TOPIC	PAGE	SECTION	COMMENT AEFI
A. Pharmacovigilance system master file	*5*	***1. Definition*** ***The pharmacovigilance system master file contains a detailed description of the Pharmacovigilance system used by the marketing authoristation holder with respect to one or more authorised medicinal products***	How should be this document submitted? Contained in registration dossier and superseding DDPS? Please clarify.
	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 most updated list of products should be available under request. The aim of the pharmacovigilance master file, as stated later, is to facilitate maintenance by uncoupling it form marketing authorization. The list of medicinal products has a high level of variability and this information should be updated very frequently in this document.
	6	***3. Content*** **(7) (d) Documentation arrangement and the location of any records in relation to pharmacovigilance activities**	Due to confidentiality issues, we understand that this requirement may be covered presenting a table of delegated activities.

TOPIC	PAGE	SECTION	COMMENT AEFI
	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. We have a proposal: 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 an historial SOP, 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).
	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 prefer to provide the competent authorities with a list of the co-marketing/license agreements between partners, and provide any of them on demand. Additional, the safety agreements are continuously updated; 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. hat 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***	This information is included in the audit reports which are already available for the Competent Authorities. The corrective and preventive actions are included too in the company audit reports and there is a deadline to resolve them. Hence, MAHs consider that this activity is not feasible for us. It shall suppose huge volume of daily work focused only on PVMF updating.

TOPIC	PAGE	SECTION	COMMENT AEFI
		has been verified.	
	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?
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).
	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***	It is not possible 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

TOPIC	PAGE	SECTION	COMMENT AEFI
		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.	during the product life cycle.
E. Signal detection and risk identification	*14*	***21.Changed risks/ new risks Following consultation of the Pharmacovigilance Risk Assessment Committee EMA may publish a list of medical events that have to be taken into account for the detection of a signal.***	How will it be this? Is it going to be similar to the IME list?
	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 have small databases in order to unify the criteria between MAH. There are guidelines on the use of statistical signal detection methods in Eudravigilance, and quantitative methods of signal detection have been designed for large spontaneous reporting system databases. Please provide guidelines on how signals will be validated.
Annex III – Electronic PSUR	*24*	***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.***	Please, clarify this sentence.
	26	***Region-specific information/Appendices to the PSUR***	What information do it contain these sections? Line-listing and Summary tabulations?