EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

30 June 2020
EMA/567192/2019
Veterinary Medicines Division

Advice on implementing measures under Article 99(6) of Regulation (EU) 2019/6 on veterinary medicinal products – Good distribution practices (GDP) for veterinary medicinal products

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Background

In July 2019, the European Commission sent a request to the European Medicines Agency for advice on good distribution practice for veterinary medicinal products.

The Agency was requested to provide the scientific recommendations by 30 June 2020 to inform the adoption of measures on GDP for veterinary medicinal products.

The GMP/GDP Inspectors Working Group formed one expert group to prepare the recommendations in relation to Good distribution practices for veterinary medicinal products. The group was composed of 14 experts selected from the European network of experts, on the basis of recommendations from the national competent authorities, and one Agency staff member.

When addressing this request, the European Commission asked the Agency to take into account:

- the view of the policy reasoning and purpose of GDP to ensure the quality and identity of veterinary medicinal products during all aspects of their distribution process, e.g. procurement, storage, distribution, transportation, documentation and record-keeping;
- the experience gained with the application of the current EU system on the human medicines side as established in the *Guidelines of 5 November 2013 on Good Distribution Practice of medicinal products for human use*;
- existing international standards and guidelines on GDP for medicinal products, *e.g.* WHO *Good distribution practices for pharmaceutical products, Guide to good storage practices for pharmaceuticals, Model guidance for the storage and transport of time and temperature-sensitive pharmaceutical products,* the 2014 PIC/S *Guide to Good Distribution Practice for medicinal products',*
- as appropriate and available, the experience gained by certain Member States (such as France, Hungary, Poland, Portugal, Romania, the United Kingdom), which have adopted national GDPs and conduct GDP inspections for veterinary medicinal products;
- the similarities and potential differences between the requirements towards GDP for human and for veterinary medicinal products;
- the fact that more often than not GDP inspections are to be performed by the same experts for both types of medicines or that the same wholesaler distributes both veterinary and human medicinal products and therefore, in order to avoid unnecessary administrative burden, it is not practicable to deviate significantly from the human side, unless practical needs dictate otherwise.

The expert group submitted their recommendations to the GMP/GDP Inspectors Working Group for comments on 4 March 2020.

The GMP/GDP Inspectors Working Group adopted the scientific advice on 2 June 2020.

Considerations and rationale for the recommendations

Article 99(6) of Regulation 2019/6 introduces provisions for measures on good distribution practice for veterinary medicinal products indicating that the European Commission shall by means of implementing acts adopt such measures.

Although no good distribution practice measures have been adopted up to now at EU level for veterinary medicines, such measures have been established in the EU in relation to medicinal products for human use[1].

The experience gained with the application of the current EU system on the human medicines side as well as experience with GDP inspections for veterinary medicinal products conducted under existing national legislation was therefore taken into account and constitutes the basis for the recommendations made in relation to veterinary medicines.

For the preparation of the advice international standards and guidelines on good distribution practice for medicinal products such as the WHO *Good distribution practices for pharmaceutical products, Guide to good storage practices for pharmaceuticals, Model guidance for the storage and transport of time and temperature-sensitive pharmaceutical products and* the 2014 PIC/S *Guide to Good Distribution Practice for medicinal products'* were taken into account.

Regulation (EU) 2019/6 aims to reduce the administrative burden, enhance the internal market and increase the availability of veterinary medicinal products, while guaranteeing the highest level of public and animal health and environmental protection. Consideration was therefore given to all these aspects in the drafting of the recommendations.

Recommendations

The recommendations provided in the Agency's advice to the Commission follow the principles of Good Distribution Practice of medicinal products for human use taking into account the specificities of the veterinary field.

The alignment of the recommendations with the corresponding measures established for the good distribution practice of human medicinal products is also supported by the fact that Good Distribution Practice inspections for both types of medicine will often be carried out by the same inspectors and that the same wholesaler may distribute both veterinary and human medicinal products. Therefore, it is essential that the future Implementing Act does not introduce any requirements more stringent than the corresponding GDP guidance for the human sector.

Additional considerations and points to note

In addition to the recommendations made the below matters were addressed and are brought to the Commission's attention for consideration in the development of the Union's legal framework.

As the transfer of ownership is an inherent component of the distribution activities of veterinary medicines the requirements for the ownership transfer for products stored in the territory of the Union/EEA to entities registered outside of the EU/EEA (also known as fiscal importation) should be defined in the Implementing Act and aligned with the outcome of the on-going discussions and future decisions made in this context for the good manufacturing practice framework[2].

[1] Guidelines of 5 November 2013 on Good Distribution Practice of medicinal products for human use
[2] https://ec.europa.eu/health/medicinal_products/consultations/importation_medicinalproducts_en

In the preparation of the advice it was noted that brokering of veterinary medicinal products is not covered in the Regulation (EU) 2019/6. However, in spite of this the necessity for adequate regulation of this activity was identified based on the following facts:

- brokering of medicinal products encompasses participation in trading of medicinal products for both the veterinary and the human sector,
- brokering activities may be performed with all actors in the supply chain (not only with manufacturers, wholesalers, in the EU/EEA or third countries, but also with retailers),
- brokers play an important role in transferring information along the supply chain, between customers (e.g. information concerning complaints or recalls) and may also have a role in alerting the parties involved about falsified, altered or unlicensed products,
- the National Competent Authorities supervising veterinary medicinal products have only marginal knowledge of the activities of brokers and no standards or legal basis to enforce if a report about a broker's misconduct is received,
- the lack of supervision of brokers entails a risk of introduction of medicinal products of unsuitable quality in the supply chain within the EU or with agents outside of the EU.

Considering that brokers are part of the supply chain of veterinary medicines and hence can impact on the integrity of the supply chain it is essential to address their activities, so that a registry of brokers operating in the EU's veterinary sector is created and compliance with good distribution practice for veterinary medicines applies also to brokers.

Advice on implementing measures for Good Distribution Practice (**GDP) for veterinary medicinal products**

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Introduction[3]

This advice provides stand-alone measures on Good Distribution Practice (GDP) for veterinary medicinal products as well as recommendations on appropriate tools to assist wholesale distributors in conducting their activities and to guarantee that veterinary medicinal products are appropriately procured, stored, transported and handled as well as to ensure control of the distribution chain and consequently maintain the quality and the integrity of veterinary medicinal products while preventing falsified medicines from entering the legal supply chain. Compliance with good distribution practices for veterinary medicinal products will ensure control of the distribution chain and consequently maintain the quality and the integrity of veterinary medicinal products.

According to Article 4(36) of Regulation (EU) 2019/6, wholesale distribution means all activities consisting of procuring, holding, supplying or exporting veterinary medicinal products whether for profit or not, apart from retail supply of veterinary medicinal products to the public. Such activities are carried out with holders of a manufacturing authorisation or other holders of a wholesale distribution authorisation of veterinary medicinal products, persons permitted to carry out retail activities in a Member State in accordance with Article 103 of Regulation (EU) 2019/6 and other persons or entities in accordance with national law of the Member State concerned.

Any person acting as a wholesale distributor of veterinary medicinal products has to hold a wholesale distribution authorisation and according to Article 101(5) of Regulation (EU) 2019/6 comply with the good distribution practice for veterinary medicinal products.

Possession of a manufacturing authorisation includes authorisation to distribute the veterinary medicinal products covered by the manufacturing authorisation. Manufacturers performing any distribution activities with their own veterinary medicinal products must therefore also comply with good distribution practice for veterinary medicinal products.

The definition of wholesale distribution does not depend on whether that distributor is established or operating in specific customs areas, such as free zones or in free warehouses. All obligations related to wholesale distribution activities (such as exporting, holding or supplying) also apply to these distributors. Relevant sections of good distribution practice for veterinary medicinal products should also be adhered to by other actors involved in the distribution of veterinary medicinal products, apart from brokers[4] which are not covered by the definition of 'wholesale distribution' under Article 4(36) of Regulation 2019/6.

Definitions

In alignment with the human medicines sector and in order to complement the definitions included in Regulation 2019/6, the following definitions required for a good understanding of the terminology used in this advice are proposed:

'Good distribution practice for veterinary medicinal products' means the part of the quality assurance which ensures that the quality of veterinary medicinal products is maintained throughout all stages of the supply chain from the site of manufacturer to the pharmacy or person authorised or entitled to

[3] Note: In order to maintain alignment of the Chapter numbers with the GDP guideline for human medicines, the numbering begins with 1. for Quality Management. The alignment will benefit the ease of reference during implementation and execution of the Implementing Act.

[4] In the context of distribution of medicinal products for human use a broker is defined as the actor conducting all activities in relation to the sale or purchase of medicinal products that do not include physical handling and that consist of negotiating independently and on behalf of another legal or natural person.

supply veterinary medicinal products to the public and other persons or entities in accordance with national law of the Member State concerned.

'Export procedure' means the procedure that allows Union goods to leave the customs territory of the Union. For the purpose of good distribution practice, the supply of veterinary medicines from an EU Member State to a contracting State of the European Economic Area is not considered as export.

'Falsified veterinary medicinal product' means any veterinary medicinal product with a false representation of:

a) its identity, including its packaging and labelling, its name or its composition as regards any of the ingredients including excipients and the strength of those ingredients;
b) its source, including its manufacturer, its country of manufacturing, its country of origin or its marketing authorisation holder;
c) or its history, including the records and documents relating to the distribution channels used.

'Free zones' and 'free warehouses' mean those parts of the customs territory of the Union or premises situated in that territory and separated from the rest of it in which:

a) Union goods are considered, for the purpose of import duties and commercial policy import measures, as not being on Community customs territory, provided they are not released for free circulation or placed under another customs procedure or used or consumed under conditions other than those provided for in customs regulations;
b) Union goods for which such provision is made under Union legislation governing specific fields qualify, by virtue of being placed in a free zone or free warehouse, for measures normally attaching to the export of goods.

'Holding' means storing veterinary medicinal products.

'Transport' means moving veterinary medicinal products between two locations without storing them for unjustified periods of time.

'Procuring' means obtaining, acquiring, purchasing or buying (including evidence demonstrating the ownership takeover) veterinary medicinal products from manufacturers, importers or other wholesale distributors.

'Qualification' means the action of proving that any equipment works correctly and actually leads to the expected results. The word 'validation' is sometimes widened to incorporate the concept of qualification.

'Supplying' means all activities of providing, selling (including evidence demonstrating the transfer of ownership), donating veterinary medicinal products to wholesalers, pharmacists, persons authorised or entitled to supply veterinary medicinal products to the public or other persons or entities in accordance with national law of the Member State concerned.

'Quality risk management' means a systematic process for the assessment, control, communication and review of risks to the quality of the drug (medicinal) product across the product lifecycle.

'Quality system' means the sum of all aspects of a system that implements quality policy and ensures that quality objectives are met (International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, Q9).

'Validation' means the action of proving that any procedure, process, equipment, material, activity or system actually leads to the expected results (see also 'qualification').

1. Quality management

1.1. Principle

Wholesale distributors must maintain a quality system setting out responsibilities, processes and risk management principles in relation to their activities[5]. All distribution activities should be clearly defined and systematically reviewed. All critical steps of distribution processes and significant changes should be justified and where relevant validated. The quality system is the responsibility of the organisation's management and requires their leadership and active participation and should be supported by staff commitment.

1.2. Quality system

The system for managing quality should encompass the organisational structure, procedures, processes and resources, as well as activities necessary to ensure confidence that the product delivered maintains its quality and integrity and remains within the legal supply chain during storage and/or transportation.

The quality system should be fully documented and its effectiveness monitored. All quality-system-related activities should be defined and documented. A quality manual or equivalent documentation approach should be established and should include a description of any differences in the quality system regarding handling of products of different types.

A responsible person should be appointed by the management, who should have clearly specified authority and responsibility for ensuring that a quality system is implemented and maintained.

The management of the distributor should ensure that all parts of the quality system are adequately resourced with competent personnel, and suitable and sufficient premises, equipment and facilities.

The size, structure and complexity of distributor's activities should be taken into consideration when developing or modifying the quality system.

A change control system should be in place. This system should incorporate quality risk management principles and be proportionate and effective.

The quality system should ensure that:

- medicinal products are procured, held, supplied or exported in a way that is compliant with the requirements of GDP;
- management responsibilities are clearly specified;
- products are delivered to the right recipients within a satisfactory time period;
- records are made contemporaneously;
- deviations from established procedures are documented and investigated;

[5] Article 101(5) of Regulation (EU) 2019/6 (EU)

- appropriate corrective and preventive actions (commonly known as 'CAPA') are taken to correct deviations and prevent them in line with the principles of quality risk management.
- the operations do not pose a risk to the environment or risk of development of antimicrobial resistance.

1.3. Management of outsourced activities

The quality system should extend to the control and review of any outsourced activities related to the procurement, holding, supply or export of medicinal products. These processes should incorporate quality risk management and include:

- assessing the suitability and competence of the contract acceptor to carry out the activity and checking authorisation status, if required;
- defining the responsibilities and communication processes for the quality-related activities of the parties involved;
- monitoring and review of the performance of the contract acceptor, and the identification and implementation of any required improvements on a regular basis.

1.4. Management review and monitoring

The management should have a formal process for reviewing the quality system on a periodic basis. The review should include:

- measurement of achievement of quality system objectives;
- assessment of performance indicators that can be used to monitor the effectiveness of processes within the quality system, such as complaints, deviations, CAPA, changes to processes; feedback on outsourced activities; self-assessment processes including risk assessments and audits; and external assessments such as inspections, findings and customer audits;
- emerging regulations, guidance and quality issues that can impact the quality management system;
- innovations that might enhance the quality system;
- changes in business environment and objectives.

The outcome of each management review of the quality system should be documented in a timely manner and effectively communicated internally.

1.5. Quality risk management

Quality risk management is a systematic process for the assessment, control, communication and review of risks to the quality of medicinal products. It can be applied both proactively and retrospectively.

Quality risk management should ensure that the evaluation of the risk to quality is based on scientific knowledge, experience with the process and ultimately links to the protection of the treated animal or animal group, the persons responsible for the animal and the treatment, the consumer of a food producing animal or the environment. The level of effort, formality and documentation of the process

should be commensurate with the level of risk. Examples of the processes and applications of quality risk management can be found in guideline Q9 of the International Council on Harmonisation ('ICH').

2. Personnel

2.1. Principles

The correct distribution of veterinary medicinal products relies upon people. For this reason, there must be sufficient competent personnel to carry out all the tasks for which the wholesale distributor is responsible. Individual responsibilities should be clearly understood by the staff and be recorded.

2.2. Responsible person

The wholesale distributor must designate a person as responsible person for good distribution practices compliance. The responsible person should meet the qualifications and all conditions provided for by the legislation of the Member State concerned[6]. The responsible person should have appropriate competence and experience as well as knowledge of and training in good distribution practices compliance.

The responsible person should fulfil their responsibilities personally and should be continuously contactable. The responsible person may delegate duties but not responsibilities.

The written job description of the responsible person should define their authority to take decisions with regard to their responsibilities. The wholesale distributor should give the responsible person the defined authority, resources and responsibility needed to fulfil their duties.

The responsible person should carry out their duties in such a way as to ensure that the wholesale distributor can demonstrate good distribution practices compliance and that public service obligations are met.

The responsibilities of the responsible person include:

- ensuring that a quality management system is implemented and maintained;
- focusing on the management of authorised activities and the accuracy and quality of records;
- ensuring that initial and continuous training programmes are implemented and maintained;
- coordinating and promptly performing any recall operations for veterinary medicinal products;
- ensuring that relevant customer complaints are dealt with effectively;
- ensuring that suppliers and customers are approved;
- approving any subcontracted activities which may impact on good distribution practices;
- ensuring that self-inspections are performed at appropriate regular intervals following a prearranged programme and necessary corrective measures are put in place;
- keeping appropriate records of any delegated duties;

[6] Article 100 (2a) of Regulation (EU) 2019/06

- deciding on the final disposition of returned, rejected, recalled or falsified products;
- approving any returns to saleable stock;
- ensuring that any additional requirements imposed on certain products by national law are adhered to.

2.3. Other personnel

There should be an adequate number of competent personnel involved in all stages of the wholesale distribution activities of veterinary medicinal products. The number of personnel required will depend on the volume and scope of activities.

The organisational structure of the wholesale distributor should be set out in an organisation chart. The role, responsibilities, and interrelationships of all personnel should be clearly indicated.

The role and responsibilities of employees working in key positions should be set out in written job descriptions, along with any arrangements for deputising.

2.4. Training

All personnel involved in wholesale distribution activities should be trained on the requirements of good distribution practices. They should have the appropriate competence and experience prior to commencing their tasks.

Personnel should receive initial and continuing training relevant to their role, based on written procedures and in accordance with a written training program. The responsible person should also maintain their competence in good distribution practices through regular training.

In addition, training should include aspects of product identification and avoidance of falsified medicines entering the supply chain.

Personnel dealing with any products which require more stringent handling conditions should receive specific training. Examples of such products include hazardous products, radio- active materials, products presenting special risks of abuse (including narcotic and psychotropic substances), and temperature-sensitive products.

A record of all training should be kept, and the effectiveness of training should be periodically assessed and documented.

2.5. Hygiene

Appropriate procedures relating to personnel hygiene, relevant to the activities being carried out, should be established and observed. Such procedures should cover health, hygiene and clothing.

3. Premises and Equipment

3.1. Principles

Wholesale distributors must have suitable and adequate premises, installations and equipment[7], so as to ensure proper storage and distribution of veterinary medicinal products. In particular, the premises should be clean, dry and maintained within acceptable temperature limits.

3.2. Premises

The premises should be designed or adapted to ensure that the required storage conditions are maintained. They should be suitably secure, structurally sound and of sufficient capacity to allow safe storage and handling of the veterinary medicinal products. Storage areas should be provided with adequate lighting to enable all operations to be carried out accurately and safely. Veterinary medicinal products should be stored suitably spaced to permit cleaning and inspection. Pallets should be kept in a good state of cleanliness and repair.

Where premises are not directly operated by the wholesale distributor, a contract should be in place. The contracted premises should be covered by a separate wholesale distribution authorisation.

Veterinary medicinal products should be stored in segregated areas which are clearly marked and have access restricted to authorised personnel. Any system replacing physical segregation, such as electronic segregation based on a computerised system, should provide equivalent security and should be validated.

Products pending a decision as to their disposition or products that have been removed from saleable stock should be segregated physically and electronically, if an electronic system is available. This includes, for example returned products. Veterinary medicinal products received from a third country but not intended for the Union market should also be physically segregated. Any product suspected of falsification and falsified veterinary medicinal products found in the supply chain, expired products, recalled products and rejected products should be immediately physically and electronically separated, if an electronic system is available and stored in a dedicated area away from all other veterinary medicinal products. The appropriate degree of security should be applied in these areas to ensure that such items remain separate from saleable stock. These areas should be clearly identified.

Special attention should be paid to the storage of products with specific handling instructions as specified in national law, such as narcotics and psychotropic substances. Special storage conditions (and special authorisations) may be required for such products.

Hazardous products, as well as products presenting special safety risks of fire or explosion, such as medicinal gases, combustibles, flammable liquids and solids, should be stored in one or more dedicated areas subject to local legislation and appropriate safety and security measures.

Receiving and dispatch bays should protect products from prevailing weather conditions. There should be adequate separation between the receipt and dispatch and storage areas. Procedures should be in place to maintain control of inbound/ outbound goods. Reception areas where deliveries are examined following receipt should be designated and suitably equipped.

[7] Article 100 (2b) of the Regulation (EU)2019/6

Unauthorised access to all areas of the authorised premises should be prevented. Prevention measures would usually include a monitored intruder alarm system and appropriate access control. Visitors should be accompanied.

Premises and storage facilities should be clean and free from litter and dust. Cleaning programmes, instructions and records should be in place. Appropriate cleaning equipment and cleaning agents should be chosen and used so as not to present a source of contamination.

There should be appropriate procedures for the clean-up of any spillage to ensure complete removal of any risk of contamination.

Vehicles should be cleaned regularly. Equipment chosen and used for the cleaning of vehicles should not constitute a source of contamination.

Premises should be designed and equipped so as to afford protection against the entry of insects, rodents or other animals. A preventive pest control programme should be in place.

Rest, wash and refreshment rooms for employees should be adequately separated from the storage areas. The presence of food, drink, smoking material or medicinal products for personal use should be prohibited in the storage areas.

3.2.1. Temperature and environmental control

Suitable equipment and procedures should be in place to check the environment where veterinary medicinal products are stored. Environmental factors to be considered include temperature, light, humidity and cleanliness of the premises.

An initial temperature mapping exercise should be carried out on the storage area before use, under representative conditions. Temperature monitoring equipment should be located according to the results of the mapping exercise, ensuring that monitoring devices are positioned in the areas that experience the extremes of fluctuations. The mapping exercise should be repeated according to the results of a risk assessment exercise or whenever significant modifications are made to the facility or the temperature controlling equipment. For small premises of a few square meters which are at room temperature, an assessment of potential risks, such as heaters, should be conducted and temperature monitors placed accordingly.

3.3. Equipment

All equipment impacting on storage and distribution of veterinary medicinal products should be designed, located and maintained to a standard which suits its intended purpose. Planned maintenance should be in place for key equipment vital to the functionality of the operation.

Equipment used to control or to monitor the environment where the veterinary medicinal products are stored should be calibrated at defined intervals based on a risk and reliability assessment.

Calibration of equipment should be traceable to a national or international measurement standard. Appropriate alarm systems should be in place to provide alerts when there are excursions from pre-defined storage conditions. Alarm levels should be appropriately set and alarms should be regularly tested to ensure adequate functionality.

Equipment repair, maintenance and calibration operations should be carried out in such a way that the integrity of the veterinary medicinal products is not compromised.

Defective vehicles and equipment should not be used and should either be labelled as such or removed from service.

Equipment not relevant for the wholesale activities should not be stored in the medicines storage area.

Adequate records of repair, maintenance and calibration activities for key equipment should be made and the results should be retained. Key equipment would include for example cold stores, monitored intruder alarm and access control systems, refrigerators, thermohygrometers, or other temperature and humidity recording devices, air handling units and any equipment used in conjunction with the onward supply chain.

3.3.1. Computerised systems

Before a computerised system is brought into use, it should be demonstrated, through appropriate validation or verification studies, that the system is capable of achieving the desired results accurately, consistently and reproducibly.

A written, detailed description of the system should be available (including diagrams where appropriate). This should be kept up to date. The document should describe principles, objectives, security measures, system scope and main features, how the computerised system is used and the way it interacts with other systems.

Data should only be entered into the computerised system or amended by persons authorised to do so.

Data should be secured by physical or electronic means and protected against accidental or unauthorised modifications. Stored data should be checked periodically for accessibility. Data should be protected by backing up at regular intervals. Back up data should be retained for the period stated in national legislation but at least five years at a separate and secure location.

Procedures to be followed if the system fails or breaks down should be defined. This should include systems for the restoration of data.

3.3.2. Qualification and validation

Wholesale distributors should identify what key equipment qualification and/or key process validation is necessary to ensure correct installation and operation. The scope and extent of such qualification and/or validation activities such as storage, pick and pack processes, should be determined using a documented risk assessment approach.

Equipment and processes should be respectively qualified and/or validated before commencing use and after any significant changes, such as repair or maintenance.

Validation and qualification reports should be prepared summarising the results obtained and commenting on any observed deviations. Deviations from established procedures should be documented and further actions decided to correct deviations and avoid their reoccurrence (corrective and preventive actions). The principles of CAPA should be applied where necessary. Evidence of satisfactory validation and acceptance of a process or piece of equipment should be produced and approved by appropriate personnel.

4. Documentation

4.1. Principles

Good documentation constitutes an essential part of the quality system. Written documentation should prevent errors from spoken communication and permits the tracking of relevant operations

during the distribution of veterinary medicinal products. All types of document should be defined and adhered to.

4.2. General

Documentation comprises all written procedures, instructions, contracts, records and data, in paper or in electronic form. Documentation should be readily available and retrievable.

Written procedures should describe the distribution activities which affect the quality of veterinary medicinal products. These include but are not limited to: receipt and checking of deliveries, suppliers and customers control, storage, cleaning and maintenance of the premises and equipment, including pest control, checking and recording of the storage conditions, protection of veterinary medicinal products during transportation, security of stock on site and of consignments in transit, withdrawal from saleable stock, handling of returned products, recall plans, validation and qualification, procedures and measures for the disposal of unusable veterinary medicinal products, procedures for investigating and resolving complaints, procedures identifying veterinary medicinal products suspected of falsification.

With regard to the processing of personal data of employees, complainants or any other natural person, Regulation (EU) 2016/679 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data.

Documentation should be sufficiently comprehensive with respect to the scope of the wholesale distributor's activities and in a language understood by personnel. It should be written in clear, unambiguous language and be free from errors.

Procedures should be approved signed and dated by the responsible person. Documentation should be approved, signed and dated by appropriate authorised persons, as required. It should not be hand-written; although, where it is necessary, sufficient space should be provided for such entries.

Any alteration made in the documentation should be signed and dated; the alteration should permit the reading of the original information. Where appropriate, the reason for the alteration should be recorded.

Documents should be retained for the period stated in national legislation but at least five years. Personal data should be deleted or anonymized as soon as their storage is no longer than necessary for the purpose of distribution activities.

Each employee should have ready access to all necessary documentation for the tasks executed.

Valid and approved procedures should be used. Documents should have unambiguous content; title, nature and purpose should be clearly stated. Documents should be reviewed regularly and kept up to date. Version control should be applied to procedures. After revision of a document, a system should exist to prevent inadvertent use of the superseded version. Superseded or obsolete procedures should be removed from workstations and archived.

Relationships and control measures for original documents and official copies, data handling and records need to be stated for all paper based, electronic and hybrid systems.

Records must be kept either in the form of purchase/sales invoices, delivery slips, or on computer or any other form, for any transaction in veterinary medicinal products received, supplied.

Records must include at least the following information: date of the transaction; name of the veterinary medicinal product including as appropriate, pharmaceutical form and strength; quantity

received, supplied, stating pack size and number of packs; name and address of the supplier, customer or consignee, as appropriate; batch number, expiry date of the veterinary medicinal products[8] and additional requirements specified by national legislation.

Records should be made at the time each operation is undertaken, if handwritten, in clear, legible and indelible handwriting.

5. Operations

5.1. Principles

All actions taken by wholesale distributors should ensure that the identity of the veterinary medicinal product is not lost and that the wholesale distribution of veterinary medicinal products is performed according to the information on the outer packaging. The wholesale distributor should use all means available to minimise the risk of falsified veterinary medicinal products entering the legal supply chain.

All veterinary medicinal products placed on the Union market by a wholesale distributor must be covered by a Union or national marketing authorisation[9] or by a permission to place on the market by national legislation.

For the purpose of parallel trade of veterinary medicinal products a wholesale distributor that is not the marketing authorisation holder shall

- notify the marketing authorisation holder and the competent authority of the source Member State of its intention to parallel trade the veterinary medicinal product to a destination Member State

and

- notify the marketing authorisation holder in the destination Member State about the veterinary medicinal product to be obtained from the source Member State and intended to be placed on the market in the destination Member State

and

- submit to the competent authority in the destination Member State the application for parallel trade in that veterinary medicinal product[10].

All key operations described below should be fully described in the quality system in appropriate documentation.

5.2. Qualification of suppliers

Wholesale distributors must obtain their supplies of veterinary medicinal products only from persons who are themselves in possession of a wholesale distribution authorisation, or who are in possession of a manufacturing authorisation which covers the product in question[11].

[8] Article 101 (7) of the Regulation (EU)2019/6
[9] Article 5 and 101 (1) of Regulation (EU) 2019/6
[10] Article 102 of Regulation (EU) 2019/6
[11] Articles 93 (1) (h), 99 (5) and 101 (1) of Regulation (EU) 2019/6

Wholesale distributors receiving veterinary medicinal products from third countries for the purpose of importation, i.e. for the purpose of placing these products on the EU market, must hold a manufacturing authorisation[12].

Where veterinary medicinal products are obtained from another wholesale distributor, the receiving wholesale distributor, must verify that the supplier complies with the principles and guidelines of good distribution practices and that they hold an authorisation. This information may be obtained from National Competent Authorities or the Union database (EudraGMDP)[13]. Appropriate qualification and approval of suppliers should be performed prior to any procurement of medicinal products. This should be controlled by a procedure and the results documented and periodically rechecked based on quality risk management principles.

When entering into a new contract with new suppliers, the wholesale distributor should carry out 'due diligence' checks in order to assess the suitability, competence and reliability of the other party. Attention should be paid to:

- the reputation or reliability of the supplier;
- offers of veterinary medicinal products more likely to be falsified;
- large offers of veterinary medicinal products which are generally only available in limited quantities;
- diversity of products handled by supplier; and
- out-of-range prices.

5.3. Qualification of customers

Wholesale distributors must ensure they supply veterinary medicinal products only to persons who are themselves in possession of a wholesale distribution authorisation or who are authorised or entitled to supply veterinary medicinal products to the public or otherwise authorised to procure veterinary medicinal products from a distributor in accordance with national law.

Checks and periodic rechecks may include requesting copies of customer's authorisations according to national law, verifying status on an authority website, requesting evidence of qualifications or entitlement according to national legislation.

Wholesale distributors should monitor their transactions and investigate any irregularity in the sales patterns of narcotics, psychotropic substances or other dangerous substances. Unusual sales patterns that may constitute diversion or misuse of veterinary medicinal product should be investigated and reported to competent authorities where necessary. Steps should be taken to ensure fulfilment of any public service obligation imposed upon them[14].

5.4. Receipt of veterinary medicinal products

The purpose of the receiving function is to ensure that the arriving consignment is correct, that the veterinary medicinal products originate from approved suppliers and that they have not been visibly or not visibly damaged during transport.

[12] Article 88 (1) of Regulation (EU) 2019/6
[13] Article 91 (1–7) and Article 100 (5c) of Regulation (EU) 2019/6
[14] Article 101 (4) of Regulation (EU) 2019/6 on veterinary medicinal products

Veterinary medicinal products requiring special storage or security measures should be prioritised and once appropriate checks have been conducted they should be immediately transferred to appropriate storage facilities.

Batches of medicinal products intended for the EU and EEA countries should not be transferred to saleable stock before assurance has been obtained in accordance with written procedures, that they are authorised for sale. For batches coming from another Member State, prior to their transfer to saleable stock, the control report referred to in Article 97 (6), (7) and (9) of Regulation (EU) 2019/6 on veterinary medicinal products or another proof of release to the market in question based on an equivalent system should be carefully checked by appropriately trained personnel.

5.5. Storage

Veterinary medicinal products should be stored separately from other products likely to alter them and should be protected from the harmful effects of light, temperature, moisture and other external factors. Particular attention should be paid to products requiring specific storage conditions.

Incoming containers of veterinary medicinal products should be cleaned, if necessary, before storage. Any activities performed on the incoming goods (e.g. fumigation) should not impact on the quality of the veterinary medicinal products.

Warehousing operations must ensure appropriate storage conditions are maintained and allow for appropriate security of stocks.

Stock should be rotated according to the 'first expiry, first out' (FEFO) principle. Exceptions should be documented.

Veterinary medicinal products should be handled and stored in such a manner as to prevent spillage, breakage, contamination and mix-ups. Medicinal products should not be stored directly on the floor unless the package is designed to allow such storage (such as for some medicinal gas cylinders).

Veterinary medicinal products that are nearing their expiry date/shelf life should be separated immediately from saleable stock physically and electronically, if an electronic system is available.

Stock inventories should be performed regularly taking into account national legislation requirements. Stock irregularities should be investigated and documented.

5.6. Destruction of obsolete goods

Veterinary medicinal products intended for destruction should be appropriately identified, held physically and electronically separated, if an electronic system is available and handled in accordance with a written procedure.

Destruction of veterinary medicinal products should be in accordance with national or international requirements for handling, transport and disposal of such products.

Records of all destroyed veterinary medicinal products should be retained for a defined period.

5.7. Picking

Controls should be in place to ensure the correct product is picked. The product should have an appropriate remaining shelf life when it is picked.

5.8. Supply

For all supplies, a document (e.g. delivery note) must be enclosed stating the date, name, pharmaceutical form of the veterinary medicinal product, strength, batch number, expiry date, quantity supplied stating pack size and number of packs, name and address of the supplier, name and delivery address of the consignee (actual physical storage premises, if different), unique number to allow identification of the delivery order, applicable transport and storage conditions15 and additional requirement specified by national legislation. For traceability purpose, records should be kept so that the actual location of the product can be known. Such records should facilitate the recall of a batch of a product, if necessary, as well as the investigation of counterfeit or potentially counterfeit pharmaceutical products.

5.9. Export to third countries

The export of veterinary medicinal products falls within the definition of 'wholesale distribution' [16]. A person exporting medicinal products must hold a wholesale distribution authorisation or a manufacturing authorisation. This is also the case if the exporting wholesale distributor is operating from a free zone.

The rules for wholesale distribution apply in their entirety in the case of export of veterinary medicinal products. However, where veterinary medicinal products are exported, they do not need to be covered by a marketing authorisation of the Union or a Member State. Wholesalers should take the appropriate measures in order to prevent these veterinary medicinal products reaching the Union market.

Where wholesale distributors supply veterinary medicinal products to persons in third countries, they shall ensure that such supplies are only made to persons who are authorised or entitled to receive veterinary medicinal products for wholesale distribution or supply to the public in accordance with the applicable legal and administrative provisions of the country concerned.

6. Complaints, returns, suspected falsified veterinary medicinal products and veterinary medicinal product recalls

6.1. Principles

All complaints, returns, suspected falsified veterinary medicinal products and recalls must be recorded and handled carefully according to written procedures. Records should be made available to the competent authorities. An assessment of returned veterinary medicinal products should be performed before any approval for resale. A consistent approach by all partners in the supply chain is required in order to be successful in the fight against falsified veterinary medicinal products.

6.2. Complaints

Complaints should be recorded with all the original details. A distinction should be made between complaints related to the quality of a veterinary medicinal product and those related to

[15] Article 101 (7) of Regulation (EU) 2019/6
[16] Article 4 (36) of Regulation (EU) 2019/6

distribution. In the event of a complaint about the quality of a veterinary medicinal product and a potential product defect, the manufacturer and/or marketing authorisation holder should be informed without delay. Any product distribution complaint should be thoroughly investigated to identify the origin of or reason for the complaint.

A person should be appointed to handle complaints and allocated sufficient support personnel.

If necessary, appropriate follow-up actions (including CAPA) should be taken after investigation and evaluation of the complaint, including where required notification to the national competent authorities.

6.3. Returned veterinary medicinal products

Returned products must be handled according to a written, risk-based process taking into account the product concerned, any specific storage requirements and the time elapsed since the veterinary medicinal product was originally dispatched. Returns should be conducted in accordance with national law and contractual arrangements between the parties.

Veterinary medicinal products which have left the premises of the distributor should only be returned to saleable stock if all of the following are confirmed:

- the veterinary medicinal products are in their unopened and undamaged secondary packaging and are in good condition; have not expired and have not been recalled;
- veterinary medicinal products returned from a customer not holding a wholesale distribution authorisation or from pharmacies or persons authorised to supply veterinary medicinal products to the public in accordance with national law of the Member state concerned should only be returned to saleable stock if they are returned within a defined acceptable time limit determined by using quality risk management principles;
- veterinary medicinal products returned by the animal owner to the pharmacy or to other persons or entities permitted in accordance with national law of the Member State should not be taken back as stock, but should be destroyed, unless otherwise specified by national legislation;
- it has been demonstrated by the customer that the veterinary medicinal products have been transported, stored and handled in compliance with their specific storage requirements;
- they have been examined and assessed by a sufficiently trained and competent person authorised to do so;
- the distributor has reasonable evidence that the product was supplied to that customer (via copies of the original delivery note or by referencing invoice numbers, batch numbers, expiry date etc., as required by national legislation), and that there is no reason to believe that the product has been falsified.

Moreover, for veterinary medicinal products requiring specific temperature storage conditions such as low temperature, returns to saleable stock can only be made if there is documented evidence that the product has been stored under the authorised storage conditions throughout the entire time. If any deviation has occurred, a risk assessment has to be performed, on which basis the integrity of the product can be demonstrated. The evidence should cover all the following steps:

- delivery to customer;
- examination of the product;
- opening of the transport packaging;

- return of the product to the packaging;
- collection and return to the distributor;
- record of temperature readings during transportation;
- return to the distribution site refrigerator.

Products returned to saleable stock should be placed such that the 'first expired first out' (FEFO) system operates effectively.

Stolen products that have been recovered cannot be returned to saleable stock and sold to customers.

6.4. Falsified veterinary medicinal products

Wholesale distributors must immediately inform the competent authority and the marketing authorisation holder of any veterinary medicinal products they identify as falsified or suspect to be falsified, stop the distribution and act on the instructions as specified by the competent authorities[17]. A procedure should be in place to this effect. It should be recorded with all the original details and investigated.

Any falsified or suspected to be falsified veterinary medicinal products found in the supply chain should immediately be segregated physically and electronically, if an electronic system is available, and stored in a dedicated area away from all other veterinary medicinal products and be appropriately labelled. All relevant activities in relation to such products should be documented and records retained.

6.5. Veterinary medicinal products recalls

There should be documentation and procedures in place to ensure traceability of products received and distributed, to facilitate product recall.

In the event of a product recall, all affected customers to whom the product has been distributed shall be informed with the appropriate degree of urgency and clear actionable instructions.

The national regulatory authority should be informed of all product recalls. If the product is exported, the third countries clients and/or the third country competent authorities must be informed of the recall as required by national legislation.

The effectiveness of the arrangements for product recall should be evaluated regularly and at least annually.

Recall operations should be capable of being initiated promptly and at any time.

The distributor must follow the instructions of a recall message, which should be approved, if required, by the competent authorities.

Any recall operation should be recorded at the time it is carried out. Records should be made readily available to the competent authorities.

The distribution records should be readily accessible to the person(s) responsible for the recall, and should contain sufficient information on distributors and directly supplied customers (with

[17] Art. 101 (6) of Regulation (EU) 2019/6

addresses, phone and/or fax numbers inside and outside working hours, batch numbers as required by national legislation and quantities delivered), including those for exported products and veterinary medicinal product samples.

The progress of the recall process should be recorded for a final report including reconciliation of the recalled product.

7. Outsourced activities

7.1. Principles

Any activity covered by the good distribution practice for veterinary medicinal products that is outsourced should be correctly defined, agreed and controlled in order to avoid misunderstandings which could affect the integrity of the veterinary medicinal product. There must be a written contract between the contract giver and the contract acceptor which clearly establishes the duties of each party.

Inspections of the contract acceptor can be carried out by representatives of the competent authority[18].

7.2. Contract giver

The contract giver is responsible for the activities contracted out.

The contract giver is responsible for assessing the competence of the contract acceptor to successfully carry out the work required and for ensuring by means of the contract and through audits that the principles of good distribution practice for veterinary medicinal products are followed. An audit of the contract acceptor should be performed before commencement of, and whenever there has been a change to, the outsourced activities. The frequency of audit should be defined based on risk depending on the nature of the outsourced activities. Audits should be permitted at any time.

The contract giver should provide the contract acceptor with all the information necessary to carry out the contracted operations in accordance with the specific product requirements and any other relevant requirements.

7.3. Contract acceptor

The contract acceptor should have adequate premises and equipment, procedures, knowledge and experience, and competent personnel to carry out the work ordered by the contract giver.

The contract acceptor should not pass to a third party any of the work entrusted to him under the contract without the contract giver's prior evaluation and approval of the arrangements and an audit of the third party by the contract giver or the contract acceptor. Arrangements made between the contract acceptor and any third party should ensure that the wholesale distribution information is made available in the same way as between the original contract giver and contract acceptor.

The contract acceptor should refrain from any activity which may adversely affect the quality of the veterinary medicinal product(s) handled for the contract giver.

[18] Article 123 (6 d) of Regulation (EU) 2019/6

The contract acceptor must forward any information that can influence the quality of the veterinary medicinal product(s) to the contract giver in accordance with the requirement of the contract.

8. Self-Inspections

8.1. Principles

Self-inspections should be conducted in order to monitor implementation and compliance with good distribution practice for veterinary medicinal products principles and to propose necessary corrective measures.

8.2. Self-inspections

A self-inspection programme should be implemented covering all aspects of good distribution practice for veterinary medicinal products and compliance with the regulations, guidelines and procedures within a defined time frame. Self-inspections may be divided into several individual self- inspections of limited scope.

Self-inspections should be conducted in an impartial and detailed way by designated competent company personnel. Audits by independent external experts may also be useful but may not be used as a substitute for self-inspection.

All self-inspections should be recorded. Reports should contain all the observations made during the inspection. A copy of the report should be provided to the management and other relevant persons. In the event that irregularities and/or deficiencies are observed, their cause should be determined and the corrective and preventive actions (CAPA) should be documented and followed up. The effectiveness of the CAPAs should be reviewed.

9. Transportation

9.1. Principles

It is the responsibility of the supplying wholesale distributor to protect veterinary medicinal products against breakage, adulteration and theft, and to ensure that temperature conditions are maintained within acceptable limits during transport and whenever possible monitor these conditions.

Regardless of the mode of transport, it should be possible to demonstrate that the veterinary medicines have not been exposed to conditions that may compromise their quality and integrity. A risk-based approach should be utilised when planning transportation.

9.2. Transportation

The required storage conditions for veterinary medicinal products should be maintained during transportation within the defined limits as described on the outer packaging by the manufacturers and by the marketing authorisation holder.

If a deviation such as temperature excursion or product damage has occurred during transportation, this should be reported to the distributor and recipient of the affected veterinary medicinal products to assess the potential impact on the quality of the veterinary medicinal product. A procedure should also be in place for investigating and handling temperature excursions.

It is the responsibility of the wholesale distributor to ensure that vehicles and equipment used to distribute, store or handle veterinary medicinal products are suitable for their use and appropriately equipped to prevent exposure of the products to conditions that could affect their quality and packaging integrity.

Where feasible, consideration should be given to adding technology, such as global positioning system (GPS) or other systems, electronic tracking devices and engine-kill buttons to vehicles, which would enhance the security of veterinary medicinal products while in the vehicle.

There should be written procedures in place for the operation and maintenance of all vehicles and equipment involved in the distribution process, including cleaning and safety precautions. Equipment chosen and used for the cleaning of vehicles should not constitute a source of contamination.

Risk assessment of delivery routes should be used to determine where temperature controls are required. Equipment used for temperature monitoring during transport within vehicles and/or containers should be maintained and calibrated at regular intervals at least once a year.

Dedicated vehicles and equipment should be used, where possible, when handling human and veterinary medicinal products. Where non- dedicated vehicles and equipment are used, procedures should be in place to ensure that the quality of the medicinal products will not be compromised.

Deliveries should be made to the address stated on the delivery note and into the care or the premises of the consignee. Veterinary Medicinal products should never be left on alternative premises.

For emergency deliveries outside normal business hours, persons should be designated and written procedures should be available.

Where transportation is performed by a third party, the contract in place should encompass the requirements of Chapter 7 (Outsourced activities). Transportation providers should be made aware by the wholesale distributor of the relevant transport conditions applicable to the consignment. Where the transportation route includes unloading and reloading or transit storage at a transportation hub, particular attention should be paid to the temperature monitoring, cleanliness and the security of any intermediate storage facilities.

Provision should be made to minimise the duration of temporary storage while awaiting the next stage of the transportation route.

9.3. Containers, packaging and labelling

Veterinary medicinal products should be transported in containers that have no adverse effect on the quality of the products, and that offer adequate protection from external influences, including contamination.

Selection of a container and packaging should be based on the storage and transportation requirements of the veterinary medicinal products; the space required for the amount of medicines; the pharmaceutical forms, also including medicated premixes; the anticipated external temperature extremes; the estimated maximum time for transportation including transit storage at customs; the qualification status of the packaging and the validation status of the shipping containers.

Containers should bear labels providing sufficient information on handling and storage requirements and precautions to ensure that the products are properly handled and secured at all times. The containers should enable identification of the contents of the containers and the source.

9.4. Products requiring special conditions

In relation to deliveries containing veterinary medicinal products requiring special conditions such as narcotics or psychotropic substances, the wholesale distributor should maintain a safe and secure supply chain for these products in accordance with requirements laid down by the Member States concerned. There should be additional control systems in place for delivery of these products. There should be a protocol to address the occurrence of any theft.

Veterinary medicinal products comprising highly active materials should be transported in safe, dedicated and secure containers and vehicles. The relevant safety measures should be in accordance with international agreements and national legislation.

For temperature-sensitive veterinary medicinal products, qualified equipment, such as thermal packaging, temperature-controlled containers or temperature-controlled vehicles, should be used to ensure correct transport conditions are maintained between the manufacturer, wholesale distributor and customer.

If temperature-controlled vehicles are used, the temperature monitoring equipment used during transport should be maintained and calibrated at regular intervals. Temperature mapping under representative conditions should be carried out and should take into account seasonal variations.

If requested, customers should be provided with information to demonstrate that products have complied with the temperature storage conditions.

If cool-packs are used in insulated boxes, they need to be located such that the product does not come in direct contact with the cool-pack. Staff must be trained on the procedures for assembly of the insulated boxes (seasonal configurations) and on the reuse of cool-packs.

There should be a system in place to control the re-use of cool- packs to ensure that incompletely cooled packs are not used in error. There should be adequate physical segregation between frozen and chilled ice packs.

The process for delivery of sensitive products and control of seasonal temperature variations should be described in a written procedure.