6 November 2015
EMA/CVMP/PhVWP/590073/2015
Committee for Medicinal Products for Veterinary Use (CVMP)

Concept paper for revision of the recommendation for the basic surveillance of EudraVigilance Veterinary data

Agreed by CVMP Pharmacovigilance Working Party	September 2015
Adopted by CVMP for release for consultation	6 November 2015
Start of public consultation	20 November 2015
End of consultation (deadline for comments)	29 February 2016

The proposed recommendation will replace 'Recommendation for the basic surveillance of Eudravigilance Veterinary data' (EMA/CVMP/PhVWP/471721/2006).

Comments should be provided using this template. The completed comments form should be sent to vet-guidelines@ema.europa.eu

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

1. Introduction

The CVMP adopted the recommendation on pharmacovigilance surveillance and signal detection of veterinary medicinal products (EMA/CVMP/PhVWP/901279/2011) in April 2015 providing an initial framework for further development of signal detection in veterinary pharmacovigilance, its practical modalities, interpretation and location in the signal management process. The recently adopted recommendation (EMA/CVMP/PhVWP/901279/2011) is applicable to post-marketing surveillance of all veterinary medicinal products (VMPs) authorised in the European Union (EU).

Signal detection is one of the tools available for surveillance of pharmacovigilance data to screen and assess data reported for a particular VMP and/or active substance as part of the continuous evaluation of their benefit-risk balance. The availability of adverse event (AE) databases, such as EudraVigilance Veterinary (EVVet) has enabled progress to be made in veterinary pharmacovigilance as the electronic tools available (in particular via the queries in the EVVet Data Warehouse (DWH)) which gives another methodology for an efficient and resource effective way of monitoring pharmacovigilance data.

This concept paper describes and discusses the need to revise the CVMP recommendation for the basic surveillance of EudraVigilance Veterinary (EVVet) data (EMA/CVMP/PhVWP/471721/2006) for centrally authorized products (CAPs) taking into account the recent adoption of the recommendation on pharmacovigilance surveillance and providing a comprehensive and streamlined surveillance process involving periodic safety update report (PSUR) assessment and signal detection within the framework of the current legislation.
The proposed recommendation is for CAPs. The aim of this document is to enhance the impact of pharmacovigilance by strengthening surveillance activities within the resources available.

2. Problem statement

The recommendation for the basic surveillance of EVVet data (EMA/CVMP/PhVWP/471721/2006) was originally developed to provide a framework for surveillance of VMPs using the electronic tools available. To date, it has only been fully implemented for CAPs, since the EU VMP database is only fully populated for these products.

In view of the recent adoption of the pharmacovigilance surveillance and signal detection of VMPs (applicable to all VMPs authorised in the EU) some overlap exists between the two recommendations. In addition some of the principles in the recommendation for basic surveillance are not in line with the recommendation for surveillance and signal detection.

In view of the pilot on PSUR assessment for CAPs based on EVVet data, further consideration of the use of the EVVet DWH for PSUR assessment and signal detection was considered necessary, to optimise surveillance and avoid duplication of work between PSUR assessment and evaluation of signal detection findings.

The pilot initiative on PSUR assessment for CAPs based on EVVet data started in 2012. This involved a selection of CAPs and allowed assessors to evaluate PSURs with support of electronically submitted pharmacovigilance data using the EVVet DWH. The MAHs involved in this pilot submitted all serious and non-serious events to EVVet and were exempt from providing a separate line listing for the PSURs in question. The experience gained in the pilot and further development and improvement of the EVVet DWH should be taken into account in the proposed recommendation.

3. Discussion (on the problem statement)

According to the current legislation the MAH is obliged to submit a PSUR to the Agency and Member States immediately upon request or at least every six months after authorisation until the placing on the market. PSURs shall also be submitted immediately upon request or at least every six months during the first two years following the initial placing on the Community market and once a year for the following two years. Thereafter, the reports shall be submitted at three-yearly intervals, or immediately upon request.

In addition the MAH shall ensure that all suspected serious adverse reactions and adverse human reactions to a VMP authorised in accordance with the provisions of Regulation (EC) No 726/2004 occurring within the Community which a health-care professional brings to his attention are recorded and reported promptly to the Member States in the territory of which the incident occurred no later than 15 days following receipt of the information.

Each Member State shall ensure that all suspected serious adverse reactions, and adverse human reactions, occurring within its territory to a VMP authorised in accordance with the provisions of Regulation (EC) No 726/2004 which are brought to its attention are recorded and reported promptly to the Agency and the MAH for the VMP, and no later than 15 days following receipt of the information.

Pharmacovigilance surveillance of CAPs is currently carried out via signal detection at predefined time-points and based on data in EVVet (serious AE reports plus voluntarily transferred non-serious reports) and in parallel assessment of PSURs submitted by MAHs at predefined time points. The PSURs contain all AE reports no matter severity. To avoid assessing the same data twice - during both signal detection and PSUR assessment – signal detection findings requiring further investigation are discussed at the Pharmacovigilance Working Party (PhVWP-V). Where necessary, following endorsement by CVMP, the MAH will be requested to specifically address issues identified in signal detection in the next PSUR. In case signal detection reveals matters that require more urgent attention, the need for a targeted PSUR shall be considered. Industry has at several occasions expressed a strong wish (during public consultation on the recommendation on pharmacovigilance surveillance and signal detection of veterinary medicinal products (EMA/CVMP/PhVWP/901279/2011) as well as at interested parties meetings) to be involved in signal management at an earlier time-point.

The industry has also expressed a strong wish for the continuation of the pilot of PSUR assessment based on EVVet data on the condition that the requirement for line listings can be reduced. The DWH has in the meantime been improved to generate the line listings with the inclusion of the narrative field and the possibility to drill directly to the individual reports. The DWH line listing hereby outperforms the line listings provided together with the PSUR. There is however a need to progress on a solution to make the DWH line listings and overall relevant EVVet data accessible to the MAH in order to ensure working on the same dataset. Experience has shown that due to inconsistencies in reporting, the data available to the MAH can be less than the data available to the authorities.

It should be explored if there are alternative (automated) routes, to the PSURs, to get independent sales figures based on number of prescriptions, orders of medicinal products, or dispatched product. Sales figures are needed to calculate ratio and incidence of AEs, which, when compared over time, is indicative of any increase or decrease in the reporting of AEs. If alternative routes can be established it would be possible to:

- Simplify the content and allow more flexibility in submission of the PSURs
- Explore access to sales figures independent of MAHs and PSUR submission

Additionally consideration of the experience gained with the pilot on PSUR assessment for CAPs based on EVVet data is necessary to establish how EVVet DWH can be used for PSUR assessment and signal detection.

The document should be expanded to include proposals allowing benefit from the analyses in signal detection surveillance in the PSUR assessment.

The document should be expanded to include proposals on reducing the administrative burden for authorities as well as MAHs while improving the overall effectiveness of pharmacovigilance surveillance and reducing duplication of efforts for assessors, which may include the following:

- MAH database access, use of EVVET data and DWH queries within or outside the system depending on how/if EVVet access policy can be solved;
- Transfer of non-serious AEs to EVVet is not obligatory although, according to Volume 9B, it is strongly recommended; analyses of the full data-set provides a good overview of all AEs no matter severity; in return of transferring all data the MAH should be relieved from including the "Line Listing" in the PSUR save in exceptional circumstances.

The following aspects should also be addressed in the revision of the recommendation for basic surveillance:

- Further guidance on the queries to be used in the EVVet DWH and on the analysis process; a stepwise tutorial is being drafted giving advice on how to use the queries and which queries to be used for e.g. PSUR assessment purposes; training in DWH queries is taking place/being planned.
- Reasons for inconsistencies between line listing generated by MAH and line listing generated by the DWH and investigating solutions to improve access of all stakeholders to the same dataset.
- PhVWP-V to continue to give advice on the signal detection findings that should be addressed by the MAH within the next PSUR. Signal detection findings that require more urgent attention may trigger a targeted PSUR.
- Exchange of data and findings with the MAH during the process to allow the MAH to focus their analysis on the rapporteur's signal detection outcome (NB this is already applicable for pharmacovigilance surveillance of human CAPs).

In addition to the revision of the recommendation, a modification of the current assessment template for PSURs, i.e. including the information already available in the Veterinary Pharmacovigilance Surveillance (VPhS) FileMaker database from the signal detection, should be considered.

4. Recommendation

The CVMP recommends revising the recommendation for the basic surveillance of EVVet data (EMA/CVMP/PhVWP/471721/2006) to address the issues outlined above.

5. Proposed timetable

Adoption of concept paper by CVMP for release for consultation: November 2015

End of consultation: February 2016

Preparation of draft revised recommendation: during 2016

Adoption by CVMP of the draft revised recommendation for consultation: beginning 2017

6. Resource requirements for preparation

The revision of this recommendation will be undertaken by the PhVWP-V and will involve the PhVWP-V secretariat and CVMP. The PhVWP-V will appoint a rapporteur from amongst its members.

It is anticipated that the revision of the recommendation will require drafting group meetings to be held as virtual meetings.

7. Impact assessment (anticipated)

The use of the data in the EVVet DWH for optimising surveillance and avoiding duplication of work in pharmacovigilance surveillance of CAPs in Europe will be of benefit for the human and animal health, the authorities and MAHs.

A surveillance strategy to include the signal detection findings for the consideration of the MAH in the next PSUR will reduce the workload on procedural aspects and the MAH will be involved in the signal management process at an earlier time-point. The MAHs should commit to transfer all data, no matter severity, to EVVet; in return the submission of a line listing in the PSUR will not be required but will be available via DWH.

This ensures a better use of the available pharmacovigilance resources in Member States, the Agency and MAHs. In addition the transparency to industry on pharmacovigilance information will be increased.

8. Interested parties

Veterinary pharmaceutical industry and EU/EEA national competent authorities, consultants and veterinarians.

9. References to literature, guidelines, etc.

European Medicines Agency and Heads of Medicines Agency (2015) Recommendation on pharmacovigilance surveillance and signal detection of veterinary medicinal products (EMA/CVMP/PhVWP/901279/2011)

European Medicines Agency (2011) Recommendation for the basic surveillance of Eudravigilance Veterinary data (EMA/CVMP/PhVWP/471721/2006)

European Commission (2011): Volume 9B - Pharmacovigilance for Medicinal Products for Veterinary Use Guidelines on Pharmacovigilance for Medicinal Products for Veterinary

European Commission (2004): Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency