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# Union procedure on the coordination of veterinary pharmacovigilance inspections

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# Union procedure on the coordination of veterinary pharmacovigilance inspections

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# 1. Introduction (background)

Article 123 (6) of Regulation (EU) 2019/6 states that the competent authorities of the Member States may carry out inspections — unannounced and announced — as part of controls. As laid down in Article 126, the competent authority concerned shall, in cooperation with the European Medicines Agency (hereinafter 'the Agency'), ensure by means of inspections that all pharmacovigilance system master files in the Union are regularly checked and that the pharmacovigilance systems are being correctly applied.

Article 126 (2) of Regulation (EU) 2019/6 provides the specific legal basis for the coordination of pharmacovigilance inspections for centrally authorised veterinary medicinal products (CAPs) by the Agency and the conduct of these inspections by the concerned competent authority.

The Guideline on Veterinary Good Pharmacovigilance Practices (VGVP) (Module: Controls and pharmacovigilance inspections) provides a high-level overview of the types of inspections performed by EU pharmacovigilance inspectorates, the factors considered for the planning of inspection programmes, the sites which may be inspected, the scope of inspections, and the basic elements of the inspection process. According to the VGVP module on Controls and pharmacovigilance inspections, pharmacovigilance inspections should be planned, coordinated, conducted, reported on, followed-up and documented in accordance with the legislative requirements, veterinary good pharmacovigilance practices and the Union procedures for pharmacovigilance inspections related to veterinary medicinal products.

This Union procedure provides guidance on the coordination of pharmacovigilance inspections conducted by EU inspectorates on behalf of the Union and relates to inspection programmes concerning centrally authorised products (CAPs) and nationally authorised products (NAPs, i.e., authorised nationally or via the mutual recognition or decentralised procedure). Effective coordination of inspections and inspection programmes is required in order to ensure appropriate inspection coverage, while at the same time minimising duplication and maximising the use of available resources. Effective coordination is also required to enable the flexible use of resources, for example, to respond to requests for triggered inspections. In addition, this procedure outlines the roles of the different parties involved in the coordination of EU inspections and inspection programmes.

This procedure should be read in conjunction with the Modules of the guidelines on veterinary good pharmacovigilance practices (VGVP) and other Union procedures on pharmacovigilance inspections related to veterinary medicinal products.

# 2. Scope

The competent authorities of the Member States, in cooperation with the Agency, are responsible for conducting routine and targeted pharmacovigilance inspections in order to verify compliance with applicable legislation and guidance. This procedure outlines the processes used for the coordination of EU inspections and inspection programmes, including:

- Processes for the design and maintenance of the CAP risk-based programme for routine pharmacovigilance inspections, which relate to the planning and coordination of supervisory authority pharmacovigilance inspections of marketing-authorisation holders (MAHs) with centrally authorised products. Processes for the design and maintenance of the national risk-based programme for routine pharmacovigilance inspections in each Member State, which

relate to the planning and coordination of supervisory authority pharmacovigilance inspections of marketing-authorisation holders (MAHs) with nationally authorised products only. National pharmacovigilance inspection programmes will include pharmacovigilance inspections that relate to MAHs with product authorisations of all types (i.e., NAPs and CAPs).

- Factors to consider for "targeted" pharmacovigilance inspections, including processes to be followed for targeted requests for inspection from the Committee for Veterinary Medicinal Products (CVMP).
- Factors to consider for non-supervisory authority inspections i.e., inspections included in the national programme of a Member State where the PSMF location is not in that Member State. Non-supervisory inspections may be routine or targeted.
- Factors to consider for the coordination of inspections in third countries, whether conducted as part of a national inspection or as part of a supervisory authority inspection.
- Factors to consider for the inspection of pharmacovigilance contractors [Commission Implementing Regulation (EU) 2021/1281, Art. 26 1b], whether conducted as part of a national inspection or as part of a supervisory authority inspection.
- Processes for the delegation of the supervisory authority responsibilities to another Member State according to Art.80 of Regulation (EU) 2019/6.

This procedure describes how different inspection programmes in the EU are integrated in order to provide appropriate inspection coverage while minimising duplication.

# 3. Coordination overview

The scheduling and conduct of inspections, in accordance with Articles 126(2) and 126(3) of Regulation (EU) 2019/6, will be driven by the preparation of inspection programmes based on a systematic and risk-based approach as outlined in Section 2.2 of the VGVP Module on controls and pharmacovigilance inspections.

In the context of CAPs, a risk-based programme for routine inspections of MAHs with CAPs will be determined by the Agency in conjunction with the supervisory authorities of the Member States (the Pharmacovigilance Inspectors' Working Group [PhV IWG], the Committee for Veterinary Medicinal Products [CVMP], and its Pharmacovigilance Working Party).

In the context of nationally authorised products, if the same pharmacovigilance system is used for products with a variety of authorisation types (including centrally authorised products, mutual recognition, decentralised and national), then the supervisory authority inspections under the abovementioned risk-based inspection programme for centrally authorised products should be applicable to all products covered by that system. If the pharmacovigilance system covers nationally authorised products only, then the supervisory authority inspection should be part of the concerned Member State's national inspection programme.

These routine programmes shall be distinct from any targeted inspections, but if a targeted inspection has been or is planned to be conducted, it may replace the planned routine inspection (see section 4.2.4).

Member States and the Agency shall cooperate in the coordination of inspections in third countries when a need to inspect sites outside the EU is identified (see section 4.2.6).

Where appropriate, inspectors from different Member States may participate in joint inspections of a MAH or pharmacovigilance contractor. The circumstances under which this may occur are described in Section 4.2.7.

In order to make the best use of the European surveillance and enforcement resources whilst maintaining a high level of public health, animal health, animal welfare and protection of the environment, it is important that the information on the planned and conducted inspections under these inspection programmes is shared in a timely manner between the national competent authorities (NCAs) and the Agency. The sharing of this information will help prevent unnecessary duplication, in some cases by adapting the scope and/or timing of the inspections, which may reduce the inspection-related resource burden for MAHs, improve inspection coverage, and ensure better and more consistent follow-up of inspections.

The combination of these complementary programmes of routine and targeted supervisory and non-supervisory authority inspections for CAPs and NAPs running in parallel constitute the EU programme of pharmacovigilance inspections.

# 4. EU pharmacovigilance inspection programme

## *4.1. Risk factors*

A risk-based approach to inspection planning allows for the frequency, scope, and breadth of inspections to be determined in line with risk factors. Examples of the factors which may be taken into consideration, as appropriate, by the competent authorities when establishing pharmacovigilance inspection programmes are described in section 2 of the VGVP Module: Controls and pharmacovigilance inspections.

## *4.2. Process*

### 4.2.1. Programme for centrally authorised products

The Agency, in conjunction with the supervisory authorities of the concerned Member States, the PhV IWG and the CVMP and its Pharmacovigilance Working Party will prepare a routine pharmacovigilance inspections programme. This programme will relate to CAPs [Regulation (EU) 2019/6, Article 126(2)], however, whenever the same system is used for products authorised via the decentralised or mutual recognition procedure or nationally authorised products, these may be added to the inspection scope if decided at national level or at the request of the Committee for Veterinary Medicinal Products (CVMP) and/or the Coordination Group for Mutual Recognition and Decentralised procedures for veterinary medicinal products (CMDV). Annex 1 provides details and an overview of the different steps in relation to the preparation of this programme.

The supervisory authority responsible for the conduct of the inspection will be determined by the location of the PSMF [Regulation (EU) 2019/6, Article 126(4)]. Once the different supervisory authorities concerned by the programme are identified, they will ensure that the inspection of the PSMF site is included in their national programme and, will notify the Agency and the CVMP in case the adoption of a specific inspection request by the CVMP is required. The situations where these inspections might be specifically requested by the CVMP are outlined in section 2.4. of the VGVP Module on controls and pharmacovigilance inspections, while the triggers for "targeted'' inspections can be found in section 2.7.2. of the same VGVP Module.

Routine inspections will be requested as system inspections as defined in section 2.7.1. of the VGVP Module on controls and pharmacovigilance inspections. Product specific examples will be used to demonstrate the operation of the pharmacovigilance system.

The scope of these inspections should be in line with the requirements outlined in section 2.7.1 of the VGVP Module controls and pharmacovigilance inspections. All the areas listed in this section should be covered in the scope of an initial supervisory authority inspection and taken into account and adjusted, as necessary, for re-inspections.

The timing of the first inspection and any re-inspection within the programme will be determined based on risk factors, examples described in section 2.2 of VGVP Module controls and pharmacovigilance inspections. In principle, all MAHs with CAPs should be inspected regularly after the Commission decision of the first CAP of the MAH. The inspection frequency may be increased or decreased based on on-going risk assessment. The supervisory authorities concerned will inform the Agency prior to or after the inspection if additional sites need to be inspected and the timeframe for those inspections. For additional sites within the EU/EEA, the competent authority where the additional site is located will be informed in a timely manner in order to plan and fit the inspection into its national programme. For additional sites outside the EU/EEA please refer to section 4.2.6 of this procedure.

### 4.2.2. Programme for nationally authorised products

Each competent authority of the Member States is responsible for preparing a yearly national programme for routine pharmacovigilance inspections which relates to MAHs with product authorisations of all types, which may include third parties.

This programme should be prepared using a risk-based approach as described in paragraph 4.2.1 above.

A national standard operating procedure should be available describing the requirements of the routine national inspection programme and the set-up of inspection planning. In drafting the national inspection programme each inspectorate should consider the information already available in-house and, if appropriate, may solicit further information from MAHs.

For the preparation of the scope of these inspections, each inspectorate should consider all the inspection information coming from the other Member States and specifically the results of pharmacovigilance inspections shared in the Union pharmacovigilance database [Regulation (EU) 2019/6, Article 74(1)]. This is relevant in terms of coordination in order to avoid unnecessary repetition and duplication of inspections or to improve and complement the coverage of activities to be inspected.

For example, if a supervisory authority (where applicable) plans to conduct an inspection of a particular MAH within their yearly programme, details of which are shared within the EU Member State inspectorates, national inspectorates may choose to amend the inspection date of the same MAH so that the findings from the supervisory authority inspection may be taken into account or may propose to the supervisory authority to cooperate in joint or coordinated inspections of the same MAH or may focus the scope to review local processes, including but not limited to the collection of safety data in that Member State, interface with the QPPV, verification of national implementation of specific risk-minimisation measures, national communications concerning safety, locally conducted safety studies, or issues linked to the national health care systems.

In situations where a MAH has no centrally authorised products, a similar approach as described above should be followed and, when considered appropriate, Member State inspectorates may choose to conduct joint or coordinated inspections of a MAH for the same reasons as described in Section 4.2.7 below.

The re-inspections considered necessary should be included in the programme for nationally authorised products.

This programme should also include the inspections scheduled in the risk-based EU programme of routine pharmacovigilance inspections of CAPs, for which the specific Member State acts as supervisory authority.

If the inspectorate receives an inspection request from the Agency, other NCAs, or from departments within the same national competent authority, a "targeted" inspection may replace a routine inspection in the EU programme.

The manner and the rationale for the prioritisation in the programme should be documented, where considered appropriate by the Member State in line with their SOPs.

### 4.2.3. Sharing EU veterinary pharmacovigilance inspection information

To make the best use of resources, both for MAHs and NCAs, and to avoid unnecessary duplication of inspections while achieving a high standard of routine pharmacovigilance surveillance, the national inspection programmes of all Member States shall be shared and coordinated with each other.

For this purpose, each NCA will be responsible for informing the EMA about the MAHs, which will be prioritised in the national routine pharmacovigilance inspections for the next year / will provisionally be inspected by the NCA in the next year.

EMA will collect all the information provided by the Member States and aggregate it in a single document. The information on planned and conducted site inspections will be updated and shared quarterly within the EU Member State inspectorates in a format to be agreed within the PhV IWG.

Member States that are planning to inspect the same MAH, are not obliged to combine or reschedule their planned inspection but are invited to communicate with each other to verify possibilities to plan a joint inspection or adjust their inspection scope and/or reprioritise and adjust their programme.

### 4.2.4. Targeted inspections

Already conducted or planned "targeted" inspections may replace planned routine inspections, in which case the programme is to be revised to reflect the new timeframe. Specific triggers for this type of inspection and some information on the scope of these inspections can be found in section 2.7.2. of VGVP Module: Controls and pharmacovigilance inspections.

In the context of CAPs, "targeted" inspections will be adopted by the CVMP.

### 4.2.5. Inspections of pharmacovigilance contractors

The legal basis for the conduct of the inspection of contractors is set out in Article 123 6(d) of Regulation (EU) 2019/6. Contractors may be inspected in the margins of a MAH inspection or in a

separate pharmacovigilance inspection depending on the type and extent of delegated pharmacovigilance activities.

### 4.2.6. Third country inspections

According to Article 27(2) of Commission Implementing Regulation (EU) 2021/1281, third parties carrying out pharmacovigilance activities may be inspected, even if the site to be inspected is located outside the Union. Member States and the Agency shall cooperate in the coordination of inspections in third countries to avoid duplication of activities and to ensure the best use of resources.

Programme for centrally authorised products:

- If CVMP or a supervisory authority considers it necessary for a third country site or sites to be inspected in order to obtain a comprehensive overview of a MAH's pharmacovigilance system, as part of either a routine or ''targeted'' inspection, the supervisory authority inspectorate is responsible for performing these inspections. These inspections will be included in the risk-based programme for the inspection of MAHs with CAPs and will normally be conducted following a request from the CVMP.
- The supervisory authority may request assistance from other Member State inspectorates to perform inspections in third countries e.g. the inspectorate of the rapporteur or co-rapporteur country. In addition, assistance may be requested from another Member State inspectorate to address linguistic needs.
- When it is not feasible for the supervisory authority inspectorate to conduct a third country inspection, the competent authority of that country may ask, in coordination with the Agency, another inspectorate to lead the inspection.

The Agency will contact local authorities in third countries as appropriate to notify them of the inspection.

Programmes for nationally authorised products:

- When a national inspectorate plans to inspect a third country site as part of its national inspection programme in relation to NAPs, it should inform the Agency and the other Member States in advance of the inspection in order to avoid duplication of inspection activity.
- The Agency and/or other Member State inspectorate will alert that national inspectorate if the third country site that the inspectorate is planning to inspect has recently been inspected or is due to be inspected by another EU/EEA inspectorate. If after the review of findings from an inspection of a third country site recently conducted by another EU/EEA inspectorate, a national inspectorate wishes to proceed with the third country site inspection (e.g. to examine product-specific issues that are specific to that Member State), the national inspectorate should inform the Agency of the reasons for the proposed inspection.
- Inspectorates from different Member States may, in coordination with the Agency, choose to conduct joint inspections of third country sites.

### 4.2.7. Delegation of tasks and work-sharing

As per Article 80 of Regulation (EU) 2019/6, a supervisory authority may delegate its responsibilities to another competent authority. The delegation should be officially recorded and

made available to all Member States. For centrally authorised products, delegations will be captured in the risk-based programme for the inspection of MAHs with CAPs. For nationally authorised products, delegations should be captured locally by the concerned NCAs.

The agreement for delegation should be valid until a new Member State accepts the role in writing or the Member State where the pharmacovigilance system master file is located resumes its role or changes. During the initial period of delegation close communication and joint inspection(s) may be required between the previous and the new supervisory authority.

A supervisory authority inspectorate may request assistance from inspectors from another Member State for the conduct of a supervisory authority inspection, even where there is no site to be inspected in the other Member State. In addition, inspectors and/or assessors from a Member State that is not the supervisory authority may request to participate in a supervisory authority inspection.

Examples of reasons for a joint Member State inspectorates' inspection are:

- to verify the implementation of national requirements;
- to review the implementation of corrective actions and preventive actions for non- compliance identified during a national pharmacovigilance inspection of the same MAH, in situations where the actions can only be fully examined at a main pharmacovigilance processing site;
- due to specific expertise relating to the MAH's pharmacovigilance system and/or to the products to be reviewed during the supervisory authority inspection;
- for training and harmonisation purposes.

For inspections within the EU, acceptance of such requests will be at the discretion of the supervisory authority and/or the Member State inspectorate receiving the request. For inspections in a third country, the Agency will play a coordinating role (see section 4.2.6).

Where instances of non-compliance are identified during national pharmacovigilance inspection(s) of an MAH conducted by non-supervisory authority Member State(s), which relate to the global pharmacovigilance system (and not solely to national issues), it may be advantageous for the concerned Member State inspectorate(s) to discuss with the supervisory authority how production of an integrated corrective and preventive action (CAPA) can be facilitated e.g. in order to avoid multiple CAPAs for the same or similar instances of non-compliance.

# 5. Implementation of EU pharmacovigilance inspections

Member States should provide sufficient resources and appoint at least one adequately qualified inspector to ensure effective determination of compliance with good pharmacovigilance practice, unless they have agreed on the delegation of their supervisory authority tasks in accordance with Article 80 of the Regulation (EU) 2019/6. The following Union procedures should be taken into account for the implementation of EU pharmacovigilance inspections:

- Union procedure on the preparation, conduct and reporting of EU pharmacovigilance inspections
- Union recommendations on the training and experience of inspectors performing pharmacovigilance inspections.

# 6. The Agency's coordination activities for CVMP requested inspections

The agency plays a key role in the coordination of pharmacovigilance inspections requested by the CVMP. This section describes the activities in which the Agency is involved as part of the coordination role, however, for the details about the preparation, conduct, reporting, and follow-up of these inspections please also refer to the Union procedure listed in Section 5.

An overview of the timelines for the different steps in the CVMP requested inspections is provided in Annex 2.

## *6.1. Preparation of an inspection request*

For each CVMP-requested inspection, an inspection request should be prepared which indicates the MAH concerned and site(s) to be inspected, the product(s) to be examined during the inspection, and, if applicable, a list of specific questions to be addressed during the inspection (system and /or product related) based on concerns from the pharmacovigilance assessors, any other issues relevant to the inspection and the target date for the availability of the inspection report(s). Interaction between inspectors, CVMP members and its Pharmacovigilance Working Party (PhVWP-V) members is encouraged during the preparation of the inspection request preparation, in particular in the case of "for cause" inspections, to ensure that the reasons for the request and any link between the request and a particular procedure that may be ongoing or anticipated (e.g. variation, etc.) are taken into account.

The inspection details will be entered in the IRIS database by the Agency's Inspections Office and the inspectors concerned will be invited to review the record and confirm the inspection details prior to CVMP adoption. After the adoption by the CVMP, the Agency's Inspections Office will initiate the coordination of this inspection.

## *6.2. Inspection team*

The Agency's Inspections Office confirms the availability of the inspectorate(s) in the EU/EEA, and the names of inspectors to be involved in order to enter their names in IRIS and perform the necessary Declaration of Interest (DOI) checks. The inspectors involved should ensure they have access to IRIS, and they should review and confirm the inspection details as entered in the database prior to CVMP adoption.

In principle, the reporting inspectorate should be from the competent authority of the Member State in whose territory the PSMF is located. However, if for any reason, this competent authority cannot fulfil this task or it is more appropriate for another Member State to take on this responsibility, the Agency's Inspections Office should determine the availability of other inspectorates and designate another reporting inspectorate. The Agency designates the reporting inspectorate according to the following sequence, subject to the availability of inspector(s):

- competent authority of the Member State in whose territory the PSMF is located i.e. the supervisory authority or delegated supervisory authority;
- the Member State where the site to be inspected is located when this site is not located in the Member State where the PSMF is located or in a third country;
- competent authority of the Member State of the rapporteur concerned by one or more products or that express an interest to participate;

- competent authority of the Member State of the co-rapporteur concerned by one or more products or that express an interest to participate;
- other Member States who agree to participate.

When it is not feasible for the selected inspectorate to conduct the requested parts of the inspection, the competent authority of that country may ask, in coordination with the Agency, another inspectorate to conduct the inspection. For the purpose of promoting harmonisation, consideration should be given to involving more than one Member State inspectorate in the conduct of CVMP requested inspections. If more than one EU/EEA inspectorate needs to be involved in the inspection, one will be designated as the "reporting inspectorate" in accordance with the set of rules mentioned above.

Where relevant or on request, and in particular for product specific issues, the reporting inspector may be assisted, or the inspection (in a third country) may be conducted, by an inspector and/or expert from the rapporteur and co-rapporteur Member State. If an inspectorate wishes to request the assistance of another inspectorate, they should indicate this to the Agency within 5 working days from the notification of the inspection.

Member States may send trainees to the inspection, subject to considerations being made regarding the size of the inspection team. Such trainee participation will not give rise to a share of the inspection fee or claims for expenses from the applicant.

The Member State inspectorate undertaking the reporting inspectorate role should ensure effective communication with the rapporteur, co-rapporteur, and the relevant assessors.

For each site to be inspected, one lead inspector should be designated (this may be the same or different people when more than one site is selected for inspection). For the selection of the lead inspector the following rules should be considered:

- Pharmacovigilance inspections in EU/EEA countries: the lead inspector will be from the inspectorate in the country where the site(s) to be inspected is/are located. This does not prevent a lead inspector of one site to be involved, as an inspection team member, in the inspection of another related site located in a different EU/EEA country.
  - When it is not feasible for the inspectorate of the country where the inspection site is located to conduct the requested parts of the inspection, the competent authority of that country may ask, in co-ordination with the Agency, another inspectorate to lead the inspection.
- Pharmacovigilance inspections in third countries: the reporting inspector, and/or (co)-rapporteur Member State/other inspectors from EU/EEA countries may act as lead inspector.

The Agency will contact local authorities in third countries as appropriate to notify them of the inspection. Inspectors are responsible for all visas, permissions, and arrangements.

The CVMP will be informed in case there are no inspection resources available.

The inspection request details will be available to CVMP members, the reporting inspectorate, and the lead inspectorate(s) via the IRIS platform.

## 6.3. Announcement and preparation of the inspection

Pharmacovigilance inspections will be announced to the MAH and/or the inspected entity (e.g. service provider) using the Agency IRIS platform, unless unannounced inspection is required. The Agency product leaders/procedure managers, rapporteurs and inspectors are copied in all relevant correspondence, as necessary.

According to the inspection announcement message, the MAH and/or the inspected entity is requested to ensure cooperation of all inspected parties and to confirm in writing that the sites accept to be inspected and that they will make all required documents available for direct access by the inspectors. The MAH/inspected entity is also requested to provide copies of an initial set of documents (including the current version of the PSMF) for the preparation of the inspection to the inspection team indicated in the announcement within a given deadline. The inspectors can then supplement this list with additional requests to the MAH/inspected entity. Documents can be uploaded/submitted via the platform or by other means as agreed with the inspection team.

The inspection should be announced within [10]* days from the date of adoption of the inspection request by the CVMP and the inspection should be prepared within [20]* days after the delivery of the documents requested from the MAH/inspected entity. Concerned inspectorates should participate in the discussion about the feasibility of the inspection as requested and the time schedule. Any change in the sites selected for inspection should be adopted by the CVMP.

For general considerations about the inspection preparation refer to section 3 of the Union procedure on the preparation, conduct and reporting of EU pharmacovigilance inspections.

## 6.4. Conduct of the inspection

The CVMP requested inspections should be conducted within [30]* days after the preparation of the inspection.

For general considerations about the conduct of the inspections refer to section 5 of the Union procedure on the preparation, conduct and reporting of EU pharmacovigilance inspections.

## 6.5. Reporting of the inspection and inspection follow-up

In the case of CVMP requested inspections, the reporting/lead inspector prepares an inspection report (IR) within [70]* days after the completion of the inspection. The final IR is shared with EMA, the MAH and CVMP and NCAs via the IRIS platform.

For general considerations about reporting inspections and follow-up of the inspection outcome refer to section 5 and 6 of the Union procedure on the preparation, conduct and reporting of EU pharmacovigilance inspections.

# Definitions

The following definitions refer to the use of the specific terms for inspections of MAHs holding marketing authorisations for CAPs. For inspections conducted under the Member State national programme the terms are defined within the national procedures and the definitions below will only be used as guidance.

- **Supervisory authority (SA):** the supervisory authority for pharmacovigilance shall be the competent authority of the Member State in which the pharmacovigilance system master file is located [Article 126(4) of Regulation (EU) 2019/6] or the competent authority of the Member State to which the role of Supervisory Authority has been delegated to [Article 126(5) of Regulation (EU) 2019/6].
- **Reporting inspectorate:** the inspectorate from an EU/EEA country that was requested and has accepted to be designated as the reporting inspector.
- **Reporting inspector:** the inspector designated by the reporting inspectorate to coordinate the preparation of the inspection, the conduct of the inspection, and the activities of the inspectors. The reporting inspector has the following general duties:
  - Coordinating the preparation of the inspection.
  - Practicalities of the inspection (with the inspectors and the MAH).
  - Conduct of the inspection
  - Preparation of the reports by the inspectors involved.
  - Checking that the timelines of the inspection are met.
  - Acting as the main contact point between the inspection team and the Agency's Inspections Office.
  - Being responsible, in conjunction with the Agency's Inspections Office , for communication between the inspectorates and inspectors involved, the rapporteur/co-rapporteur and the CVMP (the system of communication should, however, be flexible and there can be direct communication between the involved parties, including the assessors, where this is more practical).
  - Management of the live central archive related to the pharmacovigilance inspection.
  - The reporting inspector may also be the lead inspector (see below) for one or more sites.
- **Lead inspector:** the inspector who has the following duties for the pharmacovigilance inspection of at least one inspection site:
  - Evaluation of the feasibility of the inspection as requested and discussion with the reporting inspector.
  - Organisation of the practicalities of the inspection with the inspected entity.
  - Leading the conduct of the inspection on site.
  - Communication between the inspected entity and the reporting inspector/Agency's Inspections Office, as applicable (the system of communication should be flexible and there can be direct communication between the involved parties where this is more practical. In any case, the reporting inspector shall be kept informed about this communication outcome).

- Writing and signing the inspection report.

The reporting inspector and lead inspector will be the same person when only one site is concerned by the inspection.

- **Inspection report (IR):** details about the definition, availability, signatures, language, and content of the IR can be found in the Union procedure on the preparation, conduct and reporting of EU pharmacovigilance inspections.
- **Joint inspection:** an inspection with two or more Member State inspectorates participating in the same inspection at the same inspection site(s).

## References


- Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC
- 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
- Guideline on veterinary good pharmacovigilance practices (VGVP) – Module: Controls and pharmacovigilance inspections.
- Union procedure on the preparation, conduct and reporting of EU pharmacovigilance inspections.
- Union recommendations on the training and experience of inspectors performing pharmacovigilance inspections.

# Annex 1

## Preparation of the risk-based programme of pharmacovigilance inspections of MAHs with centrally authorised products

**Gathering information**

At least once per year (1Q - 2Q), the Agency will gather information regarding changes to the information currently available in the risk-based programme (e.g. changes in the location of the PSMF) and information on any new MAHs with CAP authorisations to be included in the programme with the aim of revising the programme as indicated in the following sub-section. However, as soon as the Agency becomes aware of a change in the supervisory authority e.g. change in the location of the PSMF, the Agency will communicate this information to the previous and new supervisory authority concerned due to the impact on the national authority responsible for conducting the inspection.

In addition, previous information available on CAP inspections or inspections conducted/planned at national level will also be taken into consideration (e.g. the re-inspection dates proposed by the inspectors after the conduct of the inspections proposed in this programme) in order to ensure that the scheduled year for an inspection of a particular MAH in this programme is appropriate in light of the changes in risk.

**Revision of the programme**

The programme will be a dynamic rolling cycle to be revised at least once per year to reflect the inspections already performed, the revised risk factors and the new MAHs/CAP products joining the system.

The preparation/revision of the risk-based programme will take into consideration the following rules:

a. for new MAHs to be included in the programme, the feedback from the inspectorates on when they plan to inspect the new MAHs according to their national programmes will be considered. This proposal may need to change based on risk factors and other considerations as outlined in section 4.1;

b. for the MAHs already included in the programme, the inspectorates will be asked to confirm whether a change is needed based on new risk factors identified and a justification for these changes should be provided, in particular, when the changes relate to delaying the inspection by one or more years;

c. re-inspections will be prioritised based on risk factors and will be focused on addressing critical/major findings observed in previous inspections, changes in the system and/or any product-specific issues of concern to the assessors.

The preparation/revision of the risk-based programme will take place at least once per year i.e. Q1/Q2 of each year. A second review, but without the extensive information gathering /information on new MAHs, will take place to account for PSMF changes and/or changes in the Member State inspection planning (Q3/Q4) focusing on revision steps b) and c) above.

The programme schedule should at least include the details below:

MAH;

invented name;

active substance (international non-proprietary name (INN);

PSMF country;

PSMF reference number

QPPV country;

rapporteur country;

co-rapporteur country;

Supervisory Authority (Member State where the PSMF is located, or Member State delegated the Supervisory Authority responsibility)

requestor of the inspection, i.e. Member State or CVMP;

scheduled year of the inspection;

comment field (e.g. for justifications on changes).

Delegation of the Supervisory Authority information, when applicable

Additional details concerning the inspections (e.g. inspected sites, dates of inspection, inspection findings, etc.) will be tracked in other documents and in the pharmacovigilance inspection outcome database records.

**Adoption of the programme**

This risk-based programme should be agreed by the PhV IWG and CVMP and its V-PhV WP the year before its implementation. As the programme schedule will be a live document requiring periodic revision throughout the year, it is expected to be circulated for adoption twice, in the Q2 and Q4 of the year.

The PhV IWG will be provided with each adopted revised programme schedule to ensure its implementation by the supervisory authorities concerned.

**Re-inspections**

The calculation of the next inspection date for the programme should take into account the last inspection date and the risk assessment process. The inspection cycle may be shortened or lengthened based on risk assessment.

**Overview of the steps for the preparation of the 200X-200(X+3) programme**

| Steps | Sources | Responsibility | Timelines |
|---|---|---|---|
| 1- Gathering information | SIAMED/UPD<br>Member State Inspectorates<br>Other: e.g. IRIS | Agency-Inspections Office | Q1-Q2 of each year |
| 2- Preparation and revision of the programme | SIAMED/UPD<br>Member State Inspectorates<br>Other (IRIS) | Agency-Inspections Office<br><br>PhV IWG<br>CVMP (V-PhVWP) | Q2 of each year |
| 3- Adoption of the programme | | PhV IWG<br>CVMP (V-PhVWP) | Q2-Q3 of each year |
| 4- Implementation of the programme | | Member State Inspectorates | Current and next year |

| | | | |
|---|---|---|---|
| 5- Re-inspections | | Member State Inspectorates | Define year for re-inspection based on risk assessment (Four-year cycle unless considered to be performed later/earlier) |

# Annex 2

# Activities related to pharmacovigilance inspections requested by CVMP: indicative time schedule*

| STEPS OF THE PROCEDURE | TIME ALLOWED | |
|---|---|---|
| **1. Early activities of EMA / CVMP**<br>Request for a PhV inspection<br>Initial selection /confirmation of sites<br>Set up of overall time schedule<br>Designation of the Reporting Inspectorates (usually Supervisory Authority)<br>First contacts EMA / Inspectorates concerned<br>Notification of the inspection to MAH | To be determined by EMA/CVMP<br><br><br><br>Notify MAH within [10] days of CVMP meeting<br>Notify Reporting inspectorate and other inspectorate(s) within [10] days of CVMP meeting<br>Forwarding of required documents, (within [10] days of CVMP meeting | |
| **2. Inspection preparation**<br>Notification / announcement of site inspections (via IRIS)<br>Preparation of the inspection plan<br><br>Obtaining and reviewing required documents<br>Finalisation of travel arrangements with the MAH | [20] days ✷ after the delivery of the documents requested from the MAH to the inspectorates | |
| **3. Site inspection**<br><br>*Note: The EMA should be notified as soon as possible by the Reporting Inspector of any urgent critical finding relating to the functioning of the MAH pharmacovigilance system and in particular the risk/benefit of the product(s) concerned by this inspection.* | [30] days ✷ | |
| **4. Writing and circulation of the reports**<br>Writing of the Inspection Report<br>Reply from the inspected entity /party(ies) responsible (include this as an attachment to the IR)<br>Comments from the inspectors to the Inspected entity's response (include this as an attachment to the IR) and finalise IR | [30] days ✷<br>[30] days ✷<br><br>[10] days ✷ | Total: [70] days* ✷ |
| **5. Review of the reports by EMA for adherence to applicable reference texts and EMA guidelines.** | [5 ] days ✷ | |

✷Times allowed to complete each step of the initiation, conduct, and termination of the inspection are provided in this table. These times, shown in square brackets, should be considered as indicative and can be modified, if necessary, e.g. the times for the preparation of the inspection report can be extended when the inspectors request information from the inspected entity that is necessary for the completion of the report.