Comments on EC Concept Paper on Implementating Measures for New Pharmacovigilance Legislation

Pharmacovigilance Master File, 3. Content

Location: where the QPPV resides is not always the place that the bulk of the PV activities are performed

Item (2) (b), p5: It is not clear what "experience and registrations relevant to Pharmacovigilance" means for the QPPV. Registrations for healthcare professionals exist but what about non-healthcare professionals as QPPVs? Examples or an explanation is required in a guidance document?)

3.1 List of authorised medicinal products will also be in the EVMPD, why do we have to provide this information twice?

Item (3), p6: It seems reasonable to have a list of contact person(s) for pharmacovigilance where a nomination at national level has been made (national responsible person), however to have to provide a description of their responsibilities in the Pharmacovigilance System Master File seems unnecessary. These may vary depending on country and should only need to be maintained at local national level.

Consultation item 1: No additional procedures should be described as they will be described in the procedural documents to be submitted with the Pharmacovigilance Master File.

Item (7) (b), p6: It is not clear what "a description of the resource management" for performance of pharmacovigilance activities is referring to.

Item (7) (e), p7: It is not clear what "audit trails" refers to in this context – does this mean audit plans and audit reports? Or perhaps documentation/records of compliance monitoring of the pharmacovigilance system?

Consultation item 2: Pharmacovigilance System Master File should contain a last review date. Significant changes to the Pharmacovigilance System Master File should ideally require a simple notification to the EMA, not all the separate competent authorities.

Also, what is meant by a significant change? Change of QPPV, yes, addition of a new SOP, probably not. But why should changes be notified? As I understand, a brief description of the pharmacovigilance system is submitted with the MAA. Significant changes to the PSMF may not impact upon the brief description

5. Documentation. Indexed – is a table of contents adequate or is a comprehensive index required?

Consultation item 3 Tthe MAH should only have to *list* third parties involved in pharmacovigilance activities and their roles, and not include copies of the actual agreements (just have access to these if required). To keep copies of up to date signed agreements within the Pharmacovigilance System Master File represents an unnecessary administrative burden. However, where pharmacovigilance activities have been out sourced, it is appropriate to describe this.

Consultation item 4: Acopy of the audit report should not be retained in the Pharmacovigilance System Master File, this should remain an internal document. It is sufficient to place a note concerning the main findings temporarily in the Pharmacovigilance System Master File until corrective actions/improvements have been put in place, as in the text on p8. It may be appropriate to require documentation of audit plans, but not detailed schedules.

Evidence that audits are and have been performed is acceptable. However, to include full audit reports or details of open corrective action plans could compromise both auditors and inspectors. Inspectors should independently assess a MAH's pharmacovigilance system, reading an auditor's report may bias the subsequent inspection.

Consultation item 5: The requirements for Pharmacovigilance System Master File are acceptable in principle, but could be difficult to maintain currency and accuracy that would enable it to be made available within seven days. Seven days is a tight deadline, and it is conceivable that an agency may ask for it even faster than that. There should therefore be a minimum period of time in which the Pharmacovigilance System Master File is provided, i.e. at least two working days

Quality systems for pharmacovigilance activities performed by MAHs, 13. Resource management

P10, first paragraph: Guidance is required on what is meant by "adequate" (theoretical and practical knowledge). Examples should be provided in a guidance document.

P10, second paragraph: How is a MAH expected to be able to show that sufficient authority "be ensured"?

Quality systems for PV activities performed by MAHs, 14. Compliance management

Item (d), p10: It is unnecessary to stipulate that MAHs shall check the EMA's medicines web-portal for updates every working day. This represents an unnecessary administrative burden. Instead, MAHs should be required to monitor the web-portal regularly and with appropriate frequency (this may depend on the number and type of product licenses the MAH has etc, and will in any case need to be justified in an Inspection). Some examples of acceptable levels of frequency could be given dependent upon the size of the organisation/number of MAs/risk category of approved actives. Furthermore, the EMA's website also need to be made easier to search and monitor for relevant updates.

Consultation item 6: The listed quality procedures are more than adequate. There is a balance between ensuring compliance and measuring things because they can be measured.

Consultation item 7: This is describing what should already be good practice. Having a defined timeframe in which to retain documents is better the currently ridiculous requirement to retain documents indefinitely.

Consultation item 8: Resource management – it is pleasing to note that the competent authorities will be required to have adequate numbers of pharmacovigilance staff. In light of the current economic problems affecting in particular the nations of southern and eastern Europe, it is hard to believe that this will occur. If it does not, what sanctions will the non-compliant agencies face? In

addition, if lack of personnel at a competent authority delays the assessment of a safety-related issue notified to the authority by the MAH, where does liability lie?

Signal detection – 21, final paragraph. Change the first sentence to "...by statistical analysis**, where appropriate,** within EudraVigilance.."

Consultation item 9: Quality systems should be in place and oversight of the PRAC should be strong enough to avoid any risks.

Consultation item 10: Guidanced is required on what will be expected of MAHs for signal management activities.

Consultation item 11 & 12: As these standards have yet to be finalised and the work on creating the some of the terminologies yet to start, this consultation item is irrelevant. Also, as the work on developing the EVMPD has already started and has to be completed by July of next year, it is highly improbable that objections to use of the ISO terminologies will be taken on board. The new EVMPD Legal notice includes reference to these standards. As this is a legal requirement, it is not clear why comments on this are being solicited.

Consultation item 13: Yes. For reporting all ADRs between July 2012 and July 2015 when the new EudraVigilance database is ready. How are we to report cases that are currently included in line listings but will not be required for the new PSUR format?

Pharmacovigilance System Master File – why should we have to wait until renewal or submit a variation to move from a DDPS to a Pharmacovigilance System Master File? Submitting variations will result in significant costs to MAHs and unnecessary administration for the competent authorities. The EVMPD will include the link between an authorised product and the Pharmacovigilance System Master File.

Consultation item 14: Submitting copies of clinical papers, plus translations if required, may incur significant costs to MAHs.

Consultation item 15: This infers that the full risk management plan will be made public, but previous guidance suggests that only a summary would be public. It is not possible to comment on the format and content of the risk management plan as all that we have been given is a list of section headings. For a marketing authorisation application for genericised or well established active, will a risk management plan now be required or can a waiver statement be submitted?

Consultation item 16: It is not possible to comment on the format and content of the PSUR as all that we have been given is a list of section headings.

Consultation item 17: No comments