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Comments on:

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

Concept paper submitted for public consultation

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Abbreviations	
CAPA	Corrective Action Preventive Action
DSUR	Development Safety Update Report
EEA	European Economic Area
EMA	European Medicines Agency
EU	European Union
MA	Marketing Authorisation
MAH	Marketing Authorisation Holder
MS	Member State
PSMF	Pharmacovigilance System Master File
PSUR	Periodic Safety Update Report
QPPV	Qualified person responsible for pharmacovigilance
RMP	Risk Management Plan

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II.A.3.(6)	6	Consultation Item no. 1	Additional process that should be covered is the process concerning company internal communication that ensures all relevant information is received by the pharmacovigilance department	This process applies to both communication between company departments (department to department communication) and communication between contractors (contractor to company communication). This coordination process facilitates the role of the EEA QPPV in order to successfully complete his/hers role and provides him/her with sufficient authority as to coordinate all global pharmacovigilance activities.
II.A.4.	7	Consultation Item no. 2	– It would not be appropriate to require the MAH to notify significant changes/modifications to the PSMF to the competent authorities.	– We consider notification of significant changes/modifications to the PSMF to the competent authorities to be confusing unless significant changes/modifications are defined accordingly. However this would necessitate more complex guidelines and would lead to onerous procedures. Therefore we propose to avoid this by abolishing such a requirement. According to 2010/84/EU, paragraph (7): ”[….] Applications for marketing authorisations should therefore be accompanied by a brief description of the corresponding pharmacovigilance system, which should include a reference to the location where the pharmacovigilance system master file for the medicinal product concerned is kept and available for inspection by the competent authorities.”

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				We propose the brief description of the PSMF to be submitted not in connection, or not only with connection to a MA application, but to competent authorities' pharmacovigilance departments (for example as it is already required for submission of EEA QPPV's appointment procedure). Thereafter changes to the brief description of the PSMF may be notified only to the competent authorities' pharmacovigilance departments.
			– The PSMF must be version controlled (including date of last review).	The PSMF should be version controlled. According to II.A.5. the master file shall contain a logbook recording any alteration. However, in a global perspective where high number and rate of changes would be taking place, this might prove to be a burdensome and time-consuming procedure. We propose all product lists, training records, contact details, CVs, list of SOPs to be appended to the PSMF. Any amendments to the Appendices shall not lead to different versions of the PSMF.
II.A.6.	8	Consultation Item no. 3	No.	

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II.A.7.	8	Consultation Item no. 4	– As long as specific CAPAs are pending, a copy of the audit report should be annexed to the PSMF. When all CAPAs are completed / implemented, the audit report may be retrieved from the PSMF. – Documentation of audit schedules is not considered appropriate to be annexed to the PSMF.	MAHs shall have audit reports and audit schedules available upon request but only audit reports with pending CAPAs are considered relevant to be retained to the PSMF. Replacing the audit report with a note describing the CAPAs to be implemented should be optional.
II.A.	8	Consultation Item no. 5	We overall agree with this appraisal.	Notification to the authorities concerning every change to the PSMF should be avoided, as it would lead to onerous procedures and a high number of regulatory submissions. Local diversities (i.e. in different MSs) and their impact to the working load of MAHs and competent authorities should also be taken under consideration. In Greece, for example, the number of the MA for each product is changing with every variation/renewal. As a result potential PSMF requirements concerning MA number (e.g. need for updating PSMF version with new MA numbers) would be confusing and superfluous.

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II.C.13.	10			We propose training records and training plans of company's employees involved in PV activities (but who are not members of the PV department) to be kept and be readily available for audit or inspection and only training records of the global PV department staff to be retained in the PSMF.
II.C.14.	10-11			To our understanding, paragraph *14. Compliance management* overall, seems to address compliance management in a rather austere way. We think that procedures and processes shall be in place in order to effectively cope with pharmacovigilance obligations; however 100% compliance is not always feasible to be demonstrated.
II.C.14.	10-11	Consultation Item no. 6	No.	
II.C.	11	Consultation Item no. 7	We agree.	We would like to underline the fact that the requirements described for the quality system for the performance of pharmacovigilance activities demand a considerable budget, robustly staffed pharmacovigilance departments and a proper planning of pharmacovigilance activities. This may not be always feasible and – more importantly - scientifically relevant for small companies handling a small volume of safety data.
II.D.	13	Consultation Item no. 8	We agree.	Quality system requirements for national authorities and EMA are less detailed than those described for MAHs (II.C. versus II.D.). We recommend more detailed requirements to be included in the upcoming Good Pharmacovigilance Practices for national authorities and the EMA.

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II.E.22.	14			Common methodology for signal detection and risk identification can be useful since the assessments sent out by the EMA, the competent authorities or the MAHs should not be disputed amongst them. However, the common methodology should be diversified according to the volume of safety data, in order to effectively address the needs and support competence of micro, small and medium-sized companies where the volume of data does not permit statistical methods of signal detection.
II.E.24.	15	Consultation Item no. 9	– We propose a lead MS to be appointed as described in II.E.24. for the monitoring of EudraVigilance data. This MS should be different than the lead MS for the assessment of PSURs for the same active substance – We consider that “work sharing” should also be applied to centrally approved products and a lead MS shall be appointed in addition to EMA.	– Benefits of parallel monitoring may indeed be lost by cumulating all tasks in one MS. Nevertheless, a “work sharing” procedure is more efficient. We therefore propose a lead MS to be appointed for the monitoring of data within EudraVigilance and additionally, another MS to be appointed as lead MS for the assessment of PSURs for the same active substance / product. Workload distributions amongst the MSs should follow MS dynamics (e.g. population). – We consider the above mentioned rationale to be valid also for centrally approved products and therefore a lead MS shall be appointed in addition to EMA for the monitoring of EudraVigilance data.

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II.E.26.	15	Consultation Item no. 10	As commented in II.E.22. a common methodology with differential gradations should be established, depending on the volume of data and other factors which influence the choice for the “right” method for signal detection.	
II.F.27.	16	Consultation Item no. 11	We agree.	We would like to underline the fact that all terminologies should be available through the EudraVigilance WebTrader environment and all ISO and European Pharmacopoeia Commission terminology should be accessible to MAHs free of user fees. We propose also that use of MedDRA via the EudraVigilance WebTrader environment should be free of user fees. Adverse reaction reporting is of utmost significance and micro, small and medium sized enterprises should be facilitated to apply procedures at the minimum cost.
II.F.28.	18	Consultation Item no. 12	We agree.	
II.G.	18	Consultation Item no. 13	No additional provisions are deemed necessary.	

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Annex I.1.1.(a)	19			We propose the definition of “misuse” to be changed as not to include the word “intentionally” since we consider there is no reason to distinct intentional from unintentional misuse.
Annex I.1.1.(d)	19			Occupational exposure, as defined in (d), fails to include all cases of exposure by accident. Therefore, we propose the term “occupational” to be changed to “accidental” exposure to include e.g. cases of children exposure through contact (with an adult) to products applied to the skin.
Annex I.3.3.	20			Use of pseudonyms for the patient’s identification may be misleading. Therefore, we propose use of the word “privacy” to replace Personally Identifiable Information.
Annex I.3.4.(g)	20-21			As already stated in the response for consultation item no. 5, please be informed that in Greece there is no a single MA number that follows product’s life-cycle but the MA number changes at every MA variation and every MA renewal. Therefore, it is difficult and confusing to identify products that are authorized in Greece by the MA number. For the same reason, MA number should not be a mandatory field for identification of a product through the electronic reporting procedure.

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Annex I.3.4.(o)	21			Case narrative is a comprehensive summary of the case and at present it could be reported in an official language other than English. Information included in narratives is a synopsis presented with brevity and accuracy. An English summary of the narrative would be practically inefficient to adequately capture provided information, unless it is a narrative translation. We do not consider "summary of narrative" to be scientifically appropriate, as information that may be significant for the assessment of the case could be omitted. Therefore, it should be decided whether to accept the narrative in any official EU language or only in English. We propose narratives to continue to be accepted in all EU official EU languages and if requested by the authorities for a specific case, an English translation should be timely prepared by the MAH.
Annex I	21	Consultation Item no. 14	In view of the above remarks for Annex I, we agree with the proposed format and content.	
Annex II	23	Consultation Item no. 15	We agree with the proposed format and content.	On the last paragraph of Annex II, *1.2. Format of the Risk Management Plan* it is stated that: "[…] the RMP shall be submitted electronically and in an electronic format specified by EMA and national competent authorities and published on their websites". This sentence is confusing on whether different formats of RMP may be published by EMA and the competent authorities. It should be made clear that the RMP format will be one and unique.

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Annex III	26	Consultation Item no. 16	We agree with the proposed format and content.	
Annex IV	34	Consultation Item no. 17	We agree with the proposed format and content.	

Thank you for providing us with the opportunity to review and comment on the concept paper.