PHARMIG
Verband der pharmazeutischen Industrie Österreichs

Forum der forschenden pharmazeutischen Industrie in Österreich
FOPI

IGEPHA
The Austrian Self-Medication Industry

WKO
Arznei·Drogerie·Parfümerie·Chemikalien·Farben

European Commission,
DG Health and Consumers,
Unit D5 'Medicinal products – authorisations, EMA'
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PHARMIG, FOPI, IGEPHA and Federal Association of Wholesalers and Retailers of Medicines response to the European Commission Concept Paper: INTRODUCTION OF FEES TO BE CHARGED BY THE EMA FOR PHARMACOVIGILANCE

PHARMIG - Association of the Austrian Pharmaceutical Industry, FOPI - Association of the Research and Development based Pharmaceutical Industry in Austria, IGEPHA - The Austrian Self-Medication Industry and the Federal Association of Wholesalers and Retailers of Medicines, Perfumes, Toiletry Products, Chemicals and Paints would like to thank the European Commission for the opportunity to comment on the concept paper regarding the introduction of fees to be charged by the EMA for pharmacovigilance.

Please find following our comments.

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General comments

In section 2.3 the concept paper stresses the fact that in proposing the new pharmacovigilance fees, the following principles should be respected:

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

We think that almost none of the above mentioned principles is actually met in the proposal.

In section 1 the concept paper points out that the Commission's proposal of 10 December 2008 to amend the pharmacovigilance legislation was accompanied by a Financial Statement which is now *'outdated'* and that the final proposal for introduction of fees for pharmacovigilance will be accompanied by its own financial statement. Whereas the 'outdated' 2008 Financial Statement provides insight on the calculated workload at the EMA, e.g. for the assessment of Periodic Safety Update Reports (1000 PSURs/year at 6,100 €), there is not the merest hint in the current proposal why a single PSUR assessment is now charged with a fee of 80,300 €.

We think the current proposal shall mandatory explain the basis of the calculation, especially a thirteenfold increase in comparison with the 2008

financial statement for a specific assessment where the nature of the task carried out by EMA has not been changed. Therefore it has to be said that the current proposal fails to meet the principles of proportionality and transparency (see principles a) and b) above).

According to the current proposal medicinal products are charged with the same fee for a specific pharmacovigilance related task irrespective if they are centrally authorised products (CAPs) or non-CAPs. This concept does not consider the very different benefit-risk-ratios of medicinal products as well as their patient exposure. It is supposed that the assessment of a PSUR for a high-risk product authorised in the whole European Union (population 500 million) with 1000 adverse events/year requires the same workload as an Austrian (population 8 million) purely nationally registered medicinal product with 3 adverse events/year (see also item no. 1). This is also in contradiction with the principle of proportionality (see principle a) above).

It is obvious that the sales volume of a purely nationally registered product in smaller member states like Austria cannot compete with a CAP in a market with a population of 500 million. In many cases the proposed fees for pharmacovigilance exceed the annual sales of non-CAPs even if fee reductions for SMEs are considered. The concept paper fails to address this aspect. **We are concerned that a big deal of our national marketing authorisations and their holders are threatened with extinction if the concept will be implemented as presented** (see also item no. 8).

In our opinion the concept of the new Pharmacovigilance Service Fee on the basis of a medicinal product defined by the same active substance or combination of

substances favours in an inadequate way pharmaceutical companies with many marketing authorisations on the basis of few active substances, i.e. often generic companies. Whereas generic pharmaceuticals often have the biggest patient exposure and consequently create larger quantities of adverse events because of a bigger exposure to the patients these products are excluded from signal detection since under the new pharmacovigilance legislation (besides exceptions from the EURD list) there is in general no more obligation to submit PSURs for generics. Generic companies therefore are not only spared from PSUR fees but additionally are favoured with the new Pharmacovigilance Service Fee.
We think in this aspect the current proposal is hostile to innovation and interferes with the principle of equal treatment of MAHs (see principle c) above).

Pharmacovigilance and the safety of medicines are an essential part of a public health concept. The pharmaceutical industry contributes with comprehensive efforts in research and development, the fulfilment of legal requirements during the marketing authorisation process and the conduction of post marketing surveillance. Nevertheless the safety of medicines is part of the responsibilities of public administration. **Therefore the funding of these public responsibilities must not be shifted entirely to the pharmaceutical industry.**

<u>Specific comments</u>

Consultation item no. 1: Do you agree with the proposed fee for single assessment of PSURs? If not, please explain and/or suggest alternative.

Response:

We do not agree. It is proposed *'to charge (a basic) fee of maximum 80,300 € for each assessment of a PSUR'*. The information regarding the minimum and the range of the fee is missing. The basis of the calculation is missing. This does not allow a proper assessment. As mentioned under 'General comments' there is no justification presented for the thirteenfold increase in fees for a specific assessment in comparison with the 2008 Financial Statement. The following table shows an example of a recent PSUR assessment with Austria as RMS and 15 CMS.

PSUR Assessment (3-year PSUR)

Country	in Country Currency	in EURO	Link to fee at authority homepage
AT as RMS	3.600,00	3.600,00	http://www.basg.at/ueber-uns/tarife/amtliche-nachrichten/
CMS:			
CZ	0,00	0,00	http://www.sukl.cz/uploads/Pokyny_a_formulare_anglicky/UST/UST_29_version_8.pdf
DE	0,00	0,00	http://www.gesetze-im-internet.de/amgkostv/index.html
EE	0,00	0,00	http://www.ravimiamet.ee/en/state-fees-and-assessment-fees
EL	0,00	0,00	http://www.eof.gr/web/guest/procedures?p_p_id=62_INSTANCE_gTy0&p_p_lifecycle=0&p_p_state=maximized&p_p_mode=view&p_p_col_id=column-2&p_p_col_count=1&_62_INSTANCE_gTy0_struts_action=%2Fjournal_articles%2Fview&_62_INSTANCE_gTy0_groupId=12225&_62_INSTANCE_gTy0_articleId=17058&_62_INSTANCE_gTy0_version=1.0
ES	2272,48	2272,48	http://www.aemps.gob.es/industria/tasas.do?id=1
IE	0,00	0,00	http://www.imb.ie/EN/Publications/Publications/Guide-to-Fees-Human-2010.aspx
LT	475 LTL	138,00	http://www.vvkt.lt/index.php?3703264428
LV	0,00	0,00	http://www.zva.gov.lv/doc_upl/SAM_public_pricelist.pdf
NL	0,00	0,00	http://www.cbg-meb.nl/CBG/en/human-medicines/regulatory-affairs/Fees/default.htm
NO	0,00	0,00	http://www.legemiddelverket.no/templates/InterPage____82332.aspx?filterBy=CopyToGeneral
PL	0,00	0,00	http://en.urpl.gov.pl/fees
PT	0,00	0,00	http://www.infarmed.pt/portal/page/portal/INFARMED/ENGLISH/fees.pdf
RO	0,00	0,00	http://www.anm.ro/en/html/mrp_dcp.html
SE	0,00	0,00	http://www.lakemedelsverket.se/english/product/Medicinal-products/Fees--/
UK	0,00	0,00	http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Marketingauthorisations/Variationstolicences/index.htm#6
Sum		**6.010,48**	
Average		**375,66**	

The overall cost of 6,010 € corresponds with the Commission's proposal in the 2008 Financial Statement and stands in our opinion in a realistic relation to the actual workload of a multinational PSUR assessment.

Considering the current schedule of fees in Austria MAHs would have to face an inadequate and disproportional increase of costs for the same service. The Austrian Federal Office for Safety in Health Care of the Austrian Medicines and Medical Devices Agency (AGES) charges for the assessment of a PSUR 3,600 € as a Reference Member State and 500 € as a Concerned Member State or for a purely nationally registered product, an amount which is 22fold exceeded by the proposed 80,300 € or 160fold for national PSURs, respectively. As our health authorities underline in their response to this consultation they usually make do with this charges even though there are additional fee reductions foreseen in special cases (if the PSURs are presented simultaneously by the same marketing authorisation holder; if the active ingredients are of the same type, and if the application is comparable with regard to the evaluation).

The concept paper recognises that the assessment of PSURs is based on the cumulative data available at the time of submission and, as a consequence, the workload in assessing PSURs for products which have been authorised for more than 2 years is higher. Therefore it is proposed to charge a lower fee of 40,150 € for products which have been authorised for less than 2 years.
This concept does not consider the fact that according to Article 107c of directive 2010/84/EU holders of marketing authorisations which were granted before 21 July 2012, have to submit PSURs at least every 6 months following authorisation and until the placing on the market and during the first 2 years following the initial placing on the market. As a consequence the marketing authorisation holder has to pay 80,300 €/year for at least 2 consecutive years which is considerably more than for a product authorised for more than 2 years. Furthermore it is not considered that a medicinal

product does usually not generate any adverse events during the time between the authorisation until the placing on the market. We therefore suggest that in this case no fee at all should be charged for the submission of PSURs until the placing on the market.

As already explained under general comments the concept paper does not regard the different benefit-risk-ratios of medicinal products resulting in different workload for the assessment of PSURs.

Consultation item no. 2: Do you consider relevant the concept of grouping as proposed? If not, please explain and/or suggest alternative.

Response:

It is not clear how the grouping is defined. If the submission is grouped between MAHs of the same corporate group, a case were we definitely support the idea of a fee reduction, the PSUR contains one set of data from one pharmacovigilance system, collected and evaluated at one single point under global SOPs and under the supervision of one EU QPPV. There is no additional workload in the assessment of the PSUR irrespective of the number of MAHs involved in the procedure. In this case we do not see a justification for the proposed administrative fee of 500 € for each additional MAH in a group.

If the concept refers to the grouping between MAHs of different corporate groups we consider this as not relevant in practice. Whereas safety data might be exchanged

between business competitors this is very unlikely for commercial data. Additionally there would be organisational challenges because of different PV systems etc.

Consultation item no. 3: Do you agree with the proposed fee for the assessment of PASSes? If not, please explain and/or suggest alternative.

Response:

We do not agree with the proposed fee for the assessment of PASSes because of the lack of transparency and proportionality regarding the workload for the assessment.

The 2008 Financial Statement calculated a workload of 300 study assessments/year at 6,100 € at the EMA. There is no justification presented why the assessment of each final study report for PASSes is now charged with a fee of 80,300 €. We think a current proposal shall mandatory explain the basis of the calculation, especially a thirteenfold increase in comparison to the 2008 Financial Statement for a specific assessment where the nature of the task carried out by EMA has not been changed.

Consultation item no. 4: Do you consider relevant the concept of grouping as proposed? If not, please explain and/or suggest alternative.

Response:

We do not consider relevant the concept of grouping as proposed for the same reasons as described under consultation item no. 2.

Consultation item no. 5: Do you agree with the proposed fee for the assessment of pharmacovigilance referrals? If not, please explain and/or suggest alternative.

Response:

We do not agree with the proposed fee for the assessment of pharmacovigilance referrals. The 2008 Financial Statement calculated a workload of 20 assessments/year at 72,800 € at the EMA. There is no justification presented why the assessment is now charged with a fee ranging from 80,300 € to 267,400 €. We think the current proposal shall mandatory explain the basis of the calculation.

It should be borne in mind that the maximum fee of 267,000 € with an estimated rate of 150 € per hour equals 222 working days at 8 hours.

In addition the amount of the fee does not consider the size of the market of non-CAPs. In practice this will lead to withdrawals of MAs since the sales volume of many products will not be able to bear the financial pressure of a referral procedure.

Consultation item no. 6: Do you agree with the concept of grouping as proposed? If not, please explain and/or suggest alternative.

Response:

We do not agree with the concept of grouping as proposed for the same reasons as described under consultation item no. 2.

Consultation item no. 7: Do you agree with the proposed pharmacovigilance service fee? If not, please explain and/or suggest alternative.

Response:

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

Additionally to our concerns regarding the discrimination of innovative pharmaceutical companies as described under 'General comments' we miss transparency regarding the range of the fees and their proportionality with the associated tasks.

The pharmaceutical industry has already put considerable effort in the establishment of the list of products according to Article 57(2) of the Regulation and is obliged to continuously maintain the content up to date.

Additionally, it was also made clear by EMA that literature monitoring will be only performed for selected substances and in selected journals, and that the legal obligation of the MAHs to monitor the scientific literature and to process literature

reports on adverse drug reactions will remain unchanged. Therefore, literature monitoring by EMA does not shift any task or responsibility from the MAH to the EMA and can as a consequence not be regarded as a service.

The same applies to the work that EMA will undertake in future on signal detection. The final responsibility for signal detection and evaluation remains with the MAH; therefore the EMA's activities do not shift any task or responsibility from the MAH to the EMA and can as a consequence not be regarded as a service.

We think that the pharmaceutical industry already puts tremendous effort in pharmacovigilance by fulfilling legal requirements and being charged for clearly attributable assessments of the EMA. Therefore it is our opinion that it is not justified to charge the industry with an additional lump sum for unspecified services.

Consultation item no. 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.

Response:

We agree with the general idea of a fee reduction for SMEs but we do not agree with the proposed amount of the fees. As regards PSURs, PASSes and pharmacovigilance referrals, the 50% reduction would only apply when SMEs are not involved in a grouping. It should be considered that the amount of the proposed fees is even for non-CAPs of non-SMEs unbearable.

We have numerous responses from SME member companies pointing out that the proposed fees would exceed their annual budget assigned for research, development

and surveillance or even their annual sales. In the consequence the amount of the proposed pharmacovigilance fees would lead to the withdrawal of a big deal of nationally authorised medicinal products and thus to a drastic reduction of the diversity of the pharmaceutical market and therapeutic alternatives.

As already mentioned under ‘General comments’ fees should consider the patient exposure of the medicinal product as well as the economic situation in the specific member state where the product is authorised.

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

Response:
We do not agree with the concept for the same reasons as described under consultation item no. 7.

Consultation item no. 10: What other aspects would you like to raise? Do you have additional comments?

Response:
Please see our ‘General comments’ above.

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