

Pursuant to Article 257 paragraph 13 of the Law on Medicinal Products, the Management Board of the Institute for Medicines hereby adopts the following

RULEBOOK ON PHARMACOVIGILANCE SYSTEM FOR VETERINARY MEDICINAL PRODUCTS*

I. GENERAL PROVISIONS

Article 1

This Rulebook regulates the manner of data collection, reporting and monitoring of adverse events, good pharmacovigilance practice, as well as the format, content, and summary of the *Pharmacovigilance System Master File* (hereinafter: PSMF) for veterinary medicinal products.

Article 2

Terms used in this Rulebook for natural persons in masculine gender shall include same terms in feminine gender.

Definitions

Article 3

For the purposes of this Rulebook, the following definitions shall apply:

1) **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;

2) **performance indicator** means an item of information collected at regular intervals to monitor the performance of a system;

3) **signal** means information that arises from one or multiple sources, including observations and experiments, which suggests a potentially new causal association, or a new aspect of a known causal association between an intervention and an adverse event or a set of related adverse events, that is judged likely to justify further investigation of possible causality.

Pharmacovigilance system

Article 4

The marketing authorisation holder's pharmacovigilance system established and maintained in accordance with the Law on medicinal products (hereinafter: Law) shall meet the requirements laid down in this Rulebook.

The marketing authorisation holder shall ensure that the pharmacovigilance system:

1) is fully functional;

2) is covered by a comprehensive quality management system as provided for in Articles 5 to 10 of this Rulebook;

3) includes a risk management system covering all procedures and processes necessary to optimise safe use and monitor benefit-risk balance of their veterinary medicinal products;

4) sets out clearly the roles, responsibilities and required tasks for all parties involved in operating the system;

5) provides for proper control over the system and ensures that, when needed, the necessary changes to the system to improve its operation can be carried out;

6) is clearly and unambiguously documented in the PSMF.

Marketing authorisation holder shall:

1) ensure that the qualified person responsible for pharmacovigilance has sufficient control over the pharmacovigilance system in order to promote, maintain and improve the responsibilities and tasks referred to in Article 259 of the Law, and to ensure that there is an appropriate procedure in place to identify and deal with any conflicts of interest of the qualified person responsible for pharmacovigilance;

2) have a sufficient number of competent and appropriately qualified and trained personnel working for them in the performance of pharmacovigilance activities;

3) establish and document back-up procedures to ensure business continuity with regard to the fulfilment of pharmacovigilance obligations.

All persons involved in the procedures and processes of the pharmacovigilance system established shall ensure the proper functioning of the system when fulfilling their role for the marketing authorisation holder.

Marketing authorisation holders shall retain full responsibility for all pharmacovigilance obligations subcontracted to third parties as laid down in the Law and in this Rulebook.

A suspected adverse event in accordance with these Rulebook shall be submitted on a form published on the Institute's website.

Qualified person responsible for pharmacovigilance

Article 5

The qualifications and training of the qualified person responsible for pharmacovigilance shall include documented experience in pharmacovigilance.

The qualified person responsible for pharmacovigilance shall hold a degree in veterinary medicine in accordance with the Law.

In a case that qualified person responsible for pharmacovigilance does not hold a degree in veterinary medicine, marketing authorisation holder shall ensure the permanent and continuous assistance from a veterinarian, which should be documented adequately.

II. QUALITY MANAGEMENT SYSTEM

Quality management system for pharmacovigilance

Article 6

Marketing authorisation holders shall establish and implement an adequate and effective quality management system for the performance of their pharmacovigilance activities.

The quality management system shall be described in the PSMF.

Marketing authorisation holders shall ensure that the quality management system includes detailed policies, processes and procedures:

1) on document management, training, audits, and change management covering the activities in accordance with Articles 7 to 11 of this Rulebook. Those policies, processes and procedures shall provide for a review of the quality management system at regular risk-based intervals, based on pre-defined criteria.

2) for the record management system and data collection in accordance with Articles 12 to 16 of this Rulebook, for the following pharmacovigilance activities:

- initial recording of any suspected adverse event;
- collection of additional data;
- collation of reports of suspected adverse events and additional data;
- data handling other than mentioned in points 1) to 3);
- evaluation of data;
- monitoring of quality, integrity and completeness of all information registered in the pharmacovigilance system including information reported to the The European Union pharmacovigilance database and management of duplicates;
- recording of any adverse event in the The European Union pharmacovigilance database;
- archiving of all relevant documents.

3) for risk management, monitoring of the benefit-risk balance, signal management and communication to all relevant stakeholders in accordance with Articles 17 to 21 of this Rulebook;

4) for the maintenance and availability of the PSMF in accordance with Articles 25 and 26 of this Rulebook.

Marketing authorisation holders shall:

1) clearly define the roles and responsibilities of those persons involved in pharmacovigilance activities and in documentation in accordance with paragraphs 3 to 6 of this Article;

2) set up a quality management system using the following:

- quality planning: establishing structures, integrated planning 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 implemented;
- quality improvements: correcting and improving the structures and processes where necessary.

Document management system

Article 7

Marketing authorisation holder shall set up and maintain a document management system to keep all documents related to pharmacovigilance activities.

Documents referred to in the paragraph 1 of thei article shall be archived and indexed to enable accurate and easy accessibility throughout the period of record-keeping.

Documents shall be subject to version control, as appropriate.

Documents and pharmacovigilance data relating to individual authorised veterinary medicinal products shall be retained as long as the product is authorised and for 5 years after the marketing authorisation ceases to be valid.

Training

Article 8

All personnel involved in the performance of pharmacovigilance activities shall receive initial and continuous training for their role and responsibilities in relation to the activities mentioned in Article 6, paragraphs 3 of this Rulebook, also including activities related to clinical trials, technical product complaints, standards, sales and marketing.

Marketing authorisation holders shall have a training management system in place for maintaining and developing the competences of their personnel. Information on training plans and records for pharmacovigilance activities and a reference to their location shall be kept in Annex IV, indent 4 to the PSMF.

Performance indicators

Article 9

Marketing authorisation holders shall use relevant performance indicators to continuously monitor the performance of pharmacovigilance activities and the outcome of risk minimisation measures. They shall keep a list of those performance indicators including the reason why they have been chosen and a description on how to use them in Annex IV, point 3 to the PSMF.

Audits

Article 10

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 this Rulebook and to determine its effectiveness.

The audits shall be planned to cover all pharmacovigilance activities for a defined period and verify their conformity with the policies, processes and procedures of the quality management system. They shall be conducted by individuals who have no direct involvement in or responsibility for the matters or processes audited.

Any third party contracted to carry 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.

Marketing authorisation holders shall draw up a risk-based schedule for auditing. The process for risk-based planning shall be described and the rationale for the risk-based schedule shall be documented. A list of scheduled and completed audits, including outstanding critical and major findings, shall be documented in Annex IV, point 2 to the pharmacovigilance system master file.

Corrective and preventive action and change management

Article 11

Marketing authorisation holders shall have a process in place for managing corrective and preventive actions, to mitigate any deviations detected in audits, daily operational work and findings from inspections. Associated corrective and preventative actions shall be documented for the last 5 years.

Corrective and preventive action plans requested by the competent authority shall document in writing an effective process, systematically addressing and minimising identified risk or defects. Plan shall include root cause analysis, address clear possible corrective and preventive measures, address timelines for action, and communication to relevant stakeholders.

Marketing authorisation holder shall monitor and assess the effectiveness of corrective and preventive actions. Any changes associated with those actions shall be evaluated.

Change management shall provide for a controlled process of change, including monitoring and documenting the effectiveness of the corrective or preventive actions and communication to relevant stakeholders.

III: RECORD MANAGEMENT SYSTEM, DATA COLLECTION AND MONITORING

Record management system

Article 12

The document management system referred to in Article 7 of this Rulebook shall include a record management system for receiving, recording, collating and assessing information on adverse events and for recording safety information.

The description of the record management system for recording adverse events and safety information in Section D of the pharmacovigilance system master file shall include the following information:

- 1) type of record management system used for adverse event reports, including the name of the database used, if applicable;
- 2) location where the record management system is kept;
- 3) description of functionality of the record management system;

4) operational responsibility of the personnel responsible for the record management system;

5) summary of the assessment of its fitness for purpose.

Marketing authorisation holders may use the The European Union pharmacovigilance database as their electronic record management system for recording adverse events.

In the case referred to in paragraph 3 of this Article, Section D of the PSMF shall indicate that the record management system being used is the The European Union pharmacovigilance database.

Suspected adverse event

Article 13

Marketing authorisation holders shall collect and maintain detailed records of all suspected adverse events from all sources, in accordance with article 257 paragraph 1 point 1 of the Law.

Records referred to in paragraph 1 of this Article shall include post-marketing surveillance studies and literature relating to their veterinary medicinal products, and suspected adverse events concerning use of their veterinary medicinal products outside the terms of the marketing authorisation.

Recording of adverse events

Article 14

Information concerning suspected adverse events shall be recorded and coded using internationally agreed standards. The latest version of the standards shall be used in line with the specified implementation dates.

Records of adverse events shall include at least the following:

- 1) an identifiable reporter or source (including the country code);
- 2) details of identifiable animals, humans or environment;
- 3) veterinary or human medicinal product names;
- 4) details on the adverse events.

Where the name of the product is not included in the initial report from the primary source, marketing authorisation holders shall make reasonable efforts to obtain the name or at least part of the trade name of the medicinal product concerned. If neither the name nor the trade names are known and cannot be obtained, the name of the active substances shall be recorded in the record management system.

Marketing authorisation holders shall make reasonable efforts to request further information, as necessary, to enable investigation of suspected adverse events, including the results of appropriate diagnostic tests, to ensure that adverse event data reported are complete.

Adverse event recording in the Union pharmacovigilance database

Article 15

Marketing authorisation holders shall record adverse events in the European Union pharmacovigilance database.

A language customary in the field of medical science shall be used to record non-coded information in the Union pharmacovigilance, including such information related to adverse events originating outside the Union.

Marketing authorisation holders shall regularly monitor the scientific literature to identify any adverse events concerning their veterinary medicinal products. The method for monitoring literature and the frequency with which monitoring is conducted shall take into account the risk-based approach. It shall at least cover the following topics: active substance, type of product, the stability in number and incidence of reports observed over time on the market and the stability of the pharmacovigilance profile.

Post-marketing surveillance studies

Article 16

Marketing authorisation holder may conduct post-marketing surveillance studies on their own initiative or on request of a Institute.

Voluntary post-marketing surveillance studies shall be notified to the Institute immediately after initiation. The marketing authorisation holder shall submit to the Institute the protocol and the final report within one year after completion of the data collection.

For a post-marketing surveillance study requested by Institute, the marketing authorisation holder shall submit the draft study protocol to the Institute for approval at the latest two months before the trial is conducted.

The marketing authorisation holder shall notify the Institute on the conduction of post-marketing surveillance study in Montenegro, even in a case that Institute did not request the study.

The marketing authorisation holder shall submit the study protocol, the summary of the final study report and the final study report after finalisation of the study to the Institute in a case when Institute requested the post-marketing surveillance study, and when the study was conducted in Mintenegro.

The marketing authorisation holder shall submit all relevant documents in a language customary in the field of medical science.

The marketing authorisation holder shall ensure that all information concerning the study is handled and stored in such a way that it can be correctly reported, interpreted and verified, and that the analytical dataset and statistical programmes used to generate the data contained in the final report of the study are stored electronically and are available for audits and inspections upon request of the Institute.

Risk management system

Article 17

Marketing authorisation holder shall ensure that the pharmacovigilance system includes a risk management system (hereinafter: RMS) to take appropriate action to minimise identified risks, when necessary.

RMS shall include a process for monitoring the benefit-risk balance of products and performing signal management and communication system in accordance with Article 21 to this Rulebook.

Marketing authorisation holder shall ensure continuous assessment and document the risk management measures and the outcome of risk minimisation measures in the PSMF.

Signal management process

Article 18

The signal management process shall consist of at least pharmacovigilance processes of signal detection, prioritisation, validation, assessment and documentation of outcome.

Where marketing authorisation holder is responsible for the same or a similar veterinary medicinal product as defined in the VICH Guideline 24 on Management of adverse event reports, which is authorised in different Member States through different authorisation procedures, the signal management process may be performed at active substance level for all the products combined.

Marketing authorisation holder shall perform signal management using a risk-based approach and monitor the data with a frequency proportionate to the identified risk. The risk-based approach shall take into account: type of product, length of time on the market and stability of the pharmacovigilance profile, identified and potential risks and the need for additional information. To determine the methodology, extent and frequency of the signal management process the risk-based approach shall be applied, and the rationale shall be documented in accordance with EMA *Guideline on veterinary good pharmacovigilance practices (VGVP), Module: Signal Management, EMA/522332/2020*.

Signal assessment shall analyse and evaluate the potential impact of a signal on the benefit-risk balance of a product and shall allow for relative comparison between different products or product groups, including analysis at active substance level and stratified analyses.

The outcome of the signal management process shall be recorded and the rationale shall be kept ready for inspection.

Marketing authorisation holder shall conduct at least one signal detection analysis per year for each of their active substances or products in the The European Union pharmacovigilance database.

Marketing authorisation holders using the European Union pharmacovigilance database as their record management system for adverse event reports shall perform signal management in the European Union pharmacovigilance database.

When marketing authorisation holder do not use the European Union pharmacovigilance database for signal management, they shall ensure that their record management system for adverse event reports contain all adverse event reports for which they are responsible. In particular, they shall ensure that adverse event reports concerning their veterinary medicinal products reported to the European Union pharmacovigilance database from other sources are recorded in their own database.

Monitoring benefit-risk balance

Article 19

Marketing authorisation holders shall:

- continuously monitor the benefit-risk balance of their products in light of all available information from veterinarians, other healthcare professionals, the general public, adverse event reports by other marketing authorisation holders or competent authorities recorded in the European Union pharmacovigilance database, and scientific literature;

- continuously monitor the benefit-risk balance and take necessary risk minimisation measures to optimise the safe use of their veterinary medicinal products;

- consider the potential impact of each adverse event on the benefit-risk balance of their products, unless there is no causal link between their products and the adverse event.

Conclusion on the benefit-risk balance

Article 20

Marketing authorisation holders shall annually record a conclusion on the benefit-risk balance for each of their products in the European Union pharmacovigilance database and confirm that the signal management process has been conducted.

The outcome of the signal management process shall be included in the conclusion referred to in paragraph 1 to this article if a new validated signal or signals related to medically important *Veterinary Dictionary for Drug Regulatory Activities* (VeDDRA) terms have been identified, even if no further action is considered necessary. The conclusion shall explain whether the benefit-risk balance is still considered as favourable and if any actions to improve the benefit-risk balance are deemed necessary.

When marketing authorisation holder identify a new risk or a change of the benefit-risk balance of one of their products, a summary of the analysis and a conclusion on the benefit-risk balance shall be recorded in the European Union pharmacovigilance database, and notifying the Institute.

Communication

Article 21

Marketing authorisation holders shall have an overarching communication plan that identifies the relevant stakeholders in the Montenegro and European Union, including veterinarians, other healthcare professionals, customers and the general public, and in cases of urgent safety concerns, it shall outline the approach to be taken to communicate in a timely

manner concerns arising from pharmacovigilance data or in relation to other relevant pharmacovigilance information.

The communication plan shall include information on how marketing authorisation holders:

- 1) identify the target audience;
- 2) identify effective means for communication with the intended target audience;
- 3) identify the specific objectives of the communication;
- 4) define a timetable for the communication;
- 5) ensure the relevance and clarity of the information for the intended target audience;
- 6) identify and coordinate all stakeholders involved in the communication;
- 7) give prior or simultaneous notification to the Institute of any public announcement on pharmacovigilance information, in accordance with the article 257 paragraph 8 of the Law;
- 8) measure the effectiveness of the communication.

Marketing authorisation holder shall use the data-processing network of the European Union pharmacovigilance database for communication of alerts related to pharmacovigilance data.

IV: THE PHARMACOVIGILANCE SYSTEM MASTER FILE (PSMF)

General requirements

Article 22

The information in the pharmacovigilance system master file (hereinafter: PSMF) required for marketing authorization holder to establish under Article 257 paragraph 1 point 2 of the Law shall be accurate and reflect the pharmacovigilance system in place.

The contractual arrangements between marketing authorisation holder and third parties concerning pharmacovigilance activities shall be clearly documented, detailed and up-to-date.

Marketing authorisation holder may, where appropriate, use separate pharmacovigilance systems for different categories of veterinary medicinal products. Each such system shall be described in a separate PSMF.

Content and structure of the pharmacovigilance system master file

Article 23

The PSMF shall consist of a main part describing the pharmacovigilance system, together with annexes containing detailed information.

The main part of the PSMF shall contain the following sections:

- 1) Section A containing general information regarding the PSMF:
 - PSMF reference number;
 - PSMF location for the purpose of pharmacovigilance inspections;
- 2) Section B containing information regarding the qualified person responsible for pharmacovigilance, assistant veterinary surgeon and associated back-up procedures, including:

- name, contact details and a signed statement from the marketing authorisation holder and the qualified person confirming that the qualified person concerned has the necessary means to fulfil the tasks and responsibilities required by Law;

- documentation on the marketing authorisation holder arrangements concerning the assistant veterinary surgeon referred to in Article 5 paragraph 3 of this Rulebook, if applicable, including the contact details;

- a description of back-up arrangements that apply in the absence of the qualified person responsible for pharmacovigilance or the veterinary surgeon, assisting the qualified person responsible for pharmacovigilance referred to in Article 4 paragraph 3 indent 3 of this rulebook;

3) Section C containing information on the marketing authorisation holder:

- a detailed description of the organisational structure of the marketing authorisation holder, including a parent company or group of companies associated;

- the position of the qualified person responsible for pharmacovigilance within the organisation.

4) Section D containing a description of the document management system referred to in Article 7 to this rulebook, including the record management system for adverse event recording referred to in Article 12 to this rulebook;

5) Section E containing a description of the quality management system for pharmacovigilance activities, including the following:

- a description of the processes used for pharmacovigilance activities referred to in Article 6 paragraph 3 to this Rulebook;

- a description of the training management system in place referred to in Article 8 paragraph 2 and 3 to this Rulebook;

- a description of the system used for documenting or archiving information referred to in Article 7 paragraph 3 to this Rulebook;

- a description of the system for monitoring the performance of the pharmacovigilance system as referred to in Article 9 to this Rulebook;

- a description of the responsibilities for quality assurance auditing of the pharmacovigilance system as referred to in Article 10 to this Rulebook, including auditing of subcontractors, where appropriate;

- a list of audits associated with unresolved critical or major findings;

- a description of the corrective and preventive action plan management and change management in place as referred to in Article 11 to this Rulebook;

6) Section F containing a description of the contractual arrangements with third parties concerning pharmacovigilance activities, where applicable.

The PSMF shall contain the following Annexes:

1) Annex I: a logbook containing records of all changes to the main part of the PSMF;

2) Annex II: additional information regarding the qualified person responsible for pharmacovigilance, assistant veterinary surgeon, and associated back-up arrangements:

- curriculum vitae including information on qualifications and training of the qualified person responsible for pharmacovigilance as referred to in Article 5 paragraph 1 of this Rulebook and, if applicable, Article 5 paragraphs 1 and 2 of this Rulebook;

- a description of the tasks and responsibilities of the qualified person responsible for pharmacovigilance;

- proof of registration with the pharmacovigilance database;
 - a list of the pharmacovigilance activities that have been delegated by the qualified person responsible for pharmacovigilance to third parties;
- 3) Annex III: additional information on the marketing authorisation holder:
- a list of all veterinary medicinal products covered by the PSMF, including the international non-proprietary name (INN) of the active substances, the countries in which the product is authorized, and for the products authorized in the European Union Member States, the type of procedure for authorisation and the authorisation numbers in each Member State where the product is authorised;
 - a list of reference numbers for other PSMFs held by the same marketing authorisation holder, where applicable;
 - a list of local or regional representatives for the purpose of receiving reports of suspected adverse events, including their contact details, responsibilities and territories, where applicable;
 - a list of the sites where pharmacovigilance activities listed in Article 6 paragraph 3 of this Rulebook are carried out;
- 4) Annex IV: further details about the quality management system:
- a list of documents, policies, procedures and processes used for the pharmacovigilance activities referred to in Article 6 paragraph 3 of this Rulebook;
 - a list of all scheduled and completed audits including outstanding critical and major findings;
 - a list of performance indicators and how to use them, as referred to in Article 9 of this Rulebook, as applicable;
 - the information on training plans and records referred to in Article 8 paragraphs 2 and 3 of this Rulebook;
 - a list of risk management measures and the outcome of risk minimisation measures;
- 5) Annex V: further information on contractual arrangements between marketing authorisation holders and third parties concerning pharmacovigilance activities, where applicable:
- a list of the activities or services subcontracted by the marketing authorisation holder to third parties to fulfil pharmacovigilance obligations and information on who the activities or services are subcontracted to, including the name and address any subcontractors, where applicable;
 - a list of the tasks of the qualified person responsible for pharmacovigilance referred to in Article 259 of the Law that have been totally or partially outsourced and the information on who the activities or services are subcontracted to, including the name and address of the subcontractor(s), where applicable;
 - a list of existing contracts and agreements with third parties, where applicable, including the products and territories concerned.

Where appropriate, information may be provided in the form of charts or flow diagrams.

Summary of the PSMF

Article 24

The summary of the PSMF shall contain the following information:

- 1) the PSMF reference number;

- 2) the PSMF location;
- 3) name, contact details and place of operation of the qualified person responsible for pharmacovigilance;
- 4) the signed statement referred to in Article 23 paragraph 2 point 2 indent 1 of this Rulebook;
- 5) the type of record management system used for adverse events reports including the name of the database, if applicable.

Maintenance

Article 25

Marketing authorisation holder shall:

- keep the PSMF up to date and revise it, where necessary, to take account of experience gained, and of technical and scientific progress;
- ensure that the qualified person responsible for pharmacovigilance has permanent access to the PSMF to fulfil the tasks referred to in Article 259 of the Law;
- record in a logbook any alteration to the content of the main part of the PSMF made within the last 5 years;
- indicate in the logbook the changed Section, the kind of change, the date, the person responsible and, where appropriate, the reason for the alteration;
- upon request, submit a copy of their logbook or another requested part of the pharmacovigilance system master file to the Institute within 7 days from the day of receiving the request;
- notify Institute of any change in the information provided in the summary of the PSMF by submitting a variation that do not require assessment;
- keep an electronic version of the system as described in the PSMF for 5 years after the system has been formally terminated.

The PSMF shall be subject to version control and indicate the date when it was last updated.

Location and availability

Article 26

The PSMF shall be located in the territory of Montenegro, i.e.. European Union, at the site where the main pharmacovigilance activities of the marketing authorisation holder are performed or at the site where the qualified person responsible for pharmacovigilance operates.

The PSMF may be stored or made available in electronic form, and the media used for storage or making available shall be searchable and shall remain readable over time.

A printed copy of the PSMF arranged in accordance with Article 23 paragraphs 2 and 3 of this Rulebook, or parts thereof, shall be made available when requested, for audits and inspections. The printed copy or the requested part shall be complete and legible.

The PSMF shall be permanently and immediately available for inspection at the site where it is kept, and if PSMF is kept in electronic form, it is sufficient that the data stored in electronic form are directly available.

V. CONTROLS

Controls

Article 27

Marketing authorisation holders shall be ready for controls in accordance with Article 337 of the Law and shall also ensure the following are ready for those controls:

a) their qualified person responsible for pharmacovigilance in accordance with Article 257 paragraphs 3 and 4 of the Law;

b) their representatives responsible for the reporting of adverse events in accordance with Article 20 paragraph 1 point 1 and 12 of the Rulebook on conditions for issuance of marketing authorisation for a veterinary medicinal product and Article 257 paragraph 1 point 3 of the Law;

c) any other natural or legal person carrying out pharmacovigilance activities in whole or in part, on behalf of or in conjunction with marketing authorisation holders.

Pharmacovigilance inspections may be performed as on-site or remote inspections.

Pharmacovigilance inspections

Article 28

Marketing authorisation holder shall be prepared for inspections of their pharmacovigilance system and the corresponding PSMF in accordance with Article 337 of the Law and shall ensure the same for any person mentioned in Article 27 paragraph 1 of this Rulebook.

Marketing authorisation holder may be inspected on the site where the PSMF is located or at any other site of those persons inspected in accordance with paragraph 1. With regard to a third party carrying out pharmacovigilance activities, the site to be inspected may be located within or outside the Montenegro and European Union.

Marketing authorisation holder shall, at the request of the Institut, provide the necessary information for inspections.

Pharmacovigilance inspections may be either routine inspections or targeted inspections, and they may be product-specific or inspections of the general pharmacovigilance system. On the occasion of an inspection, marketing authorisation holders shall:

a) present proof that they have personnel, systems and facilities in place to meet their pharmacovigilance obligations and that they are ready for inspection at any time;

b) present proof in regard to their contractual arrangements, including a clear description of the roles and responsibilities of third parties to whom pharmacovigilance activities are subcontracted and provisions for their inspection and audit;

c) demonstrate that the pharmacovigilance system is in compliance with legislation or relevant pharmacovigilance guidelines;

d) provide information on the corrective and preventive action plan management and demonstrate the functionality and the implementation of any change management.

e) at the request of the Institute to communicate the corrective and preventive action plan.

Entry into force

Article 29

This Rulebook shall enter into force on the eighth day following its publication in the “Official Gazette of Montenegro” and shall apply upon the expiry of 12 months from the date of entry into force.

The provisions of this Rulebook relating to the obligation of the marketing authorisation holder to enter reports of suspected adverse events into the European Union pharmacovigilance database shall apply from the date of Montenegro’s accession to the European Union.

*The provisions of the **Commission Implementing Regulation (EU) 2021/1281** of 2 August 2021 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 have been incorporated into these Rulebook