Response to
"Introduction of Fees to be charged by the EMA for Pharmacovigilance"

Introduction

Objectives of the fees for pharmacovigilance are funding of the EMA's activities related to the new area of pharmacovigilance. In the introductory statement is pointed out that the proposed fees are meant to take into account the principles of

(1) proportionality,
(2) transparency,
(3) equal treatment of MAHs,
(4) reduction of administrative complexity, and
(5) avoidance of double charging of MAHs.

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

The suggested fee level does not correspond with the principles 1, 3, and 5.

Proportionality

The level of the proposed fees is oriented towards the current level of type II variations for centrally authorised products (CAP) but shall apply to all medicinal products irrespective of the authorisation route, i.e. also include nationally authorised products (NAPs). A major problem with that view is the size of the target market for the respective marketing authorisation. In a simplified view, CAPs have a target market of 502 million inhabitants while the national markets have considerably smaller numbers, e.g. Cyprus 0.9 million, the Netherlands 17 million, the UK 62 million, and Germany 82 million inhabitants.

The alternative would be to apply the EMA's suggestion to pure NAPs accordingly. In this case, fee levels for the listed countries would then be in the following ranges.

CY	51 up to 3410 EUR
NL	0 as all variations are included in the annual fee
UK	792 up to 38,744 GBP
DE	1,900 up to 16,100 EUR.

Equal treatment of MAHs

Although an orientation of the fee level based on the estimated workload of the EMA seems reasonable at first sight, it completely neglects the business situation of MAHs. Especially smaller to medium size companies or generics companies with only small market shares then would have to invest by far bigger portions of their turnover for pharmacovigilance as compared to those companies with a big market share. In point 3.5, a reduction for smaller companies is envisaged by EMA but is based on the size of the company which not necessarily must relate to the turnover it may have with the medicinal product in question.

Double charging

In addition to the consideration of the market size, it must be considered to avoid double charges by EMA and a national competent authority (NCA) in those cases where the NCA already charges an annual fee covering most of the NCA's activities such as e.g. in the Netherlands. An agreement has to reached between the EMA and the respective NCA in this matter with the aim to stick close to the

current national rules in the different countries. Finally, it is highly likely that the NCA will be involved in the evaluation of the pure NAPs anyway.

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

The suggested fee level does not correspond with the principles 2 and 4.

Transparency and less complexity
In general, grouping of PSURs seems to be quite attractive but in reality it will not work out as easy as described in the concept paper. As long as all MAHs involved in the grouping of a PSUR belong to the same legal entity, this concept might be realised without major additional workload. This advantage immediately vanishes with the involvement of MAHs of different legal entities. Moreover, problems of confidentiality as well as different readiness to discuss and/or implement safety measures suggested as a consequence of the PSUR certainly will arise in the latter scenario. The workload involved in both applying for a grouping and organising the procedure on the MAHs' side is not very likely to be low. Finally, the organisational burden involved with this procedure will not speed up this process.

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

The suggested fee level does not correspond with the principles 2 and 4.

Transparency and less complexity
As already lined out in the response to item n°1, the general level of fees should be closer oriented to the national fees for type II variations - "Why pay a CAP level fee for a small market?".
In addition to that, it has to be considered what type of activity would be performed by the PRAC, e.g. simple assessment of a protocol amendment involving less workload or a full protocol assessment. The suggested flat fee "one for all" also does not differentiate between PASSes triggered by the EMA/NCA and those voluntarily started by MAHs which certainly is worth being considered to be adapted to the regulatory situation.

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

The suggested fee level does not correspond with the principles 2 and 4.

Transparency and less complexity
Until now it is not really sure whether grouping can be helpful for MAHs in this context. It can be expected that only comparatively few cases existed where grouping would be applicable and easy to manage by both MAHs and EMA. Therefore it might be better and easier to reduce the general level of fees for PASSes rather than to introduce administratively complex fee reduction facts for various regulatory situations. Additionally, it is not clear to what level the NCAs will be involved with PASSes that would be imposed by them rather than by the EMA and thus how they would participate/benefit from this fee.

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

The suggested fee level does not correspond with the principles 1, 2, and 4.

Proportionality
As already lined out in the response to item n°1, the general level of fees should be closer oriented to the national fees for type II variations. The suggested fee level by far would exceed this level for all NAPs and even go beyond the amount that is currently charged for a new national MA. It is not clear what the rationale is behind that, as a MAA is not only related to the agency's workload (the MAH certainly has quite some on its side as well!) but also constitutes the right to market a medicinal in a certain territory and thus earn money from this right. If the fees related to that right would exceed the possible earnings by far this certainly is not proportional.

Transparency and less complexity
Unfortunately, the suggested reduction of fees depending on the agency's workload is not further specified in detail. Therefore, it remains unclear how and to what extent reductions will apply to which regulatory circumstances. If e.g. reduction will be decided on a case by case evaluation of the referral, this is not transparent for MAHs. In general, a referral should not involve any costs as it needed to be covered by the general pharmacovigilance fees already paid by the MAH at that time.

Consultation item n°7*: Do you agree with the proposed pharmacovigilance service fee? If not, please explain and/or suggest alternative.*

The suggested fee level does not correspond with the principles 1 and 5.

Proportionality
The EMA states in the concept paper that the suggested fees shall be related to "the conduct of pharmacovigilance activities". While the agency already charges an annual fee for CAPs that currently covers amongst others pharmacovigilance activities this is not the case for NAPs in all European countries. As already lined out in the response to item n°1, NAPs should only have national level fees corresponding to their territories of authorisation.

Equal treatment and double charging
It is not clear what the rationale of a separate pharmacovigilance service fee would be with especially taking into account that most pharmacovigilance activities already have a fee suggested in this concept paper. Moreover it is not clear why a NAP that already is incurring to an annual fee which is currently covering pharmacovigilance activities by the NCA should have to pay an additional fee to the EMA for the same activities. At least it is not very likely that the NCAs will reduce their currently charged national annual fee in order to reduce the MAHs' burden imposed from the European level.
It can also considered to be double charging of MAHs if NAPs still incur variation fees for national pharmacovigilance related changes which would be triggered by the EMA after receiving a separate fee while this would not happen for CAPs.

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

In general, fee reduction for smaller companies is very welcomed. However, as lined out in response to item n° 1, a closer consideration of the business side of MAHs might be advisable. Moreover, a reduction might not only be based on the size of a company but also on the type of medicinal product as e.g. generics or homeopathic products are very likely to generate less workload to the EMA compared to new chemical or biological medicinal products. Therefore, a generally lower level of fees or dropping of some suggested types thereof might turn out to be a better solution for both EMA and MAHs.

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

See response to previous item.

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

In summary, it has to be stated that the concept paper does not meet the principles lined out in its introduction, i.e. proportionality, transparency, equal treatment of MAHs, reduction of administrative complexity, and avoidance of double charging of MAHs. Moreover it does not reflect the intention the European Commission communicated in the course of the legal process from 2008 onwards. An unaltered implementation of the views expressed in the EMA's concept paper on pharmacovigilance related fees would certainly not lead to reduce costs nor administrative burden for MAHs.
Why should a pharmaceutical company try either to develop new medicinal products for a market or make cheaper products available in a competitive market if this will foreseeably not lead to any profit because of too high fees? An unaltered implementation of the views expressed in this concept paper will probably not improve the safety of medicinal products in Europe but very likely lead to a significant reduction of the diversity of medicinal treatment available for patients in Europe, especially in smaller and/or low profit markets.