European Index of Consumer Prices published by Eurostat pursuant to Council Regulation (EC) No 2494/95 of 23 October 1995 concerning harmonised indices of consumer prices[19] should be used.

(21) In order to allow for a sustainable operation of the pharmacovigilance activities of the Agency and an appropriate balance between the fee revenue and the underlying costs, the power to adopt acts in accordance with Article 290 of the Treaty on the Functioning of the European Union should be delegated to the Commission in respect of amendments to the amounts, the reductions, the methods of calculation and the performance information laid down in the Annex to this Regulation, notably through monitoring the inflation rate in the EU and in light of the experience acquired with the actual application of this Regulation. It is of particular importance that the Commission carry out appropriate consultations during its preparatory work, including at expert level. The Commission, when preparing and drawing up delegated acts, should ensure a simultaneous, timely and appropriate transmission of relevant documents to the European Parliament and to the Council.

(22) Since the objective of this Regulation, namely to ensure adequate funding of pharmacovigilance activities carried out at the level of the Union, cannot sufficiently be achieved by the Member States and can, by reason of the scale of the measure, be better achieved at Union level, the Union may adopt measures, in accordance with the principle of subsidiarity as set out in Article 5 of the Treaty on European Union. In accordance with the principle of proportionality, as set out in that Article, this Regulation does not go beyond what is necessary in order to achieve that objective.

For reasons of predictability, legal certainty and proportionality, the annual flat fee should be levied for the first time by 31 January or by 1 July, depending on the date of entry into force of this Regulation. The fees for union-wide pharmacovigilance procedures should be levied for the first time after a reasonable time period, following the entry into force of this Regulation, has elapsed.

HAVE ADOPTED THIS REGULATION:

Article 1

Subject matter and scope

[19] OJ L 257, 27.10.1995, p.1.

1. This Regulation shall apply to fees for pharmacovigilance activities relating to medicinal products for human use authorised in the Union under Regulation (EC) No 726/2004 and Directive 2001/83/EC which shall be levied by the European Medicines Agency (hereinafter the 'Agency') on marketing authorisation holders.

2. This Regulation determines the activities performed at Union level for which fees are due, the amounts and the rules of payment of those fees and the level of remuneration of the rapporteurs.

3. Micro enterprises within the meaning of Recommendation 2003/361/EC shall be exempted from any fee under this Regulation.

4. The fees provided for in this Regulation shall apply without prejudice to the fees laid down in Council Regulation (EC) No 297/95[20].

Article 2

Definitions

For the purposes of this Regulation the following definitions shall apply:

1. 'Chargeable unit' means each individual entry in the database referred to in Article 57(1)(l) of Regulation (EC) No 726/2004 based on information from the list of all medicinal products for human use authorised in the Union referred to in Article 57(2) thereof.

2. 'Medium enterprise' means a medium-sized enterprise within the meaning of Recommendation 2003/361/EC;

3. 'Small enterprise' means a small enterprise within the meaning of Recommendation 2003/361/EC;

4. 'Micro enterprise' means a micro enterprise within the meaning of Recommendation 2003/361/EC.

Article 3

Types of fees

1. The fees for pharmacovigilance activities shall consist of the following:

   (a) fees for Union-wide procedures as provided for in Articles 4, 5 and 6 (hereinafter 'fees for procedures');

   (b) an annual flat fee as provided for in Article 7.

2. Where a fee is levied by the Agency in accordance with paragraph 1(a), the Agency shall remunerate the rapporteur in the Pharmacovigilance Risk Assessment

[20] OJ L 35, 15.2.1995, p. 1.

Committee appointed by the Member State or the rapporteur in the coordination group (hereinafter 'the rapporteur') for the work they carry out for the Agency or the coordination group. This remuneration shall be paid in accordance with Article 9.

Article 4

Fee for assessment of periodic safety update reports

1. The Agency shall levy a fee for the assessment of periodic safety update reports referred to in 107e and 107g of Directive 2001/83/EC and in Article 28 of Regulation (EC) No 726/2004.

2. The amount of the fee is laid down in Part I of the Annex.

3. Where only one marketing authorisation holder is subject to the obligation to submit a periodic safety update report in the context of the procedures referred to in paragraph 1, the Agency shall levy the total amount of the applicable fee on that marketing authorisation holder.

4. Where two or more marketing authorisation holders submit periodic safety update reports in the context of the procedures referred to in paragraph 1, the Agency shall divide the total amount of the fee among those marketing authorisation holders in accordance with Part I of the Annex.

5. Where the marketing authorisation holder referred to in paragraphs 3 and 4 is a small or medium-sized enterprise, the amount payable by the marketing authorisation holder shall be reduced as laid down in Part I of the Annex.

6. The Agency shall levy the fee under this Article by issuing a separate invoice to each marketing authorisation holder concerned within thirty calendar days from the submission date of the periodic safety update report established in accordance with Article 107c(4) of Directive 2001/83/EC. Fees due under this Article shall be paid to the Agency within thirty calendar days from the date on which the invoice is received by the marketing authorisation holder.

Article 5

Fee for assessment of post-authorisation safety studies

1. The Agency shall levy a fee for post-authorisation safety studies referred to in Article 21a(b) or Article 22a(1)(a) of Directive 2001/83/EC and Article 9(4)(cb) or Article 10a(1)(a) of Regulation (EC) No 726/2004 for the assessment thereof carried out under Articles 107n to 107q of Directive 2001/83/EC and Article 28b of Regulation (EC) No 726/2004.

2. The amount of the fee is laid down in Part II of the Annex.

3. Where the obligation to conduct a post-authorisation safety study referred to in paragraph 1 is imposed on more than one marketing authorisation holders, the same concerns applying to more than one medicinal products, and where the marketing authorisation holders concerned conduct a joint post-authorisation safety study, the amount payable by each marketing authorisation holder shall be levied as laid down in Part II section 3 of the Annex.

4. Where the obligation to conduct a post-authorisation safety study is imposed on a marketing authorisation holder which is a small or medium-sized enterprise, the amount payable by the marketing authorisation holder shall be reduced, as laid down in Part II of the Annex.

5. The Agency shall levy the fee under this Article by issuing an invoice to each marketing authorisation holder within thirty calendar days from the receipt of the final study report by the Pharmacovigilance Risk Assessment Committee. Fees due under this Article shall be paid within thirty calendar days from the date on which the invoice is received by the marketing authorisation holder.

6. Marketing authorisation holders who are charged the fee under this Article shall be exempted from any other fee charged by a competent authority for the submission of studies referred to in paragraph 1.

Article 6

Fee for assessments in the context of referrals initiated as a result of the evaluation of pharmacovigilance data

1. The Agency shall levy a fee for the assessment carried out in the context of a procedure initiated as a result of the evaluation of pharmacovigilance data under Articles 107i to 107k of Directive 2001/83/EC, under the second subparagraph of Article 31(1) thereof or under Article 20(8) of Regulation (EC) No 726/2004.

2. The amount of the fee is laid down in Part III of the Annex.

3. Where only one marketing authorisation holder is involved in the procedure referred to in paragraph 1, the Agency shall levy the total amount of the fee on that marketing authorisation holder, as laid down in Part III of the Annex.

4. Where two or more marketing authorisation holders are involved in the procedure referred to in paragraph 1, the Agency shall divide the total amount of the fee among those marketing authorisation holders in accordance with Part III of the Annex.

5. Where the marketing authorisation holder referred to in paragraphs 2 or 3 is a small or medium-sized enterprise, the amount payable by that marketing authorisation holder shall be reduced as laid down in Part III of the Annex.

6. The Agency shall levy the fee under this Article by issuing a separate invoice to each marketing authorisation holder involved in the procedure within thirty calendar days from the public announcement of the procedure in accordance with Article 107j(1) of Directive 2001/83/EC or from the date on which the matter was referred to the

Agency under the second subparagraph of Article 31(1) of Directive 2001/83/EC or under Article 20(2) of Regulation (EC) No 726/2004. Fees due under this Article shall be paid within thirty calendar days from the date on which the invoice is received by the marketing authorisation holder.

Article 7

Annual flat fee

1. For its pharmacovigilance activities relating to information technology systems under Article 24, Article 25a, Article 26, Article 57(1)(l) of Regulation (EC) No 726/2004, monitoring of selected medical literature under Article 27 thereof and signal detection under Article 28a thereof, the Agency shall levy once per year a flat fee as laid down in Part IV of the Annex.

2. The fee shall be levied on holders of marketing authorisations for all medicinal products authorised in the Union in accordance with Directive 2001/83/EC, on the basis of the chargeable units corresponding to those products. Chargeable units corresponding to products authorised in accordance with Regulation (EC) No 726/2004 shall not be subject to the annual flat fee.

   The total annual payable amount for each marketing authorisation holder shall be calculated by the Agency on the basis of the chargeable units as defined in Article 2(1) of this Regulation which correspond to the information recorded on 1 January of each year. This amount shall cover the period from 1 January to 31 December of that year.

3. The amount of the annual flat fee per chargeable unit is laid down in Part IV of the Annex.

4. Where the marketing authorisation holder is a small or medium-sized enterprise, the amount payable by the marketing authorisation holder shall be reduced as laid down in Part IV of the Annex.

5. A reduced annual flat fee, as laid down in Part IV of the Annex, shall apply in respect of medicinal products referred to in Article 10(1) and Article 10a of Directive 2001/83/EC and in respect of authorised homeopathic medicinal products and authorised herbal medicinal products, as defined respectively in Article 1(5) and Article 1(30) of Directive 2001/83/EC.

6. Where the marketing authorisation holder of medicinal products referred to in paragraph 4 is a small or medium-sized enterprise, only the reduction set out in paragraph 3 shall apply.

7. The Agency shall levy the annual flat fee by issuing invoices to marketing authorisation holders at the latest on 31 January of every calendar year for that calendar year. Fees due under this Article shall be paid within 30 calendar days from the date on which the invoice is received by the marketing authorisation holder.

8. The Agency shall retain the fee revenue from the annual flat fee.

Article 8

Fee reductions and exemptions

1. Any marketing authorisation holder claiming to be a small or medium-sized enterprise and, therefore, to be entitled to a reduced fee under Articles 4 to 7, shall make a declaration to that effect to the Agency within 30 calendar days from the receipt of the invoice from the Agency. The Agency shall apply the reduction on the basis of that declaration where the required conditions are met.

2. Any marketing authorisation holder claiming to be a micro enterprise and to be entitled to the exemption under Article 1 shall make a declaration to that effect to the Agency within 30 calendar days from the receipt of the invoice from the Agency. The Agency shall apply the exemption on the basis of that declaration.

3. Any marketing authorisation holder claiming to be entitled to a reduced annual flat fee under Article 7(5) shall make a declaration to that effect to the Agency. The Agency shall apply the reduction on the basis of that declaration where the required conditions are met. Where the declaration is made by the marketing authorisation holder after the receipt of the invoice from the Agency, the declaration shall be done within 30 calendars days from the receipt of that invoice.

4. The Agency may request, at any time, evidence that the conditions for a reduction of fees or for an exemption from fees are fulfilled. In that case, the marketing authorisation holder claiming or having claimed to be entitled to a reduction or an exemption under this Regulation, shall submit to the Agency the information necessary to demonstrate compliance with the relevant conditions.

5. Where a marketing authorisation holder claiming or having claimed to be entitled to a reduction of or an exemption from fees under this Regulation fails to demonstrate that it is entitled to such a reduction or exemption, the amount of the fee laid down in the Annex shall be increased by 10% and the Agency shall levy the resulting full applicable amount or, as appropriate, the balance to the resulting full applicable amount.

Article 9

Payment of remuneration by the Agency to rapporteurs

1. The Agency shall remunerate rapporteurs in accordance with Article 3(2) in the following cases:

   (c) where the Member State has appointed a member of the Pharmacovigilance Risk Assessment Committee who acts as rapporteur for the assessment of periodic safety update reports referred to in Article 4;

   (d) where the Member State has appointed a representative in the coordination group who acts as rapporteur in the context of the assessment of periodic safety update reports referred to in Article 4;

(e) where the Member State has appointed a member of the Pharmacovigilance Risk Assessment Committee who acts as rapporteur for the assessment of post-authorisation safety studies referred to in Article 5;

(f) where the Member State has appointed a member of the Pharmacovigilance Risk Assessment Committee who acts as rapporteur for the referrals referred to in Article 6.

Where the Pharmacovigilance Risk Assessment Committee or the coordination group decides to appoint a co-rapporteur, the remuneration shall be divided between the rapporteur and the co-rapporteur.

2. The corresponding amounts of the remuneration for each of the activities listed in paragraph 1 are laid down in Parts I, II and III of the Annex.

3. The remuneration provided for in paragraph 1 shall be paid only after the final assessment report for a recommendation which is intended for adoption by the Pharmacovigilance Risk Assessment Committee has been made available to the Agency.

4. The remuneration provided for in paragraph 1 for the work of the rapporteur and any related scientific and technical support shall be without prejudice to the obligation of Member States not to give committee members and experts instructions which are incompatible with their own individual tasks as rapporteur or with the tasks and responsibilities of the Agency.

5. The remuneration shall be paid in accordance with the written contract referred to in the first subparagraph of Article 62(3) of Regulation (EC) No 726/2004. Any bank charges related to the payment of that remuneration shall be borne by the Agency.

Article 10

Mode of payment of the fee

1. The fees shall be paid in Euro.

2. Payments shall be made only after the marketing authorisation holder has received an invoice issued by the Agency.

3. Payments shall be made by means of a transfer to the bank account of the Agency. Any bank charges related to the payment shall be borne by the marketing authorisation holder.

Article 11

Identification of the payment of the fee

1. In every payment the marketing authorisation holder shall indicate the remittance reference. For payments made by on-line payment system, the reference number generated is regarded as remittance number.

2. If the purpose of the payment cannot be established, the Agency shall set a deadline by which the marketing authorisation holder shall notify it in writing of the purpose of the payment. If the Agency does not receive a notification of the purpose of the payment before expiry of the deadline, the payment shall be considered invalid and the amount concerned shall be refunded to the marketing authorisation holder.

Article 12

Date of payment of the fee

The date on which the full amount of the payment is received in the bank account held by the Agency shall be considered to be the date on which the payment has been made. A deadline for payment shall be considered to have been observed only if the full amount of the fee has been paid in due time.

Article 13

Refund of fee amounts paid in excess

1. Excess amounts shall be refunded by the Agency to the marketing authorisation holder. However, where an amount paid in excess is under EUR 100 and the marketing authorisation holder concerned has not expressly requested a refund, the amount paid in excess shall not be refunded.

2. It shall not be possible to count any amounts paid in excess towards future payments to the Agency.

Article 14

Provisional estimate of Agency budget

The Agency shall, when producing an estimate of the overall expenditure and income for the following financial year in accordance with Article 67(6) of Regulation (EC) No 726/2004, include detailed information on income from fees relating to pharmacovigilance activities. This information shall distinguish between the annual flat fee and the fees for each procedure referred to in Article 3(a). The Agency shall also provide specific analytical information on its revenue and expenditure related to pharmacovigilance activities, allowing to distinguish between the annual flat fee and each of the fees for procedures referred to in Article 3(a).

Article 15

Transparency and monitoring

1. The amounts and rates laid down in Parts I to IV of the Annex shall be published on the website of the Agency.

2. The Executive Director of the Agency shall provide the Commission and the Management Board annually with information on the components that may have a bearing on the costs to be covered by the fees provided for in this Regulation. This

information shall include a cost breakdown related to the previous year and a forecast for the following year. The Executive Director of the Agency shall also provide the Commission and the Management Board once per year with the performance information set out in Part V of the Annex based on the performance indicators referred to in paragraph 3.

3. Within one year from the entry into force of this Regulation, the Agency shall adopt a set of performance indicators taking into account the information listed in Part V of the Annex.

4. The inflation rate as measured by means of the European Index of Consumer prices as published by Eurostat pursuant to Regulation (EC) No 2494/95 shall be monitored in relation to the amounts set out in the Annex. The monitoring shall take place for the first time after this Regulation has been applied during a full calendar year and, thereafter, annually.

5. In view of the monitoring referred to in paragraph 4, the Commission may, where necessary, adjust the amounts of the fees and the amounts of the remuneration of rapporteurs laid down in the Annex, in accordance with Article 16. Those adjustments shall take effect on 1 April following the entry into force of the corresponding amending act.

Article 16

Amendment

1. The Commission shall be empowered to adopt delegated acts to amend Parts I to V of the Annex.

2. Any amendments to the amounts shall be based on an evaluation of the costs of the Agency and the costs of the assessments provided by the rapporteurs as laid down in Article 9 or on the monitoring of the inflation rate referred to in Article 15(4).

Article 17

Exercise of the delegation

1. The power to adopt delegated acts is conferred on the Commission subject to the conditions laid down in this Article.

2. The power to adopt delegated acts referred to in Article 16 shall be conferred on the Commission for an indeterminate period of time from [*].

3. The delegation of powers referred to in Article 16 may be revoked at any time by the European Parliament and by the Council. A decision to revoke shall put an end to the delegation of the power specified in that decision. It shall take effect the day following the publication of the decision in the Official Journal of the European

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[*] Date of entry into force of the basic legislative act or any other date set by the legislator.[*To be adapted by the legislator]*

Union or at the later date specified therein. It shall not affect the validity of any delegated acts already in force.

4. As soon as it adopts a delegated act, the Commission shall notify it simultaneously to the European Parliament and to the Council.

5. A delegated act adopted pursuant to Article 16 shall enter into force only if no objection has been expressed either by the European Parliament or the Council within a period of two months of notification of that act to the European Parliament and the Council or if, before the expiry of that period, the European Parliament and the Council have both informed the Commission that they will not object. That period shall be extended by two months at the initiative of the European Parliament and the Council.

Article 18

Transitional provisions

The fees referred to in Articles 4, 5 and 6 and Parts I, II and III of the Annex shall not apply to those procedures at Union level which are initiated before the fortieth day following the entry into force of this Regulation.

Article 19

Entry into force and application

1. This Regulation shall enter into force on the twentieth day following that of its publication in the Official Journal of the European Union.

2. The annual flat fee referred to in Article 7 and specified in Part IV of the Annex shall be levied for the first time by [31 January or by 1 July following the entry into force of this Regulation whichever date is the earliest], and by 31 January every year thereafter. [In case the annual flat fee is levied for the first time on 1 July, 50 % of the full flat fee shall be levied.][*To be adapted by the legislator]*

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Brussels,

For the European Parliament	*For the Council*
The President	*The President*

ANNEX

PART I

Fee for assessment of periodic safety update reports referred to in Article 4: amounts levied by the Agency and level of remuneration of rapporteurs

1. The fee for the assessment of periodic safety update reports is EUR 19 500 per procedure. The corresponding remuneration of the rapporteur is EUR 13 100.

2. In application of Article 4(5), small and medium-sized enterprises shall pay 60 % of the applicable amount.

3. For the purpose of calculating the amount to be levied on each marketing authorisation holder in application of Article 4(4), the Agency shall calculate the proportion of chargeable units held by each marketing authorisation holder concerned of the total number of chargeable units held by all marketing authorisation holders involved in the procedure.

   The share payable by each marketing authorisation holder shall be calculated by:

   (i) dividing the total amount of the fee among the marketing authorisation holders concerned proportionately to the number of chargeable units,

   (ii) subsequently applying the reduction as per paragraph 2 of Part I of this Annex and the exemption referred to in Article 1(3), where relevant.

4. Where reductions and exemptions apply, the remuneration of the rapporteur shall be adapted proportionally. Where the Agency subsequently collects the full applicable amount including the 10 % increase as provided for in Article 8(5), the remuneration of the rapporteur shall be adapted proportionally.

PART II

Fee for assessment of a post-authorisation safety study referred to in Article 5: amounts levied by the Agency and level of remuneration rapporteurs

1. The fee for the assessment of a post authorisation safety study is EUR 43 000. The corresponding remuneration of the rapporteur is EUR 18 200.

2. In application of Article 5(4), small and medium-sized enterprises shall pay 60 % of the applicable amount.

3. Where marketing authorisation holders concerned conduct a joint post-authorisation safety study referred to in Article 5(3), the amount payable by each marketing authorisation holder shall be levied by the Agency by evenly dividing the total amount of the fee among those marketing authorisation holders. Where relevant, the reduction laid down in paragraph 2 of Part II of this Annex or, where appropriate, the exemption referred to in Article 1(3), shall be applied to the share payable by the marketing authorisation holder.

4. Where reductions and exemptions apply, the remuneration of the rapporteur shall be adapted proportionally. Where the Agency subsequently collects the full applicable amount including the 10 % increase as provided for in Article 8(5), the remuneration of the rapporteur shall be adapted proportionally.

PART III

Fee for assessment in the context of referrals initiated as a result of the evaluation of pharmacovigilance data referred to in Article 6: amounts levied by the Agency and level of remuneration of rapporteurs

1. The fee for the assessment of the procedure referred to in Article 6(1) is EUR 168 600. The corresponding remuneration of the rapporteur is EUR 45 100.

2. In application of Article 6(5), small and medium-sized enterprises shall pay 60 % of the applicable amount.

3. For the purpose of calculating the amount to be levied on each marketing authorisation holder in application of Article 6(4), the Agency shall calculate the proportion of chargeable units held by each marketing authorisation holder concerned of the total number of chargeable units held by all marketing authorisation holders involved in the procedure.

   The amount payable by each marketing authorisation holder shall be calculated by:

   (i) dividing the total amount of the fee among the marketing authorisation holders concerned proportionately to the number of chargeable units,

   (ii) subsequently applying the reduction laid down in paragraph 2 of Part II of this Annex and the exemption referred to in Article 1(3), where relevant.

   Where reductions and exemptions apply, the remuneration of the rapporteur shall be adapted proportionally. Where the Agency subsequently collects the full applicable amount including the 10 % increase as provided for in Article 8(5), the remuneration of the rapporteur shall be adapted proportionally.

PART IV

Annual flat fee referred to in Article 7

1. The annual flat fee is EUR 60 per chargeable unit.

2. In application of Article 7(4), small and medium-sized enterprises shall pay 60 % of the applicable amount.

3. Holders of marketing authorisations for medicinal products referred to in Article 7(5) shall pay 80 % of the amount applicable to the chargeable units corresponding to those products.

PART V

Performance information

The following information shall relate to each calendar year:

Number of Agency staff involved in pharmacovigilance activities as per the legislation applicable during the reference period, specifying staff allocated to activities corresponding to each of the fees referred to in Articles 4 to 7.
Number of hours outsourced to third parties with specification of the activities concerned and cost incurred.
Overall pharmacovigilance costs and a breakdown of staff and non-staff costs relating to activities corresponding to each of the fees referred to in Articles 4 to 7.
Number of procedures relating to the assessment of periodic safety update reports, as well as number of marketing authorisation holders and number of chargeable units per procedure; number of reports submitted per procedure and number of marketing authorisation holders that have submitted a joint periodic safety update report.
Number of procedures relating to the assessment of post-authorisation safety studies; number of marketing authorisation holders having carried out such studies and number of marketing authorisation holders that have submitted a joint study.
Number of procedures relating to the referrals initiated on the basis of pharmacovigilance data as well as number of marketing authorisation holders and number of chargeable units involved per marketing authorisation holder and per procedure.
Number of marketing authorisation holders that have claimed a small and medium-sized enterprise status involved in each procedure; number of marketing authorisation holders whose claim has been denied. Number of marketing authorisation holders that have claimed a micro enterprise status; number of marketing authorisation holders whose claim for fee exemption has been denied.
Number of marketing authorisation holders of medicinal products referred to in Article 7(5) that have benefitted from reduced annual flat fees; number of chargeable units per marketing authorisation holders concerned.
Number of invoices sent out/ annual fees charged in respect of the annual flat fee and average and overall amount invoiced to marketing authorisation holders. Number of marketing authorisation holders that have claimed a small and medium-sized enterprise or a micro enterprise status for each annual application of the annual flat fee; number of marketing authorisation holders whose claim has been denied.
Attribution of rapporteurships and co-rapporteurships per Member State per type of procedure

LEGISLATIVE FINANCIAL STATEMENT

1. FRAMEWORK OF THE PROPOSAL/INITIATIVE

1.1. Title of the proposal/initiative

REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

on fees payable to the European Medicines Agency (EMA) for the conduct of pharmacovigilance activities in respect of medicinal products for human use

1.2. Policy area(s) concerned in the ABM/ABB structure[21]

Public Health (Heading 3B of MFF)

1.3. Nature of the proposal/initiative

☐ The proposal/initiative relates to **a new action**

☐ The proposal/initiative relates to **a new action following a pilot project/preparatory action**[22]

☑ The proposal/initiative relates to **the extension of an existing action**

☐ The proposal/initiative relates to **an action redirected towards a new action**

1.4. Objectives

1.4.1. The Commission's multiannual strategic objective(s) targeted by the proposal/initiative

Resource-efficient, smart and inclusive growth.

1.4.2. Specific objective(s) and ABM/ABB activity(ies) concerned

Specific objective No

Ensure proper implementation of measures to monitor safety of medicines through implementation at the level of the Union of the pharmacovigilance legislation of the Union

ABM/ABB activity(ies) concerned

Public Health (Heading 3B of MFF)

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21 ABM: Activity-Based Management – ABB: Activity-Based Budgeting.

22 As referred to in Article 49(6)(a) or (b) of the Financial Regulation.

1.4.3. Expected result(s) and impact

Specify the effects which the proposal/initiative should have on the beneficiaries/groups targeted.

The main effect is the introduction of fees to be paid by marketing authorisation holders of medicinal products for human use for the conduct of pharmacovigilance activities by the European Medicines Agency as per the applicable legislation, including scientific assessment performed by rapporteurs in the framework of Union-wide pharmacovigilance procedures.

The expected impact on the EMA is to be able to collect fees to ensure adequate financing in order to cover the estimated cost for the conduct of pharmacovigilance activities as assigned to it by the 2010 legislation on pharmacovigilance that became applicable in July 2012.

Marketing authorisation holders (MAH) are proposed to be charged a fee per procedure when involved in one of the Union-wide pharmacovigilance procedures. It is also proposed that all MAH of medicinal products for human use with a valid authorisation be charged a flat-rate fee for general pharmacovigilance activities of the EMA, as assigned to the Agency by the applicable legislation on pharmacovigilance.

It is proposed that rapporteurs from the national competent authorities be remunerated for the assessment services that that provide in the framework of the Union-wide pharmacovigilance procedures. This remuneration, based on average cost estimations, is included in the proposed fees.

1.4.4. Indicators of results and impact

Specify the indicators for monitoring implementation of the proposal/initiative.

The monitoring will be related to the implementation of the annual budget of the EMA. The annual activity report on the performance of the EMA will provide reliable performance information as provided for in the proposed Regulation and key indicators such as:

– the actual number of Union-wide pharmacovigilance procedures and their qualitative content,

– the amount of actual cost for each type of procedure and for general pharmacovigilance activities,

– the minimum, maximum and average number of marketing authorisations and marketing authorisation holders (MAH) per procedure, as well as other indicators such as ranges representing a high percentage of the cases,

– the annual fee revenue per procedure and the annual fee revenue from the flat fee.

Based on data on actual cost and fee revenue, the Commission may consider whether there is a need to revise the fees, after experience has been gained.

1.5. Grounds for the proposal/initiative

1.5.1. Requirement(s) to be met in the short or long term

The new pharmacovigilance legislation is already applicable and it foresees that pharmacovigilance activities be financed through new fees. The proposed legislation will only deal with fees for EMA (and not fees charged by national competent authorities for which the Union is not competent).

1.5.2. Added value of involvement of the Union

The European Medicines Agency is a European decentralised Agency set up by Regulation (EC) No 726/2004. Hence, decisions on its funding are to be taken at the level of the Union. Only the Union can act to introduce these fees for pharmacovigilance.

1.5.3. Lessons learned from similar experiences in the past

Feedback from public consultation that took place from 18 June 2012 to 15 September 2012 indicated that fees for pharmacovigilance should be cost-based and as much as possible follow the principle of payment for service.

1.5.4. Compatibility and possible synergy with other appropriate instruments

The proposed Regulation will apply in parallel to the existing Council Regulation (EC) No 297/95 on fees payable to the EMA for the Evaluation of Medicinal Products.

1.6. Duration and financial impact

☐ Proposal/initiative of **limited duration**

(1) ☐ Proposal/initiative in effect from [DD/MM]YYYY to [DD/MM]YYYY

(2) ☐ Financial impact from YYYY to YYYY

☑ Proposal/initiative of **unlimited duration**

– Implementation with a start-up period from YYYY to YYYY,

– followed by full-scale operation.

1.7. Management mode(s) envisaged[23]

☐ **Centralised direct management** by the Commission

☑ **Centralised indirect management** with the delegation of implementation tasks to:

– ☐ executive agencies

– ☑ bodies set up by the Communities[24]

– ☐ national public-sector bodies/bodies with public-service mission

(3) ☐ persons entrusted with the implementation of specific actions pursuant to Title V of the Treaty on European Union and identified in the relevant basic act within the meaning of Article 49 of the Financial Regulation

☐ **Shared management** with the Member States

☐ **Decentralised management** with third countries

☐ **Joint management** with international organisations ***(to be specified)***

If more than one management mode is indicated, please provide details in the "Comments" section.

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[23] Details of management modes and references to the Financial Regulation may be found on the BudgWeb site: http://www.cc.cec/budg/man/budgmanag/budgmanag_en.html

[24] As referred to in Article 185 of the Financial Regulation.

2. MANAGEMENT MEASURES

2.1. Monitoring and reporting rules

Specify frequency and conditions.

The Agency will provide the Commission and the Management Board twice per year with detailed and aggregated performance information and indicators relating to pharmacovigilance activities and fees.

2.2. Management and control system

2.2.1. Risk(s) identified

Insufficient fee income, given the difficulty to predict the exact actual frequency, scope and cost of all the Union-wide pharmacovigilance procedures and activities occurring in a given year.
Incomplete collection of invoiced fees.

2.2.2. Control method(s) envisaged

Regular monitoring and reporting from the Agency to the Commission on the level of performance, the level of collection of fees and unitary and aggregated cost-related components relevant to the estimation of fee levels.

2.2.3. Costs and benefits of controls and probable non-compliance rate

Administrative procedures of the Agency will be set up so that existing monitoring tables, cost-account tables and activity-based system provide information on cost breakdown of procedures and activities that will be funded by the fees set up by this Regulation.

2.3. Measures to prevent fraud and irregularities

Specify existing or envisaged prevention and protection measures.

In addition to the application of all regulatory control mechanisms, the responsible Commission's services will devise an anti-fraud strategy in line with the Commission's anti-fraud strategy (CAFS) adopted on 24 June 2011 in order to ensure inter alia that its internal anti-fraud related controls are fully aligned with the CAFS and that its fraud risk management approach is geared to identify fraud risk areas and adequate responses. Where necessary, networking groups and adequate IT tools dedicated to analysing fraud cases related to the financing implementing activities of this Regulation will be set up. In particular a series of measures will be put in place such as: – decisions, agreements and contracts resulting from the financing implementing activities of this Regulations will expressly entitle EMA, the Commission, including OLAF, and the Court of Auditors to conduct audits, on-the-spot checks and inspections;

– regular training on issues related to fraud and irregularities is given to all staff involved in fee and contract management as well as to auditors and controllers.

3. ESTIMATED FINANCIAL IMPACT OF THE PROPOSAL/INITIATIVE

3.1. Heading(s) of the multiannual financial framework and expenditure budget line(s) affected

– Existing budget lines

In order of multiannual financial framework headings and budget lines.

Heading of multiannual financial framework	Budget line	Type of expenditure	Contribution			
3	Number 17.0310* Subsidy to the European Medicines Agency	Diff./non-diff.[25]	from EFTA countries[26]	from candidate countries[27]	from third countries	within the meaning of Article 18(1)(aa) of the Financial Regulation
	[XX.YY.YY.YY]	non-diff.	YES	NO	NO	NO

**17.0312 as from 01/01/2014*

– New budget lines requested N/A

In order of multiannual financial framework headings and budget lines.

Heading of multiannual financial framework	Budget line	Type of expenditure	Contribution			
	Number [Heading……..]	Diff./non-diff.	from EFTA countries	from candidate countries	from third countries	within the meaning of Article 18(1)(aa) of the Financial Regulation
	[XX.YY.YY.YY]		YES/NO	YES/NO	YES/NO	YES/NO

* The annual subsidy to the EMA is paid under this budget line. However, all pharmacovigilance activities under this proposal are considered to be fee-financed. Consequently, no impact is foreseen on the budget of the Union.

[25] Diff. = Differentiated appropriations / Non-Diff. = Non-differentiated appropriations.

[26] EFTA: European Free Trade Association.

[27] Candidate countries and, where applicable, potential candidate countries from the Western Balkans.

3.2. Estimated impact on expenditure

This part must be completed on the spreadsheet on budget data of an administrative nature (second document in the annex to this financial statement) to be uploaded to CISNET for interdepartmental consultation purposes.

3.2.1. Summary of estimated impact on expenditure : N/A

EUR million (to three decimal places)

Heading of multiannual financial framework:	Number	[Heading ……..…….]

DG: <…….>			Year **N**[28]	Year **N+1**	Year **N+2**	Year **N+3**	Enter as many years as necessary to show the duration of the impact (see point 1.6)			**TOTAL**
• Operational appropriations										
Number of budget line	Commitments	(1)								
	Payments	(2)								
Number of budget line	Commitments	(1a)								
	Payments	(2a)								
Appropriations of an administrative nature financed from the envelope of specific programmes[29]										
Number of budget line		(3)								
TOTAL appropriations for DG <…….>	Commitments	=1+1a +3								
	Payments	=2+2a +3								

[28] Year N is the year in which implementation of the proposal/initiative starts.

[29] Technical and/or administrative assistance and expenditure in support of the implementation of EU programmes and/or actions (former 'BA' lines), indirect research, direct research.

• TOTAL operational appropriations	Commitments	(4)								
	Payments	(5)								
• TOTAL appropriations of an administrative nature financed from the envelope for specific programmes		(6)								
TOTAL appropriations under HEADING <….> of the multiannual financial framework	Commitments	=4+ 6								
	Payments	=5+ 6								

If more than one heading is affected by the proposal / initiative:

• TOTAL operational appropriations	Commitments	(4)								
	Payments	(5)								
• TOTAL appropriations of an administrative nature financed from the envelope for specific programmes		(6)								
TOTAL appropriations under HEADINGS 1 to 4 of the multiannual financial framework (Reference amount)	Commitments	=4+ 6								
	Payments	=5+ 6								

Heading of multiannual financial framework	**5**	'Administrative expenditure'

EUR million (to three decimal places)

		Year **N**	Year **N+1**	Year **N+2**	Year **N+3**	Enter as many years as necessary to show the duration of the impact (see point 1.6)			**TOTAL**
DG: <…….>									
• Human resources									
• Other administrative expenditure									
TOTAL DG <…….>	Appropriations								

TOTAL appropriations for HEADING 5 of the multiannual financial framework	(Total commitments = Total payments)								

EUR million (to three decimal places)

		Year **N**[30]	Year **N+1**	Year **N+2**	Year **N+3**	Enter as many years as necessary to show the duration of the impact (see point 1.6)			**TOTAL**
TOTAL appropriations under HEADINGS 1 to 5 of the multiannual financial framework	Commitments								
	Payments								

[30] Year N is the year in which implementation of the proposal/initiative starts.

3.2.2. Estimated impact on operational appropriations

– ☑ The proposal/initiative does not require the use of operational appropriations

– ☐ The proposal/initiative requires the use of operational appropriations, as explained below:

Commitment appropriations in EUR million (to three decimal places)

Indicate objectives and outputs ⇩			Year **N**		Year **N+1**		Year **N+2**		Year **N+3**		Enter as many years as necessary to show the duration of the impact (see point 1.6))						**TOTAL**	
	OUTPUTS																	
	Type[31]	Average cost	Number	Cost	Number	Cost	Number	Cost	Number	Cost	Number	Cost	Number	Cost	Number	Cost	Total Number	Total Cost
SPECIFIC OBJECTIVE No 1[32]…																		
- Output																		
- Output																		
- Output																		
Subtotal for specific objective n° 1																		
SPECIFIC OBJECTIVE n° 2…																		
- Output																		
Subtotal for specific objective n° 2																		
TOTAL COST																		

31 Outputs are products and services to be supplied (e.g.: number of student exchanges finances, number of km of roads built, etc.).

32 As described in point 1.4.2. 'Specific objective(s)…'.

3.2.3. Estimated impact on appropriations of an administrative nature

3.2.3.1. Summary

– ☑ The proposal/initiative does not require the use of appropriations of an administrative nature

– ☐ The proposal/initiative requires the use of appropriations of an administrative nature, as explained below:

EUR million (to three decimal places)

	Year N[33]	Year N+1	Year N+2	Year N+3	Enter as many years as necessary to show the duration of the impact (see point 1.6)			TOTAL
HEADING 5 of the multiannual financial framework								
Human resources								
Other administrative expenditure								
Subtotal HEADING 5 of the multiannual financial framework								

Outside HEADING 5[34] of the multiannual financial framework								
Human resources								
Other expenditure of an administrative nature								
Subtotal outside HEADING 5 of the multiannual financial framework								

TOTAL								

The administrative appropriations required will be met by the appropriations of the DG which are already assigned to management of the action and/or which have been redeployed within the DG, together if necessary with any additional allocation which may be granted to the managing DG under the annual allocation procedure and in the light of budgetary constraints.

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33 Year N is the year in which implementation of the proposal/initiative starts.

34 Technical and/or administrative assistance and expenditure in support of the implementation of EU programmes and/or actions (former 'BA' lines), indirect research, direct research.

3.2.3.2. Estimated requirements of human resources N/A

– ☐ The proposal/initiative does not require the use of human resources.

– ☐ The proposal/initiative requires the use of human resources, as explained below:

Estimate to be expressed in full time equivalent units

		Year **N**	Year **N+1**	Year N+2	Year N+3	Enter as many years as necessary to show the duration of the impact (see point 1.6)		
• Establishment plan posts (officials and temporary agents)								
XX 01 01 01 (Headquarters and Commission's Representation Offices)								
XX 01 01 02 (Delegations)								
XX 01 05 01 (Indirect research)								
10 01 05 01 (Direct research)								
• External personnel (in Full Time Equivalent unit: FTE)[35]								
XX 01 02 01 (CA, INT, SNE from the "global envelope")								
XX 01 02 02 (CA, INT, JED, LA and SNE in the delegations)								
XX 01 04 **yy**[36]	- at headquarters							
	- in delegations							

35 CA= Contract Agent; LA = Local Agent; SNE = Seconded National Expert; INT = agency staff ('Intérimaire'); JED = 'Jeune Expert en Délégation' (Young Experts in Delegations).

36 Sub-ceiling, for external staff covered by operational appropriations (former "BA" lines).

XX 01 05 02 (CA, SNE, INT - Indirect research)							
10 01 05 02 (CA, SNE, INT - Direct research)							
Other budget lines (specify)							
TOTAL							

XX is the policy area or budget title concerned.

The human resources required will be met by staff from the DG who are already assigned to management of the action and/or have been redeployed within the DG, together if necessary with any additional allocation which may be granted to the managing DG under the annual allocation procedure and in the light of budgetary constraints.

Description of tasks to be carried out:

Officials and temporary staff

External staff

3.2.4. Compatibility with the current multiannual financial framework

– ☑ Proposal/initiative is compatible the current multiannual financial framework.

– ☐ Proposal/initiative will entail reprogramming of the relevant heading in the multiannual financial framework.

Explain what reprogramming is required, specifying the budget lines concerned and the corresponding amounts. […]

– ☐ Proposal/initiative requires application of the flexibility instrument or revision of the multiannual financial framework.[37]

Explain what is required, specifying the headings and budget lines concerned and the corresponding amounts. […]

3.2.5. Third-party contributions

– ☑ The proposal/initiative does not provide for co-financing by third parties.

– ☐ The proposal/initiative provides for the co-financing estimated below:

Appropriations in EUR million (to three decimal places)

	Year **N**	Year **N+1**	Year **N+2**	Year **N+3**	Enter as many years as necessary to show the duration of the impact (see point 1.6)			Total
Specify the co-financing body								
TOTAL appropriations cofinanced								

[37] See points 19 and 24 of the Interinstitutional Agreement.

3.3. Estimated impact on revenue

– ☑ Proposal/initiative has no financial impact on revenue.

– ☐ Proposal/initiative has the following financial impact:

  – ☐ on own resources

  – ☐ on miscellaneous revenue

EUR million (to three decimal places)

Budget revenue line:	Appropriations available for the current financial year	Impact of the proposal/initiative[38]						
		Year **N**	Year **N+1**	Year **N+2**	Year **N+3**	Enter as many years as necessary to show the duration of the impact (see point 1.6)		
Article …….								

For miscellaneous 'assigned' revenue, specify the budget expenditure line(s) affected.

[…]

Specify the method for calculating the impact on revenue.

[…]

[38] As regards traditional own resources (customs duties, sugar levies), the amounts indicated must be net amounts, i.e. gross after deduction of 25% for collection costs.

ANNEX: DETAILS OF CALCULATIONS

General remarks

It is proposed that the entire cost relating to pharmacovigilance activities at the level of the Union as per the applicable legislation is recouped through fees. Cost estimations and calculations in this Annex are based on this principle and, therefore, the proposed measures are not expected to have any financial impact on the budget of the Union.

The cost estimations comprise cost of the Agency activities and cost of rapporteurs' assessment activities. The amounts to be respectively retained by the Agency and paid to rapporteurs where assessment has taken place are estimated accordingly.

Amounts that are proposed for remuneration of rapporteurs are based on the estimated average cost of assessment work in the context of the pharmacovigilance procedures of the Union.

The costing table provides four general headings of cost:

(1) Periodic Safety Update Reports assessment (procedural cost, both for the Agency and rapporteurs of Member States)

(2) Post Authorisation Safety Study assessment (procedural cost, both for the Agency and rapporteurs of Member States)

(3) Pharmacovigilance (Safety) Referral (procedural cost, both for the Agency and rapporteurs of Member States)

(4) Other cost: non-procedural cost, only incurred by the Agency. This heading includes ICT systems (e.g. EudraVigilance database, repository of periodic safety update reports), literature monitoring, ADR ('adverse drug reaction': reports on adverse effects of medicines) management and signal detection and risk management, within the scope of the Agency's responsibilities.

Remuneration of rapporteurs of Member States is foreseen for work provided with respect to headings (1), (2) and (3), i.e. for the three Union-wide pharmacovigilance procedures. These three procedures will entail procedure-based fees, calculated based on cost estimation of the Agency's and rapporteurs' activities.

As regards the EMA's cost in heading 'Other', it is proposed to recoup this cost through an annual flat fee to be charged to marketing authorisation holders for authorised products registered by the Agency based on the list referred to in Article 57(2) of Regulation EC No 726/2004, using chargeable units as defined in the proposed Regulation. Cost estimations under this heading (4) include only costs of the Agency, whereas Member States may continue charging national fees to cover costs at national level.

Periodic Safety Update Reports assessment

The estimated number of periodic safety update reports assessment procedures expected by the Agency is 600 per year. The total estimated cost related to these assessments is € 11,3 m per year (€ 3,4 m Agency cost and € 7,9 m rapporteur remuneration). The average cost for the

proposed procedure-related fee is € 19 500 per procedure[39]. The average part of the cost on which the proposed rapporteur remuneration is based is € 13 100 per procedure.

Post-Authorisation Safety Study assessment

The estimated number of post-authorisation safety study assessments expected by the Agency is 35 per year. The total estimated cost related to these assessments is € 1,5 m per year (€ 0,9 m Agency cost and € 0,6 m rapporteur remuneration). The average cost on which the proposed procedure-related fee is based is € 43 000 per procedure. The average part of the cost on which the proposed rapporteur remuneration is based is € 18 200 per procedure.

Pharmacovigilance Referral assessment

The estimated number of Pharmacovigilance Referral assessments expected by the Agency is 40 per year. The total estimated cost related to these assessments is € 6,7 m per year (€ 4,9 m Agency cost and € 1,8 m rapporteur remuneration). The average cost on which the proposed procedure-related fee is based is € 168 600 per procedure. The average part of the cost on which the proposed rapporteur remuneration is based is € 45 100 per procedure.

Mechanism of charging the fee for procedures for periodic safety update reports, post-authorisation safety studies and pharmacovigilance referrals

For periodic safety update reports and pharmacovigilance referral procedures, the fee will be divided among marketing authorisation holders involved in the procedure by charging them proportionately to the respective number of marketing authorisations (chargeable units) held by each marketing authorisation holder. For post-authorisation safety study procedures, the fee is proposed to be divided among all marketing authorisation holders having the obligation to produce the study by charging equal parts to each marketing authorisation holder. Further division of the cost may take place between marketing authorisation holders which have taken part in the study.

Furthermore, the amount charged to marketing authorisation holders that are small and medium-sized enterprises will be reduced to 60% and marketing authorisation holders that are micro-enterprises will not be charged any fee.

Mechanism of remunerating rapporteurs

Rapporteurs' remuneration is included in the calculation of the fee for each Union-wide pharmacovigilance procedure. Full rapporteur remuneration is based on estimated average cost per procedure. The applicable rapporteur remuneration follows the same pattern as the actual fee revenue per procedure, i.e. a reduced fee revenue entails a proportionately reduced rapporteur remuneration.

Other pharmacovigilance activities of the Agency

This heading of estimated cost of the Agency is taken into account in the calculations of the annual flat fee charged to all marketing authorisation holders with respect to their marketing authorisations (chargeable units, as recorded by the Agency based on the list laid down in Article 57(2) of Regulation (EC) No 726/2004). Marketing authorisations of centrally authorised products are not subject to this fee, as they are already charged an annual fee, in

[39] Amounts that are used for fee levels and rapporteur remuneration have been rounded to the nearest hundred euros. Administrative cost is included.

accordance with Council Regulation (EC) No 297/95, which is assumed to cover non-procedure related pharmacovigilance activities for those products.

The total estimated cost for the Agency under this heading is € 19,1 m. Calculations in the impact assessment based on this figure led to a proposed amount for the full flat fee of € 60 per marketing authorisation, that should be counted in a consistent way for all marketing authorisation holders based on chargeable units. It is proposed that marketing authorisation holders that are small and medium-sized enterprises pay 60% of the full fee and that micro-enterprises be exempted from the payment of the annual flat fee. Furthermore, a fee reduction of 20% is proposed for marketing authorisation holders for medicinal products referred to in Article 10(1) and Article 10a of Directive 2001/83/EC, as well as for authorised herbal medicinal products and authorised homeopathic medicinal products.

Workload and cost estimation tables

Summary table of overall cost estimations

Activities	EMA	Rapporteurs / NCA	Total
Union-wide pharmacovigilance procedures			
PSUR assessment	€3 435 671	€7 857 374	€11 293 045
PASS assessment	€866 456	€636 778	€1 503 234
Pharmacovigilance referrals assessment	€4 887 616	€1 803 405	€6 691 021
Subtotal procedures	**€9 189 743**	**€10 297 557**	**€19 487 300**
Other pharmacovigilance activities of the EMA			
Other	€18 825 914	€232 606	€19 058 520
Grand total	**€28 015 657**	**€10 530 163**	**€38 545 820**

1. Periodic safety update reports assessment

Activities					EMA				Rapporteurs / NCA				Total cost
					Nr of hours required	Hourly rate / wage	Frequency per year	EMA total	No. of hours required	Hourly rate / wage	Frequency per year	Rapporteur total	
PSUR assessment	1			Preparation of list of harmonised submission dates for selected active substances	53,75	124,1	2	€13 341					
	2			Preparation of PRAC advice and updated EURD list following request for changes from MAH	21,5	124,1	10	€26 682					
	3			Validation of PSUR, preparation of data for Rapporteur from Eudravigilance database and other sources	11,9	124,1	600	€886 074					
					5,1	79,5	600	€243 270					
	4			Preparation of PRAC, CHMP/CMDh outcome	21,2	124,1	600	€1 578 552					
					9,1	79,5	600	€434 070					
	5			PRAC Staff time related to PSUR	81	124,1	11	€110 573	194	109	11	€232 606	
					81	79,5	11	€70 835					
	6			CHMP/CMDh Staff time related to PSUR	27	124,1	11	€36 858	32	109	11	€38 368	
					40,5	79,5	11	€35 417					
	6 a			Evaluation/assessment of PSUR applications					116	109	600	€7 586 400	
Subtotal PSUR								**€3 435 671**				**€7 857 374**	**€11 293 045**
Average per procedure								**€5 726**				**€13 096**	**€18 822**

2. Post-authorisation safety study assessment

Activities					EMA				Rapporteurs / NCA				Total cost
					Nr of hours required	Hourly rate / wage	Frequency per year	**EMA total**	No. of hours required	Hourly rate / wage	Frequency per year	**Rapporteur total**	
PASS assessment	7		PASS Protocol	Preparation of request including scientific questions and pre-submission meeting	25	124,1	35	€108 588					
	8			Summary outcome of protocol and outcome documents for PRAC	42,5	124,1	35	€184 599					
	9			Summary outcome of protocol amendments and outcome documents for PRAC	27,5	124,1	35	€119 446					
	10			Summary of study report and outcome of report documents for PRAC and CHMP/CMDh	60	124,1	35	€260 610					
	11			PRAC Staff time related to PASS	54	124,1	11	€73 715	130	109	11	€155 870	
					54	79,5	11	€47 223					
	12			CHMP/CMDh Staff time related to PASS	27	124,1	11	€36 858	32	109	11	€38 368	
					40,5	79,5	11	€35 417					
	12a			Evaluation/assessment of PASS applications					116	109	35	€442 540	
				Sub-total PASS				**€866 456**				**€636 778**	**€1 503 234**
				Average per procedure				**€24 756**				**€18 194**	**€42 950**

3. Pharmacovigilance referral assessment

Activities					EMA				Rapporteurs / NCA				Total cost
					Nr of hours required	Hourly rate / wage	Frequency per year	EMA total	No. of hours required	Hourly rate / wage	Frequency per year	Rapporteur total	
Pharmacovigilance **Refferal**	13		Initiation	Preparation of procedure including scope of procedure, identification of products involved, List of Questions, analyses of in-house data	73,8	124,1	40	€366 343					
					73,8	79,5	40	€234 684					
	14		Assessment	Preparation of outcome documents for PRAC and CHMP/CMDh (temporary measures, list of outstanding issues, recommendations, opinions), analyses of in-house data, organisation of oral explanations, scientific advisory groups/expert meetings and public hearings	300	124,1	40	€1 489 200					
					300	79,5	40	€954 000					
	15		post - assessment	Preparation and publication of information on webportal, communication, translations, access to document requests and re-examinations of applicable	193,75	124,1	40	€961 775					
					193,75	79,5	40	€616 125					
	16			PRAC Staff time related to referrals	54	124,1	11	€73 715	130	109	11	€155 870	
					54	79,5	11	€47 223					
	17			CHMP/CMDh Staff time related to referrals	54	124,1	11	€73 715	65	109	11	€77 935	
					81	79,5	11	€70 835					
	17a			Evaluation/assessment within PhV Refferals					360	109	40	€1 569 600	
				Sub-total PhV Referrals				**€4 887 616**				**€1 803 405**	**€6 691 021**

4. Other costs of the Agency related to pharmacovigilance

Activities				EMA				Rapporteurs / NCA				Total cost
				Nr of hours required	Hourly rate / wage	Frequency per year	EMA total	No. of hours required	Hourly rate / wage	Frequency per year	Rapporteur total	
Other	18	Literature monitoring	Outsourced literature monitoring and entering of data in EudraVigilance	8153	124,1	1	€1 011 787					
	19		Quality control of the outsourced activities and entered data	4455	124,1	1	€552 866					
		ICT	IT development and software maintanace				€4 882 643					
			IT infrastructure maintanace				€2 061 636					
	22	Signal detection + ADRs handling + Risk management	Scientific validation of product and substance data submitted by the MAHs (outsorced)	22390	124,1	1	€2 778 599					
	23		Clinical validation of signals, signal management by scientific staff and provision of analysis from EudraVigilance database and other data sources at the request from MS	10 197	124,1	1	€ 1 265 455					
				2 499	79,5	1	€198 670					
	24		Management of RMPs including procedural support through PRAC, monitoring the outcome of risk minimisation measures and preparation of documents for publication for CAPs and for NAPs at the request of a member state.	17820	124,1	1	€2 211 462					
				6534	79,5	1	€519 453					
	25		Monitoring the effectiveness of public health measures (e.g. risk management systems, through outsources studies of their outcomes using longitudinal patient databases).	7643	124,1	1	€948 496					
	26		Coordination of pharmacovigilance inspections, information gathering on non-compliance and follow-up	6534	124,1	1	€810 869					
				3861	79,5	1	€306 950					

	27			Translations of communication related material and of data received from the public in relation to referrals	3370	124,1	1	€418 217					
	28			PRAC Staff time (remaining)	891	124,1	1	€110 573					
					891	79,5	1	€70 835					
	29			PRAC meeting costs				€564 503	194	109	11	€232 606*	
	30			CHMP meeting costs				€112 901					
Sub-total other								**€18 825 914**				**€232 606**	**€19 058 520**

*reimbursement to PRAC members

Estimation of the overall impact of the proposed legislation on the budget of the Agency

	Year 2014*	Year 2015	Year 2016	Year 2017	Year 2018	Year 2019	Year 2020
FTE **	**0**	**38**	**38**	**38**	**38**	**38**	**38**
Annual salaries**	**€0**	**€5 108 855**	**€5 108 855**	**€5 108 855**	**€5 108 855**	**€5 108 855**	**€5 108 855**
Annual cost other than personnel	€11 277 314	€22 906 802	€22 906 802	€22 906 802	€22 906 802	€22 906 802	€22 906 802
Rapporteurs' remuneration	€5 265 082	€10 530 163	€10 530 163	€10 530 163	€10 530 163	€10.530.163	€10 530 163
Total cost	***€16 542 396***	***€38 545 820***	***€38 545 820***	***€38 545 820***	***€38 545 820***	***€38.545.820***	***€38 545 820***
Income PhV Fees	***€16 542 396***	***€38 545 820***	***€38 545 820***	***€38 545 820***	***€38 545 820***	***€38.545.820***	***€38 545 820***
Balance	**0**	**0**	**0**	**0**	**0**	**0**	**0**

**based on the assumption that the Regulation becomes applicable in summer 2014*

***incremental to 23 FTE as per financial statement of the 2008 legislative proposal, COM(2008) 664 final*

The distribution by grades is as follows:

Posts	2015	2016	2017	2018	2019	2020
AD12	1	1	1	1	1	1
AD9	4	4	4	4	4	4
AD8	9	9	9	9	9	9
AD6	13	13	13	13	13	13
Total AD	**27**	**27**	**27**	**27**	**27**	**27**
AST3	7	7	7	7	7	7
AST1	4	4	4	4	4	4
Total AST	**11**	**11**	**11**	**11**	**11**	**11**
Total posts	**38**	**38**	**38**	**38**	**38**	**38**

The human resources required could be met by staff redeployed within the Agency or additional staff under the strict condition that sufficient posts are available within the context of the global legislative financial statements' revision exercise and the annual allocation procedure for agencies, in the light of budgetary constraints which are applicable to all EU bodies.

Agency data used for calculations of cost

1. Productive working days/year	**2012**	**2016**
	198	**199**
2. Standard working hours/year	**2012**	**2016**
Standard working hours/day	8 *	8 *
x number of productive days/year	198	199
Total number of productive hours/year	**1 584**	**1 592**
3. Average staff cost	**2012**	**2016**
Average salary items *AD*	138 579	142 655
Overhead (non-salary cost, building, equipment, support and management)	57 991	51 638
Total staff cost AD	**196 570**	**194 293**
Average salary items *AST*	75 043	77 250
Overhead (non-salary cost, building, equipment, support and management)	50 920	44 456
Total staff cost AST	**125 963**	**121 706**
Average salary items *Contract Agent*	48 538	53 360
Overhead (non-salary cost, building, equipment, support and management)	47 970	41 833
Total staff cost Contract Agent	**96 508**	**95 193**
Notes:	**2012**	**2016**
Weighting on salary items assumed (including exchange rate)	148	130
Employers pension contribution included	no	yes

Source: EMA

*A working week of 40 hours is applied to all calculations.