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INTRODUCTION OF FEES TO BE CHARGED BY THE EMA FOR PHARMACOVIGILANCE

SUMMARY OF THE REPLIES TO THE PUBLIC CONSULTATION PAPER

This document does not represent an official position of the European Commission. The suggestions contained in this document do not prejudge the form and content of any future proposal by the European Commission.
This document is solely intended to present a factual summary of the comments to the public consultation.

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Glossary

ADR: Adverse Drug Reaction

CAP: Centrally Authorised Product

CMDh: Coordination Group for Human Medicinal Products

EMA: European Medicines Agency

EV: EudraVigilance database (of ADRs)

HMA: Heads of Medicines Agencies

MA: Marketing Authorisation

MAH: Marketing Authorisation Holder

MRP / DCP: Mutual Recognition Procedure / Decentralised Procedure

NAP: Nationally Authorised Product

NCA: National Competent Authority

PASS: Post-Authorisation Safety Study

PRAC: Pharmacovigilance Risk Assessment Committee at the EMA

PSUR: Periodic Safety Update Report

QPPV: Qualified Person Responsible for Pharmacovigilance

On 18 June 2012 the European Commission published a Concept Paper[1] on the introduction of fees to be charged by the European Medicines Agency for pharmacovigilance. The consultation period ended on 15 September 2012.

The Commission received 85 replies (9 requesting confidentiality):

- 66 from industry, associations and individual companies
    - including 30 from SMEs
- 12 from national competent authorities (NCA),
    - AT, DE, DK, EL, ES, IRL, MT, NL, NO, SE, and UK
    - HMA,
- 4 from civil societies and other associations,
- 3 from individual persons.

This document summarises the responses to the public consultation on the concept paper. It is in no way to be understood as an endorsement of any comment. For the sake of brevity, consultation items are not reproduced. Therefore, this summary should be read in conjunction with the consultation items set out in the concept paper.

The public consultation is part of the on-going impact assessment exercise. The information and views gathered in this public consultation will be taken into consideration in the impact assessment process.

1. GENERAL REMARKS

The public consultation was appreciated by stakeholders. However, the vast majority of respondents did not support or fully support the proposed fees, notably as regards the amounts proposed. There was generally a view that the concept paper did not present sufficient information about the basis for the estimations (in terms of workload and costs) of the proposed fees.

Many respondents question the benchmarks that have been used and consider as a more appropriate approach the time used and the associated costs for the work. The majority of the respondents consider the proposed fees as being too high and without sufficient justification and transparency.

The vast majority of the respondents made reference to the financial statement of 2008[2] questioning the significant increase in the proposed fee levels compared with this financial statement and the lack of sufficient explanation or justification for such an increase. It is argued that the amendments made to the initial legal proposal during the legislative process were not of such type or magnitude to justify such a sharp increase in

[1] http://ec.europa.eu/health/files/pharmacovigilance/2012-06_concept_paper_en.pdf

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

the amount of fees. Also, some argue that the fees in the financial statement of 2008 are more closely aligned with those of the NCAs which charge separately for pharmacovigilance activities.

Many respondents from industry argue that the proposed fees are contrary to the objective of the legislation to reduce the costs and the unnecessary administrative burden for the pharmaceutical industry. Some have estimated that the proposed fees would lead to an increase by more than 50% of their budget for fees and, for some pharmaceutical companies, even double this budget. The need for transparency is emphasised, as well as the importance that marketing authorisation holders are not charged twice for the same assessment work. Industry, in particular, flags the risk of possible duplicative fees charged by EMA and NCAs and expects a reduction of national fees whenever work is shifted to the EMA.

The Concept Paper has put forward the possibility of grouping of MAHs for many of the proposed fee types (for the purposes of paying one single fee), as a result of which MAHs would in many cases not need to pay the maximum or full fee. However, the grouping to share the fee for PSUR and PASS assessments was not supported by the vast majority of respondents who argued that this would not work in practice as it would require the sharing of confidential information between MAHs not belonging to the same legal entity (see *2.3. Concept of grouping applied to PSURs, PASSes and Pharmacovigilance Referrals [Consultation items 2, 4 and 6]*).

Many respondents consider that proposed fees would unfairly affect companies with a large portfolio of products with well-established safety profiles and many MAs. Such comments come mainly from industry stakeholders representing generics, homeopathics, well-established-use and over-the-counter medicinal products, including allergen manufacturers.

Almost all SMEs express concern about the proposed fee levels, stating that even with the proposed fee reductions, the availability of their products would be under threat.

Many NCAs express criticism that the concept paper lacks information about the distribution of fees to the NCAs acting as rapporteurs and co-rapporteurs during the assessment procedures. On this point, especially industry advocates an analysis of the actual tasks carried out by the EMA secretariat and the NCAs in each instance.

There are also calls for further clarity on how the proposed fees have been established and questions on whether the benchmarks correspond to the scope and volume of documents to be reviewed, activities to be undertaken and number of staff involved; they call for proportionality between the fees and the nature of the work actually carried out. Some respondents acknowledge the difficulty of having a fee adjusted to each individual procedure/product, and rather advocate setting up a single fee or a simple range of fees based on well-defined and justified criteria for each procedure corresponding to the associated workload.

A number of respondents, especially from industry, consider that some pharmacovigilance activities, e.g. referrals and literature monitoring, should be at least partly covered by the EU budget as these activities are linked to the protection of public health.

2. SUMMARY OF COMMENTS

2.1. Fee for assessments of Periodic Safety Update Reports (PSUR) [Consultation item 1]

In general, the principle of charging a fee for the assessment of a PSUR has not been objected to, except when there is a risk of a possible double charging for essentially the same work (e.g. when a PSUR submission would coincide with a renewal assessment). However, the proposed levels of the fee, benchmarked against a Type II Variation procedure, have been criticised, mainly by industry, but also by some National Competent Authorities.

The main criticism to the proposed fee stems from the feeling that benchmarking against a Type II Variation is not fully justified, in order to reflect the real workload associated with the assessment of PSURs. Some replies from industry suggest that the workload of a PSUR assessment is lower than a type II Variation, whereas others from NCAs suggest that the workload could be higher.
Some respondents refer to the need for more precise and transparent cost calculations in order to arrive at the cost of an 'average' assessment. Others would prefer a greater number of levels of fees, based on criteria related to the assessment effort, e.g. the number of ADRs or literature cases (or a reduction for products whose safety profile is well established).

It is also pointed out that the expected number of PSUR assessments should be estimated in relation to the possible effect on the budget of the EMA.

The relevance of using the two-year period following the authorisation as a method of approximation of the assessment workload (and the related fee) is questioned, notably for products where the benefit/risk profile has been well established. In this respect, comments both from industry and NCAs point out that the frequency of PSUR submission, as defined by the EU reference date list, could be taken into account. Many comments argue that the workload in the first two years could actually be higher than afterwards. It is however generally recognised that the administrative complexity of the fee system should be minimal.

Some respondents point out that the 'cascade effect' on overall amounts charged to industry for subsequent procedures should be taken into account (e.g. a PSUR leading to a referral leading to a variation).

As an alternative benchmark, the existing renewal fee for a centrally authorised product is often proposed, because considered to require similar workload. Possible duplication of PSUR assessment and renewal assessment for newer products is signalled in this repect. Alternatively, national fee levels are quoted as a potential benchmark, namely fees paid by industry for MRP and DCP products.

Also, as non-CAPs are subject to subsequent national variation fees, concerns are expressed over a possible violation of the principle of equal treatment (of CAPs and non-CAPs).

2.2. Fee for assessments of Post Authorisation Safety Studies (PASS) [Consultation item 3]

Overall, the benchmark (Type II Variation) has been questioned and it is argued that the data to be assessed is not comparable, in that a PASS assessment concerns a single report whereas a Type II variation may include several studies and may be more complex, as it may require a revision of several sections of the product information. Where the PASS results lead to an update of the MA of a non-CAP through a variation, for which fees are normally charged, there is concern that MAHs would be charged two separate fees for these activities which are related.

It is proposed that the fee for PASSes should be based on several criteria, such as the methods used for the PASS and the amount and type of data collected; however, to avoid complexity, comments suggest setting a fee or a simple fee range closer to the PASS assessment fee included in the financial statement of 2008.

Especially some respondents from industry express concerns about the discrepancy where no separate variation (and, consequently, no variation fee) will be required in the case of PASS leading to a change in the MA for CAPs, whereas for non-CAPs, a subsequent variation will still be required and charged for.

2.3. Concept of grouping applied to PSURs, PASSes and Pharmacovigilance Referrals [Consultation items 2, 4 and 6]

While a number of respondents support the concept in general, as a means to reduce the actual amounts to be paid, most of the comments refer to the need to clarify whether MAHs belonging to the same mother company or group of companies (and MAHs having concluded agreements or exercising concerted practices concerning the placing on the market of the medicinal product(s) concerned), should to be taken as ‘the same marketing authorisation holder’ (as per Commission Communication OJ C 229, 22 July1998). They argue that they should be considered as a single legal entity and that this should not be considered as grouping. In addition, comments state they should not be charged additional administrative fees.

Grouping for submitting PSURs is generally considered very difficult in practice (sharing of commercial data, different standard operating procedures, difficulty to divide the work and to coordinate between different QPPVs, ...), except for entities belonging to the same mother company. In this respect, it is pointed out that producing a single PSUR with all the information, data and analysis coming from independent companies seems unrealistic. Consequently, comments from industry express concern that the anticipated savings through grouping would not materialise in practice.

Some respondents consider grouping for PASSes as an option but draw the attention to some practical/legal constraints. While grouping for the PASSes may facilitate the collaboration between independent MAHs to conduct PASS jointly (as foreseen in the pharmacovigilance legislation), it would require a model-based system for the fee assignment that complies with the principles of proportionality, equal treatment of MAHs and with competition laws. Where PASSes are conducted jointly by different MAHs, it is proposed that the total PASS fee (including any administrative fees) is equally divided amongst all concerned MAHs for the same PASS.

The concept of grouping is considered more relevant in the case of referrals, (where it is already now possible to pay one single referral fee), but several respondents, notably the generics industry, request clarification about how the fee would be divided.

Several respondents consider the administrative fee of 500€ as being too high. Most NCAs consider that the administrative fee should not be retained in full by the EMA.

In some replies it is pointed out that the concept of grouping is not applicable for some specific products, e.g. for allergen extracts.

2.4. Pharmacovigilance referrals [Consultation item 5]

The benchmark used, i.e. assessment of initial MA application, is heavily criticised. The proposed fee for pharmacovigilance referrals involving full benefit-risk assessment is considered by many as too high and the work is not considered to be comparable to assessing an initial marketing authorisation application. This is especially underlined by the generics industry. Also, it is pointed out that the assessment of an initial MA is much broader including also non-clinical data and data on chemistry, manufacturing and controls, whereas in the referral, the focus is on the new information that triggered the referral. Recognising that the workload for each referral will vary, some respondents express preference to have one single fee. In any event, there is a general call for better explanation and justification of the workload involved.

Many respondents from the generic industry argue that they are more likely to be subject to several referrals due to their broad portfolio compared to innovator companies, which is claimed to be disproportionate considering the comparative turnovers.

Some respondents suggest a fee reduction for referrals initiated by PRAC within the same class of medicinal products (referring to the same ATC code).

Others consider that if a referral fee will be charged, the amount should be within the range of what is already in place for referrals initiated by MAHs.

Also, some respondents point out that the fact that in addition a Type II variation may be requested, which is also subject to a fee, should also be considered in the referral fee.

As regards payments to the PRAC rapporteurs and co-rapporteurs for their assessments, some respondents refer to the appointment principles laid down in EMA document of 28 June 2012 whereby the co-rapporteurship is automatically granted to the Member State triggering the referrals involving non-CAPs or CAPs/non-CAPs. In view of this, attention is drawn to the risk that referrals could be initiated as a revenue generating exercise, rather than in response to a genuine safety concern.

Some respondents consider that the referrals should be supported at least partly through the EU contribution to EMA.

2.5. Pharmacovigilance service fee [Consultation item 7]

Some respondents, notably those representing the larger companies in the innovative sector, argue that the concept of an annual fee might be acceptable for certain well-specified pharmacovigilance activities which constitute a service to the MAHs. However,

there is call for more transparency in respect of the tasks which are covered by an annual pharmacovigilance service fee. The fee should also be proportionate to the costs of these activities. At the same time, many respondents from the industry point to the risk of double-charging, as many NCAs already charge annual fees for pharmacovigilance.

Particular concern is expressed by the generic industry, as many of its companies may have a large portfolio (e.g. around 1000 active substances) which would lead to extremely high charges for the proposed pharmacovigilance service fee alone. Similar concerns are expressed by other companies having products with a well-known safety profile which does not change much and generating very few ADR reports) and for companies with low-volume/low sales. They consider that MAHs belonging to the same group of companies (as one legal entity) and acting under one pharmacovigilance system master file should only be required to pay one annual fee per active substance. Some representatives of the generic industry argue for a reduced fee for generics, as they would not generate the same amount of work as innovator products.

Several respondents consider that the proposed fee unduly favours MAHs with only one medicinal product with several strengths in several Member States, as opposed to MAHs with a broad product portfolio with different active substances but only marketed in a small number of Member States. Some SMEs note that if such a fee is charged, it should be per substance and MAH, without adding charges for additional strengths, formulations or pack sizes.

However, concern is expressed that annual fees are already charged by most Member States for non-CAPs and that there is a risk of multiple charging, if an annual fee is also charged by EMA for the same activities (charging twice for the same work). Assurances are being sought by the industry that the Member States will not charge such a fee if EMA introduces an annual pharmacovigilance service fee.

Some NCAs are questioning the proposed pharmacovigilance service fee. Assuming that there are some 3,500 active substances in the EU in addition to a number of combinations of substances, it is unknown how many MAHs per substance/combination of substances would have to pay the fee. It is claimed that it is therefore not possible to assess if the fee is excessive or appropriate. While several NCAs express support for an annual fee, they consider that the proposed annual pharmacovigilance service fee level is disproportionally high. They also request clarification about what proportion of the fee would be transmitted to the NCAs for the work they carry out.

In addition, some respondents point out that CAPs are currently paying an annual fee of which 30% (ca. 28.770 €) is foreseen for pharmacovigilance and inspection costs. As it is proposed to continue to charge this fee, it is argued that there should be an analysis of the use of the revenue from this fee to ensure that a new annual fee would cover only new activities, which are not covered by the current annual fee.

Many respondents argue that these general pharmacovigilance activities should be at least co-financed by the EU and the Member States.

Some civil society organisations express their disagreement with the proposed service fee as the general activities that are proposed to be covered by this fee do not include support to PRAC members (financial compensation for their participation). They consider that pharmacovigilance fees could also be used to cover the costs of measures that NCAs and

patients and healthcare professionals' organisation are taking to encourage patients and healthcare professionals to report suspected ADRs. To cover the costs for these activities, they propose to increase the proposed service fee to 1.250€, to be partially redistributed to NCAs, or to increase the current annual fee proportionally.

ICT tools and services

Some of the respondents support the concept that MAHs should contribute to the general maintenance of EudraVigilance and the PSUR repository. Many industry respondents point out, however, that they have already had to invest heavily in ICT tools and databases to comply with the new pharmacovigilance requirements, thus questioning the need to include ICT services in the annual fee. Also the submission of information (and maintaining the information up to date) on medicinal products by the MAHs to the Article 57(2) database reportedly entails a heavy workload with considerable costs and it is not perceived acceptable to be charged a fee in this context.

Many manufacturers of non-prescription medicines argue against the annual service fee as they consider that companies, which have products with a well-established safety profile and few ADR reports, will hardly benefit from the signal detection of EMA on the basis of EudraVigilance data.

Literature monitoring

Several industry respondents emphasize that they are already required to carry out literature monitoring of their products and that they will not be relieved from this responsibility, despite the fact that EMA will monitor certain substances in selected literature. Therefore, the charging of a fee for this activity is highly questioned as it cannot be regarded as a service to the industry. Moreover, as the EMA literature monitoring will not benefit all companies and products, some respondents argue that it would be unfair to charge all companies for this activity.

Many respondents also argue that the same is true for signal detection in that the MAHs will continue to bear the responsibility for signal detection and evaluation for their products.

2.6. Fee incentives for SMEs [Consultation items 8 and 9]

In general, the proposal for fee reductions for SMEs and full exemption for microenterprises is welcomed.

Some industry representatives argue that, in addition to the proposed reduced fees for SMEs, there should also be reductions for orphan medicinal products as well as for other low volume/low sales products (to avoid that they may be withdrawn from the market due to the additional pharmacovigilance costs).

Some suggest using a similar methodology as for the MedDRA subscriptions, whereby the companies are charged on the basis of their turnover.

Several respondents request clarification on how SMEs with non-CAPs should apply for SME status at EMA in case a reduced annual fee for SMEs is charged.

Some SMEs consider that further distinction should be introduced between the different types of SMEs, e.g. suggesting that medium-sized SMEs be granted 50% reductions and small SMEs 75%.

Many respondents, particularly from the generic industry, point out that the number of substances or combination of substances of a MAH is not necessarily related to the size of the company, especially when comparing the innovative and generic industry.

Most NCAs argue that they should receive the non-reduced share of the fee, irrespective of the reduction granted to SMEs (or any other reduction).

2.7. Other comments [Consultation item 10]

Whilst the 2008 estimations accompanying the legislative proposal are currently outdated, and recognising that the final adopted legislation is not identical to the 2008 proposal, a number of respondents consider that the proposed new amounts should not be completely out of proportion with the 2008 figures.

There are requests for information about the anticipated revenues for EMA, based on the proposed fees, and how this links with their costs, in order to be able to assess whether the proposed fees are reasonable.

Respondents expect a fair treatment: e.g. an increase in companies' fees budgets which is in proportion with their size; or taking into account the specificity of some products that generate very limited revenues, as argued for instance in the case of diagnostic products or products with a very limited availability.

Whilst the 2008 Financial Statement and Impact Assessment indicated that all costs associated with activities from the proposal should be recouped through fees, a number of respondents, mainly from industry, argue that pharmacovigilance activities should be partially publicly funded. Also, they expect an analysis of the possible effect on EMA's budget.

Most NCAs (national competent authorities) underline the importance of introducing a transparent method for distribution of the fees between the EMA and the NCAs. A significant number of NCAs state that NCA's share should not be affected by any reduction of the fee. Many NCAs request a separate pharmacovigilance inspection fee, in order to pay directly the inspectors from the NCAs that have participated in the inspection. Another suggestion is to introduce fees for (assessing amendments to) risk management plans ('RMPs'), as PRAC will also be involved.

Some respondents also call for an independent arbitration service where there are disputes concerning the fees.

Some organisations representing civil society call for redistribution of pharmacovigilance fees to NCAs, which could give grants to civil society organisations for their participation in pharmacovigilance activities, and to use pharmacovigilance fees to support financially civil society PRAC members.
In addition, there are suggestions to charge fees to cover the development of guidelines and organising public hearings.