Implementing measures in order to harmonise the performance of the pharmacovigilance activities provided for in Directive 2001/83/EC and Regulation (EC) No. 726/2004

The Concept Paper Submitted for public consultation

Responses and questions from Vigilex

II.A. Pharmacovigilance system master file

QUESTIONS:

2. Location
- What is meant by the word 'operates'?. PV operations may be located in various countries in the EEA and QPPV oversees/operates in all EEA sites of relevance. Furthermore contracted QPPV may be located elsewhere and operate from a location where there is no company affiliate.

- The PSMF should be located at the site of the QPPV: what if the MAH has a contracted QPPV?

- Is an electronic PSMF accessible by the QPPV acceptable in fulfilling the requirement of 'The PSMF should be located at the site of the QPPV'?

3. Content
- (2) (a) What is meant by 'description of delegated tasks'?
  - ☐ MAH to QPPV or
  - ☐ QPPV to others
- (2) (b) What is meant by 'registrations'?

6. Delegation
- Is it correct to assume that the description of delegated activities and/or services, as well as copies of signed agreements, relates to the system relevant for and products authorised in the EEA only?

7. Audit
- Should all audits be recorded, or only those impacting products authorised in the EEA?
- The expression 'main findings' of the audits needs further clarification e.g. critical findings as defined in the EEA or what?

8. Inspection
- Does 'a copy' mean specifically a paper copy, or is a copy in an electronic format by email or CD-rom acceptable?
- Upon request of a copy, should annexes also be provided as e.g. indicated in II.B. section 11 on performance indicators?

CONSULTATION no 2
Our response: No. As the MAH is expected to keep PV Master File up to date and it is foreseen that regular changes are made, notifying CAs would be unnecessarily cumbersome for CAs and MAH alike. The PV Master File should contain the date when it was last reviewed (even if no changes were made) as this is normal document management and is already stipulated in section 5 of II. A. However, notifying changes to the PV system as they happen has been a huge administrative and financial burden on MAHs. If notifications of changes to CAs is still necessary, it should be defined what constitutes a significant change/modification (e.g. change in safety databases, outsourcing of major PV tasks) and instead of having to notify all national agencies separately for products that are not authorised under the centralised procedure, it would be desirable to just notify one central point. If the PV system master file is being used as previously the DDPS, the agencies' PV inspectorates would be the main parties to be interested in the changes, so the notifications could for example be sent to the PV inspectorate of the country where the QPPV is located and any national agencies who want to know about changes that have occurred could get request the relevant information from the EMA PV inspectorate as needed.

CONSULTATION no 3
Our response: No, as both description of the delegated activities and/or services as well as the copies of signed agreements will provide that information. It is suggested to include copies of the agreements as annexes and not in the body of the text.

CONSULTATION no 4
Our response: No. Requiring copies of an audit report will potentially negatively impact the quality of audits of the PV systems by QA. It will become extremely difficult for auditors to conduct audits truly independently and against the highest quality.
Yes: It is fine to ask for audit schedules as it provides insight as to audit approach and the number of audits conducted.

CONSULTATION no 5
No, the level of detail required AND the need to have it continuously up-to-date makes it a very resource-demanding exercise.
The DDPS was a helpful tool for both authorities and companies to obtain a quick overview of how key PV aspects were dealt with. The requirement to keep the PV Master File succinct has disappeared in the text in this Concept Paper and it threatens to become a 'paper monster' without much benefit

Specific example where the requirements lead to a huge document: It is suggested to include copies of all signed agreements. We feel that, rather than having these in the master file, a list of all agreements outlining the nature of the agreement should be included, as otherwise the document will become huge for companies who have a lot of partners. The same principle as for documented processes and procedures could be applied; i.e. that an overview which references the location is part of the master file.

II.B. Quality Systems - common obligations

QUESTIONS

10. Audit
-The requirement to audit the quality system not less frequently than every two years requires further clarification e.g.:
- Does this mean an audit of HQs every two years?
- An audit of HQs and all affiliates every two years?
- Or / and …?

- Will this also mean that the quality systems in place at the respective CAs must be audited every two years?
- An audit of the quality system is mandated not less frequently than every two years. If a company has a valid ISO-9001 certificate, including yearly audits, is that considered adequate?

II.C. Quality Systems- MAH

QUESTIONS

13. Resource Management
- Duties of managerial and supervisory staff are not defined in job descriptions in all countries (this is often culturally determined). Other means are sometimes used, such as describing them in procedures or department descriptions; would that be acceptable?
- Comment: Training records signify the initial and on-going training of staff in an adequate manner; mandating training plans is, in some organisations, an administrative activity and does not actually ensure adequate training is conducted. Training is, moreover, (and particularly in PV) required when e.g. non-compliance occurs and changes in regulations.
- Does the statement 'appropriate instructions on critical processes…. shall be provided' mean that procedures should be in place?

CONSULTATION no 6

Our response: No, compliance management, in terms of meeting requirements in time and in full, is an inherent part of every activity in PV. As such, it is suggested to minimise this section with a requirement that adequate processes and procedures must ensure compliance in terms of meeting requirements in time and full.

CONSULTATION no 7
Our response: In principle yes, but some details are over-regulated such as the need for training plans as an unnecessary burden for e.g. small organisations

II.E. Signal Detection and risk identification

QUESTIONS:

26. Signal detection audit
- Will MAHs have access to the audit trail depicting the signal detection activities of national competent authorities and EMA?
- If not, how and at what stage will MAHs be informed about the detection of signals and how validated signals have been investigated?
- How will national competent authorities, EMA and MAHs further collaborate after the identification of a signal?

CONSULTATION no 9
Our response: Work sharing is definitely efficient and a good principle. Currently, competence levels in the MSs vary and the risk exists of inconsistency in evaluations. Moreover, experience over time shows that approaches in the MSs towards MAHs vary considerably, creating inequality.
It is advised that minimally two countries, (ideally coupling less and more experienced) are evaluating. Moreover, and very important, is to ensure products in one class are dealt with in an equal way and so, by one pair.

CONSULTATION no 10
Our response: Proposed revision is sufficiently clear. We recommend, however, that at least two countries perform the evaluation and that the pairing includes less and more experienced parties. It is also very important to ensure products in one class are dealt with in an equal way and this can be achieved by using the same pairing.

Annex I – Electronic submissions of suspected adverse reactions

CONSULTATION no 14

Our response: Yes, we broadly agree.

QUESTION

This describes the narrative comments of SERIOUS ADRs. Can we conclude from this that non-serious cases can be submitted without narrative? (We would advise against this, as the narrative is a valuable section in case assessment and the case may also be upgraded along the way, so it is more efficient to have the narrative in place from the outset).

Annex II – Risk management plans

CONSULTATION no 15

Our response: The proposed format and content are difficult to follow for generic products as the MAH will not be in possession of most of the data. It would be desirable to have guidance on format and content for 'abridged' RMPs for generics.