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Guideline on veterinary good pharmacovigilance practices (VGVP)

Module: Pharmacovigilance systems, their quality management systems and pharmacovigilance system master files

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1. Introduction

This module of the guidelines on veterinary good pharmacovigilance practices (VGVP) addresses the basic requirements on the pharmacovigilance system, its integral quality management system and the pharmacovigilance system master file (PSMF) that marketing authorisation holders for veterinary medicinal products authorised in the European Union (EU) should establish and maintain.

This module should be read in conjunction with Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC and Commission Implementing Regulation (EU) 2021/1281 of 2 August 2021, in particular Article 17(5), laying down rules for the application of Regulation (EU) 2019/6 of the European Parliament and of the Council as regards good pharmacovigilance practice and on the format, content and summary of the pharmacovigilance system master file for veterinary medicinal products.

This module should also be read in conjunction with the other modules of the guideline on veterinary good pharmacovigilance practices (VGVP), pharmacovigilance inspection procedures and national legislations, as applicable.

This guidance is applicable to any veterinary medicinal product in the EU, authorised via any marketing authorisation procedure including registered homeopathic veterinary medicinal products [Regulation (EU) 2019/6, Article 87(5)].

2. Pharmacovigilance system

According to Article 77 of Regulation (EU) 2019/6, marketing authorisation holders shall establish and maintain a system for collecting, collating and evaluating information on the suspected adverse events concerning their authorised veterinary medicinal products ('pharmacovigilance system'), enabling them to fulfil all their pharmacovigilance obligations.

The overall objectives of a pharmacovigilance system are:

- promoting the safe and effective use of veterinary medicinal products, in particular through providing timely information about the safety of veterinary medicinal products and their impact to public health, animal health, animal welfare and the environment;
- detecting and taking measures to prevent harm to animals and humans from adverse events and harm to the environment arising from the use of or exposure to authorised veterinary medicinal products within or outside the terms of the marketing authorisations; and
- complying with the legal requirements for pharmacovigilance tasks and responsibilities.

The pharmacovigilance system of the marketing authorisation holder shall be fully functional [Commission Implementing Regulation (EU) 2021/1281, Article 2(2)(a)] and described clearly and unambiguously in the pharmacovigilance system master file [Commission Implementing Regulation (EU) 2021/1281, Article 2(2)(f)]. The marketing authorisation holder may, where appropriate, use separate pharmacovigilance systems for different categories of veterinary medicinal products [Commission Implementing Regulation (EU) 2021/1281, Article 21(3)]. For example, a single marketing authorisation holder may establish more than one pharmacovigilance systems specific for particular types of veterinary medicinal products (vaccines, pharmaceuticals, etc.). Each such system shall be described in a separate pharmacovigilance system master file [Commission Implementing Regulation (EU) 2021/1281 Article 21(3)]. For each veterinary medicinal product, the marketing authorisation holder shall not have more than one pharmacovigilance system [Regulation (EU) 2019/6, Article 77(2)] described in a pharmacovigilance system master file.

The marketing authorisation holder shall be responsible for the pharmacovigilance of the veterinary medicinal product(s) for which it holds a marketing authorisation and shall continuously evaluate by appropriate means the benefit-risk balance of their veterinary medicinal product(s) and, if necessary, take appropriate measures to minimize the risk. The marketing authorisation holder's risk management system consists of all procedures and processes for monitoring the benefit-risk balance of veterinary medicinal products and performing signal management and includes communication, as referred to in Articles 16 to 20 of the Commission Implementing Regulation (EU) 2021/1281. Marketing authorisation holders shall ensure continuous assessment and document the risk management measures and the outcome of risk minimisation measures in the pharmacovigilance system master file [Commission Implementing Regulation (EU) 2021/1281, Article 16(3)] for the veterinary medicinal products for which specific safety monitoring requirements exist.

Where the pharmacovigilance tasks have been contracted/subcontracted out by the marketing authorisation holder to a third party, those arrangements shall be set out in detail in the pharmacovigilance system master file [Commission Implementing Regulation (EU) 2021/1281, Articles 21(2) and 22(3e)]. The marketing authorisation holder shall retain full responsibility for all pharmacovigilance obligations contracted/subcontracted to third parties as laid down in the Regulation (EU) 2019/6 and in the Commission Implementing Regulation (EU) 2021/1281, Article 2(7), and therefore the arrangements with third parties should cover how oversight and compliance with legal requirements can be ensured. Contracted/subcontracted person(s) or any other third party carrying out pharmacovigilance activities in whole or in part, on behalf of or in conjunction with marketing authorisation holders, shall accept to be audited by or on behalf of marketing authorisation holders.

The marketing authorisation holder shall comply with good pharmacovigilance practice for veterinary medicinal products. In addition to this Module and the Module on Controls and Pharmacovigilance Inspections, for key pharmacovigilance processes dedicated Modules are included in veterinary good pharmacovigilance practice guidance, as follows:

- Module on Collection and recording of suspected adverse events for veterinary medicinal products.
- Module on Signal management.
- Module on Communication.

2.1. Qualified person responsible for pharmacovigilance (QPPV)

The QPPV designated by the marketing authorisation holder should have oversight of the pharmacovigilance system in terms of structure and performance and be in a position to ensure the fulfilment of the tasks described in Article 78 of Regulation (EU) 2019/6, either directly or through delegation and supervision in accordance with Articles 77 and 78 of Regulation (EU) 2019/6. The oversight referred to above should cover the functioning of the marketing authorisation holder's pharmacovigilance system in all relevant aspects, including:

- quality control and assurance procedures;
- standard operating procedures;
- PSMF preparation and maintenance;
- database operations;
- safety reporting;
- signal management;

- post-marketing surveillance studies;
- communication to stakeholders;
- contractual/subcontractual arrangements, compliance data (e.g. in relation to the quality, completeness and timelines for safety reporting and signal management), audit reports;
- preventive or corrective action plan preparation and implementation; and
- training of personnel in relation to pharmacovigilance.

It is recognised that this role of the QPPV may impose extensive tasks on the QPPV, depending on the size and nature of the pharmacovigilance system and the number and type of veterinary medicinal products covered by the marketing authorisation holder's pharmacovigilance system. The QPPV may therefore delegate specific tasks, with appropriate oversight, to appropriately qualified and trained individuals, e.g. acting as experts on the safety aspects of certain veterinary medicinal products, provided that the QPPV maintains system oversight and overview of the safety profiles of all veterinary medicinal products. Such delegation should be documented in the PSMF. In case the QPPV has not completed veterinary surgeon training, marketing authorisation holders shall make arrangements to ensure that the QPPV is assisted by a veterinary surgeon on a continuous basis [Commission Implementing Regulation (EU) 2021/1281, Article 3(2)].

The hierarchical relationship of the QPPV shall be defined in an organisational chart together with those of other managerial and supervisory staff. In case the tasks of the QPPV are outsourced to a third party those arrangements shall be specified in detail in the contract and included in the PSMF [Regulation (EU) 2019/6, Article 77(9)].

Usually the QPPV will be designated to a single pharmacovigilance system and respective PSMF. It is acceptable for the same QPPV to provide services for more than one marketing authorisation holder, for a shared or for separate pharmacovigilance systems (e.g. in the case of subcontractor QPPV) or, if required, to fulfil the role of QPPV for more than one pharmacovigilance system of the same marketing authorisation holder, provided that the QPPV is able to fulfil duly all obligations.

Back-up arrangements that apply in the absence of the QPPV or of the veterinary surgeon, assisting the QPPV, if applicable, as referred to in Commission Implementing Regulation (EU) 2021/1281, Article 2(6), should be in place and described in the PSMF.

In addition to the QPPV, the marketing authorisation holder shall designate a local or regional representative for the purpose of receiving reports of suspected adverse events who is able to communicate in the languages of the relevant Member States [Regulation (EU) 2019/6, Article 77(3)]. The local or regional representative should report to the QPPV in relation to the pharmacovigilance tasks and responsibilities. The QPPV may also act as the local representative. The marketing authorisation holder shall ensure that the QPPV has sufficient authority to influence the performance of the quality management system with regard to pharmacovigilance and the pharmacovigilance activities of the marketing authorisation holder. The marketing authorisation holder should therefore ensure that the QPPV has authority over and access to the PSMF and approves/authorises any changes to it. The authority over the pharmacovigilance system and the PSMF allows the QPPV to implement changes to the system as well as to initiate regulatory action in response to emerging safety concerns. Furthermore, the marketing authorisation holders shall ensure that there is an appropriate procedure in place to identify and deal with any conflicts of interest of the QPPV [Commission Implementing Regulation (EU) 2021/1281, Article 2(3)].

When a marketing authorisation holder intends to expand its veterinary medicinal product portfolio, for example by acquisition of another company or by purchasing individual marketing authorisations from another marketing authorisation holder, the QPPV should be notified well before the transfer of pharmacovigilance activities in order to ensure that the potential impact on the pharmacovigilance system can be assessed and the system can be adapted accordingly. The QPPV should be involved in determining what pharmacovigilance data is to be requested from the other marketing authorisation holder, either pre- or post-acquisition. In this situation, the QPPV should review the sections of the contractual arrangements that relate to responsibilities for pharmacovigilance activities and safety data exchange (either as part of a general template or on a case by case) and have the authority to request amendments.

When a marketing authorisation holder intends to establish a partnership with another marketing authorisation holder, organisation or person that has a direct or indirect impact on the pharmacovigilance system, the QPPV should be informed in sufficient time to allow for required changes to the pharmacovigilance system to be made and be involved in the preparation of the corresponding contractual arrangements so that all necessary provisions relevant to the pharmacovigilance system are included to enable the QPPV to fulfil the responsibilities listed in Article 78 of Regulation (EU) 2019/6.

2.2. Quality management system

Marketing authorisation holders shall establish and use quality management systems that are adequate and effective for the performance of their pharmacovigilance activities.

Quality management system means a formalised system that provides for comprehensive processes, procedures, and responsibilities for achieving quality policies and objectives to coordinate and direct an organisation's activities and improve its effectiveness and efficiency in this regard on a continuous basis [Commission Implementing Regulation (EU) 2021/1281, Article 1(a)].

While there has to be compliance with these legal requirements, the implementation of a quality system should be adapted to the respective organisation. The application of the quality system should be adapted to how crucial each pharmacovigilance task is for fulfilling the objectives for each veterinary medicinal product covered by a pharmacovigilance system. The quality system shall be based on all the following activities [Commission Implementing Regulation (EU) 2021/1281, Article 4(6)]:

- Quality planning: establishing structures and planning integrated and consistent processes.
- Quality adherence: carrying out tasks and responsibilities in accordance with quality requirements.
- Quality control and assurance: monitoring and evaluating how effectively the structures and processes have been established and how effectively the processes are being carried out.
- Quality improvements: correcting and improving the structures and processes where necessary.

Processes to monitor the performance and effectiveness of a pharmacovigilance system and its quality system include:

- reviews of the systems by those responsible for management;
- audits;
- compliance monitoring;
- inspections;

- evaluating the effectiveness of actions taken with veterinary medicinal products for the purpose of minimising risks and supporting their safe and effective use.

The quality management system shall be described in the pharmacovigilance system master file [Commission Implementing Regulation (EU) 2021/1281, Article 4]. Relevant documents include:

- documents on assignment of roles, responsibilities and authorities to all personnel directly involved in pharmacovigilance tasks;
- job descriptions defining the duties of the managerial and supervisory staff;
- training plans and records;
- instructions for the compliance management processes;
- appropriate instructions on the processes to be used in case of urgency, including business continuity;
- performance indicators where they are used to continuously monitor the good performance of pharmacovigilance activities;
- reports of audits and follow-up audits, including their dates and results;
- the methods of monitoring the efficient operation of the quality system and, in particular, its ability to fulfil the quality objectives;
- records to demonstrate that deficiencies and deviations from the established quality system are monitored, that corrective and preventive actions have been taken, that solutions have been applied to deviations or deficiencies and that the effectiveness of the actions taken has been verified.

2.2.1. Written procedures

An essential element of any pharmacovigilance system is that there are clear written procedures in place. The quality management system shall include detailed policies, processes and procedures, documented in the PSMF, for at least, but not necessarily limited to, pharmacovigilance activities listed in Chapter 4 of Commission Implementing Regulation (EU) 2021/1281:

1. Initial recording of suspected adverse event.
2. Collection of additional data.
3. Collation of reports of suspected adverse events and additional data.
4. Data handling other than mentioned in points (1) to (3) of this list.
5. Evaluation of data.
6. Monitoring the quality, integrity and completeness of all information registered in the pharmacovigilance system including, but not restricted to, the information reported to the Union pharmacovigilance database and management of duplicates.
7. Recording of adverse event in the Union pharmacovigilance database.
8. Archiving of all relevant documents.
9. Risk management system including processes for:

    9.1. signal management [Commission Implementing Regulation (EU) 2021/1281, Article 17];

9.2. continuous monitoring of the benefit-risk balance of veterinary medicinal products [Commission Implementing Regulation (EU) 2021/1281, Articles 18 and 19];

9.3. overarching communication plan [Commission Implementing Regulation (EU) 2021/1281, Article 20].

10. Document management system [Commission Implementing Regulation (EU) 2021/1281, Article 5].

11. Training [Commission Implementing Regulation (EU) 2021/1281, Article 6].

12. Audit [Commission Implementing Regulation (EU) 2021/1281, Article 8].

In each area, the marketing authorisation holder should be able to provide evidence of a system that supports appropriate and timely decision making and action. The list of written procedures should also be available and should comprise the procedural document reference number, title, effective date and document type (for all standard operating procedures, work instructions, manuals etc.) and details on how the procedures can be accessed. Procedures belonging to service providers and other third parties should be clearly identified. Documents relating to specific local/country procedures need not be listed, but a list may be requested on a per country basis.

2.2.2. Performance indicators

The organisation shall use relevant performance indicators [Commission Implementing Regulation (EU) 2021/1281, Article 7] to continuously monitor the performance of pharmacovigilance activities in relation to the quality requirements in accordance with legislation and guidance. The items of information that can be collected at regular intervals to track the performance of the system should be realistic and measurable, such as submission timeliness or quality of reports / reports free of errors. A list of these performance indicators including the reason why they have been chosen, if applicable, and a description on how to use them should be included in Section E.3 of the PSMF.

2.2.3. Audits

Marketing authorisation holders shall perform audits of the pharmacovigilance system at regular risk-based intervals to ensure that it complies with the requirements set out in Commission Implementing Regulation (EU) 2021/1281 and to determine the pharmacovigilance system effectiveness. Audits of the pharmacovigilance system should ensure that it complies with the legal requirements, the human resource management, the compliance management, the record management and data retention and to ensure its effectiveness. A report shall be drawn up on the results for each audit and any follow-up audits and these shall be sent to the QPPV and management responsible for the matters audited, as applicable, to ensure that management cooperates with the QPPV to address the findings. The report should include the results of audits of organisations or persons the marketing authorisation holder has delegated tasks to, as these are part of the marketing authorisation holder‘s pharmacovigilance system. The risk-based audit schedule and the report on each audit and follow-up audit, including their dates and results shall be documented in Section E and Annex 4 of the PSMF, as applicable. The process for risk-based planning shall be described and the rationale documented in the PSMF [Commission Implementing Regulation (EU) 2021/1281 Article 8(3)]. Contracted/subcontracted person(s) or any other third party carrying out pharmacovigilance activities in whole or in part, on behalf of or in conjunction with marketing authorisation holders, shall accept to be audited by or on behalf of marketing authorisation holders [Commission Implementing Regulation (EU) 2021/1281, Article 6(2)].

2.2.4. Corrective and Preventive Action Plan

The marketing authorisation holder's corrective and preventive action plan shall document in writing a robust, effective and useful process systematically addressing and minimizing identified risk or defects. It shall be clear and precise and address timelines for action [Commission Implementing Regulation (EU) 2021/1281, Article 9]. Marketing authorisation holders shall monitor the implementation and assess the effectiveness of corrective and preventive actions. If there are changes associated with the corrective and preventive actions, those changes shall be evaluated and be part of a controlled process of change (change management) and communicated to relevant stakeholders.

In particular as a consequence of audits, corrective action(s), including a follow-up audit on deficiencies identified, shall be taken where necessary. Additionally, corrective and preventive actions should be drawn for non-compliance identified during inspections by the competent authorities aiming at monitoring the compliance of marketing authorisations holders with legally required pharmacovigilance tasks and responsibilities. Associated corrective and preventive actions shall be documented for the last 5 years.

2.2.5. Training of personnel for pharmacovigilance

Achieving the required quality for the conduct of pharmacovigilance processes and their outcomes by an organisation is intrinsically linked with the availability of a sufficient number of competent and appropriately qualified and trained personnel.

All personnel involved in the performance of pharmacovigilance activities shall receive initial and continued training [Commission Implementing Regulation (EU) 2021/1281, Article 6(1)]. For marketing authorisation holders, this training shall relate to the roles and responsibilities of the personnel.

The organisation shall keep training plans and records for documenting, maintaining and developing the competences of personnel [Commission Implementing Regulation (EU) 2021/1281, Article 6(2)]. Training plans should be based on training needs assessment and should be subject to monitoring.

The training should support continuous improvement of relevant skills, the application of scientific progress and professional development and ensure that staff members have the appropriate qualifications, understanding of relevant pharmacovigilance requirements as well as experience for the assigned tasks and responsibilities. All staff members of the organisation should receive and be able to seek information about what to do if they become aware of a safety concern.

There should be a process in place within the organisation to check training results in the appropriate levels of understanding and conduct of pharmacovigilance activities for the assigned tasks and responsibilities, or to identify unmet training needs, in line with professional development plans agreed for the organisations as well as the individual staff members.

Adequate training should also be considered by the organisation for those staff members to whom no specific pharmacovigilance tasks and responsibilities have been assigned but whose activities may have an impact on the pharmacovigilance system or the conduct of pharmacovigilance. Such activities include but are not limited to those related to clinical trials, technical product complaints, medical information, sales and marketing, regulatory affairs, legal affairs and audits.

Appropriate instructions on the processes to be used in case of pharmacovigilance-related urgency, including business continuity, shall be provided by the organisation to their personnel.

2.2.6. Document management system

The organisation shall record all pharmacovigilance information and ensure that it is handled, stored, saved and archived to allow accurate reporting, interpretation and verification of that information.

A document management system shall be put in place for all documents related to pharmacovigilance activities, ensuring their retrievability as well as traceability of the measures taken to investigate safety concerns, of the timelines for those investigations and of decisions on safety concerns, including their date and the decision-making process. The document management system referred to in Article 5 of Commission Implementing Regulation 2021/1281 shall include a record management system for receiving, recording, collating and assessing information on adverse events [Commission Implementing Regulation 2021/1281, Article 10(1)].

All information technology (IT) systems, (electronic) storage spaces and record management systems including database systems used as part of pharmacovigilance activities should be located, designed, constructed, adapted and maintained to suit their intended purpose in line with the quality objectives for pharmacovigilance. These systems should be subject to appropriate checks, qualification and/or validation activities to prove their suitability for the intended purpose. Evidence on validation status of the system(s) used should be available upon request, if applicable. There should be appropriate structures and processes in place to ensure that pharmacovigilance data and records are protected from destruction during the applicable record retention period.

As part of a record management system, specific measures should be taken at each stage in the storage and processing of pharmacovigilance data to ensure data security, integrity and confidentiality. This should involve strict limitation of access to records and to databases to authorised personnel respecting the confidentiality of the data. For systems critical for the conduct of pharmacovigilance it should be ensured to build into the system the creation of a record of all pharmacovigilance data changes and deletions (a system generated "audit trail"). For change or deletion of pharmacovigilance data the reason should be documented. Audit trails need to be available.

2.2.7. Quality management system requirements for pharmacovigilance tasks contracted/subcontracted by the marketing authorisation holder

Where a marketing authorisation holder has contracted/subcontracted part or all of its pharmacovigilance tasks, it shall retain full responsibility for ensuring that an effective quality management system is applied in relation to those tasks. All legislative and guidance requirements are also applicable to the other organisation (third party) to which the tasks have been contracted/subcontracted even if it is located outside the EU.

When contracting/subcontracting tasks to a third party, the marketing authorisation holder shall conclude contract(s) with the third party and these should be detailed, up-to-date and clearly document the allocation of tasks and responsibilities between the marketing authorisation holder and the third party. A description of the contracted/subcontracted activities and/or services and a list of the contracts with contractors/subcontractors, specifying the veterinary medicinal product(s) and territory(-ies) concerned, shall be included in the PSMF [Commission Implementing Regulation (EU) 2021/1281, Article 22(3)(e)(iii)]. The third party may be subject to inspection at the discretion of the competent or supervisory authority in the relevant Member State depending on the location of the contractor/subcontractor organisation and /or the tasks and responsibilities delegated to them.

Contractual arrangements should be prepared with the aim of enabling compliance with the legal requirements by each party involved. The third party may not subcontract any task assigned to it by the marketing authorisation holder without the marketing authorisation holder’s written consent. When

preparing contractual arrangements, the marketing authorisation holder should include sufficiently detailed descriptions of the delegated tasks, the related interactions and data reconciliation, together with, for example, agreed definitions, tools, assignments and timelines. The contractual arrangements should also contain clear information on the practical conduct of the outsourced tasks, including those for the maintenance of pharmacovigilance databases, if applicable. Further, they should indicate which processes are in place for verifying whether the agreed arrangements are being adhered to on an ongoing basis. In this respect, e.g. regular risk-based audits of the third party by the marketing authorisation holder are required.

2.3. Pharmacovigilance system master file (PSMF)

2.3.1. Summary of the pharmacovigilance system master file

Article 8(1)(c) of Regulation EU 2019/6 requires a summary of the applicant's pharmacovigilance system master file to be included in the marketing authorisation application, which, in accordance with Article 23 of Commission Implementing Regulation 2021/1281, shall include the following elements:

- The pharmacovigilance system master file reference number.
- The pharmacovigilance system master file location.
- Name, contact details and place of operation of the QPPV.
- A signed statement from the marketing authorisation holder and the QPPV that the QPPV has the necessary means to fulfil the tasks and responsibilities requested by Regulation (EU) 2019/6.
- The type of record management system used for adverse events reports including the name of the database, if applicable.

At the time of the granting of a marketing authorisation, the information from the summary of the applicant's pharmacovigilance system master file (QPPV name, contact details and location, PSMF reference number and location) will be stored in the Union product database and communicated to the Union pharmacovigilance database by means of the interconnection as foreseen in Article 74(2) of Regulation (EU) 2019/6. Information on all pharmacovigilance system master files must be registered in the database and while each PSMF and QPPV will be linked to one or more veterinary medicinal products, each product authorised under Regulation (EU) 2019/6 should be linked to a single PSMF and the respective designated QPPV.

Marketing authorisation holders shall ensure that the entries in the Union product database for veterinary medicinal products are always up-to-date, including the information about the QPPV, name and contact details (telephone numbers for continuous availability, email address, postal address and operational location of the QPPV) and PSMF reference number and location information. Upon a change in any of the information in the summary of the applicant's pharmacovigilance system master file, the relevant variation not requiring assessment [Regulation (EU) 2019/6, Article 61] shall be submitted to the database in accordance with the list provided in the Annex of Commission Implementing Regulation (EU) 2021/17 establishing a list of variations not requiring assessment in accordance with Regulation (EU) 2019/6 of the European Parliament and of the Council and within 30 days following the implementation of that variation. Readily available up to date information will facilitate identification of the competent authorities of the Member States responsible to carry out inspections of the pharmacovigilance system master files located in their Member State and any changes to those (i.e. the Supervisory Authorities, see the VGVP Module on Controls and Pharmacovigilance Inspections, section 2.3).

Each PSMF can be declared only in one location in the applicant's summary of pharmacovigilance system master file and subsequently in the Union product database and this single location should be registered as part of controlled organisation data. The address of the location of the PSMF provided should be a physical office address which reflects either the site in the EU where the main pharmacovigilance activities of the marketing authorisation holder are performed or the site where the QPPV operates. This address may be different to that of the applicant/marketing authorisation holder, for example it may be a different office of the marketing authorisation holder or the address of a third party undertaking the main activities. Where the PSMF is held in electronic form, the location stated must be a site where the data stored can be directly accessed, and this is sufficient in terms of a practical electronic location. When determining the main site of pharmacovigilance activity, the marketing authorisation holder should consider the most relevant EU site for the pharmacovigilance system since the relative importance of particular activities may vary according to the veterinary medicinal products and fluctuate in the short term. The marketing authorisation holder should have an appropriate rationale for the location decision. In the situation where the main activities take place outside the EU, or where a main site cannot be determined, the location should default to the site where the QPPV operates.

2.3.2. Pharmacovigilance system master file content

The PSMF is a legal requirement in the EU and is applicable for any veterinary medicinal product authorised in the EU, irrespective of the marketing authorisation procedure. The required content and management of the PSMF in accordance with the Commission Implementing Regulation (EU) 2021/1281 applies irrespective of the organisational structure of a marketing authorisation holder, including any contracting/subcontracting or delegation of activities, or their location. Irrespective of the location of other activities, the QPPV's residence, the location at which he/she carries out his/her tasks and the PSMF location must be within the EU. Following European Economic Area (EEA) agreements, the QPPV may also reside and operate in Norway, Iceland or Liechtenstein. The content of the pharmacovigilance system master file should reflect availability of global safety information for veterinary medicinal products authorised in the EU, presenting information on the pharmacovigilance system applied at global, regional and national level, as applicable. The content shall be indexed to allow for efficient navigation in the document and follow the structure described in the Commission Implementing Regulation (EU) 2021/1281,, Article 22, on the format and content of the pharmacovigilance system master file. The PSMF shall describe the pharmacovigilance system in place at the current time.

The PSMF shall consist of a main part and Annexes containing the information described in the Commission Implementing Regulation (EU) 2021/1281, Article 22, and as shown in Table 1. The sections in the main part of the PSMF should contain information that is fundamental for the description of pharmacovigilance system whereas the corresponding Annexes should include supplementary information for each section that may change frequently.

Table 1. PSMF content overview

PSMF section	Main Part	Annexes
Information on the PSMF	Section A	Annex 1 – Logbook
QPPV, Assisting veterinary surgeon, and back up procedures	Section B	Annex 2
Marketing Authorisation holder information	Section C	Annex 3

PSMF section	Main Part	Annexes
Document management system (including record management system for adverse event recording)	Section D	
Quality management system for pharmacovigilance activities	Section E	Annex 4
Contractual arrangements between marketing authorisation holders and third parties concerning pharmacovigilance activities	Section F	Annex 5

2.3.3. Pharmacovigilance system master file location, availability and maintenance

The requirements for the location, availability and maintenance of the PSMF are provided in Article 79(6) of Regulation (EU) 2019/6 and in Articles 24 and 25 of the Commission Implementing Regulation (EU) 2021/1281.

When pharmacovigilance activities are shared between marketing authorisation holders it is advised that the partners agree on how to mutually maintain the relevant sections within their own pharmacovigilance system master files. Accessibility of the PSMF to all the applicable marketing authorisation holder(s), and its provision to competent authorities should be defined in written agreements. It is vital that marketing authorisation holder(s) can gain assurance that the pharmacovigilance system used for its veterinary medicinal products is appropriate and compliant.

According to Article 24(3) of Commission Implementing Regulation 2021/1281 the PSMF itself shall be subject to version control and indicate the date(s) when it was last updated. Any alteration to the content of the main part of the PSMF made within the last 5 years shall be recorded in a logbook, indicating

- the changed section;
- the kind of change;
- the date of change;
- the person responsible for the change;
- where appropriate, the reason for the alteration [Commission Implementing Regulation (EU) 2021/1281, Article 24(4)].

Changes to the information in the Annexes do not need to be tracked in the form of a logbook and version control should be adjusted to the type of information. For example, information in the Annexes of the PSMF that is being regularly updated, such as veterinary medicinal product lists or compliance figures, may include outputs from controlled systems (such as electronic document management systems or regulatory databases). The information and superseded versions of such content may be managed outside of the PSMF content itself, provided that the history of changes is maintained and available to competent authorities and the Agency on request. Marketing authorisation holders need to ensure that the obligations concerning the timely provision of an up to date PSMF can be met.

Definitions

Please refer to the VGVP Glossary for relevant definitions.