TOPIC	PAGE	SECTION	COMMENT
A. Pharmacovigilance system master file	*5*	***3. Content*** ***(1)*** **A list of medicinal products relevant to the pharmacovigilance system master file including the name of the medicinal product, international non-proprietary name (INN) of active substance(s), procedure under which the product have been authorised, authorisation number, Member State(s) in which the authorisation is valid including information on whether the medicinal product has been actually placed on the market.**	The list of medicinal products is considered also worthwhile to be included in this document taking into account the high level of variability of DCP/MRP evaluation and this information should be updated very frequently in this document. The most updated list of products should be available under request. The aim of this document, as stated later, not to be linked to the regulatory status.
	7	***Consultation item no. 2: The aim of the pharmacovigilance master file is two-fold: to concentrate information in one global document and to facilitate maintenance by uncoupling it from the marketing authorisation. Therefore changes to the content of the master file will be no longer subject to variation obligations. Would it be nevertheless appropriate to require the marketing authorisation holder to notify significant changes/modifications to the master file to the competent authorities in order to facilitate supervision tasks? If so, how should this be done? Should the master file contain a date when it was last reviewed?***	Taking into account the content of this document it is then appropriate not to be submitted to variation obligations. Our proposal is the following: Treat the master file as a SOP: Any minor change will be included in an annex signed by responsible person/s of the change, as a SOP history tracking changes, and the significant changes will produce a new version. All versions will be kept in the MAH and they can be required by the competent authorities under request. For this, it would be necessary to define significant changes/modifications (as change of Qualified Person for Pharmacovigilance and/or its back-up, etc).

TOPIC	PAGE	SECTION	COMMENT
	8	***6.Delegation*** ***In those cases the pharmacovigilance system master file shall contain a description of the delegated activities and/or service provisions relating to the fulfilment of pharmacovigilance obligation, indicating the parties involved, roles undertaken and concerned product(s) and*** ***territory(ies). Copies of the signed agreements shall be included in the master file.***	Copies of the signed agreements should be filed a part from the PMF, due to many safety agreements are annexed to license agreements where confidential information about business/marketing of MAH is included. We consider more appropriate to provide the competent authorities with a list of the co-marketing/license agreements between partners, and provide any of them under request. Additionally, the safety agreements are updated frequently; therefore it would difficult and low operating to handle all this information in the same document.
	8	***7. Audit*** ***Immediately after an audit report has been received that requires corrective or preventive action, the MAH shall lace a note concerning the main findings of the audit on the PMF. That note may be removed once the corrective and preventive actions have been fully implemented, which is taken to mean that correction and/or sufficient improvement can be demonstrated or has been verified.***	This information is included in the audit reports which are already available for the Competent Authorities. The corrective and preventive actions are also included in the company audit reports and there is a deadline to resolve them. Our proposal is to include a statement signed by the Quality Assurance responsible in which is set forth that the audit report is available.
	8	***Consultation item no. 4: Should a copy of the audit report be retained in the master file?*** ***Would it be appropriate to require documentation of audit schedules?***	Why the main findings should be included on the pharmacovigilance master file if the competent authorities will have access to the company audit reports? The companies can show the audit plan but the audit report should be shown under request. Additionally, if we have to include this information and the PMF has to be shared with licensors, sensible and confidential information for the company will be showed to them.

TOPIC	PAGE	SECTION	COMMENT
	8	***8. Inspection*** ***The markeging authorization holder shall submit the copy at the latest seven days after receipt of the request at its own expenses.***	Taking into account that some updates in a pharmacovigilance master file can involve exchange of information between different affiliates and companies of the group, and it could be also in vacation period, we think that seven days is a period of time too short. Please, consider to extend the period to 30 working days.
C. Quality systems for the perfomance of pharmacovigilance activities by mah	*10*	***13. Resource management*** ***Appropriate instructions on critical processes, including business continuity, shall be provided.***	Please, clarify this sentence. Do you mean a contingency plan?
	10	***14. Compliance management*** ***(d) ensure that the product information is kept up to date with the current scientific knowledge, including the conclusions of the assessment and recommendations made public by means of the European medicines web-portal. To this end, the marketing authorisation holder shall check the European medicines web-portal for any relevant updates, including consultations and notifications of procedures, on each working day.***	Instead of checking the web-portal every day, could it be possible to subscribe us to any alert list provided by EMA? Nowadays, there are many agencies that have this alert system.
	11	***Consultation item no. 6: ; in relation to processes for taking corrective and improvement actions or in relation to the detection of duplicates of suspected adverse reaction reports in the Eudravigilance database?***	Any MAH has internal procedures to avoid duplicate cases during the data entry of any new case. Should not it be enough? We do not know how to detect duplicates through Eudravigilance database because we will not have access to all the cases (for example, from other partners).

TOPIC	PAGE	SECTION	COMMENT
	11	***15. Record management*** ***Pharmacovigilance system-related documents shall be retained as long as the system as described in the pharmacovigilance master file exists and for a further 10 years after it has ceased to exist. Product-related documents shall be retained as long as the marketing authorisation exists and for further at least 30 years after the marketing authorisation has ceased to exist.***	It is difficult to guarantee that the MAH keeps the documentation for 30 years when this MAH ceases its activity. Apart from that, we consider that the safety information about product has been sent to competent authorities during the product life cycle.
	14	***22. Methodology*** ***The Pharmacovigilance Risk Assessment Committee shall perform a regular review of the methodology to be used and publish recommendations, if appropriate.***	Please, publish recommendations about signal detection, above all for companies who has small databases in order to unify the criteria between MAH. Please, provide a common method.
Annex I. Electronic submissions of suspected adverse reactions	*19*	***4*** ***(n) Reason for nullification or amendment for nullification and amendment reports***	We would like to know how we can specify that the case is an amendment report.
Annex III – Electronic PSUR	*24*	***7. Unless otherwise specified in the list of union reference dates and frequency of submission two options are foreseen for products containing the same combination of active substances. The MAH shall either submit stand-alone PSUR for the combination of active substances with cross-reference to the single-substance PSUR(s), authorised to the same MAH or provide the combination data within one of the single active substance PSURs.***	Do you mean that in case we have a combination of hydrochlorothiazide and valsartan and another product with valsartan, we can submit a PSUR of the combination alone with a cross-reference to the single substance, or the combination data inside the PSUR of single substance? Please, clarify.
	25	***11. Literature***	Please, clarify if this section is with regard to the studies or case reports.

TOPIC	PAGE	SECTION	COMMENT
	26	***20. Region-specific information*** ***21.Appendices to the PSUR***	What information is contained in these sections? Line-listing and Summary tabulations?
	26	***Consultation item no.16: Do you agree the proposed format and content? Please comment.***	In general, we think that the new proposal for PSUR is fine for brand products, but not for generics. Will be the same content and format for generic and brand products? Additionally, we do not find a correlation between the information that we provide in the current section, Overall Safety Evaluation (like interactions, overdose and special patient groups) in this proposed format and content. What section of the PSUR should deal with this information?

GENERAL COMMENTS

As general comment, we think that the scope and content of the implementing measures are more focused on brand products than generic products, especially, with regard to the format and content of the PSUR.