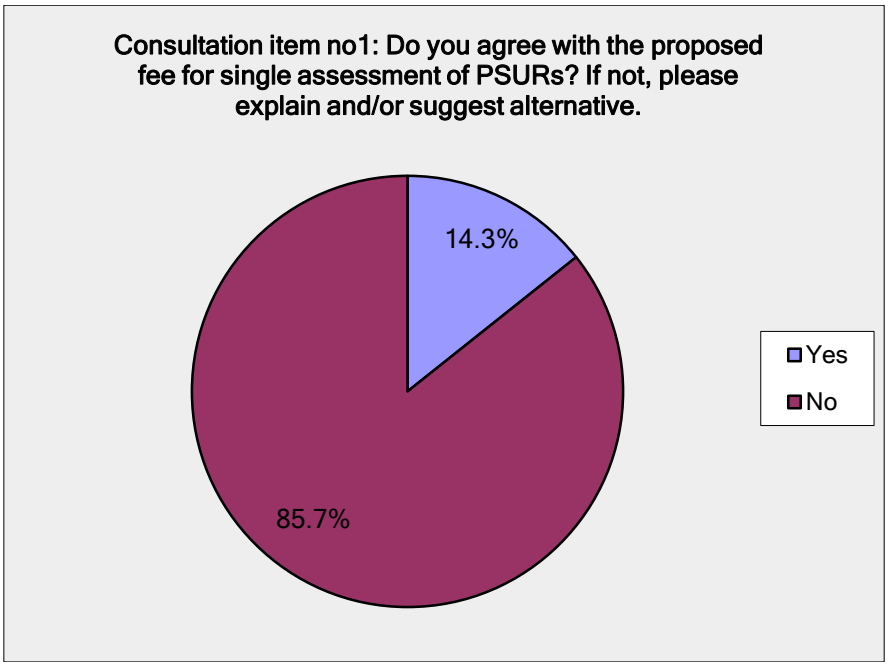
PIPA MEMBERSHIP COMMENTS ON CONCEPT PAPER ON INTRODUCTION OF FEES TO BE CHARGED BY THE EMA FOR PHARMACOVIGILANCE SEPTEMBER 2012

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



Explain and/or suggest an alternative:

- The content and complexity of a PSUR (number of ICSRs reported, complexity of studies and RMPs) should be taken into account when determining the fees e.g. €80,300 would be an unreasonable fee for a product is in receipt of only 10 ADRs each year.

- The length and complexity of these documents varies considerably between different medicinal products. We think that the length of the document should be taken into account and fees scaled accordingly. We also think for products with orphan status these fees should be substantially reduced.

- The fee proposed seems adequate for centralised procedure marketing authorisations. Nevertheless it must be clarified what the minimum fee would be and what factors would trigger the fee to rise.

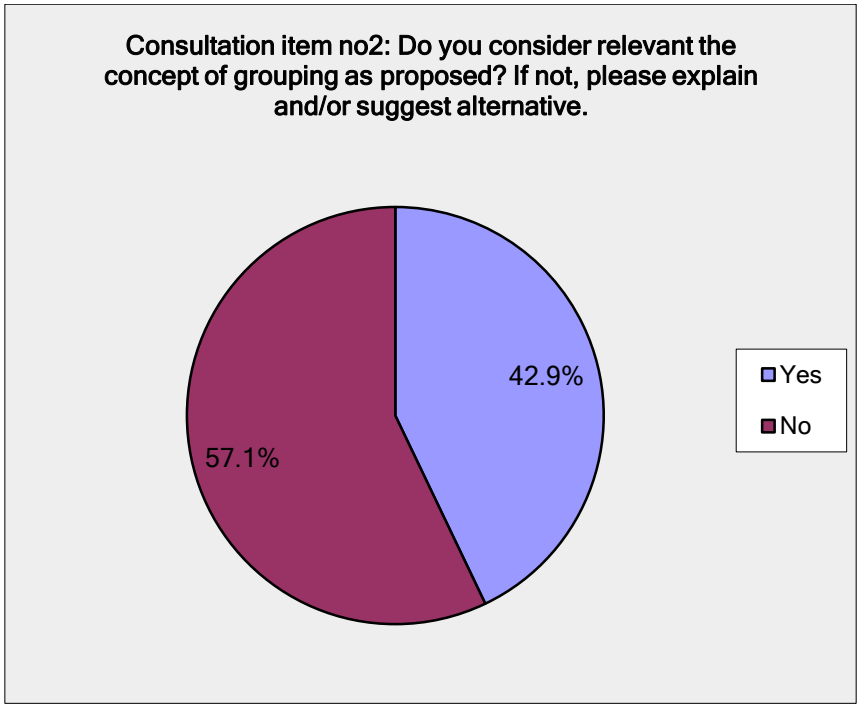
- A pro-rata fee depending on the number of markets and type of licence i.e. national being the lowest fee.

- Quite simply we wouldn't exist anymore.

- As there is no way of producing a single PSUR across Europe, this will become a money-making exercise for the EMA, who will charge every company the single assessment fee, regardless of how much there is to read in each one. The proposed fee will drive companies who have low margin generics out of the market, and those who can stay the course will have to increase prices significantly to cover the assessment fee.

- The price of the fee should be based on the complexity of the PSUR and how long it takes to assess. For example, one product that is likely to require yearly PSURs generates about 4 cases a year. There will be no clinical trial data to present in the PSUR. Is it fair that the company pay as much for the assessment of a minimal number of cases and the occasional published study as for a product that has an active clinical trial programme generating significant new safety information?

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



Explain and/or suggest an alternative:

- In principle the idea seems to be acceptable taking the general comments into account. Referring to (98/C 229/03) all MAHs involved in a European procedure like a DCP have to be taken as one entity. There would be no administrative fee in this occasion.

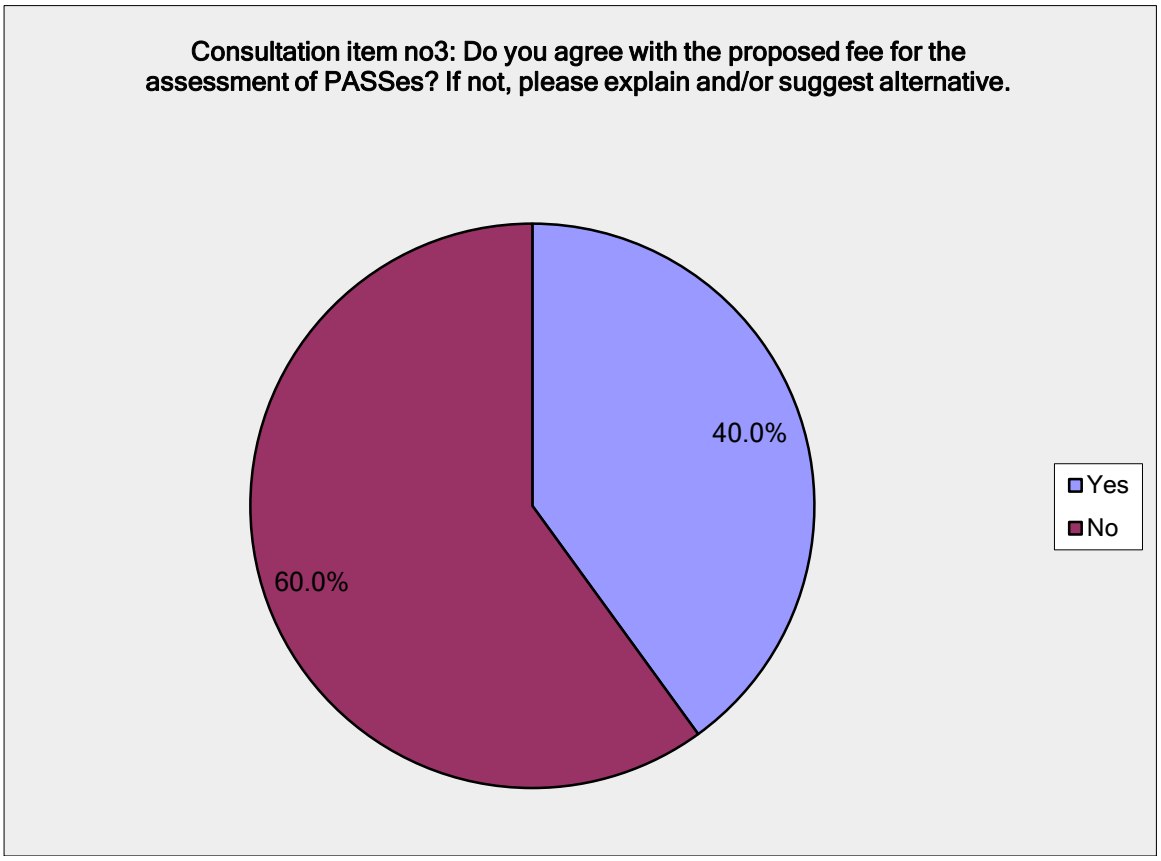
- I'm not sure how this would work - one company will always end up doing more work than others and how would you enter into a group?

- It's vital, if the plans go ahead.

- This is completely impractical. How does the EMA propose that companies with no shared database produce a combined PSUR without divulging commercially sensitive information and which all their QPPVs approve within a 90-day period? The majority of generic companies are in competition with each other, but even if they weren't, the numbers of MAHs across Europe for some products will be enormous and the associated administration could take longer than preparation of individual PSURs..

- Suggest that the EMA receive the PSURs from each company, appoint someone to analyse the data and produce a composite report, and then assess that report.

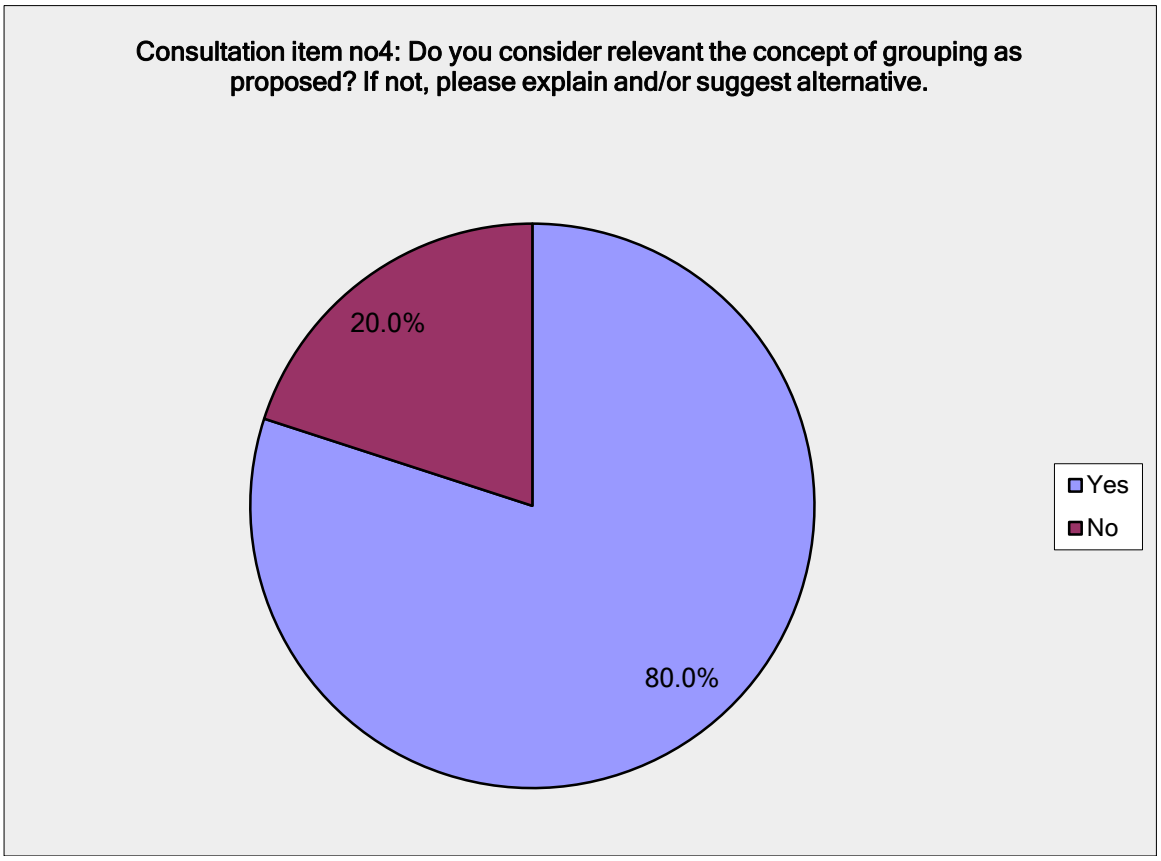
Consultation item n°3: Do you agree with the proposed fee for the assessment of PASSes? If not, please explain and/or suggest alternative.



Explain and/or suggest an alternative:

- The size and complexity of the PASS should be taken into account when determining fees.
- It is anticipated that a PASS is imposed to MAH(s) based on specific license(s). Therefore it is recommended that the MAH submits the final study report as part of a variation to these licenses together with proposed updates for product literature. The PASS assessment should be part of this type II variation and the competent authority should initiate the review by PRAC. The complete procedure should be covered by the variation fee of the competent authority(ies) involved. This would strengthen the approach and speed up the process to update the labelling of the affected products. Therefore there should not be a separate fee for PASS assessment.
- Our company would become bankrupt.

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

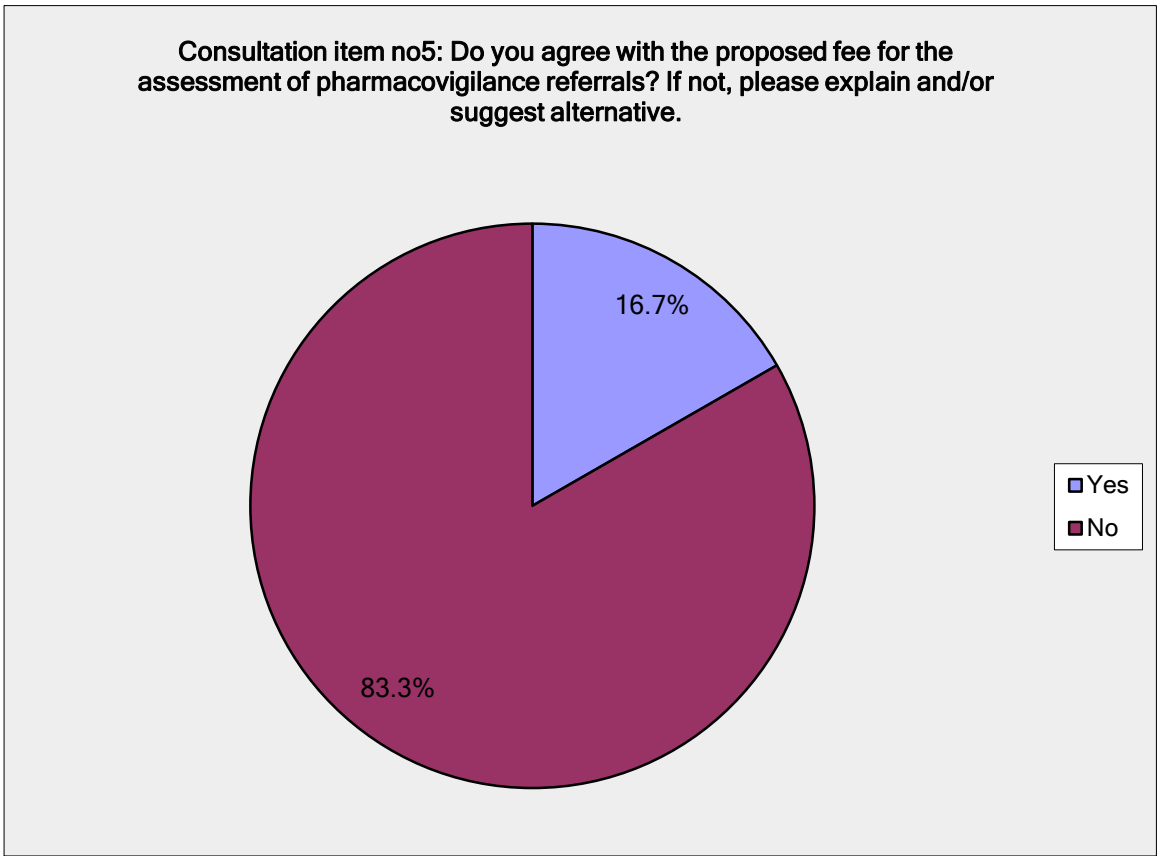


Explain and/or suggest an alternative:

- In principle the idea is acceptable taking the general comments into account. Referring to (98/C 229/03) e.g. all MAHs involved in a European procedure like a DCP have to be taken as one entity.

- This would be the only way to survive.

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.



Explain and/or suggest an alternative:

- The fees should be based on the time taken for review and the nature of the review material. The fees should be itemised as prices per unit of activity for transparency and reduce the burden on smaller companies who will not be able to afford the proposed range of fees: €80,300 to a maximum of 267,400€.

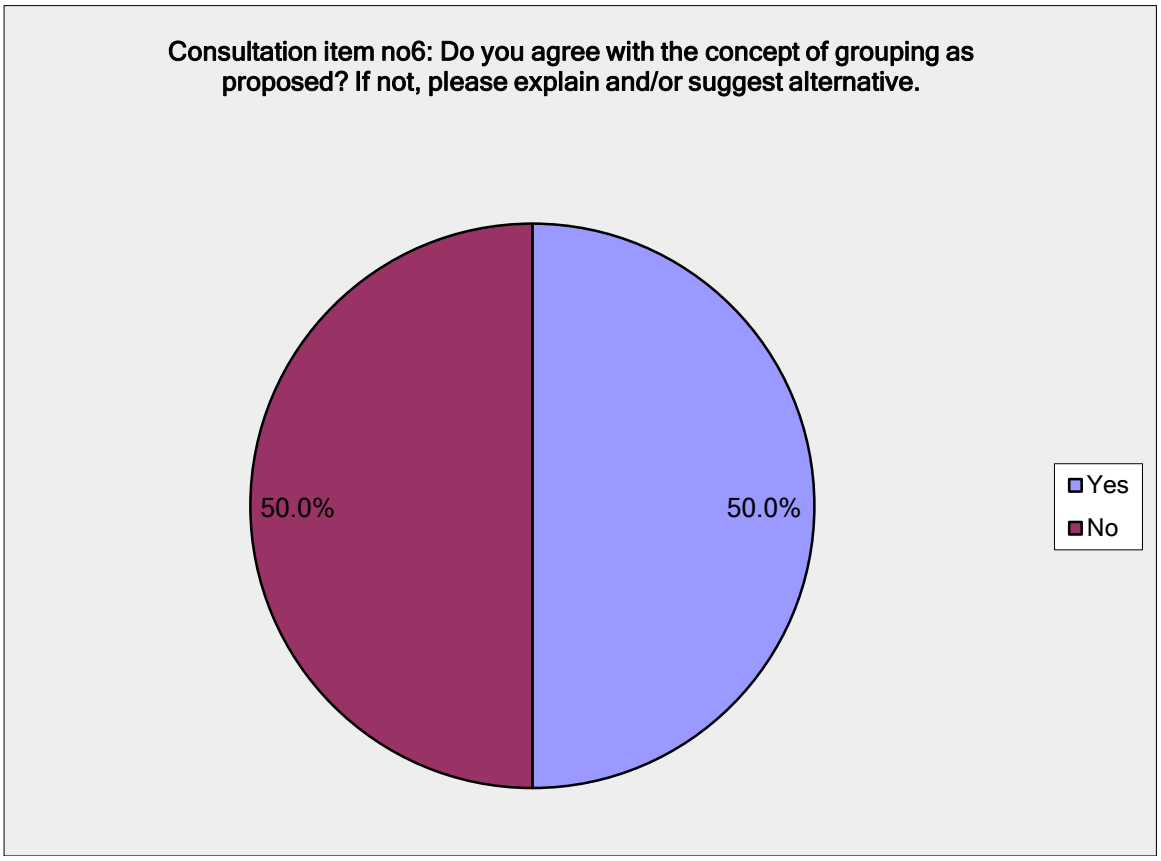
- The suggested PV referral fees seem excessive considering it is the MAH who is required to perform surveillance and benefit:risk analysis of their products and will use this analysis for example to suggest new safety labelling. The MAH is required to review both individual safety cases and the overall benefit:risk for the PSUR (which will also have EMA fees for review) and this seems a duplication of costs.

- In this case both the upper and the lower end of the fees are known. Nevertheless it remains unclear what exactly makes the fee rise.

- I am concerned that the level of fees may mean that this could be used as a backdoor way of removing products from the market because the possible cost of a referral for low margin products (e.g., the recent referral of pholcodine to the CHMP) could be far in excess of the income that a product can generate.

- For established medicines, the cost should be proportionate to the income generated by the product, unless the authorities are prepared to accept the risk that low cost products will disappear from the market overnight, as soon as a referral is made.

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

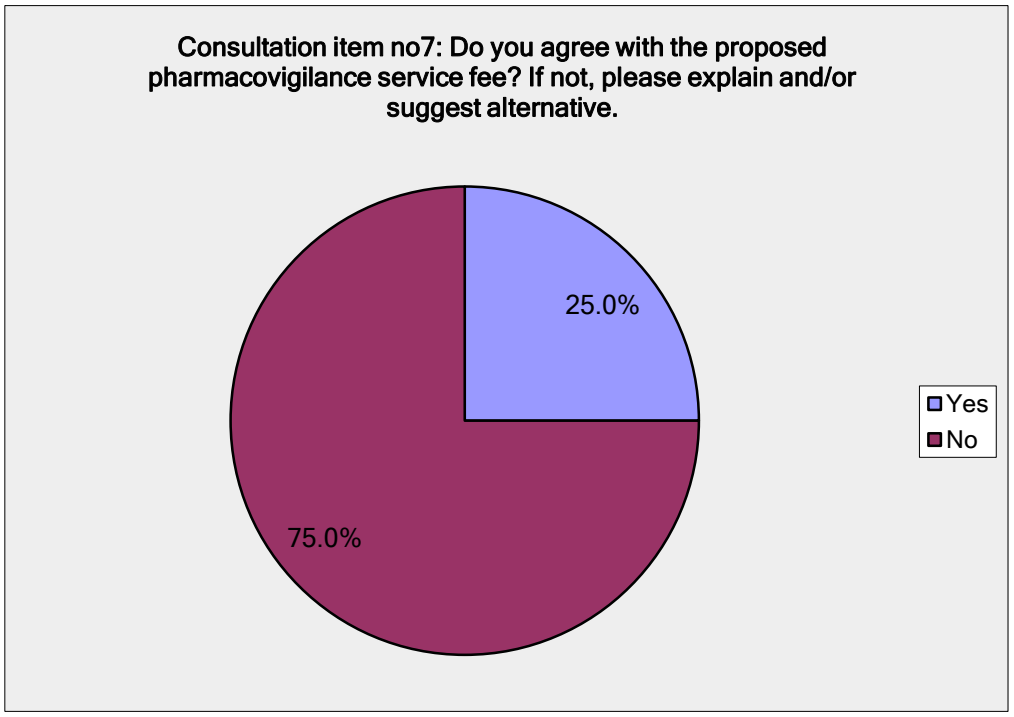


Explain and/or suggest an alternative:

- In principle the idea is acceptable taking the general comments into account. Referring to (98/C 229/03) e.g. all MAHs involved in a European procedure like a DCP have to be taken as one entity.

- This cannot work unless the EU sets up systems to co-ordinate such an approach.

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



Explain and/or suggest an alternative:

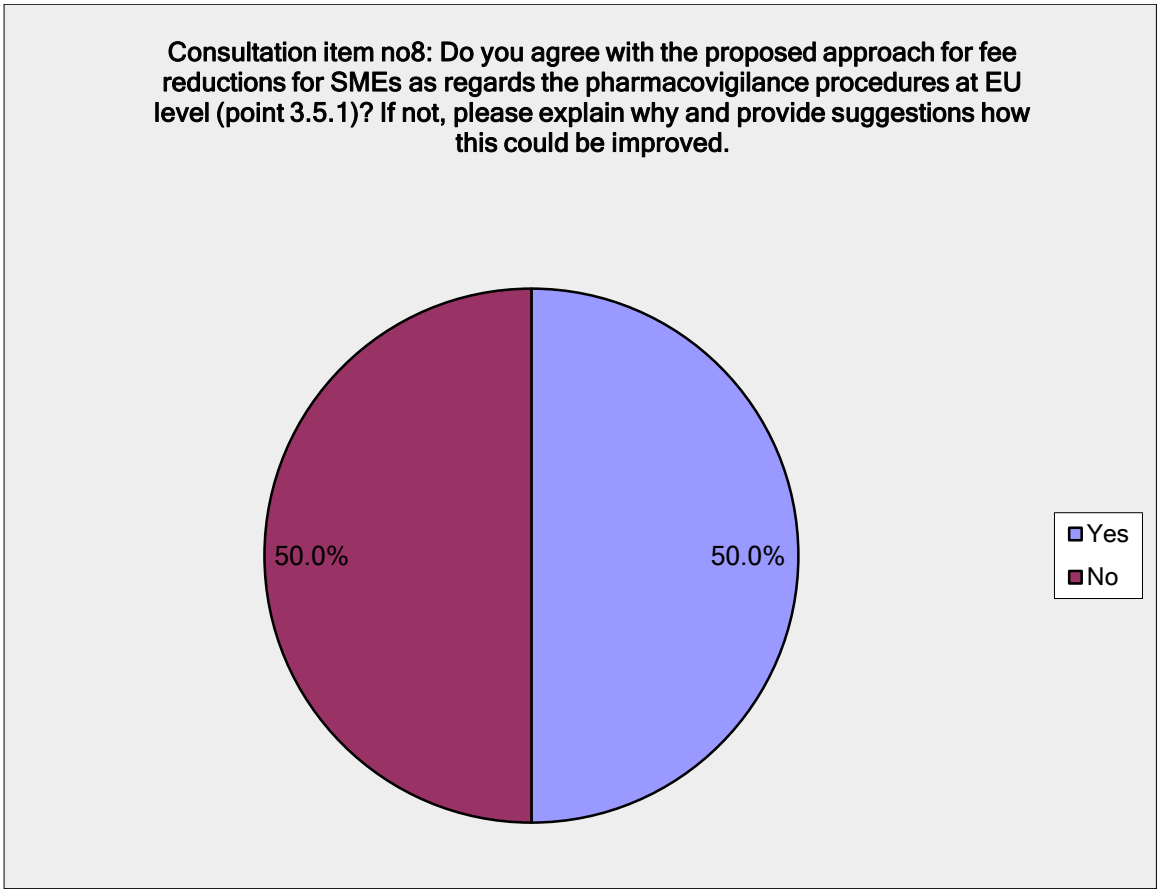
- The PV service fee should be proportionate to the activity of a product. For an old product for which minimal ADRs are received and no PSURs are required, the fee should be made null and void. The PV service fee at €1,000 should instead consist of a range of fees reaching up to a maximum of €1,000 in accordance with the activity of a product and the size of the MAH concerned.

- Again there is a maximum given only. No other values are available and no idea what product would cost how much.

- In principle the idea is acceptable taking the general comments into account. Referring to (98/C 229/03) all MAHs involved in a European procedure e.g. DCP have to be taken as one entity. Nevertheless the fee should be reduced depending on the turnover of the product affected. Especially MAHs with numerous products but small turnover per product the fees proposed will reduce profitability of small products unacceptably.

- Companies already pay fees to national authorities. It is difficult to see what companies with national licences will get for their €1000 per product. The EMA has already proposed charging outrageous levels of fees for PSUR assessment and referrals to PRAC. Companies are still required to perform weekly literature searches for their actives, for which they already pay. If this had been removed from the legislation and been replaced by something less prescriptive, then there might be some justification for some fee to cover centralised literature searching. For the majority of established/elderly national products, the input from the EMA will be negligible, but the cost of the service fee will be significant. Many products generate no, or very few cases, and therefore will have very few cases to report. For example, one company with 25 licences generates a maximum of 10 spontaneous adverse events per year, and have never had to report a case from the literature. This company will have to pay approximately €18,000 per year, so each case they receive will cost €1,800 in EMA fees. A proportionate system based on use of the system would be fairer, possibly based on the number of cases reported.

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

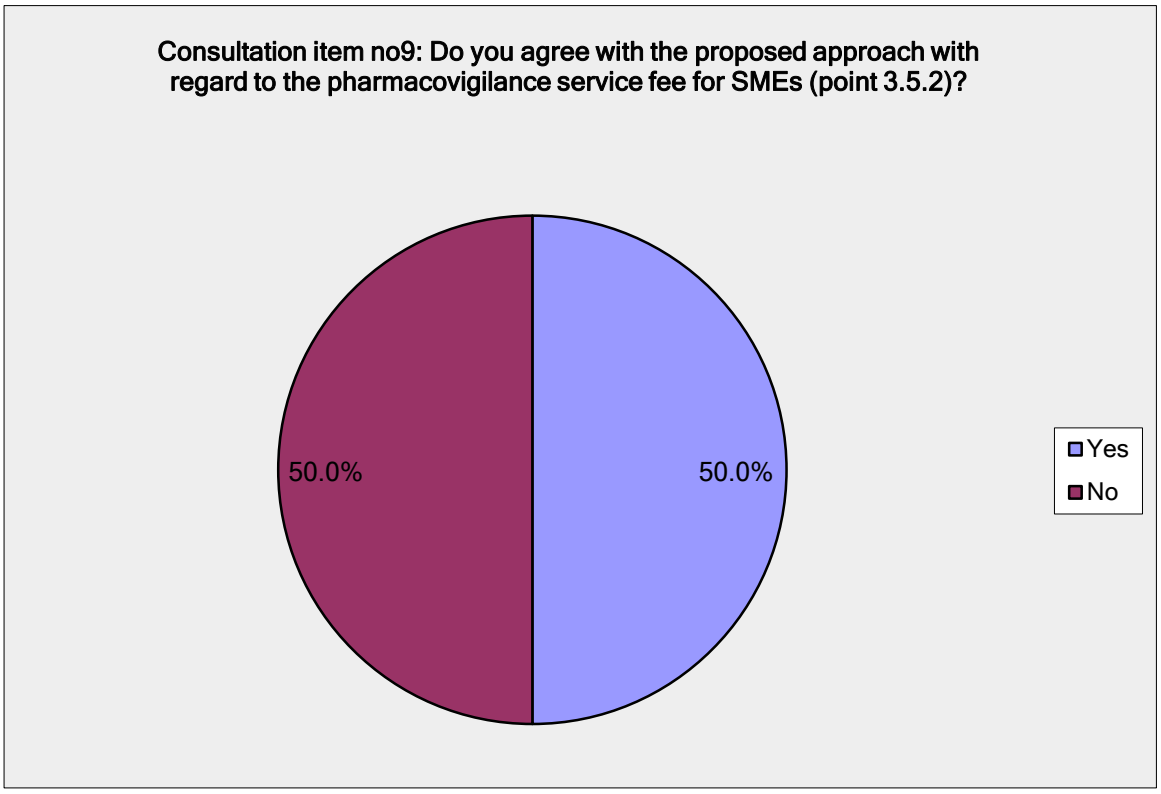


Explain and/or suggest an alternative:

- We think there should be a sliding scale depending on size of the company, volume of complaints and if fees will be shared by the grouping system.

- It is welcomed that SMEs should get a 50% reduction and micro enterprises will be exempted completely. Nevertheless the fees should be reduced depending on the turnover of the product affected. Especially MAHs with numerous products but small turnover per product the fees proposed will reduce profitability of small products unacceptably. SME fee reduction should not stop while grouping. The intention to provide fee reduction to SMEs is to lower the burden of fees for smaller companies in relation to the bigger ones. This idea is not affected at all by grouping as big companies may group as well.

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



Explain and/or suggest an alternative:

- The fee should be reduced depending on the turnover of the product affected (alternatively please refer to #III). Especially SMEs with numerous products but small turnover per product the fees proposed will reduce profitability of small products unacceptably.

- Charges should be proportionate to use of the system, not the size of the company.

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

- It appears the proposed PV fees are penalising companies with innovator products. Not only will high fees be charged for PSURS but variations for non-CAPs will be subject to the same fees, the latter seems unreasonable. If all products will be subject to a PV service fee, fees should not apply to variations for non-CAPs.

- The grouping idea used throughout the concept paper to split costs between MAH's with the same products and therefore reduction of burden of fees for an individual MAH is not relevant to products with no generics or biosimilars – which is often the case for innovative biotechnology products. The concept paper makes no concessions for orphan drug products which by their very nature are less frequently used therefore generating relatively less safety reports and signals. Therefore as it currently stands these niche products will shoulder a higher burden in terms of fees due to their specialist nature which will not encourage innovation in areas of specialist unmet medical need in the future.

- MAHs should be interpreted as one company/entity as described in the Commission communication on the Community marketing authorisation procedures for medicinal products (98/C 229/03) footnote 27 (http://ec.europa.eu/health/files/eudralex/vol-1/com_1998/com_1998_en.pdf#page=11). With regard to grouping only MAHs exceeding this group of companies would start a grouping. Within a group acc. footnote 27 an administrative would not occur.

- In case the fees need to be split it seems to be more adequate to take into account the number of MAs and the type of MA (CP, DC/MR or purely national). It seems not to be adequate that an MAH holding 10 CP MAs involved would pay the same aliquot as an MAH being involved with a single national MA in a small country. In the fee calculation it must be taken into account what the target group of the MA is (e.g. CP Europe with a population of~ 500 millions or a national license in e.g. Slovenia with a population of ~2 millions) (Source eurostats - http://epp.eurostat.ec.europa.eu/tgm/web/_download/Eurostat_Table_tps00002FlagDesc.xls).

- It is recommend to stagger the fees depending on the countries affected:
  - CP or MA in > 22 countries – full proposal
  - MA in ≥ 16 up to 22 countries – ¾ of fees proposed
  - MA in ≥ 8 up to 15 countries – ½ fee
  - MA in > 3 up to 7 countries – ¼ fee
  - MA in up to 3 countries – 1/10 fee

- For grouping and the PASS fee a fixed amount is given. While for the other fees there is a maximum fee given the minimum fee remains often unclear and what the fee makes to raise as well. This makes it very difficult to comment.