Overview of comments received
on Volume 9B Revision October 2009

of The Rules Governing Medicinal Products in the European Union

- Guidelines on Pharmacovigilance for Medicinal Products for Veterinary Use -

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

Stakeholder no.	Name of organisation or individual
1	International Federation for Animal Health Europe (IFAH-Europe)
2	Agence Française de Sécurité Sanitaire des Aliments (AFSSA)
3	Agence Fédérale des Médicaments et des Produits de Santé (AFMPS)
4	European Group for Generic Veterinary Products (EGGVP)
5	PHARMAQ

1.1. General comments – overview

Stakeholder no.	General comment (if any)	Outcome (if applicable)
1	**Date of entry into force of Volume 9B** Marketing authorisation holders will need to update their internal procedures according to the final Volume 9B and will only be able to complete this exercise once the document is finally published. This must be taken into consideration by introducing a minimum 6 months transition period from the date of publication of the document to the one of its entry into force.	*The Agency would recommend to the Commission services a 6 month transition phase for entry into force.*
1	**Periodic Safety Update Reports (PSURs)** The section on PSUR introduces many additional constraints with regards to e.g. presentation of the data, incidence rates calculation, with no obvious added value to the evaluation of the safety profile of the product. Also such information cannot always be automatically generated by companies' systems and having to produce these manually only increases the risk of errors and delays in providing unnecessary information. Secondly, draft Volume 9B lacks flexibility with regard to the reduced frequency of PSURs for well established products; this further goes against the concept of PSUR synchronisation that is also referred to in the document. Therefore, a more pragmatic approach focused on the safety evaluation would be welcomed. The June 2009 HMAv Reflection Paper further acknowledges the need 'to provide adequate and simple surveillance' and this should already be reflected in Volume 9B.	*Please see relevant section (Part I.6) for response on this concern.*
4	**Periodic Safety Update Reports (PSURs)** As a general comment we would like to express our concern for the growing administrative burden related to the PSURs. In principle, we do favour the pharmacovigilance system over the old renewal system. It is a good thing to have information on serious (unknown) adverse reactions available as soon as possible. However, it seems that the transition from a PSUR based system towards a database based system (electronic reporting) is leading to duplication of the administrative burden. From a 5 yearly renewal we changed to a 3 year PSUR and now towards a continuous electronic reporting. In some countries not only serious adverse reactions must be reported electronically but also the non-serious events and	*Please see relevant section (Part I.6) for response on this concern.*

Stakeholder no.	General comment (if any)	Outcome (if applicable)
	eventually all events must be included in the PSUR as well without the possibility for applicants to use the EMEA database to prepare the listings. When all events are already reported electronically, it is not clear what the use of the periodic PSUR still is. A choice should be made between a periodic PSUR system with only serious unknown events reported electronically within 2 weeks (as this is new information) or a continuous system were a database is kept up to date on all adverse reactions, but then no requirement for a periodic reporting should exist. In addition it is very important that all memberstates do follow the same system. Even though the text of volume 9B cannot overrule the legal texts, it is important to limit the administrative requirements as much as possible as the costs for defending old products are a real concern within the industry.	
5	All in all, this Volume 9 B is a great improvement to the old Volume 9. It appears clearer and more specific in areas which may have been unclear before	*The comment is much appreciated.*

1.2. Specific comments on text

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
555/1.2	5	**Draft Volume 9B v 3.1:** National legislation in some MS requires a nominated individual in that country who has specific legal obligations in respect of pharmacovigilance at a national level. **Comments:** "National legislation in some MS requires a nominated individual in that country who has specific legal obligations in respect of pharmacovigilance at a national level" **Proposed change (if any):** It would be very helpful if a list of countries with such national legislation could be included in an annex.	*Not accepted. It appears that the maintenance of such a list would need frequent updating due to changes in national legislation and therefore be at risk of being frequently outdated.*
555 - 558	1	**Draft Volume 9B v 3.1:** National legislation in some MS requires a nominated individual in that country who has specific legal obligations in respect of pharmacovigilance at a national level. One such individual may also act as the QPPV for the whole EEA. Alternatively, the QPPV for the EEA may be a separate person, additional to requirements under the relevant national regulations. **Comments:** Volume 9B should not promote such national obligation. **Proposed change (if any):** Please delete the section: "~~National legislation in some MSs requires a nominated individual in that country who has specific legal obligations ... to requirements under the relevant national regulations~~."	*Not accepted. This is to be considered a clarification of the situation set by national legislation, which cannot be overruled by Volume 9B, and is intended as guidance to MAHs.*

[1] Line numbers refer to draft Volume 9B of the Rules Governing Medicinal Products in the European Union. Version 3.1 – consultation http://ec.europa.eu/health/files/pharmacos/news/volume_9b_master_draft_v3.1_en.pdf

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
559/ 1.2	4	**Draft Volume 9B v 3.1:** The QPPV should be appropriately qualified, with documented experience in all aspects **Comments:** What does "appropriately qualified" mean and what is meant by "documented experience in all aspects"? **Proposed change (if any):** [None]	*Question noted. To be appropriately qualified, the QPPV needs to have sufficient training and experience and an appropriate background to be able to execute the actions and responsibilities described in legislation for establishing and maintaining a functioning pharmacovigilance system. Since the systems vary between MAHs due to e.g. the size of the company, different numbers of products and authorisations, the qualifications can vary. Documented evidence indicates that above mentioned elements such as training, work and other experience, and the educational background must be documented by traceable documentation e.g. certificates, diplomas or other records.*
612 - 613	1	**Draft Volume 9B v 3.1:** The QPPV should also act as the MAHs contact point for pharmacovigilance inspections or should be made aware by the MAH of any inspection and be available at inspection. **Comments:** We welcome involvement of the EU QPPV only it should be stated that inspections and outcome should be in English for the QPPV participation to be of relevance. **Proposed change (if any):** Please amend as follows: "... or should be made aware by the MAH of any inspection and be available at inspection, <u>if necessary</u>. <u>In such cases, the inspection should be carried out in English and the inspection report be written in English</u>.	*Partly accepted. Concerning the availability of the QPPV, the QPPV should be aware and be contactable during any inspection. Ideally, the QPPV should be present. Concerning use of language, this is specified in other procedural guidance. The following change is made to draft Volume 9B.* "The QPPV should also act as the MAHs contact point for pharmacovigilance inspections or should be made aware by the MAH of any inspection and be <u>contactable, and ideally be</u> available ~~at~~ <u>during</u> inspection.
705 onwards 2.3	1	**Draft Volume 9B v 3.1: 2.3** Detailed description of the pharmacovigilance system **Comments:** Experience with the DDPS to date has demonstrated that such document creates more administrative burden on industry and competent authorities than it brings any added value to the marketing authorisation dossier. There is now a strong will from industry and competent authorities to move	Not accepted. While the practical benefit of a concept for a pharmacovigilance master file – similar to the one being developed for medicines for human use - would benefit both industry and regulators, at the present time it is considered that a clear legal basis is needed in order to first introduce the concept of the PhV master file and then to replace the requirement for the DPPS submission with each marketing authorisation application.

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		towards the concept of 'PhV Master File' (PVMF). Such document would include all the items of the DDPS as given in lines 731 to 853 and be available on the site where the EU QP is located or upon request. Thus it will no longer be part of the dossier and will prevent heavy administrative burden associated with its update. Under this concept, Part I of the dossier would only include the following necessary information: - The name of the QPPV located in the EEA including its business address and contact details; - A statement certifying the availability of the services of the QPPV and of the necessary means for the collection and notification of any adverse event. - A reference to the PhV Master File (PVMF) and of the site where it is located. **Proposed change (if any):** IFAH-Europe strongly encourages the Commission to introduce this concept in Volume 9B by amending section 2.3 accordingly.	
708-710	1	**Draft Volume 9B v 3.1:** The DDPS, including the proof of the availability of the services of the QPPV and the proof that the MAH has the necessary means for the collection and notification of any adverse event, should be provided in Part 1 of the MAA. **Comments:** **Proposed change (if any):** Please amend as follows: The ~~DDPS, including the~~ proves of the availability of the services of the QPPV and of the necessary means for the collection and notification of any adverse event should be provided in Part 1 of the MAA.	*Not accepted. This point is related to the comment above and a legal basis is needed in order to introduce the concept of the PhV Master File and to replace the requirement for the DDPS submission with each marketing authorisation application.*
715/2.3.1	5	**Draft Volume 9B v 3.1:** The DDPS should be supported by documentation maintained by the company	*Not accepted. Further guidance documents are currently under development concerning the DDPS and it is considered more appropriate to await those. Meanwhile, additional*

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		Comments: **Proposed change (if any):** Would it be possible to exemplify the kind of documentation relevant for supporting the DDPS?	*guidance can be requested from competent authorities.*
726 onwards/ 2.3.3	4	**Draft Volume 9B v 3.1:** 2.3.3 Elements of the detailed description of the pharmacovigilance system that should be described in the application for a marketing authorisation **Comments:** Procedures in place: Do all the subjects in the list need a separate written procedure or can all those subjects be described in 1 procedure? **Proposed change (if any):**	*Question noted. Not all the items in the list need a separate procedure. One procedure may cover all or some of the items (see Part I section 2.3.3 c)). It is up to the MAH to decide the number of procedures necessary to describe the pharmacovigilance activities indoors. The DDPS document should, however, clearly state that all topics are covered by written procedures and if any is missing justification should be provided.*
728 onwards	1	**Draft Volume 9B v 3.1:** 2.3.3 Elements of the detailed description of the pharmacovigilance system that should be described in the application for a marketing authorisation **Comments:** **Proposed change (if any):** Information listed under Items a) to i) shall constitute the company PhV Master File available on the site where the EU QP is located and upon request.	*Not accepted. This point is related to comments above and a legal basis is needed in order to introduce the concept of the PhV Master File and to replace the requirement for the DDPS submission with each marketing authorisation application.*
801/ 2.3.3	4	**Draft Volume 9B v 3.1:** The DDPS should indicate the processes for which written procedures are available. **Comments:** The understanding is that the DDPS only relates to pharmacovigilance processes. The current text might be read as to include all processes within a company **Proposed change (if any):** we propose to add the word pharmacovigilance.	*Not accepted. It is true that the DDPS only relates to pharmacovigilance, however there may be written procedures that do cover the listed items but are not strictly related to pharmacovigilance (i.e. training). It is considered that the addition of the word "pharmacovigilance" would not necessarily provide with additional clarification, as the topics to be covered are listed.*

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
801/2.3.3	5	**Draft Volume 9B v 3.1:** A list and copies of the global and EEA procedures should be available within two working days on request by the competent authorities. **Comments:** This is a relatively short amount of time. When is the clock started and stopped if a competent authority makes such a request? **Proposed change (if any):** Specify when the clock starts and stops.	*Accepted. The clock starts at the time of the request and stops at the time of receipt by competent authority. As the written procedures are already drafted and in force, these should therefore be easily available to the authorities. The timelines indicated cover the period to retrieve those and to send them to the authorities, however excludes any aspects of time needed for preparing and drafting the procedures themselves. The request may be related to procedures with different clock-stop timelines. Specifications are added to Volume 9B.* "A list and copies of the global and EEA procedures should be available within two working days after receipt by the MAH of ~~on~~ competent authorities request ~~by the competent authorities~~."
834/ 2.3.3	4	**Draft Volume 9B v 3.1:** Staff should be appropriately trained for performing pharmacovigilance related activities. **Comments:** What is "appropriately trained"? **Proposed change (if any):** If this means all relevant personnel should be trained according to the standards within the company a text change is proposed.	*Partly accepted. Revision of the text may be appropriate however "appropriately trained" means according to the legislative requirements so that they are aware of their role and duties concerning pharmacovigilance according to their position in the company. Staff should receive and maintain sufficient knowledge of the pharmacovigilance system either to perform pharmacovigilance related activities or to insure that calls and other reports related to adverse events are correctly captured. A specification is introduced in Volume 9B.* "Staff should be appropriately trained for performing pharmacovigilance related activities, taking into account their role within the company. "
886 896-896	1	**Draft Volume 9B v 3.1:** Monitoring the quality of reports. Submission of reports judged to be of poor quality may result in the follow-up procedures of MAHs being scrutinised. **Comments:** With regard to the quality of the reports, the limits and specificities of spontaneous reporting in the veterinary field should be acknowledged; reporting	*Not accepted. The limitations of reporting in veterinary pharmacovigilance are known and accounted for in the overall assessment of the safety profile of products and when considering regulatory actions.*

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		in veterinary medicines is not limited to health professionals and the pressure for complementary analyses is limited in comparison to human medicines. Thus in some cases, poor quality of reports is difficult to avoid and this should be reflected **Proposed change (if any):** Please amend as follows: "Monitoring the quality of reports. Submission of reports judged to be of poor quality, taking into account the limits of reporting in the field of veterinary medicines, may result in the follow-up procedures of MAHs being scrutinised."	
1176-1177	1	**Draft Volume 9B v 3.1:** "Adverse events identified from the worldwide-published scientific literature should also be reported." **Comments:** The above should be limited to peer reviewed literature only. **Proposed change (if any):** Please amend as follows: "Adverse events identified from the worldwide-published peer reviewed scientific literature should also be reported."	*Accepted.*

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
1199-1200	1	**Draft Volume 9B v 3.1:** "For all VMPs, independent of the authorisation procedure, the MAH should report, on an expedited basis, all serious adverse events occurring in the EEA, and all serious and unexpected adverse events in animals, human adverse reactions and suspected transmission of infectious agents occurring outside the EEA, which are brought to his attention by a veterinarian or other health-care professional or other source. Such reports should be sent to the NCA in whose territory the incident occurred." **Comments:** We feel that the above text could benefit from clarification with regard to third country reports. It should further be aligned with the EV Vet Reporting schema (version 1.02, 12.02.2009). **Proposed change (if any):** Please amend the paragraph to comply with the agreed EMEA Schemas for the Guidance on the Electronic Data Interchange Version 1.02 - 12 February 2009, as follows: The MAH should report on an expedited basis: → All serious adverse events occurring in the EEA to the NCA in whose territory the incident occurred and All serious and unexpected adverse events in animals, human adverse reactions and suspected transmission of infectious agents occurring outside the EEA to the EV Vet database.	*Partly accepted.* "For all VMPs, independent of the authorisation procedure, the MAH should report, on an expedited basis: • All serious adverse events occurring in the EEA to the NCA in whose territory the incident occurred; • All serious and unexpected adverse events in animals, human adverse reactions and suspected transmission of infectious agents occurring outside the EEA to the EV Vet database."
1219	1	**Draft Volume 9B v 3.1:** "These reports should be reported promptly, and in no case later than 15 calendar days for receipt, to the NCA in whose territory the serious adverse event occurred." **Comments:** '15 calendar days' is used here for the	*Accepted. This will be considered throughout the document.*

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		first time; previous lines 886, 903, 1168 and so on only refer to '15 days'. The wording would benefit from consistency to prevent confusion. **Proposed change (if any):** Please harmonise the wording throughout the document by replacing all '15 days' with '15 calendar days'	
1223-1225	1	**Draft Volume 9B v 3.1: "**The MAH shall additionally ensure that all reports on serious adverse events occurring in the EEA are available to the RMS." **Comments:** This sentence is irrelevant as cases already are available to the RMS by the following means: the MAH is responsible for sending all serious report to the CA where the case occurred; it is then the NCA responsibility to send the report within 15 days to EV Vet DB where it thus becomes available to all NCAs including the Reference Member State. **Proposed change (if any):** Please delete the sentence: "~~The MAH shall additionally ensure that all reports on serious adverse events occurring in the EEA are available to the RMS~~".	*Partly accepted. The whole paragraph is deleted:* "~~For products authorised……..are available to the RMS.~~"
1329	1	**Draft Volume 9B v 3.1:** , a single report should be submitted relating only to the animal which experienced the adverse reaction. **Comments:** Terminology that is not aligned with VICH should not be used. **Proposed change (if any):** Also on line 1329, the text should be amended as follows: "... a single report should be submitted relating only to the animal which experienced the adverse ~~reaction~~ event."	*Accepted.*
1342	1	**Draft Volume 9B v 3.1:** A short explanation should be included in the dose details to indicate which parent was treated.	*Partly accepted. The sentence will now read* "A short explanation should be included in the dose details and narrative to indicate which parent was treated."

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		Comments: This is not possible in the schema; the explanation should thus go in the narrative. **Proposed change (if any):** Please amend as follows: "A short explanation should be included in the narrative ~~dose details~~ to indicate which parent was treated."	
1362-1365	1	**Draft Volume 9B v 3.1:** if they are also coded using VeDDRA List of Clinical Terms for reporting adverse events in Animals to Veterinary Medicinal Products and the VeDDRA List of Clinical Terms for reporting adverse events in Human Beings to Veterinary Medicinal Products (VeDDRA terminology) . **Comments:** The text should refer to the combined VeDDRA list adopted by CVMP in June 2009; the same comment applies to Annex 4. **Proposed change (if any):** Please amend as follows: "... if they are also coded using ~~VeDDRA List of Clinical Terms for reporting adverse events in Animals to Veterinary Medicinal Products ... (See Annex 4. References)~~ the combined VeDDRA List of Clinical Terms for Reporting Suspected Adverse Reactions in Animals and Humans to Veterinary Medicinal Products (see annex 4). Please also delete references 17 and 18 in Annex 4 and replace with the reference above.	*Partly accepted. The word "combined" would however be deleted and reference shortened. The section will read as follows:* "…if they are also coded using the VeDDRA List of Clinical Terms for reporting adverse events in animals and humans ~~in Animals to Veterinary Medicinal Products and the VeDDRA List of Clinical Terms for reporting adverse events in Human Beings to Veterinary Medicinal Products (VeDDRA terminology)~~"
1394	1	**Draft Volume 9B v 3.1:** If neither the numbers exposed nor affected are known, a notional figure of one should be used. **Comments:** A notional figure of 1 is acceptable in companion animals but may be inappropriate in a herd situation. **Proposed change (if any):** Please amend as follows:	*Partly accepted. The sentence will read as follows* "If neither the numbers exposed nor affected are known, a notional figure ~~of one~~ should be used, which should be justified. If the exact numbers of animals exposed are not known, an estimation should always be provided. It is not acceptable to omit this information. "

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		"a notional figure of one should be used, unless otherwise justified."	
1410	1	**Draft Volume 9B v 3.1:** Source of report, e.g. spontaneous, clinical trial, post-authorisation safety studies. **Comments:** The scope of veterinary PhV excludes clinical trials; thus they should be removed. **Proposed change (if any):** Please amend 5 as follows: "5. Source of report, e.g. spontaneous, ~~clinical trial~~, post-authorisation safety studies."	*Not accepted. Adverse reactions from clinical trials following authorisation do fall within the scope of pharmacovigilance. In addition, terminology is brought in line with VICH and to be used throughout the document. The sentence is clarified and now reads* "Source of report, e.g. spontaneous, ~~clinical trial,~~ post-authorisation safety studies and clinical studies."
1433-1434 1462	1	**Draft Volume 9B v 3.1:** 1. The person who administered the VMP (e.g. animal owner, veterinary surgeon etc.). Include identifier (name/initials) and relevant occupation/qualification of person. **Comments:** This requirement is not part of the data elements guideline, which only requires 'Who administered the VMP' (see R.18.17.26). This comment also applies to line 1462. **Proposed change (if any):** Please amend 1. on lines 1433 and 1462 as follows: "1. The person who administered the VMP (e.g. animal owner, veterinary surgeon etc.). ~~Include identifier (name/initials) and relevant occupation/qualification of person."~~	*Accepted.*
1542	3	**Draft Volume 9B v 3.1: For inclusion in category "O1" (inconclusive),** **Comments:** I can't understand the difference between O1 and O; in both , there is other factors/causes prevent a conclusion being drawn **Proposed change (if any):** Suppression of O1 category	*Not accepted. The O1 – Inconclusive category has been used for some time. It is helpful to distinguish a sub-set of data which might yield more information when followed-up at a later stage from data for which no more information is available. i.e. reports classified as O.*

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
1544	3	**Draft Volume 9B v 3.1: For inclusion in category "N" (unlikely)**, **Comments:** A positive definition of N case would be rather accurate Cases where sufficient information exists to establish beyond reasonable doubt that the event has physiopathogenic explanation different from VMP (please specify this physiopathogenic explanation) **Proposed change (if any):** Cases where sufficient information exists to establish beyond reasonable doubt that the event has physiopathogenic explanation different from VMP (please specify this physiopathogenic explanation)	*Partly accepted. The existing explanation of category N is clear, however the reference to a physiopathogenic explanation in the proposed definition is an unnecessary complication. The text is, however amended as follows:* "..., cases where sufficient information exists to establish beyond reasonable doubt that there is an alternative explanation to the adverse event that is not related to a VMP "
1620/ 4.9	4	**Draft Volume 9B v 3.1: "**e.g. the lay press or other media, reasonable attempt should be made to obtain the minimum ninformation that constitutes an individual adverse event…" **Comments:** A "reasonable attempt" is very subjective. **Proposed change (if any):**	*Comment noted. 'Reasonable' allows flexibility and the exercise of judgement, which is what is required here.*

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
1700/ 6.1	4	**Draft Volume 9B v 3.1**: The requirement for the submission of a PSUR applies irrespective of whether the VMP is marketed or not. **Comments:** : When no sales are made, the PSUR is basically empty and only a administrative burden. It would be easier to sent just a letter confirming that the product is not (yet) on the market **Proposed change (if any):** "The requirement for the submission of a PSUR applies irrespective of whether the VMP is marketed or not, however if the product is not marketed within a country the PSUR can be replaced by a written statement that the product has not been on the market for the last PSUR period."	*Partly accepted. A reference to the section concerning abridged PSURs is included to address this comment.* "The requirement for the submission of a PSUR applies irrespective of whether the VMP is marketed or not, however in certain circumstances an abridged PSUR is considered sufficient (see Chapter 6.3.2)." *Subsequently, Vol 9B needs to be amended by adding a new, 7th bullet point after Line 2125 of draft Vol 9B v. 3.1.:* • estimated date for initially placing the product on the market
1734-1736	1	**Draft Volume 9B v 3.1:** It is strongly recommended that, before submitting the PSUR, the MAH should make sure that all reports from the line listings have been submitted electronically (without duplicate reporting) as described **Comments:** While reporting of all cases electronically could be supported in the future, it is still too early in the process. Furthermore, this would need to be balanced with decrease requirements for PSURs. **Proposed change (if any):** Please amend as follows: "Where possible, it is ~~strongly~~ recommended that, before submitting the PSUR, the MAH should make sure that all reports from the line listings have been submitted electronically (without duplicate reporting) as described in Part III..."	*Not accepted. As the technology is available for electronic reporting, this should be possible also for non-expedited reports. While there is, however, no legal basis for requesting electronic reporting of non-serious reports, such cannot be considered mandatory. For safety surveillance purposes it is important that all reports are in one database.*
1734-1735/6.2.2.1	4	**Draft Volume 9B v 3.1:** It is strongly recommended that, before submitting the PSUR, the MAH should make sure that all reports from the line listings have been submitted electronically (without duplicate reporting) as described	*Not accepted. The PSUR contains an overall benefit/risk evaluation, and currently also includes an incidence calculation, therefore providing with a different type of assessment than only the submission of single reports into a database.*

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		Comments: Here we refer to our general comment. When all reports are submitted electronically, why still submit the PSUR? The database should be used to signal possible safety issues earlier and on a continious basis. To submit electronically and via a PSUR is just a duplication of the work for applicants. **Proposed change (if any):**	In a PSUR adverse events over a certain time frame are evaluated scientifically in relation to the use of the VMP (benefit/risk evaluation). This is currently not possible by the use of data in Eudravigilance Veterinary. Signals may lead to the need for a PSUR, in which the potential signals will be evaluated and a conclusion drawn on their impact on the safety of the product. See also comment above for a further explanation of the basis for the recommendation.
1750-1753	1	**Draft Volume 9B v 3.1:** The PSUR cycle should be based on the EU Birth Date (EBD, date of the first marketing authorisation within the European Union) of a VMP or its International Birth Date (IBD, date of the first marketing authorisation for the product granted to the MAH in any country in the world), or the EU HBD (EU Harmonised Birth Date for VMPs included in the work sharing initiative on PSUR assessments). **Comments:** Other harmonisation practices already in application should also be reflected here. **Proposed change (if any):** Please amend as follows: "... or the EU HBD (EU Harmonised Birth Date for VMPs included in the work sharing initiative on PSUR assessment) or as agreed between the MAH and the concerned NCAs.	Not accepted. Additional options for setting birth dates, as proposed, would provide a potential for disharmonisation within the European union, which should be discouraged. In comparison to previous requirements, the EU HBD has already been added and it is desirable to gain some experience with this EU HBD before modifying the requirements.

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
1824-1825	1	**Draft Volume 9B v 3.1:** For all other authorised VMPs, the PSUR should be written in the national language or in English, if agreed by the concerned NCA. **Comments:** If the above is kept, it is likely that the national language will become the norm rather than the exception. English should however be the norm. Also for the benefit of the PSUR work-sharing initiative, synchronised PSURs are prepared in English. **Proposed change (if any):** Please amend as follows: "For all other authorised VMPs, the PSUR should be written ~~in the national language or~~ in English~~, if agreed by the concerned NCA~~. If requested by the MAH and agreed by the concerned NCA, the national language may be used."	Partly accepted. It is considered that certain PSURs would need to be written in English, specifically where there is collaboration between Member States during the authorisation procedure or in other agreed initiatives. Vol 9B is modified. "For VMPs authorised via the centralised, mutual recognition, decentralised or ex-concertation procedures, for VMPs participating in the PSUR work sharing project and for VMPs, which have been subject to a referral, the PSUR should be written in English. For all other authorised VMPs, the PSUR should - if submitted to one Member State only - be written in the national language or in English, as agreed with the concerned NCA. If this PSUR is to be submitted to two or more Member States, the PSUR should be written in English."
1875	1	**Draft Volume 9B v 3.1:** Tablets to be expressed in numbers of tablets; **Comments:** The above could also be expressed in 'amount of active substance' **Proposed change (if any):** Please amend as follows: "Tablets to be expressed in numbers of tablets or in amount of active substance."	*Not accepted. Tablets in different strengths will be used in different groups of authorised species. For an incidence calculation an overall amount of active substance is of no use.*
1904	1	**Draft Volume 9B v 3.1:** Table on standard body weights. **Comments:** We recommend using the body weights referred to in VICH guidance. **Proposed change (if any):** Please amend the table with the following body weights: Dairy cow and beef bullock: ~~550~~ 500 Slaughter calf: ~~150~~ 160	*Not accepted. Following clarification with the sender of the comment, no change would be necessary as the comment was due to a misunderstanding.*

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		Sow/boar: ~~160~~ 130; Fattening pig: ~~60~~ 95; Weaner: ~~25~~ 20	
1904	2	**Draft Volume 9B v 3.1:** Table on standard body weights. **Comments:** I have noticed that there is no standard weight given for rabbits **Proposed change (if any):** .(1.5 kg as standard weight?)	*Accepted. Vol 9B now refers to rabbits at a standard weight of 1.5 kg.*
1911-1913	1	**Draft Volume 9B v 3.1:** For immunological VMP, the number of animals treated may be considered equivalent to the total number of doses sold. Any calculations should take into account the recommended treatment regimen (initial course plus booster doses). **Comments:** We support '1 animal = 1 dose' and propose deleting the last sentence of the above paragraph. **Proposed change (if any):** Please amend the section as follows: "For immunological VMP, the number of animals treated may be considered equivalent to the total number of doses sold. ~~Any calculations should take into account the recommended treatment regimen (initial course plus booster doses)~~."	*Not accepted. These data are needed for the worst case scenario: taking into account both the initial course plus booster dose reduces the number of treated animals.*
1923/ 6.3.1.5	4	**Draft Volume 9B v 3.1:** In addition, an incidence for lack of efficacy in target species after recommended use should be calculated, when relevant. **Comments:** `when relevant´ Who is to decide when it is relevant? **Proposed change (if any):**	*Question noted. Both the MAH when preparing a PSUR and an NCA when assessing a PSUR are to consider and decide whether there are reasonable grounds (e.g. antibiotics or antiparasitics - resistance) to calculate an incidence for lack of efficacy.*
1943-1945	1	**Draft Volume 9B v 3.1:** For PSURs covering 3 years	*Not accepted. A split per calendar year facilitates different approaches in assessment, in some cases even split per*

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		sales volume should be broken down by calendar year and the ratio of the number of animals with adverse event to the amount of VMP sold should be computed for each of the years concerned by the report. **Comments:** The split per calendar year is unnecessary and unjustified; it should thus be deleted. **Proposed change (if any):** Please delete the sentence: "~~For PSURs covering 3 years sales volume should be broken down by calendar year and the ratio of the number of animals with adverse event to the amount of VMP sold should be computed for each of the years concerned by the report~~."	*month would be useful (e.g. for detecting periodic clustering). NCAs need yearly splits for comparison of pharmacovigilance issues of different VMPs over the same time periods.*
1966-1972	1	**Draft Volume 9B v 3.1:** The analysis of the adverse events reported should be supported by tables or tabulations summarising the main findings. It may be helpful, especially for PSURs which contain a large number of adverse events, to introduce summary tabulations and prepare separate tables e.g. for serious expected reactions, serious unexpected reactions, non-serious unlisted reactions (not mentioned in the SPC), or on basis of VEDDRA categories on organ level (e.g. System Organ Class (SOC) or Preferred Term (PT) level). Examples of tables have been developed and may be used … **Comments:** Such requirement will lead to significant additional work and is not necessarily justified. **Proposed change (if any):** Please delete the sentence: "~~It may be helpful, especially for PSURs which contain a large number of adverse events, to introduce summary tabulations and prepare separate tables ... Examples of tables have been developed and may be used (see Annex 2.3 Templates for tables for use as necessary in preparing and assessing Periodic~~	*Not accepted. A PSUR is intended to be more than only a compilation of all adverse event reports received during a specific time period, and therefore needs to include a scientific evaluation of pharmacovigilance data over a certain time period. These data cannot be presented only by automatically extracting reports from the database (as requested in general comment no 2). With the PSUR the MAH performs a critical assessment of the pharmacovigilance data to evaluate and defend the safety of the product over time.* *Summary tabulations may be helpful in presenting the results and to facilitate the illustration of new issues in particular.*

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		~~Safety Update Reports (PSURs))~~".	
2010-2016	1	**Draft Volume 9B v 3.1: 6.3.1.8 Other Information** Adverse events arising from prescription errors or medication errors, including those due to invented names of VMPs or similar appearance (e.g. mix-up with another VMP) should be reported in PSURs. Where names convey misleading therapeutic connotations, there may be a risk for misuse or abuse of the product. Adverse events arising from such misuse or abuse should be reported in PSURs. A summary report on medication errors, including those due to name confusion, occurring with the VMP should be submitted as an annex to the PSUR. **Comments:** This section is clearly taken from Volume 9A on human medicinal products and is of no added value to VMPs. **Proposed change (if any):** Please delete section 6.3.1.8; alternatively, please amend as follows: "A summary report on medication errors, including those due to name confusion, occurring with the VMP should be submitted as an annex to the PSUR, <u>when available</u>".	*Not accepted. All requirements on reporting in PSURs are based on the availability of identified reports.*

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
2072/ 6.3.1.11	4	**Draft Volume 9B v 3.1:** and, as necessary, separately in a searchable and sortable format **Comments:** ` and, as necessary, separately in a searchable and sortable format´ . Does ´as necessary´ mean it is needed in all cases? If it is a typo and should be read as `if necessary´ who will decide whether it is needed. Could an applicant be required to submit the PSUR (partly) in an electronic format? **Proposed change (if any):**	*Question noted. Electronic submission of a searchable and sortable format of the line listing is useful specifically when PSURs contain a high number of reports.* *An electronic format (excel or xml) of line listings facilitate the assessment of data by NCAs. This facilitation is important especially concerning large line listings. Searchable and sortable is especially needed for VeDDRA terms. To facilitate this it is considered of high importance to have VeDDRA terms in separate column in the line listing instead of combining VeDDRA terms in a text field together with text concerning "description of presented signs, diagnosis, including timing and duration". Electronic versions are requested to be submitted in addition to the usual line listing included in the PSUR (usually in pdf format for IT- security).* *The requirement of a searchable and sortable format concerning VeDDRA terms is best met by separating in the line listing VeDDRA terms into one new column and to maintain the column "description of presented signs and diagnosis, including timing and duration" for the narrative. In consequence of the above (Part I. Chapter 6.3.1.11) the following changes are needed:* *Line 2092 of draft Vol 9B v.4.1:* "xii) presenting signs/diagnosis ~~(to include VeDDRA terminology)~~, including timing and duration xiii) VeDDRA terminology (for description of signs/diagnosis) xiv) MA comments – brief, informative narrative xv) Causality assessment (A, B, O, O1, N code)Causality assessment (A, B, O, O1,N code)" *Line 4789, 4790 (Headings of columns in PSUR line listing template):* *Modified:* Presenting signs/diagnosis ~~(VeDDRA)~~

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
			New: VeDDRA terminology *Line 4797 (Heading of column in PSUR line listing template):* *New:* VeDDRA terminology
2074-2077	1	**Draft Volume 9B v 3.1:** In order to relate the data review to the line listings, it is necessary to separate data e.g. relating to different formulations (dosage form(s) and strength(s)), target species (if the VMP is authorised for use in more than one species), reaction type (that is, serious, non-serious, human adverse event, etc.), and the country where the event occurred. **Comments:** The above request to separate data is very stringent and unjustified in some cases, e.g. product with few adverse events. Thus, this should only be done when necessary and be limited to the dosage form and reaction type. **Proposed change (if any):** Please amend as follows: "In order to relate the data review to the line listings, it may be ~~is~~ necessary in some cases to separate data ~~e.g.~~ relating to different ~~formulations (~~dosage form(s) and ~~strength(s)), target species (if the VMP is authorised for use in more than one species),~~ reaction type (that is, serious, non-serious, human adverse event, etc.) ~~and the country where the event occurred~~."	*Not accepted. See also above.* *Separated data in the line listings facilitate assessment by NCAs and the criteria for separation have been agreed within the regulatory network. The alternative approach is to provide the line listings in an electronic searchable and sortable format (excel or xml) in addition to including it as part of the PSUR.*

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
2135-2138	1	**Draft Volume 9B v 3.1:** As part of the renewal application documents related to safety, the MAH needs to prepare or submit either a PSUR Summary Bridging Report supported, if needed, by a PSUR Addendum Report, or one PSUR in circumstances where the PSUR submission schedule is in synchrony with the renewal submission schedule. **Comments:** Flexibility must be kept at the time of the single renewal when either a PSUR Summary Bridging Report or one PSUR can be submitted under any circumstances - see also main comment on page 2. **Proposed change (if any):** Please amend as follows: "As part of the renewal application documents related to safety, the MAH needs to prepare or submit either a PSUR Summary Bridging Report supported, if needed, by a PSUR Addendum Report, or one PSUR ~~in circumstances where the PSUR submission schedule is in synchrony with the renewal submission schedule~~)."	*Not accepted. Renewal and PSUR are different procedures, which seldom correlate in their schedules.* *Normally several PSURs will have been submitted before renewal – thus for the renewal a PSUR Summary Bridging Report is needed. This may be accompanied by a PSUR Addendum Report in cases when the DLP of the last submitted PSUR is long ago. The following amendment is introduced in Vol 9B to clarify the requirement:* As part of the renewal application documents related to safety, the MAH needs to prepare or submit a PSUR Summary Bridging Report <u>which is</u> supported, if needed, <u>either</u> by • a PSUR Addendum Report, or • one PSUR in circumstances where the PSUR submission schedule is in synchrony with the renewal submission schedule. *The comment concerning lines 2135-2138 is relating to the uncertainty of what is to be submitted for renewal. Experience with renewal submissions so far shows that there is a need for more clarification on the definition of a Summary Bridging Report, by modifying Lines 2155-2156 of draft Vol 9B v 4.1 as follows:* "A Summary Bridging Report should contain the following for the period covered by all <u>previously submitted</u> ~~subsequent~~ PSURs".
2166-2167	1	**Draft Volume 9B v 3.1:** An overview of exposure data (estimation of the total number of animals exposed in the time period) as well as incidence data (in animal and in human); **Comments:** This is in contradiction with section 6.3.1.5 where human reactions are excluded from	*Partly accepted. Amended Vol 9B will read:* "An overview of exposure data (estimation of the total number of animals exposed in the time period) as well as incidence data <u>and overview of human reactions</u>"

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		incidence calculation (line 1918). **Proposed change (if any):** Please amend as follows: "An overview of exposure data (estimation of the total number of animals exposed in the time period) as well as incidence data ~~(in animal and in human)~~.	
2214-2215	1	**Draft Volume 9B v 3.1:** For any VMPs, submission of PSURs at a lower frequency than once every 3 years is not possible. **Comments:** The above statement lacks consideration for well established use VMPs for which the frequency could be significantly decreased. Also a lower frequency is proposed in line 2990. **Proposed change (if any):** Please amend the sentence as follows: "For <u>well established</u> ~~any~~ VMPs, submission of PSURs at a lower frequency than once every 3 years is ~~not~~ possible."	*Not accepted. The current requirements are based on legislation. The issue will be considered in any future review of the legislation.*
2234-2256	1	**Draft Volume 9B v 3.1: 6.4.3 Reference Safety Information** [… <u>The CSID is strongly encouraged to be submitted in addition to the regularly enclosed SPCs (in national languages, see section 6.3.1.3) of all VMPs for which the synchronised PSUR is prepared.</u> For more information regarding the CSID refer to Heads of Agencies website (…)…] **Comments:** To align with the agreed principles of the pilot phase on work-sharing, we recommend using the terminology 'Core Safety Data Sheet (CSDS)' instead of 'Core Safety Information Document'. Where such document is provided, it has been agreed that SPCs do not need to be added to the PSUR. Also discussions are still on-going with regard to the content of the CSDS; thus Volume 9B should not enter	*Partly accepted.* *Amendment of Vol 9B will read:* **" <u>6.4.3 Core Safety Data Sheet (CSDS)</u>** An objective of a **…** This information is especially important in the framework of the PSUR synchronisation / PSUR assessment <u>work share</u> initiative (see above).It is recommended for MAHs participating in this initiative to prepare a Core Safety <u>Data Sheet</u> <u>(CSDS)</u> written in English, which consists of the <u>core</u> safety relevant sections from the SPCs of the VMPs for which the synchronised PSUR is submitted…… For more information regarding the <u>CSDS</u> refer to <u>the</u> Heads of Medicinal Agencies website (see Annex 4 – References)." *The following editorial change is also introduced:* *Line 2232:* "The principles <u>of PSUR synchronisation / PSUR work share initiative on PSUR assessment</u> are outlined on the

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		into details and only refer to the Heads of Agencies website for further information. **Proposed change (if any):** Please amend as follows: **6.4.3 ~~Reference~~ Core Safety ~~Information~~ Data** … It is recommended for MAHs participating in this initiative to prepare a Core Safety Data Sheet ~~Information Document (CSID)~~ (CSDS) written in English~~, which consists of an extract of all safety relevant sections from the SPCs of the VMPs for which the synchronised PSUR is submitted…The CSID is strongly encouraged to be submitted in addition to the regularly enclosed SPCs (in national languages, see section 6.3.1.3) of all VMPs for which the synchronised PSUR is prepared~~. For more information ~~regarding the CSID~~ refer to the Heads of Agencies website.”	Heads of Medicines Agencies.”
2532-2533	1	**Draft Volume 9B v 3.1:** To communicate the outcome of evaluation of safety concerns as appropriate to veterinarians and other health-care professionals and as necessary to the public, through timely and appropriate methods of communication and to assess the impact of such communications; **Comments:** MAHs are very likely to be contacted following the release of such communication, thus it would be more appropriate for the competent authorities to first liaise with the MAHs before any information is communicated to veterinarians and other health care professionals or the public - see also comments to Part IV. **Proposed change (if any):** Please amend as follows: “To communicate, following exchange with the concerned MAHs, the outcome of evaluation of safety concerns as appropriate to veterinarians and other health-care professionals and as necessary to the public, through timely and appropriate methods of communication and to assess the impact of such	*Partly accepted. While MAHs would be involved during the evaluation and would therefore be aware of the issue, efficient communication between regulators and marketing authorisation holders is of value and therefore the following amendment is introduced to Vol 9B.* “To communicate the outcome of evaluation of safety concerns as appropriate to veterinarians and other health-care professionals and as necessary to the public, through timely and appropriate methods of communication and to assess the impact of such communications; Before or at the same time the communication takes place, the MAH would normally be informed. “

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		communications."	
2657-2658/ 1.3.2.1	4	**Draft Volume 9B v 3.1:** Every effort should be made to obtain complete information. **Comments:** "every effort" seems to be a bit vague. **Proposed change (if any):** The ~~Every effort should be made to obtain complete~~ information obtained should be as complete as possible.	*Accepted.*
2710/1.3.3	4	**Draft Volume 9B v 3.1:** The NCA should make every effort to ensure that adverse event reports contain sufficient information to identify such duplicates, e.g. from **Comments:** Again `every effort´ seems a bit vague. Furthermore, it is now only to the point to avoid duplications. We propose to bring the text in line with 1.3.2.1 **Proposed change (if any):** The NCA should ~~make every effort to~~ ensure that adverse event reports contain ~~sufficient~~ information as complete as possible in order to be able to identify such duplicates, e.g. from....	*Partly accepted. A change is necessary as follows:* 'The NCA should ensure that adverse event reports contain as much information as possible in order to identify such duplicates, e.g. from…'
2779/1.3.6	5	**Draft Volume 9B v 3.1:** A signal should be considered as information reported on a possible causal relationship between an adverse event and a VMP, the relationship being unknown or previously incompletely documented. **Comments:** In my understanding, one spontaneously reported event will not constitute a signal. Is it really meant to be written like this? **Proposed change (if any):** A signal should be considered as information reported on a possible causal relationship between **reoccurring adverse events** and a VMP, the relationship being unknown or previously incompletely documented	*Accepted.*

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
2833/1.3.7	5	**Draft Volume 9B v 3.1:** Trigger III More than 3 adverse event reports involving death of the animal(s) within three months after the initial placing on the market (launch) of a new VMP. **Comments:** "More than 3 adverse event reports involving death within three months after the initial placing on the market should be a trigger type III for investigations." This trigger seems poorly adapted to production intensive species. This trigger may work fine in species where mortalities are not expected, whereas it does not work so well e.g. for farmed fish. **Proposed change (if any):** Maybe a note could be included that in production intensive species the mortality rate must exceed the „normal" level?	*Partly accepted. A change is necessary as follows:* *'For animals managed and treated as a group (see Glossary), more than 3 adverse event reports involving mortality above the expected level within three months after the initial placing on the market of a new VMP.'*
2990-2992	1	**Draft Volume 9B v 3.1:** Circumstances where <u>less frequent submission</u> of PSURs may be appropriate include: • Products authorised through line-extensions to existing VMPs; • Newly authorised generic VMPs. **Comments:** This section must also include well established products and be consistent with lines 2214 – 2215. **Proposed change (if any):** Please amend as follows: "Circumstances where less frequent submission of PSURs may be appropriate include: • <u>Well-established VMPs, i.e. products demonstrating a steady benefit:risk balance over 3 PSURs;</u> • Products authorised through line-extensions to existing VMPs; Newly authorised generic VMPs."	*Not accepted.* *Well-established VMPs would already be on a 3-year PSUR cycle. There is no legal basis for a longer interval.* *(This also applies to IFAH's comment on lines* 2214-2215).

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
3556-3720/ 2.2	4	**Draft Volume 9B v 3.1:** **Comments:** The reasons for setting up a separate crisis system for centralised products only is not clear. Safety issues for European products should be dealt with the same way, whether they are centrally, decentrally or nationally authorised products. An additional system could lead to more administrative burden **Proposed change (if any):**	*Comment noted. Efforts will be made to harmonise systems/approaches among competent authorities within the European Regulatory network.* *As the crisis management plan will need to be updated to reflect new EMA structures and especially responsibilities; to reflect on the appropriate way to include nationally authorised products that do or could involve agency action; and to benefit from the experienced gained on the human side in the development of the Incident management plan and the pilot project implementing this plan, Part II section 2.2 (lines 3556-3742) is now deleted from Volume 9B. The following related changes have been made:* *Part II Section 1.1:* *Lines 2551-2552: bullet point deleted: ~~the Crisis Management Plan for CAPs (see Part II Section 2.2…),~~* *Part II Section 2.1.4.3:* *Line 3513: Footnote 8 deleted: ~~The concept, terms and definition are to be updated in accordance with the future approach for medicinal products for human use, which is under development.~~* *Lines 3517-3520: Deletion of text under subheading Crisis management:* *A Crisis Management Plan, agreed with the CVMP, has been implemented by the Agency in close consultation with the European Commission (see Annex 4. References ~~Part II Section 2.2 Crisis Management Plan regarding Centrally Authorised Products).~~* *Annexes: Annex 4 References:* *After line 4861: add new reference: European Medicines Agency. Crisis Management Plan regarding Safety Issues for Centrally Authorised Products or Veterinary Use (Doc. Ref. EMEA/CVMP/159/04)* *http://www.ema.europa.eu/docs/en_GB/document_library/Ot*

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
			her/2009/10/WC500004980.pdf
3605-3611	1	**Draft Volume 9B v 3.1:** 2.2.3.1 European Veterinary Crisis Group In order to deal successfully with a crisis relating to VMPs, a European Veterinary Crisis Group needs to be created. For logistical reasons, and rapid and efficient issue management, the core members of the European Veterinary Crisis Group must be kept to a minimum. Due to logistical and time constraints, some meetings may need to take place without all members being present. Where feasible, tele- or video-conferencing facilities may be used. Of course additional members and expertise may be co-opted into the European Veterinary Crisis Group as need arises C**omments:** This section lacks involvement of industry. **Proposed change (if any):** Please amend as follows: "... the core members of the European Veterinary Crisis Group must be kept to a minimum and include at least one representative of the MAH(s) concerned..."	*Not accepted. MAHs would be informed and consulted to ensure effective communication, however the MAHs would not participate in the decision making.*
4003/ 3.3.2.6	4	**Draft Volume 9B v 3.1:** Where possible, in order to ensure a coordinated approach, efforts should be made to reach a consensus on the proposed action to be taken, through discussion within the PhVWP-V. **Comments:** "Where possible" is not very clear and could be deleted **Proposed change (if any):** ~~Where possible, in~~ In order to ensure a coordinated approach, efforts should be made to reach a consensus on the proposed action to be taken, through discussion within the PhVWP-V.	*Accepted.*

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
4005/ 3.3.2.6	4	**Draft Volume 9B v 3.1:** Where appropriate, the RMS should communicate with the MAH on the reasons for the conclusions reached by the MS and the action that should be taken by the MAH. **Comments:** "Where appropriate" is strange in this context. As this text relates to a situation in which actions are taken, it is always appropriate to communicate with the applicant the reasons for the proposed actions. **Proposed change (if any):** ~~Where appropriate,~~ ~~t~~The RMS should communicate with the MAH on the reasons for the conclusions reached by the MS and the action that should be taken by the MAH.	*Partly accepted. A specification will be included in Vol 9B.* "Where the RMS concludes that action is necessary ~~appropriate~~, the RMS should communicate with the MAH on the reasons for the conclusions reached by the MS and the action that should be taken by the MAH. "
4015-4018/ 3.4.2.6	4	**Draft Volume 9B v 3.1:** **Comments:** The communication with the MAH and the role of the MAH in this situation is unclear. **Proposed change (if any):**	*Comment noted. Volume 9B v 3.1 states in line 4000 that the MAH is to be informed. Here, however, the emphasis is on the timing of the communication to other authorities within the network. Thus any NCA will initiate the appropriate suspension procedure according to national requirements which includes communication to the MAH on proposed actions.*

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
4035/ 3.4.2.7	5	**Draft Volume 9B v 3.1:** In addition it may be appropriate to inform veterinarians and other healthcare professionals and the general public about safety concerns related to MRP and DCP VMPs in other ways (e.g. public statements). It is important that consistent information is provided in all concerned EU/EEA countries. In such cases, the RMS should propose the content of the information to be provided, and whenever possible, this should be agreed by the CMS and, if necessary considered by the PhVWP-V. **Comments:** It says; in case of public statements about safety concerns, the RMS should propose the content of the information to be provided and should be agreed by the CMS and if necessary considered by the PhVWP-V. Will the MAH have any influence on the content in such statements? Considering the fact that MAHs are given the right to evaluate preliminary public assessment reports for consideration of commercially sensitive data. **Proposed change: -**	*Safety concerns are primarily different to the commercially confidential information to be deleted from public assessment reports. The MAHs would be involved during evaluation and then informed of the actions in relation to a safety concern and thereby be informed of the intended communication.*
4059 / 4.1	4	**Draft Volume 9B v 3.1:** The purpose of the RA System is to alert, with the appropriate degree of urgency, other MSs, the Agency and the European Commission and about newly available pharmacovigilance data for VMPs **Comments:** It is not clear what is meant by "appropriate degree" of urgency. **Proposed change: -**	*Comment noted. The urgency is defined by the measure to be taken for which the urgency may differ (suspension, withdrawal of MA, batch recall on one hand, some SPC changes on the other hand). Therefore no clear definition of urgency can be given, but needs to be considered and decided by the notifying MS.*
4393/ 4.3	5	**Draft Volume 9B v 3.1:** To comply with EU legislation on the protection of individuals with regard to the	*Not accepted. It is indicated that "electronic transmission of adverse events should be operated on the principles of*

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		processing of personal data, electronic transmission of adverse events should be operated on the principles of anonymised information. (2741-2745) When an NCA receives a report of a serious adverse event in animals or a human adverse reaction that occurred in its territory following the use of a CAP, this NCA is responsible for ensuring that such a reaction is reported to the Agency. Such reports must be submitted to the Agency promptly and in no case later than 15 days following receipt of the information, and they should contain the NCAs assessment in addition to the details provided by the MAH. **Comments:** Does this mean that all personal data should be anonymized in EVVet reports i.e. veterinarians, animal owners and human patients? In the template on line 4742 (2.1 on page 130/168 (EU template for MAHs for reporting adverse events), confidentiality is not mentioned under the section for veterinarian / physician / pharmacist but it is mentioned under animal owner / human patient.Section 3 and 4 of this template will include details of the Vet/physician/pharmacist (section 3) and details on the animal owner/human patient (section 4). The template indicates that section 4 should be anonymised whereas section 3 need not be anonymised ie. the full name of the veterinarian should be reported. Section 4.3 starting on line 4392, does not separate between veterinarians (section 3 in the above referenced template) and animal owners (section 4, above template). However, if the veterinarian is the primary source then he/she (the way I read section	*anonymised information". The personal data needs to be anonymised in accordance with national legislation. The anonymisation mainly relates to second line reporting, i.e. when data is introduced into the electronic database EVVet.* *Volume 9B is amended as follows in this section, and the EU templates for reporting adverse events will be amended accordingly.* "To comply with EU legislation on the protection of individuals with regard to the processing of personal data, electronic transmission of adverse events should be operated on the principles of anonymised information in accordance with national legislation."

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		4.3 starting on line 4392) would also be entitled to anonymity in the report. **Proposed change (if any):** If applicable, specify that this paragraph describes privacy protection and, in section 4.3 lines 4392-4403, that the name of health care personnel (vet/physician/pharmacist) will not be anonymised in the report	
4426-4227 and 4448-4451	1	**Draft Volume 9B v 3.1:** It is strongly recommended that non-expedited adverse events are sent to the EVVet database and when required, to the relevant NCAs. From the technical point of view, non-expedited reports should be sent exactly via the same reporting systems as being in use for the submission of expedited reports, in accordance with Situation IV in the schemas for the guidance on the electronic data interchange of safety data for veterinary medicinal products in the EEA, see Annex 6 **Comments:** Electronic reporting of all cases should not be strongly recommended at this stage, especially while requirements for PSURs remain the same. Also situation IV is not described in the EMEA Schemas for the Guidance on the Electronic Data Interchange Version 1.02 (12 February 2009), simply because such route has not yet been finally agreed by all parties. Finally there should be no additional requirements to send a case to the NCA, where it is already available in the EV Vet database. **Proposed change (if any):** Please amend as follows: "It is ~~strongly~~ recommended that non-expedited adverse events are sent directly to the EV Vet database ~~and when required, to the relevant NCAs.~~" "From the technical point of view, non-expedited	*Partly accepted. To make optimal and efficient use of the electronic reporting and analysing facilities it is considered necessary to recommend and to provide the option of reporting all relevant data electronically. At present, some of the non-expedited and/or non-serious data are indeed only provided by paper in the PSUR. It is considered that the electronic availability of such data increases the surveillance capabilities of the system since it facilitates data review and analysis of a large set of data using the same tools as for analysing expedited adverse events.* *Vol 9B is amended as follows:* "Where possible, it is strongly recommended that non-expedited adverse events are sent to the EV Vet database and when required, to the relevant NCAs." "From the technical point of view, non-expedited reports should preferably be sent ~~exactly~~ via the same reporting systems as being in use for the submission of expedited reports~~, in accordance with Situation IV in the schemas for the guidance on the electronic data interchange of safety data for veterinary medicinal products in the EEA, see Annex 6.~~"

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		reports should preferably be sent ~~exactly~~ via the same reporting systems as being in use for the submission of expedited reports~~, in accordance with Situation IV in the schemas for the guidance on the electronic data interchange of safety data for veterinary medicinal products in the EEA, see Annex 6...~~"	
4581-4582	4	**Draft Volume 9B v 3.1:** In a WEB Trader Message Transmission a Safety Message can be considered successfully transmitted… **Comments:** Duplication, can be deleted. **Proposed change (if any):**	*Accepted.*
4624/7	5	**Draft Volume 9B v 3.1:** The field "date of most recent information" (R.09) taken together with the field "Sender identifier" (H.0.5), the field "Report identification number" (R.01) and the field "Unique case registration number" (R.05) provide a mechanism for each receiver to identify whether the report being transmitted is an initial or follow-up report. For this reason these items are considered critical for each transmission. A precise date should be used (i.e. day, month, year) **Comments:** Initial receive date vs. most recent info date. If the initial receive date differs from the most recent info date, will the report be perceived as a follow-up report? In some cases it will be possible to receive further information about a case before reporting it for the first time. Then these two dates will differ despite being an initial report. **Proposed change (if any):**	*Question noted. The initial receipt date may differ from the most recent information date, however the 15 day timeline applies from the initial receipt date.*
4672/Table III.9.A	5	**Draft Volume 9B v 3.1:** Table III.9.A: Examples of different scenarios for which case nullifications should and should not be carried out	*Question noted. Indeed, both examples 7 and 10 are very similar and example 10 is deleted in Table III.9.A to avoid confusion.*

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		Comments: What is the difference between example 7 and example 10? And who is meant by *initial sender* in example 10? Is this the MAH who first submitted the EVVet report or is it the primary reporter in the field? **Proposed change (if any):**	~~10 The drug taken belongs to another MAH (e.g. a product with the same active substance but marketed under a different invented name). The case should not be nullified.It is recommended that the initial sender informs the other MAH about this case. The original organisation should also submit a follow-up report to provide this new information.~~
4676-4677	1	**Draft Volume 9B v 3.1:** All other registered users have access to the data that they have submitted to EudraVigilance Veterinary. **Comments:** The policy must provide for MAH to have access to all their products' data. **Proposed change (if any):** Please refer to the IFAH-Europe position dated 15/04/2009 and submitted to EMEA in response to the public consultation on the EMEA draft EV Access Policy for medicines for veterinary Use (EMEA/113700/2008).	*Partly accepted. While the proposal is accepted in principle, it is at present time not possible to implement. The access rights will be established with the implementation of the EVVet access policy.*
4687/ 11	5	**Draft Volume 9B v 3.1:** Further initiatives are ongoing to automate the data transfer of the relevant product information from the local NCA product databases to the EVVetMPD. **Comments:** Does this mean there will be no need for MAH to send product reports in the future? **Proposed change (if any):**	*Question noted. MAHs for veterinary products may be asked in future to send product data. Access is constrained by availability of product data.*
4739	1	**Draft Volume 9B v 3.1:** Annex. 1. Glossary **Comments:** Terminology that is not aligned with VICH should not be used. **Proposed change (if any):** 'Adverse reaction' and 'serious adverse reaction' should be deleted. The terms 'adverse event' and 'serious adverse event' are aligned with VICH and sufficient.	*Not accepted. We should keep the definitions of 'adverse reaction' and 'serious adverse reaction' as they are explicit and distinguish adverse reactions from lack of efficacy.*
4739	1	**Draft Volume 9B v 3.1:** Annex. 1. Glossary	*Accepted. Proposed terms are included and in addition a*

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		Comments: Missing terms – Clinical trial HBD, Harmonised Birth Date **Proposed change (if any):**	*definition of 'third country' has been added.*
4739	3	**Draft Volume 9B v 3.1:** Adverse event - Any observation in animals, whether or not considered to be product-related, that is unfavourable and unintended and that occurs after any use of VMP (off-label and on-label uses). Included are events related to a suspected lack of expected efficacy according to approved labeling or noxious reactions in humans after being exposed to VMP(s). Ref. VICH Topic GL24 Adverse reaction - A reaction to a veterinary medicinal product which is harmful and unintended and which occurs at doses normally used in animals for the profylaxis, diagnosis or treatment of disease or to restore, correct or modify a physiological function. Ref. Article 1 (10) of Directive 2001/82/EC, as amended. This guideline will not include the word "suspected" when making full text reference to adverse reactions, serious adverse reactions, human adverse reactions. **Comments:** Imprecision of the definition of the Serious adverse event & the Serious adverse reaction : Example of anaphylaxis benign when treated and fatal without. Addition adverse events that need to be parenterally treated by vet. **Proposed change (if any):**	*Not accepted.* *The suggestion to include treatment of an adverse reaction as a benchmark of its seriousness is impractical as such information is not always reported.*
4787-4789	1	**Draft Volume 9B v 3.1:** **MARKETING AUTHORISATION HOLDER:** **MARKETING AUTHORISATION NO:**	*Partly accepted. MA No is necessary to specify which authorisations the line listing refers to.* *The following changes are made in Vol (B, involving deletion of items:*

Line no.[1]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		PERIOD OF REPORT FROM …/…/… TO …/…/…. NO. OF DOSES SOLD ON AN ANNUAL BASIS: YEAR=……NO.=……YEAR=……NO.=……YEAR=…… NO.=…… **Comments:** - 'MARKETING AUTHORISATION N°' should be deleted, because there may be several numbers; - The request for information on 'number of doses per year' and '% of incidence' is irrelevant to the line listing. **Proposed change (if any):** Please delete: ~~- MARKETING AUTHORISATION N°~~ ~~- Nº. OF DOSES SOLD ON AN ANNUAL BASIS and~~ ~~% INCIDENCE~~	~~"No of doses sold in the EEA during period",~~ ~~"Dose units",~~ ~~"% Incidence",~~ ~~"No of doses sold on an annual basis"~~ *The following are maintained* "Product*",* "MAH*", "*MA No*",* "Period of Report*"*
5263	5	**Draft Volume 9B v 3.1:** Also, when a Safety report is being sent by a MAH to a competent authority (CA), and this CA forwards the message to the EVVet central database (after including its causality assessment), this Safety Report will not be available to the MAH. When a Safety Report is being sent by a MAH directly to the EVVet central database and to the CA, the follow-up message from the CA to the EVVet central database will still not be visible to the MAH. **Comments:** When a safety report is forwarded from a CA (after including its causality assessment) to the EVVet database, this report will not be available to the MAH. If the CA causality assessment differs from that of the MAH, it would be very interesting for the MAH to know. **Proposed change (if any):** Add that the MAH will be informed about the causality assessment included by the CA.	*Partly accepted. The following is added to Vol 9B.* "The MAH will be informed about the causality assessment concluded by the CA, when and if considered relevant by the CA. "

2. Interested parties (organisations or individuals) that commented on the draft document (EMA/430286/2007 – draft v 3.1) following the close of the public consultation

Stakeholder no.	Name of organisation or individual
6	Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL),
7	European Medicines Agency

2.1. Specific comments on text

Line no.[2]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
3879	6	**Draft Volume 9B v 3.1**: "The PSUR submission schedule to be followed in the CMS is the one in place in the RMS, unless otherwise agreed during MRP or DCP. This should be decided on a case by case basis." **Comment:** According to current PSUR synchronisation / PSUR work share in assessment initiative the DLPs on the lists for active substances should be taken into account in all Member States. The proposed change would be in line with current obligation for all Member States. Proposed change: **"unless otherwise agreed during MRP or DCP. The RMS should take into account the PSUR synchronisation / PSUR work share initiative on PSUR assessment (see website of the Heads of Medicinal Agencies, Annex 4., References). For active substances which are on the lists for PSUR synchronisation, the PSUR submission schedule should follow the listed DLPs. ~~This should be decided on a case by case basis.~~**	*Partly accepted. Vol 9B is amended as follows:* **"unless otherwise agreed during MRP or DCP. The RMS should take into account the PSUR synchronisation / PSUR work share initiative on PSUR assessment (see website of the Heads of Medicinal Agencies, Annex 4., References). For active substances which are on the lists for PSUR synchronisation, *it is recommended that* the PSUR submission schedule should follow the listed DLPs. ~~This should be decided on a case by case basis.~~**
3881-3882	6	**Draft Volume 9B v 3.1**: "The RMS will evaluate the PSUR and circulate a preliminary assessment report, in accordance with CMDv SOPs " **Comment:** This is not correct: CMDv does not publish SOPs	*Accepted*

[2] Line numbers refer to draft Volume 9B of the Rules Governing Medicinal Products in the European Union. Version 3.1 – consultation http://ec.europa.eu/health/files/pharmacos/news/volume_9b_master_draft_v3.1_en.pdf

Line no.[2]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		Proposed change: **"The RMS will evaluate the PSUR and circulate a preliminary assessment report, <u>in accordance with CMDv guidance documents</u> "**	
3881-3885	6	**Draft Volume 9B v 3.1**: " The RMS will evaluate the PSUR and circulate a preliminary assessment report, in accordance with CMDv SOPs, to the CMS within the specified time schedule. The CMS should respond on the RMS preliminary assessment report. The RMS will distribute the final assessment report to the CMSs and the MAH. This assessment report will, if requested by the RMS or a CMS due to disagreement or need for advice, be discussed at a PhVWP–V meeting." **Comment:** The Assessment of work share PSURs not reflected. The proposed change would be in line with current obligation for all Member States. **Proposed change:** "…be discussed at a PhVWP-V meeting. <u>In case the VMP is participating in PSUR synchronisation / PSUR work share initiative on PSUR assessment the RMS will liaise with the PSUR-RMS (P-RMS) for that product. (see website of the Heads of Medicinal Agencies, Annex 4., Reference)."</u>	*Accepted.*
3891	6	**Draft Volume 9B v 3.1**: : " …applied for by the MAH should be agreed." **Comment:** Amendment of PSUR submission dates in line with PSUR synchronisation / PSUR work share initiative on PSUR assessment not reflected. Update needed. The proposed change would be in line with current obligation for all Member States. **Proposed change:** " …applied for by the MAH should	*Partly accepted. Vol 9B is amended as follows:* …applied for by the MAH should be agreed <u>between RMS and CMSs. Adherence to listed DLPs included in PSUR synchronisation / PSUR work share initiative on assessment of PSURs *is recommended*</u>.

Line no.[2]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		be agreed between RMS and CMSs. Adherence to listed DLPs included in PSUR synchronisation / PSUR work share initiative on assessment of PSURs should always have highest priority.	
3892-3896	6	**Draft Volume 9B v 3.1**: "Given the variability…www.hma.eu." **Comment:** Update to status of PSUR work share initiative needed. **Proposed change:** "Given the variability of resources available and making most effective use of these resources without duplication of work the Heads of Medicinal Agencies initiated the PSUR synchronization / PSUR work share initiative on PSUR assessment. Lists of active substances with harmonized DLPs for harmonized PSUR submission and guidance documents on how to participate in this procedure can be found on the Heads of Medicinal Agencies website: http://www.hma.eu. "	*Partly accepted. Vol 9B is amended as follows:* "Given the variability of resources available and *in order to make* most effective use of these resources without duplication of work the Heads of Medicinal Agencies initiated the PSUR synchronization / PSUR work share initiative on PSUR assessment. Lists of active substances with harmonized DLPs for harmonized PSUR submission and guidance documents on how to participate in this procedure can be found on the Heads of Medicinal Agencies website: http://www.hma.eu. "
4324	7	**Draft Volume 9B v 3.1:** Part III. 2. Overview of the available electronic reporting systems in the EU, section 2.2 on the Simplified electronic reporting form **Comments:** Additional clarification related to an improvement being implemented during 2009 on the EVWEB site to clarify the different Member States policies to the use of SEF. **Proposed change (if any):** The following text should be added in section 2.2 on the Simplified electronic reporting form: "Some competent authorities do not allow using SEF and instead have alternative electronic reporting tools available or require the use of EVWEB.	*Accepted.*

Line no.[2]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		The different Member States policies and corresponding links to the relevant competent authorities' website are listed on the EVVet Website prior to accessing SEF."	
4662-4665	7	**Draft Volume 9B v 3.1:** Part III. **9. Handling of duplicate reports** **Comments:** Further amendmends need to be included to take into account latest technical improvements related to duplicate detection. **Proposed change (if any):** [Modify lines 4662-4665]: When a sender has identified a duplicate it is recommended to nullify one report while ensuring that the remaining report contains all additional information that would be present in the nullified report. ~~In addition, in case of duplicate reports where one report needs to be nullified, the update of the remaining case should be performed in the form of a follow up report, if it is considered that complementary information of the nullified case should be included in the case that is considered as the master report.~~ [Add after table Table III.9.A]: Specific duplicate detection software is also available by the European Medicines Agency and allows screening of the database for duplicate reports based on a specific algorithm developed and tested for EudraVigilance Veterinary data. This application allows linking two or more reports that are considered duplicates, hence no reports would be nullified by the European Medicines Agency through the use of the duplicate detection software. When reports are linked, one report will be selected as the principal report but there will be no transfer of information from any of the	*Accepted*

Line no.[2]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		linked reports, instead it will remain possible to continue sending follow-up reports to any of the linked duplicate reports. The data analysing tools take into account when reports have been linked to avoid e.g. VeDDRA terms to be counted twice.	

Line no.[2]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
4815-4816	6	**Draft Volume 9B v 3.1**: Annexes. 3. Eudranet mailboxes for use in communication **Comment:** Update is necessary, new Mail-Box to be added Proposed change: **Add** "V.CMD-PSUR Periodic Safety Update Reports: MRP/DCP, PSUR synchronisation / work share initiative on PSUR assessment"	*Accepted.*
4902	6	**Draft Volume 9B v 3.1: Annex 4 References**: **Comment:** in different places in Vol 9B reference is made to either HMA in general or HMA PSUR workshare initiative. These references are still missing. **Proposed change:** Add Heads of Medicines Agencies (HMA), http://www.hma.eu PSUR synchronisation / PSUR work share initiative on PSUR assessment of the Heads of Medicines Agencies, The Heads of Medicines Agencies>Veterinary Medicines > Heads of Agencies > About HMA > Working Groups > PSSG - PSUR synchronisation Sub Group, http://www.hma.eu/236.html	*Accepted.*
5030	7	**Draft Volume 9B v 3.1:** Annex 5.2, section 4. Registration to EVVet - organisation and user management	*Accepted.*

Line no.[2]	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		Comments: During the Veterinary Joint Implementation Group meeting on 15 July 2009 it was agreed that with the present electronic reporting system it seems not appropriate to require certain MAHs, with no or very limited reports, to register. In particular smaller and local MAHs with no third country reports (for which direct reporting to EVVet central database would still be required (see reporting schemas)). It would be up to the discretion of the competent authority to allow certain MAHs to limit their electronic reporting activity to the use of SEF or any other locally available electronic reporting system. It was considered that this change would still be in line with the current Volume 9B Guideline on monitoring of compliance with pharmacovigilance inspections for veterinary medicinal products, since the "as applicable" wording in *"The detailed description of the pharmacovigilance system should include the following elements, as applicable:"* may be used by MAHs to argument for non-registration to EVVet. It was also agreed that for those MAHs that would be allowed for non-registration, the situation would be constantly reviewed to ensure that in case of increased reporting or third country reports such MAH would still be required to register to EVVet. **Proposed change (if any):** Add the following text to section 4. Registration to EVVet: "In principle all MAHs in the EU need to register to EudraVigilance Veterinary in order to ensure compliance with the reporting requirements for the 15-day third country reports that should be send directly to the central database. It is considered however to the discretion of the competent authority to allow specific MAHs that have a history of no or very limited reporting to postpone the registration until necessary and in any case when third country reports would be due."	