European Medicines Agency
Post-authorisation Evaluation of Medicines for Human Use

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Dear Peter,

Subject: European Commission's Public Consultation on an Assessment of the European Community System of Pharmacovigilance

First of all the EMEA would like to thank the European Commission for the opportunity to provide feedback on the "Assessment of the European Community System of Pharmacovigilance". The Agency welcomes the Assessment as a major positive development in looking at the future of the EU Pharmacovigilance System, the various challenges such system is facing, and how such challenges might be addressed, in the best interest of public health.

Two sets of comments/proposals are attached: Annex 1 provides the EMEA viewpoint in the context of the Agency's role as the coordinator of the EU Phamacovigilance System and Annex 2 provides the viewpoint of both the CHMP and PhVWP, as recently adopted by both fora.

The EMEA is looking forward to further contribute to the next steps of this important process initiated by the European Commission.

Yours Sincerely,

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ANNEX 1

EMEA Comments/Proposals on the Assessment of the European Community System of Pharmacovigilance

I General Comments

1. The EMEA is of the view that the ideal EU Pharmacovigilance System should have the following characteristics:
   - A system that is capable of achieving the highest standards of public health protection, with proactive planning for safety in addition to early detection of harm.
   - A system that is able to support risk management throughout the life-cycle of medicinal products irrespective of the authorisation route.
   - A system that allows use of the available resources in an optimal way.
   - A system that leads to robust and timely decisions, based on a best evidence model.
   - A system that delivers appropriate, timely and coordinated regulatory action and which communicates effectively with all stakeholders.
   - A system that is supported by high-quality, independent scientific research, including some public funding and/or public/private partnerships.
2. The report (by Fraunhofer) of the Assessment is very comprehensive, however some aspects are mentioned in the main text but do not reach the recommendations section. One of these is the use of regional centre approaches for proactive pharmacovigilance and active surveillance, a concept which already exists in some Member States.
3. Whilst the Assessment covers very thoroughly the methods of collecting data, especially in terms of spontaneous reporting, the relative contribution of other methods, such as pharmacoepidemiology for instance, is not as detailed.
4. The report makes many useful proposals on how to move forward in pharmacovigilance in the future. However, some of the recommendations are rather vague and there is no mention of who should implement such proposals. For instance, in section 10.4.1 there is a recommendation for replacing the sequential approach with a cyclical one; this proposal could be further developed.

II Specific Comments and Recommendations

The specific comments and recommendations have been grouped in two parts: (1) recommendations requiring legislative changes and (2) other recommendations for the strengthening of the EU Pharmacovigilance System.

II.1 Recommendations requiring legislative changes

Areas for which existing legislation could be strengthened or new legislation could be introduced relate to:

1. Reporting obligations:
   - Taking into account the availability of a database accessible to all Regulatory Authorities in the EEA, reporting obligations could be simplified by establishing a single reporting point for all MAHs irrespective of the licensing route. The introduction of such single reporting point should not affect the current legal responsibilities of the Regulatory Authorities at national level.

- Reporting obligations could be simplified by expediting all serious (EU and non-EU) suspected ADRs.

2. Risk minimisation:

   - Heterogeneity still exists in national legislation on certain pharmacovigilance related aspects, characterised by specific national requirements. This heterogeneity has created and will continue to create difficulties in implementing risk minimisation measures (such as patient registries, informed consent, product supply and distribution controls) in a harmonised way across the EU. A harmonised risk minimisation toolbox could therefore be developed and implemented.

3. Decision making:

   - Regulatory timelines could be shortened, especially for referrals. In addition, provisional SPC changes (USR-like) could be considered, where appropriate, whilst safety referrals are ongoing. This would also facilitate early communication with HCPs and patients.

   - Legal possibilities could be explored for timely extension of EU regulatory action based on active substance (i.e. automatic action from the originator to generic products).

4. Monitoring and compliance:

   - The concept of the Qualified Person (QP) for pharmacovigilance is linked in the legislation only to the MAA for a given product and the MAH for that product. It would assist in the oversight of the pharmacovigilance system if the QP role and the pharmacovigilance system could be identified with the "corporate entity" at EU level, that includes the multiple legal entities and MAH identities that exist with it. Such a "corporate entity" does not exist in the EU legislation at present. It could perhaps be identified as the "operator of the pharmacovigilance system" or similar concept, if a satisfactory legal concept can be established for this. The aim being to have one pharmacovigilance system per company with one QP responsible for that system.

   - The introduction of a different concept of Supervisory Authority for the pharmacovigilance system than current provisions that apply to manufacturers and importers could be envisaged. For practical reasons the Supervisory Authority for pharmacovigilance should be the Member State were the QP for pharmacovigilance is located.

   - It is felt that additional tools are needed regarding non-compliance by MAHs. A possibility could be to include suspension of a MA as a regulatory option in cases of serious non-compliance.

5. Data sources:

   - Positive experiences have been reported from several Member States regarding consumer reporting of ADRs. This could have particular utility also for OTC medicines. Consumer reporting at EU level could therefore be considered as a new reporting requirement.

   - The regular and frequent provision of drug usage (consumption) data by MAHs could be made mandatory.

6. Reducing regulatory burdens:

   - The establishment of a legal basis for a Pharmacovigilance System Master File (PSMF), which describes the Pharmacovigilance system of the applicant or the MAH, could be envisaged. Since such PSMF is not product specific, it would reduce the administrative burden of frequent variations to a MA. This process would also ensure that the same PSMF can be used for any product regardless of the authorisation route.

7. Communication:

   - Communication by the MAH to cease marketing of a medicinal product due to concerns over safety should be communicated to Regulatory Authorities at an earlier stage than currently stipulated in Community legislation, since the current legal provisions do not provide sufficient time for the Regulatory Authorities to adequately fulfil their task in the protection of public health.

II.2 Other recommendations

Other recommendations for the strengthening of the EU Pharmacovigilance System relate to:

1. Improved data sources and methodologies:

   - The development and implementation of new and/or improved tools for influencing HCPs to prescribe safely should be considered.

   - An evidence-based approach should be applied to the decision making in pharmacovigilance. This should incorporate new concepts such as the best evidence model

   - EU healthcare databases should be further developed and integrated wherever possible in order to provide a robust data source for conducting pharmacoepidemiology studies.

   - Data sources should be expanded to include the e-medical record. This electronic record would potentially link hospital, community and drug usage data and as such has the potential of being a very important new methodology in future pharmacovigilance at population level.

   - Regional centre approaches should be further developed and funded to support proactive pharmacovigilance. As this would be a re-inforcing of existing resources it is possibly a cost-effective way to achieve early gains by the existing system.

   - A network of centres of excellence, including academia, should be developed in order to carry out the research necessary for proactive pharmacovigilance and risk management.

   - There is currently no validated quantitative methodology for carrying out benefit-risk assessment and therefore such methodology should be established. It needs to be recognised that there is no guarantee, however, that this would be feasible, or that it would replace entirely the current qualitative expertise and peer review based approaches.

   - To our knowledge no objective evaluation of the actual impact on public health outcomes has ever been carried out in relation to establishing pharmacovigilance systems. There is also no methodology available to do this at present. It may be possible to draw on experience from health technology assessment in order to attempt this in future.

2. Resource related issues:

   - A more precise evaluation of resource needs in pharmacovigilance should be carried out.

   - The use of the majority of the existing resources in spontaneous reporting should be re-evaluated. Optimally, some resources should be re-deployed or new resources acquired to support proactive pharmacovigilance and risk management (specifically risk assessment, minimisation, communication).

- This optimisation of resources could partly be achieved by better implementation of EudraVigilance e.g. by use of automated signal detection methods instead of the manual paper-based traditional methods as well as by reducing, where possible, any duplication of work.

- Work needs to be undertaken in order to increase compliance with electronic reporting of clinical trial SUSARs, especially for non-commercial sponsors. Clear roles and responsibilities should be established for the evaluation of SUSARs.

- Duplication of work in signal detection and evaluation should be reduced by defining clear roles and responsibilities and by work-sharing. This should include a collaboration of the NCAs and the EMEA.

- The Community should support high quality independent organisations able to conduct research in pharmacovigilance (including a network of centres of excellence).

- Funding which is public or obtained from public/private partnerships should be ensured for the conduct of safety studies (including pharmacoepidemiology, regional centre active surveillance, centres of excellence/academia) according to public health needs.

- The European Commission should consider specifically to support pharmacovigilance research within the VII Framework Programme.

- The possibility of call-for-tender procedures should be investigated as a means of allocating public funds to pharmacovigilance research areas with the most public health need.

- In view of many aspects, including pandemic, there should be specific support for high quality epidemiological studies on vaccines.

- Some resource should be considered for the conduct of pharmacoepidemiology studies based on EU healthcare databases that contain exposure/outcome data.