25 May 2018
EMA/CVMP/PhVWP/519126/2017
Committee for Medicinal Products for Veterinary Use (CVMP)

Overview of comments received on 'Revised recommendation for the basic surveillance of EudraVigilance Veterinary (EVVet) data for centrally authorised products (CAPs)' (EMA/CVMP/PhVWP/171122/2016)

Interested parties (organisations or individuals) that commented on the draft document as released for consultation.

Stakeholder no.	Name of organisation or individual
1	AnimalHealthEurope (formerly known as International Federation for Animal Health Europe)

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1. General comments – overview

Stakeholder no. (See cover page)	General comment	Outcome
1	IFAH-Europe welcomes the opportunity to comment on this draft and fully supports the need for the revision of the 2006 Recommendation paper. We appreciate the reference to the issues raised by industry in the consultation on the concept paper, and the recognition of the desire expressed by industry to be involved in signal detection at an earlier time point (line 153). We also appreciate the pilot phase approach and the willingness, as expressed in line 25, to address the increasing administrative burden associated with PSUR preparation. It is in relation to the latter that IFAH-Europe would like to make a profound suggestion to CVMP/PhVWP, that it should develop, in cooperation with IFAH-Europe experts, a more in-depth understanding of the impact of proposals for pharmacovigilance systems to the administrative burden of marketing authorisation holders (MAHs). Perhaps via a more in-depth or prior consultation to collect data for an impact assessment. This increased mutual understanding is essential to avoid situations of where the CVMP/PhVWP believes it is proposing reductions in administrative burden, while the MAHs believe that the completely opposite situation will occur. In this current document we believe that the measures proposed do not represent a significant simplification of PSURs for the MAH, because by adding differences into production of reports between products (CAPs vs non-CAPs), if the MAH takes this approach it actually adds administrative burden.	The issues related to additional work for the marketing authorisation holders (MAHs) are understood. However, as highlighted in the recommendation due to the absence of a fully populated product database, the scope of this document was limited to centrally authorised products (CAPs) only and therefore from the outset it was acknowledged that a single approach would not be possible for all products. Notwithstanding this, a number of MAHs agreed to participate in the pilot exercise and their contributions and experiences have provided valuable insight for improvement of the recommendation and methods outlined in the document. Although the recommendation stated that this would be voluntary for those MAHs who wish to apply the approach, this aspect has been reiterated in the document for clarity. Concerning the simplified PSUR, it should also be noted that the structure of the simplified PSUR followed proposals previously expressed at meetings/workshops held with stakeholders, namely waiving the need for provision of the electronic line listing and summary of product characteristics provided non-expedited reports were submitted to EudraVigilance Veterinary (EVVet) via a single point of entry/mode. However on the basis of the consultation comments received and feedback from both MAHs and regulators taking part in the pilot, the structure for a PSUR

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	We would like to highlight the following points that we feel are critically important: To minimise increases in administrative burden it should be confirmed that the Recommendation is VOLUNTARY for MAHs, as implied in lines 175-176 Make the simplified PSUR meaningful (please find more details in the specific comments below lines 114-120). IFAH-Europe would like to stress that an interim transition period until the future legislation comes into operation, where two systems would run in parallel i.e. maintaining simplified/risk-based/synchronised PSURs until the signal management process is established, should be avoided as the animal health industry does not have the resources to run two systems. This would be in addition a major failing in one of the stated objectives of the review of the legislation. As this document demonstrates, it will be very important to move as soon as possible to a single more efficient system based on just signal management processes. A second general point concerns the absence of an assessment of the quality of the current data situation in EVVet, although the potential existence of poor quality data is mentioned in lines 188-9. Furthermore, there is no estimation of the consequences of an increased number of reports for the signal detection activities. When it is acknowledged that statistical results are more reliable if based on a significant quantity of data (line 188), the quality expected from additional data on non-serious AEs or AEs collected in third countries	submitted in accordance with this recommendation has been further reduced. Quality of the database is important. A good system and good education are necessary to ensure a good quality of data. The implementation of the revised recommendation will imply the transmission of non-serious cases into EVVet for CAPs. This is not expected to increase the proportion of poor quality cases into EVVet. It is the responsibility of all stakeholders to check the quality of the data and to gather as much information as possible before electronic submission, and this applies to all cases regardless of the region of occurrence, seriousness, expedited nature. Ensuring a high quality standard of information is always important and it is independent of the number of cases that are reported to EVVet. In future, it is possible that MAHs would submit all adverse events received for all types of products regardless of authorisation rout, and not only for CAPs.

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	is not discussed. Poor data quality will simply raise the background noise without providing added values to the process. Although not the main focus of this guidance, the quality of the data collected and entered in EVVet is key for a future improvement of the signal detection process and deserves discussion e.g. data collection processes, including follow-up practice of MAHs and NCAs.	

2. Specific comments on text

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
19-27	1	**Comment:** Line 23-24 refers to implementation for CAPs – what is the timeframe/legal basis? i.e. can this be enforced as mandatory prior to the revision of legislation? And what would be the timeframe for including other procedures? Considering that line 66 says 'within current legislative framework' this pilot should be voluntary on agreement between EMA and individual MAHs. Lines 25 – 26 mentions that proposals are made to minimise the admin burden for MAHs, however any approach which handles different products (CAPs, others) or timeframes or different routes of transfer of adverse events data creates multiple approaches and complexity in MAHs systems – this substantially increases administrative burden. To treat some individual CAPs differently will require appropriate modification and validation of MAH PhV databases on an ongoing basis as individual CAPs enter the pilot. **Proposed change:** Please modify lines 25 to 27 to read: "However it is accepted that this proposal will significantly increase the administrative burden for MAH and it should therefore be initiated on a voluntary basis with the agreement of individual MAHs. The revised recommendation will be trialled in a pilot phase	The implementation for CAPS is not mandatory under the current legislation. Both the pilot and the recommendation were envisaged to be voluntary for MAHs. The timeframe for including other procedures cannot be envisaged at this stage. Proposed change partly accepted. The suggested sentence can be added to the introduction, where it fits better, but with some modification of the text to read as follows: "The recommendation and the principles described will be implemented on a voluntary basis with the agreement of individual MAHs, particularly as it is accepted that this proposal may increase the administrative burden for some MAHs".

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		with the agreement of individual MAHs before full implementation".	
45	1	**Comment:** IFAH-Europe very much welcome exchanges with the MAH	Comment noted.
55	1	**Comment:** The PSUR proposed is recognised as being non-compliant however non-compliance such as not including a blank line listing template in a PSUR with no cases can be a reason for rejection of a PSUR by some NCAs. **Proposed change:** Please make sure that all NCAs are completely aligned with this approach.	Partly accepted. When adopting this recommendation, representatives of the NCAs accept receipt of simplified PSURs which are not fully compliant with Volume 9B, therefore no rejection of a simplified PSUR should occur, as long as the simplified PSUR is in line with the content described in the recommendation and it is clearly identified as a simplified PSUR submitted in accordance with this recommendation.
59	1	**Comment:** While it is recognized that the DWH queries in EVVet will only be used by regulators, the MAH will need to – initially - perform the in-depth analysis (see line 156). Therefore, the MAH is indirectly affected and thus should be engaged in discussion on what the appropriate queries are for the investigation of certain signals since there are several "reasonable" ways to approach them. **Proposal:** Please add a sentence in line 59 after "The analysis of data in EVVet by means of DWH queries is intended solely for regulators." E.g. "A description of the queries and of the statistical methods applied will be shared with MAHs prior to use, so that the MAHs will have the opportunity to provide comments and run similar queries in their own database."	Partly accepted. "When requested by MAHs, a copy of the output of the surveillance findings, if necessary also including description of the queries and statistical methods applied can be provided" is added to the text in the recommendation.

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61	1	**Comment:** The pilot is due to commence before end of consultation. **Proposed change:** Please clarify what is the rationale and objectives for these timelines.	As detailed in the consultation document, the pilot was foreseen to take place in parallel to the public consultation to make optimal use of time and to avoid prolonging the development of this revised recommendation. The comments gathered during the consultation as well as the feedback from the pilot were intended to be used to improve the recommendation.
101 -111	1	**Comment:** Please confirm that redirection of non-serious EU/EEA AEs to NCAs is automatic and do not need any additional action for MAH. Indeed, there is already disharmonisation of e-reporting at NCA level e.g. two NCAs require third country serious reports, one NCA has recently requested that individual cases are sent rather than batches of cases (note: if non-serious cases are included this could be a significant burden to accommodate the request of this NCA. One NCA does not accept e-reports. Harmonisation of the above with standard procedures should be undertaken before any further changes are made to the scope of e-reporting. **Proposed change:** To simplify and decrease admin burden at MAH, a single and unique reporting route to EV VET should be applicable for ALL types of reports	It is confirmed that redirection of reports submitted to EVVet is automatic. N.B. However for a limited number of Member States, due to specific national requirements MAHs still need to submit some adverse events directly to the NCA. Proposed change not accepted. Reporting of ALL types of reports to EVVet would be ideal, but as discussed above this is constrained by specific national requirements and the proposed approach is still voluntary and both MAHs and NCAs have to agree.
117	1	**Comment:** A LL is generally created during the development of a PSUR to enable cases to be sorted, statistics to be developed and the narrative to be	Partially accepted. It is recognised that there may be some discrepancies between the lists of cases in the two systems (EVVet and

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		written. Therefore there is NO reduction in administrative burden. Unless all NCAs send all non-serious AEs to MAHs and to EVVet, there is a risk that the LL in EVVet will have more/different cases than the MAH's database.	MAH's) for different reasons. The pilot provided the opportunity to identify possible shortcomings/solutions on this level and how this may impact on the overall analysis, if at all. In addition, it should be clarified that the proposal to waive the requirement for the PSUR LL was to address the desires previously expressed by stakeholders.
114-120	1	**Comment**: As discussed above these proposals do not actually simplify PSUR creation to any meaningful extent. A much more radical proposal needs to be developed to reduce MAH administrative burden and make this attractive to MAHs. **Proposed change:** E.g. the simplified PSUR should consist of sales data, results of literature searching and MAH results of signal detection / conclusions only.	Partially accepted. AnimalHealthEurope's proposed change was considered, together with the feedback received from MAHs and regulators participating in the pilot. The simplified PSUR structure for use with this recommendation has been further reduced in the revised recommendation. The simplified structure to be presented in accordance with the revised recommendation now comprises sales data (exposure/incidence estimates) and a thorough critical discussion justifying the benefit-risk balance of the product and supporting the conclusions and any actions recommended. It should be highlighted that the MAH needs to take the main responsibility for assessing the safety of the product even in the future which should form the basis of their thorough critical benefit-risk evaluation.
127	1	**Comment**: The type of products/situations described for submission of a simplified PSUR seem to be the least likely to have a signal.	Not accepted. Unnecessary. The voluntary status is already stated from the outset and emphasised in the executive summary and

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		Proposed change: Please add new bullet point: "- Agreement of MAH to participate in program."	introduction, for example.
137/139	1	**Comment:** 'Non-urgent safety issue' is not otherwise defined. MAHs are aware of situations where NCAs consider a single case a non-urgent safety issue – hence, the logic seems that with an individual case a full PSUR may be required; does this notification of a 'non serious issue is identified' apply to all MAHs or only to those 'participating' in the pilot? **Proposed change:** Please clarify.	The comment is noted and upon further reflection the text has been revised to further simplify the PSUR requirements (i.e. only a single simplified PSUR structure) and reference to a 'non-urgent safety issue' has now been excluded from the recommendation.
142	1	**Comment:** Submission of a PSUR within 30 days could be a major challenge for a large PSUR – this should not become a default timeline. **Proposed change**: Please modify line 142 to clarify.	Partly accepted. A targeted PSUR would be necessary only if urgent safety issues are identified. In such a case, the procedure needs to be speeded up and, in accordance with the current legislation may need to be provided "immediately upon request". However, the following wording has been introduced for clarity: "unless another time-frame has been requested".
151	1	**Comment:** Because of the significant increase in administrative burden this proposal must be voluntary for MAHs **Proposed change:** Please add new bullet point: "– MAH has agreed to be part of the pilot."	Not accepted. Unnecessary. The voluntary status is already stated from the outset and emphasised in the introduction, for example.
157	1	**Comment:** as the MAH does not have access to the same dataset as the regulators it is unclear how the in-depth analysis can occur; this is particularly relevant	Accepted. The text in the recommendation has been updated for improved clarity. This is only going to be requested from

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		where regulators should be accessing all data relative to an active ingredient rather than only to one MAH's product(s). Transferring workload of regulators to MAHs is unlikely to be seen as strong motivation for MAHs to participate. **Proposed change**: Please clarify that this is only going to be requested from MAHs who volunteer for the pilot.	MAHs who volunteer for the pilot at this time.
176	1	**Comment**: Please confirm that MAHs can decline to participate in the pilot.	Confirmed. MAHs can decline to participate in the pilot.