



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

21 September 2023  
EMA/INS/PhV/216087/2022  
Quality and Safety of Medicine Department  
Inspections Office

## Annual report of the Pharmacovigilance Inspectors' Working Group for 2021 and 2022

Adopted by the PhV IWG on 21 September 2023

---

**Official address** Domenico Scarlattilaan 6 • 1083 HS Amsterdam • The Netherlands

**Address for visits and deliveries** Refer to [www.ema.europa.eu/how-to-find-us](http://www.ema.europa.eu/how-to-find-us)

**Send us a question** Go to [www.ema.europa.eu/contact](http://www.ema.europa.eu/contact) **Telephone** +31 (0)88 781 6000

An agency of the European Union



## List of Abbreviations

CAP	Centrally Authorised Product
CHMP	Committee for Medicinal Products for Human Use
CVMP	Committee for Veterinary Medicinal Products
DWH	Data Warehouse (DHW)
EVDAS	EudraVigilance Data Analysis System
EV-Vet	EudraVigilance -Veterinary
GVP	Good Pharmacovigilance Practices
ICSR	Individual Case Safety Report
MAH	Marketing Authorisation Holder
MS	Member State
NCA	National Competent Authority
PhV IWG	Pharmacovigilance Inspectors Working Group
PhVWP-V	Pharmacovigilance Working Party (Veterinary Medicinal Products)
PRAC	Pharmacovigilance Risk Assessment Committee (Human Medicinal Products)
PSMF	Pharmacovigilance System Master File
SSR	summary safety reports
VGVP	Guideline on veterinary good pharmacovigilance practices

## Table of contents

<b>1. Introduction .....</b>	<b>4</b>
<b>2. Meetings.....</b>	<b>4</b>
<b>3. Pharmacovigilance inspections relating to centrally authorised medicinal products .....</b>	<b>5</b>
3.1. General overview .....	5
3.2. Categorisation of findings for CHMP requested inspections conducted in 2021-2022.....	7
3.3. Categorisation of findings for CVMP requested inspections conducted in 2021-2022.....	9
<b>4. Harmonisation topics.....</b>	<b>10</b>
4.1. Human pharmacovigilance legislation.....	10
4.2. Implementation of the new veterinary pharmacovigilance legislation .....	10
4.3. Joint inspections.....	11
4.4. Training and development .....	11
4.5. Medicinal products for human use .....	12
4.6. Medicinal products for veterinary use.....	13
<b>5. Liaison with other groups.....</b>	<b>13</b>
5.1. Interaction with the PRAC.....	13
5.2. Interaction with the CVMP Pharmacovigilance Working Party .....	14

# 1. Introduction

This document is the thirteenth annual report of the Pharmacovigilance Inspectors Working Group (PhV IWG). The PhV IWG was established by the European Medicines Agency (hereinafter "the Agency") within the scope of Article 57(1)(i) of Regulation (EC) No 726/2004. Following a report on its first year of operation, the PhV IWG [mandate](#) was endorsed by the Heads of Medicines Agencies on 18-19 May 2009 and by the Agency's Management Board on 1 October 2009, thereby formally establishing the PhV IWG.

The PhV IWG focuses on the harmonisation and coordination of pharmacovigilance related activities at EU (hereinafter the "Union") level. The group's role and activities are described in more detail in its [work plan](#). The group supports the coordination of the provision of pharmacovigilance inspection related advice and provides a link to other groups such as the Committee for Medicinal Products for Human Use (CHMP), the Committee for Medicinal Products for Veterinary Use (CVMP), the Pharmacovigilance Risk Assessment Committee (Human Medicinal Products) (PRAC [H]), and the Pharmacovigilance Working Party (Veterinary Medicinal Products) (PhV WP [V]).

This annual report for 2021-2022 has been drawn up in line with the format and objectives of the 2021-2024 [work plan](#).

The activities outlined in the annual report for 2021 and 2022 were carried out in line with the Agency's business continuity plan and prioritisation of activities for the COVID-19 pandemic.

# 2. Meetings

The plenary meetings, involving pharmacovigilance inspectors working with human medicinal products and pharmacovigilance inspectors working with veterinary medicinal products, were held remotely (due to the COVID-19 pandemic) on the following dates in a virtual setting:

- 25 March 2021;
- 10 June 2021;
- 30 September 2021;
- 9 December 2021;
- 24 March 2022;
- 23 June 2022;
- 28 September 2022;
- 1 December 2022.

Meetings included a joint session and two separate sessions, one dedicated to human and one to veterinary medicinal products only.

In addition, several virtual meetings took place using teleconferencing or equivalent settings:

- For human medicinal products: ad-hoc presentations on pharmacovigilance inspection topics (COVID-19 products; pharmacovigilance inspection programme; Digital Business Transformation – IRIS EMA inspection coordination) in PRAC meetings were organised, as necessary.
- For veterinary medicinal products: ad-hoc presentations on pharmacovigilance inspection topics (pharmacovigilance inspection programme; Digital Business Transformation – IRIS EMA inspection

coordination) were organised for the CVMP and PhVWP-V. Ad-hoc meetings within EMA and the expert group of pharmacovigilance inspectors and assessors were organised on the implementation of the new veterinary pharmacovigilance legislation.

### **3. Pharmacovigilance inspections relating to centrally authorised medicinal products**

#### **3.1. General overview**

For human medicinal products, the CHMP with input from the PRAC and in conjunction with the competent authority of the MS in whose territory the pharmacovigilance system master file is located (supervisory authority) and the inspectors' working group, have created and maintained a programme for inspection in relation to CAPs, in accordance with GVP Module III on pharmacovigilance inspections and the Union procedure on the coordination of Union pharmacovigilance inspections.

For veterinary medicinal products, the CVMP supported by the Pharmacovigilance Working Party, in conjunction with the competent authority of the MS in which territory the MAH's QPPV is located (according to Volume 9B guidelines on pharmacovigilance regulatory obligations and pharmacovigilance inspections of veterinary medicinal products) and the inspectors' working group, have created and maintained a programme for inspection in relation to CAPs.

With the new legal provisions on veterinary pharmacovigilance contained in the Veterinary Medicinal Products Regulation (Regulation (EU) 2019/6) and Commission Implementing Regulation (EU) 2021/1281) applicable since 28 January 2022, the competent authorities (supervisory authorities) responsible for performing the inspection is determined by the location of the pharmacovigilance system master file. From 28 January 2022 the programme for inspections in relation to CAPs was adjusted to take into account the supervisory authority role.

The inspections covered by these programmes are prioritised based on the potential risk to public health, the nature of the products, extent of use, number of products that the MAH has on the EEA market and other risk factors.

The focus of these inspections is to determine whether the MAH has the personnel, systems, and facilities in place to meet its regulatory pharmacovigilance obligations for CAPs in the EEA. These inspections are requested as system inspections with one or more specific products selected as examples, for which specific information can be traced and verified through the various processes. This provides practical evidence for the functioning of the MAH's pharmacovigilance system in the Union and its compliance with the regulatory requirements.

In general, it is anticipated that national inspection programmes will fulfil the need for the routine inspections included in this programme and therefore it is expected that the inspection programme is achieved mainly through the national programmes. However, there are situations where these inspections might be specifically requested by the CHMP or CVMP, as applicable, (e.g. global pharmacovigilance sites in third countries; additional sites within the Union are identified for inspection and require joint inspections involving the Member State concerned by that site and the supervisory authority). For cause inspections are also reflected in this programme as they may replace the need for routine inspections.

During the lockdowns and travel restrictions due to the COVID-19 pandemic in 2021 and part of 2022, inspections continued, and they were mostly conducted virtually. In September 2022, the coordination of pharmacovigilance inspections requested by EMA's committees for human and veterinary medicines under the centralised procedure was transferred to the IRIS platform, a secure online platform for

handling product-related scientific and regulatory procedures, that EMA launched in 2018, as part of EMA's digital transformation programme.

The key benefits of the coordination of inspections using IRIS are efficiency gains for EMA, MAHs/applicants and the Union regulatory network, increased security, reduced risk of unintentional disclosure of confidential information, and better knowledge management. To ensure a smooth rollout, several training sessions were organised for EMA staff, NCA inspectors, and [industry users](#).

The results presented in Tables 1 and 2 show the number of inspections conducted in relation to the human and veterinary pharmacovigilance inspection programmes for 2021 and 2022, respectively, and split by the type of site inspected.

**Table 1** - Human pharmacovigilance inspections conducted in 2021 and 2022 in the context of the programme for the pharmacovigilance inspection of companies with Centrally Authorised Products (CAPs)

2021	QPPV/PSMF (MAH) site	Global PhV site	Subcontractor/ Licensing partner/affiliate site	Total
CHMP requested	6	0	4	10
National inspection programmes	31	0	11	42
<b>Total</b>	<b>37</b>	<b>0</b>	<b>15</b>	<b>52</b>

2022	QPPV/PSMF (MAH) site	Global PhV site	Subcontractor/ Licensing partner/affiliate site	Total
CHMP requested	3	1	1	5
National inspection programmes	50	0	8	58
<b>Total</b>	<b>53</b>	<b>1</b>	<b>9</b>	<b>63</b>

**Table 2** - Veterinary pharmacovigilance inspections conducted in 2021 and 2022 in the context of the programme for the pharmacovigilance inspection of companies with CAPs

2021	QPPV (MAH) site	Global PhV site	Subcontractor/ Licensing partner/affiliate site	Total
CVMP requested	4	1	0	5
National inspection programmes	6	0	0	6
<b>Total</b>	<b>10</b>	<b>1</b>	<b>0</b>	<b>11</b>

<b>2022</b>	<b>QPPV (MAH) site</b>	<b>Global PhV site</b>	<b>Subcontractor/ Licensing partner/affiliate site</b>	<b>Total</b>
CVMP requested	2	0	0	2
National inspection programmes	5	0	0	5
<b>Total</b>	<b>7</b>	<b>0</b>	<b>0</b>	<b>7</b>

### **3.2. Categorisation of findings for CHMP requested inspections conducted in 2021-2022**

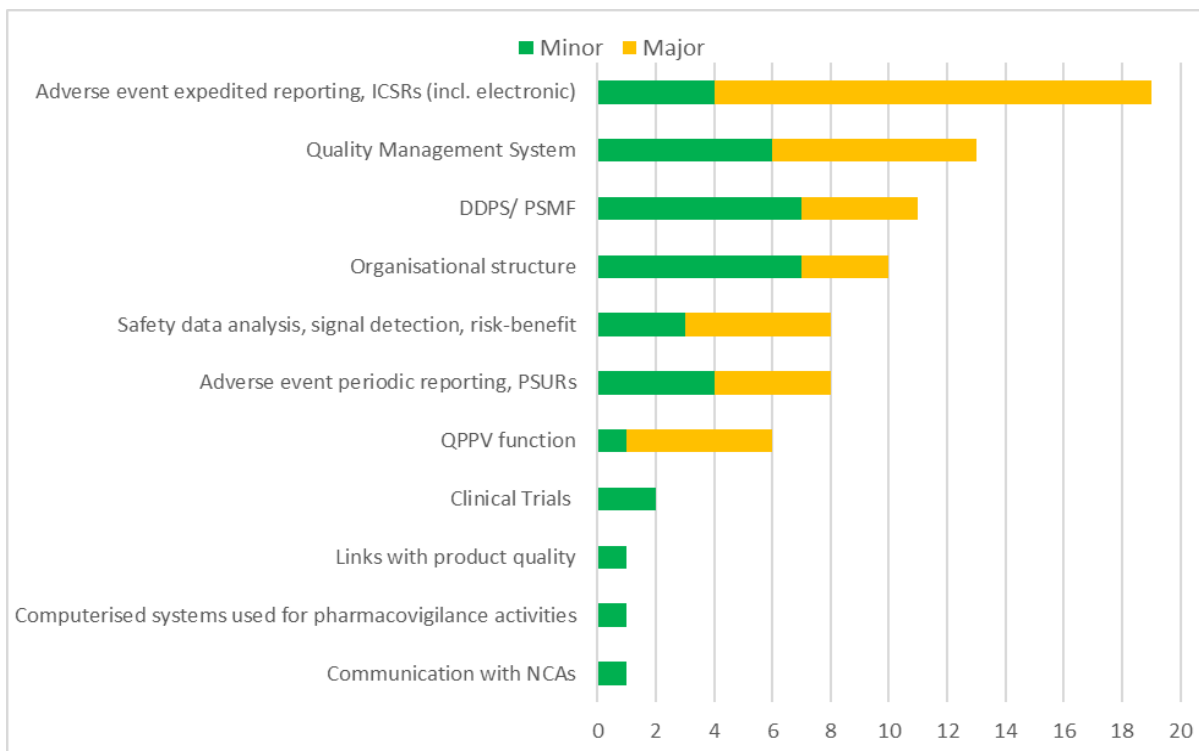
A total of 80 deficiencies, comprising 0 critical, 43 major (53.75%) and 37 minor (46.25%) findings were recorded for the CHMP requested inspections conducted in 2021 (period covered from 01/01/2021 until 31/12/2021).

A total of 24 deficiencies, comprising 0 critical, 5 major (20.8 %) and 19 minor (79,2 %) findings were recorded for the CHMP requested inspections conducted in 2022 (period covered from 01/01/2022 until 31/12/2022).

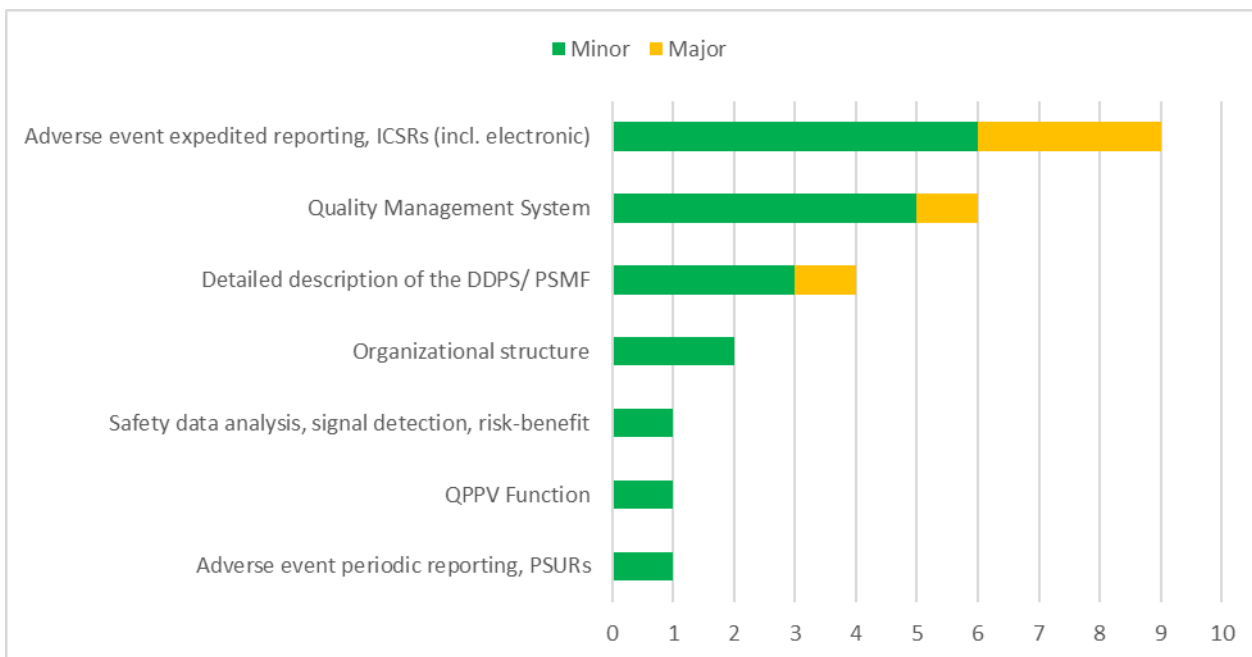
The main findings observed during inspections conducted in 2021 and 2022 are detailed in Figure 1 and 2 below in accordance with the categorisation of pharmacovigilance inspection findings agreed by the PhV IWG. The three most common areas with findings identified during inspections conducted in 2021 and 2022 were the following:

- adverse event expedited reporting, Individual Case Safety Reports (ICSRs);
- quality management system;
- Pharmacovigilance System Master File (PMSF).

**Figure 1** - Number of findings related to the main categories graded as critical, major, and minor for CHMP inspections conducted in 2021



**Figure 2** - Number of findings related to the main categories graded as critical, major, and minor for CHMP inspections conducted in 2022



### 3.3. Categorisation of findings for CVMP requested inspections conducted in 2021-2022

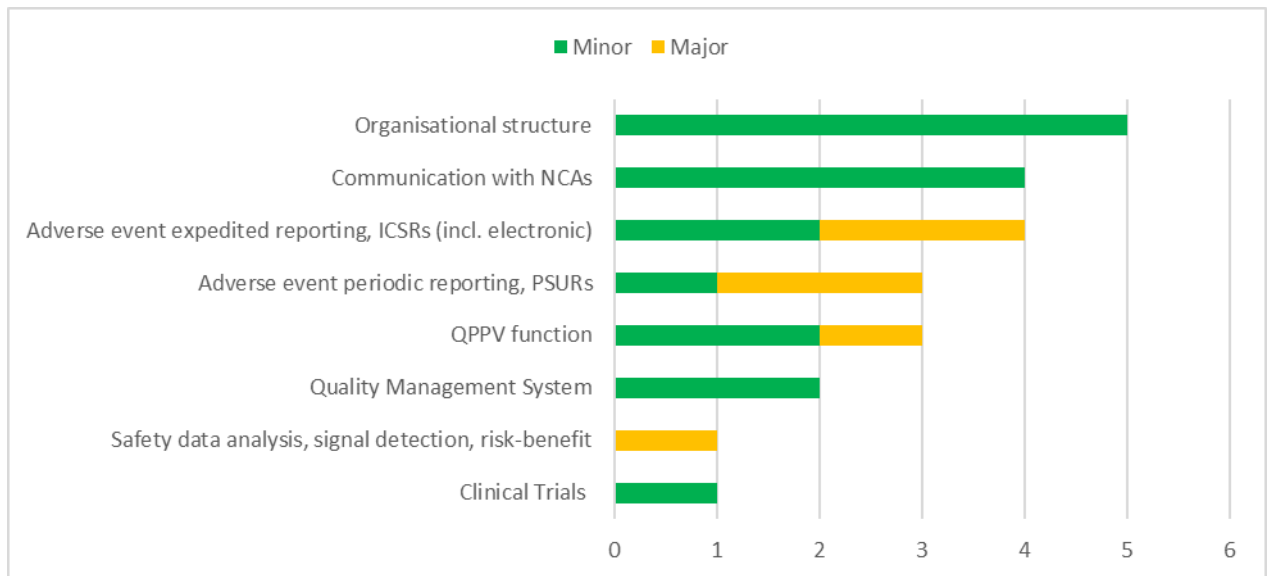
A total of 23 deficiencies, comprising 0 critical, 6 major (26.1%) and 17 minor (73.9%) findings were recorded for the CVMP requested inspections conducted in 2021 (period covered from 01/01/2021 until 31/12/2021).

A total of 9 deficiencies, comprising 1 critical (11,1 %), 1 major (11,1 %) and 7 minor (77,8 %) findings were recorded for the CVMP requested inspections conducted in 2022 (period covered from 01/01/2022 until 31/12/2022).

The main findings observed during inspections conducted in the 2021 and 2022 are detailed in Figure 3 and 4 below in accordance with the categorisation of pharmacovigilance inspection findings agreed by the PhV IWG. The three most common areas with findings identified during inspections conducted in 2021 were the following:

- organisational structure;
- communication with NCAs;
- adverse event expedited reporting, ICSRs (incl. electronic).

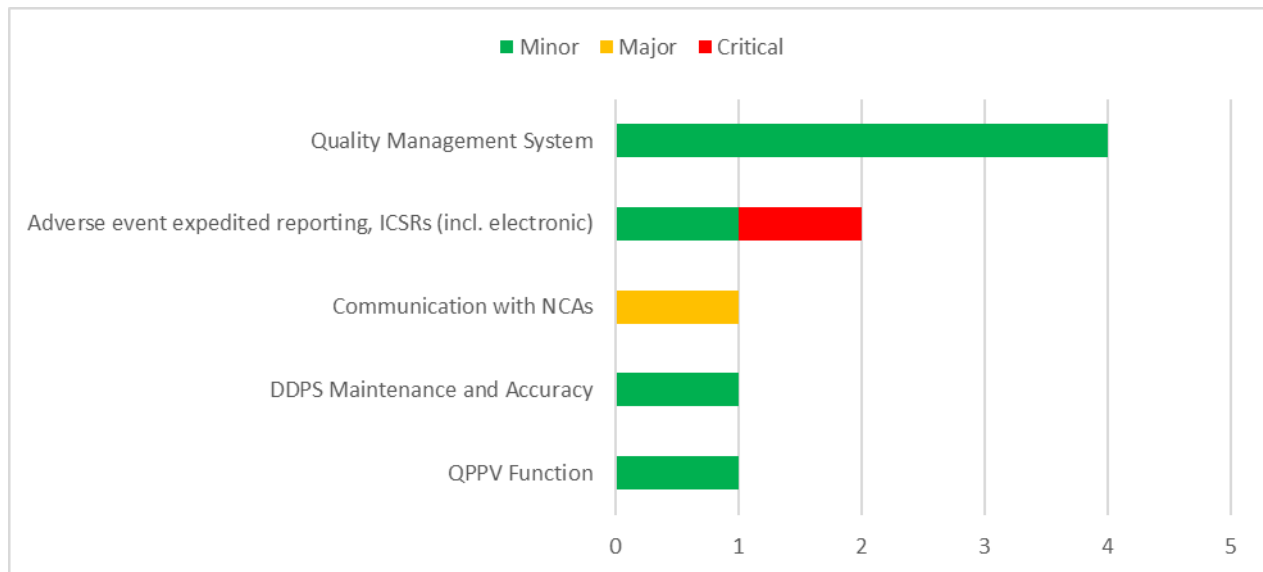
**Figure 3** - Number of findings related to the main categories graded as critical, major, and minor for CVMP inspections conducted in 2021



The three most common areas with findings identified during inspections conducted in 2022 were the following:

- quality management system;
- adverse event expedited reporting, ICSRs (incl. electronic).
- communication with NCAs;

**Figure 4** - Number of findings related to the main categories graded as critical, major, and minor for CVMP inspections conducted in 2022



## 4. Harmonisation topics

### 4.1. Human pharmacovigilance legislation

In order to support further harmonisation for the mutual recognition of pharmacovigilance inspections within the Union and in connection with human medicinal products, in 2021 and 2022 the group was involved in the revision of existing inspection procedures and guidance for pharmacovigilance inspections:

- Revision of the Union procedure on record keeping and archiving of documents obtained or resulting from pharmacovigilance inspections (Rev 01);

In addition, the group contributed to the preparation of the:

- Concept Paper on Pharmacovigilance to support the revision of the pharmaceutical legislation to the European Commission;
- GVP Module XVI Addendum III - Pregnancy prevention programme and other 5 pregnancy-specific risk minimisation measures.

### 4.2. Implementation of the new veterinary pharmacovigilance legislation

In order to support the implementation of the new pharmacovigilance legislation and in connection with veterinary medicinal products in 2021 and 2022 the group continued the work on the following guidance documents and Union procedures:

- Guideline on veterinary good pharmacovigilance practices (VGVP) Module on Pharmacovigilance systems, their quality management systems and pharmacovigilance system master files (published);
- VGVP Module on Controls and pharmacovigilance Inspections (published);

- Union procedure on preparation, conduct, reporting and follow up of pharmacovigilance inspections (Rev 1) and its Appendix 1 on pharmacovigilance inspection report and appendix 2 on Template for collecting information on Pharmacovigilance issues for the attention of the inspectors/assessors (published);
- Union guidance on record keeping and archiving of documents obtained or resulting from pharmacovigilance inspections (published, combined with Human Medicines guidance);
- Union procedure on coordination of veterinary pharmacovigilance inspections (on going).

The group also contributed to the preparation of the:

- VGVP Module on Collection and recording of suspected adverse events for veterinary medicinal products (published);
- VGVP Module on Signal Management (published);
- VGVP Module on Veterinary pharmacovigilance communication (published);
- VGVP Glossary (published).

In addition, the group has been involved in the collection of database requirements in relation to Regulation (EU) 2019/6, Article 74(1) provision to record the results of pharmacovigilance inspections in the pharmacovigilance database.

The work on the development of pharmacovigilance compliance monitoring reports for inspectors is on-going.

### **4.3. Joint inspections**

From the total of 9 CHMP pharmacovigilance site inspections requested and conducted in 2021, 5 inspections were joint inspections involving more than one MS (see Table 1 in Section 3). From the total of 5 CHMP pharmacovigilance site inspections requested and conducted in 2022, no inspections were joint inspections involving more than one MS.

From the total of 5 CVMP pharmacovigilance site inspections requested and conducted in 2021, 1 inspection was a joint inspection involving more than one MS (see Table 2 in Section 3). From the total of 2 CVMP pharmacovigilance site inspections requested and conducted in 2022, no inspection were joint inspections involving more than one MS (see Table 2 in Section 3).

### **4.4. Training and development**

No Pharmacovigilance Inspectors Working Group training course took place during 2021 due to the Agency's business continuity plan for the COVID-19 pandemic.

Training ([via webinar](#)), including Q&A session, on PSMF and inspection topics for veterinary medicines was provided to stakeholders on 8 December 2021 by the EMA Inspections Office and inspectors.

A virtual Pharmacovigilance Inspectors' Working Group training course took place, from 29 to 30 September 2022. The training organisation was supported by the programme committee (Germany [BVL], Croatia [Halmed], Netherland [IGJ], Spain [AEMPS], [H+V]). Inspectors and assessors of both, veterinary and human units of Member States (Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovenia, Spain, Sweden) as well as

inspectors, assessors/experts from non-EU countries (Australia, Canada, Brazil, Switzerland, USA) participated.

- Key objectives of the training:
  - to promote awareness and better understanding of legislation and/or guidance, as applicable, with focus on good pharmacovigilance practices (GVP) and Union procedures on pharmacovigilance inspections and their implementation in relation to human medicinal products.
  - to promote awareness and better understanding of the new Veterinary Medicinal Products Regulation (Regulation (EU) 2019/6 and Commission Implementing Regulation (EU) 2021/1281) and guidance, as applicable, and its implementation in relation to veterinary medicinal products;
  - to share experiences from inspections (human and veterinary) conducted by individual MS to promote further harmonisation of inspection approaches and sharing best practices;
  - to build an understanding, promote further interaction between assessors and inspectors and improve the coordination of inspection and the verification of pharmacovigilance compliance;
- The following topics were presented and/or discussed in the human and veterinary medicinal products related workshops:
  - Risk-based approach to the selection of MAHs to be inspected;
  - remote inspections;
  - inspection of IT systems.
- The following topics were presented and/or discussed in the human medicinal products related workshops:
  - EudraVigilance Data Analysis System (EVDAS) for quality and compliance;
  - pre-authorization inspections;
  - inspections of post-authorisation safety studies;
  - inspections of additional risk minimisation measures
  - harmonisation of the grading of findings.
- The following topics were presented and/or discussed in the veterinary medicinal products related workshops:
  - Inspections under the New Veterinary legislation/requirements;
  - veterinary IT systems and reports.
  - harmonisation in grading of findings.

#### **4.5. Medicinal products for human use**

- The PhV IWG has prepared and is maintaining the 2021-2024 risk-based programme for routine pharmacovigilance inspections of MAHs related to human CAPs.

- Pharmacovigilance inspectors also provided recommendation(s) to the PRAC in relation to pharmacovigilance inspections or related assessment issues.
- During the PhV IWG meetings held in 2021 and 2022, discussions on the following topics took place:
  - the impact of the COVID-19 pandemic on PhV inspections;
  - Brexit - Protocol on Ireland/Northern Ireland;
  - sharing and discussion of inspection report findings;
  - sharing of pharmacovigilance inspection information;
  - development of peer review of case studies;
  - EudraVigilance and EudraVigilance Data Analysis System;
  - Digital Business Transformation - EMA inspection coordination;
  - Medical literature monitoring of ICSRs;
  - risk-based inspection planning;
  - queries on guidance/legislation interpretation.

#### **4.6. Medicinal products for veterinary use**

- The PhV IWG has prepared and is maintaining the 2021-2023 risk-based programme for routine pharmacovigilance inspections of MAHs related to veterinary CAPs. These programmes (human and veterinary) are not publicly available as they contain confidential information.
- During the PhV IWG meetings held in 2021 and 2022, discussions on the following topics took place:
  - The impact of the COVID-19 pandemic on PhV inspections;
  - Regulation (EU) 2019/6 on veterinary medicinal products and corresponding implementing and delegated acts;
  - development of peer review of case studies;
  - sharing and discussion of inspection report findings;
  - EudraVigilance -Veterinary (EV-Vet) and Data Warehouse (DWH);
  - Digital Business Transformation - EMA inspection co-ordination;
  - risk-based inspection planning;
  - queries on guidance/legislation interpretation.

## **5. Liaison with other groups**

### **5.1. Interaction with the PRAC**

During the COVID-19 pandemic the PRAC was frequently updated on the impact of the COVID-19 pandemic on pharmacovigilance inspections planning and conduct.

The unprecedented increase in suspected ADR reporting following the marketing authorisation of COVID-19 vaccines required a review of processes and adjustments to the existing regulatory measures to intensify the monitoring of MAHs' compliance with pharmacovigilance requirements. For all COVID-19 vaccines, a proactive approach was endorsed by PRAC, which included:

- early communication with pharmaceutical companies to request information on the pharmacovigilance system in place and business continuity plans;
- pre-authorisation inspections for MAHs new to the Union and or to the centralised procedure;
- early post-authorisation inspections of the pharmacovigilance systems of the MAHs for COVID-19 vaccines to assess:
  - their readiness to process a large amount of safety data and produce complete and accurate monthly summary safety reports (SSRs);
  - their ability to promptly detect signals and evaluate new information that may impact the benefit-risk balance of those vaccines;
  - the existence and appropriateness of business continuity plans and mechanisms to actively manage evolving situations.

The purpose of these measures was to ensure that the MAHs had the resources and systems in place to support intensive monitoring, which was a key consideration for regulators in their decision to allow a more rapid EU approval process for COVID-19 vaccines.

Presentation to the PRAC on the new IRIS platform for the coordination of pharmacovigilance inspections requested by EMA's committees was provided (GVP Inspection IRIS launched September 2022).

## **5.2. Interaction with the CVMP Pharmacovigilance Working Party**

- The PhV IWG interacted with assessors on topics related to:
  - Regulation (EU) 2019/6 on veterinary medicinal products and corresponding implementing and delegated acts;
  - interaction between assessors and inspectors;
  - updates on inspections planned and conducted;
  - follow-up of pharmacovigilance inspections;
  - preparation and maintenance of the risk-based programme for routine pharmacovigilance inspections of MAHs connected with veterinary CAPs.