EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

21 October 2024
EMA/INS/PhV/471069/2024
Quality and Safety of Medicine Department
Inspections Office

Annual report of the Pharmacovigilance Inspectors' Working Group for 2023

Adopted by the PhV IWG on 15 October 2024

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
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

List of Abbreviations

ADR	Adverse drug reactions
CAP	Centrally Authorised Product
CAPA	Corrective and preventive actions
CHMP	Committee for Medicinal Products for Human Use
CVMP	Committee for Veterinary Medicinal Products
DWH	Data Warehouse (DHW)
EVCTM	EudraVigilance Clinical Trial Module
EVDAS	EudraVigilance Data Analysis System
EVPM	EudraVigilance Post-Authorisation Module
EV-Vet	EudraVigilance -Veterinary
GCP	Good Clinical Practices
GVP	Good Pharmacovigilance Practices
ICSR	Individual Case Safety Report
KPI	Key performance indicators
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)
PIC	Pharmaceutical Inspection Co-operation Scheme
PRAC	Pharmacovigilance Risk Assessment Committee (Human Medicinal Products)
PSMF	Pharmacovigilance System Master File
QMS	Quality management system
QPPV	Qualified Person responsible for Pharmacovigilance
VGVP	Guideline on veterinary good pharmacovigilance practices

Table of contents

1. Introduction

This document is the fourteenth 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 Veterinary Medicinal Products (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 2023 has been drawn up in line with the format and objectives of the 2024-2026 work plan.

2. Meetings

The plenary meetings, involving pharmacovigilance inspectors working with human medicinal products and pharmacovigilance inspectors working with veterinary medicinal products, were held on the following dates:

- 23-24 March 2023 (hybrid meeting).
- 22 June 2023 (virtual meeting).
- 21-22 September 2023 (virtual meeting).
- 06 December 2023 (hybrid meeting).

Meetings included a joint session of relevance to both human and veterinary matters, and two separate sessions which dealt with human and veterinary matters separately.

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

- For human medicinal products: ad-hoc presentations on pharmacovigilance inspection topics may be delivered to the PRAC meetings as necessary, but this did not occur during 2023.
- For veterinary medicinal products: ad-hoc presentations on pharmacovigilance inspection topics were organised for the PhVWP-V meetings, as necessary. 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 (hereafter known as the 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 EU pharmacovigilance inspections.

For veterinary medicinal products, the CVMP supported by the Pharmacovigilance Working Party, in conjunction with the supervisory authority and the inspectors' working group, have created and maintained a programme for inspection in relation to CAPs, in accordance with VGVP Module on Controls and pharmacovigilance Inspections and the Union procedure on the coordination of veterinary pharmacovigilance inspections.

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 listed in GVP Module III on pharmacovigilance inspections and VGVP Module on Controls and pharmacovigilance Inspections.

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.

Since September 2022, the coordination of pharmacovigilance inspections requested by EMA's committees for human and veterinary medicines under the centralised procedure has been managed through 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 results presented in Tables 1 and 2 show the number of inspections conducted in relation to the human and veterinary pharmacovigilance inspection programmes for 2023, respectively, and split by the type of site inspected.

Table 1 - Human pharmacovigilance inspections conducted in 2023 in the context of the programme for the pharmacovigilance inspection of companies with CAPs

2023	QPPV/PSMF (MAH) site	Global PhV site	Subcontractor/ Licensing partner/affiliate site	Total
CHMP requested	6	0	3	9
National inspection programmes	23	0	4	27
Total	**29**	**0**	**7**	**36**

Table 2 - Veterinary pharmacovigilance inspections conducted in 2023 in the context of the programme for the pharmacovigilance inspection of companies with CAPs

2023	QPPV/PSMF (MAH) site	Global PhV site	Subcontractor/ Licensing partner/affiliate site	Total
CVMP requested	7	0	0	7
National inspection programmes	2	0	0	2
Total	**9**	**0**	**0**	**9**

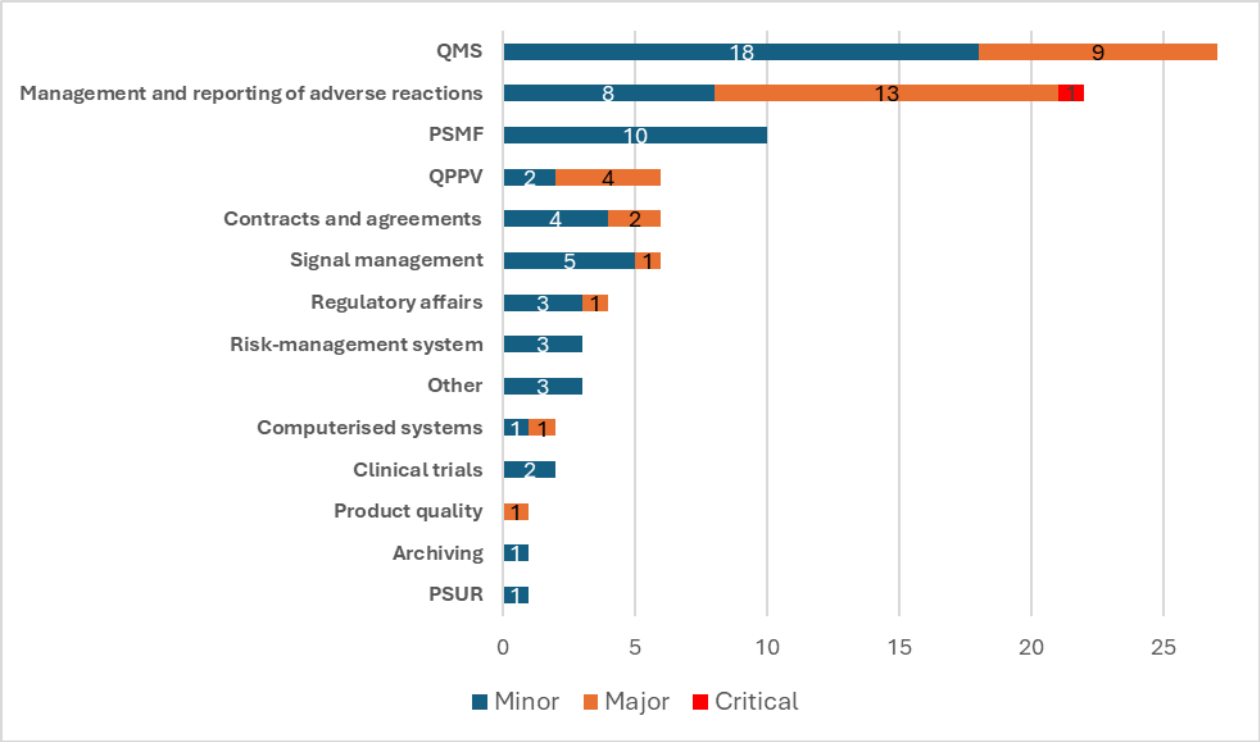
3.2. Categorisation of findings for CHMP requested inspections conducted in 2023

A total of 94 deficiencies, comprising 1 critical (1.06%), 32 major (34.04%) and 61 minor (64.89%) findings were recorded for the CHMP requested human medicines pharmacovigilance inspections conducted in 2023 (period covered from 01/01/2023 until 31/12/2023).

The main findings observed during inspections conducted in 2023 are detailed in Figure 1 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 2023 were the following:

- Quality Management System (QMS).
- Management and reporting of adverse reactions.
- Pharmacovigilance System Master File (PSMF).

Figure 1 - Number of findings related to the main categories graded as critical, major, and minor for CHMP requested inspections conducted in 2023



In 2023, a total of 27 findings in the QMS were detected. Nine were classified as major findings related to training, KPIs, audit and Corrective and Preventive Actions (CAPA) processes, and written instructions (SOPs, manuals, etc.). The remaining 18 were classified as minor findings related solely to written instructions (SOPs, manuals, etc.).

3.3. Categorisation of findings for CVMP requested inspections conducted in 2023

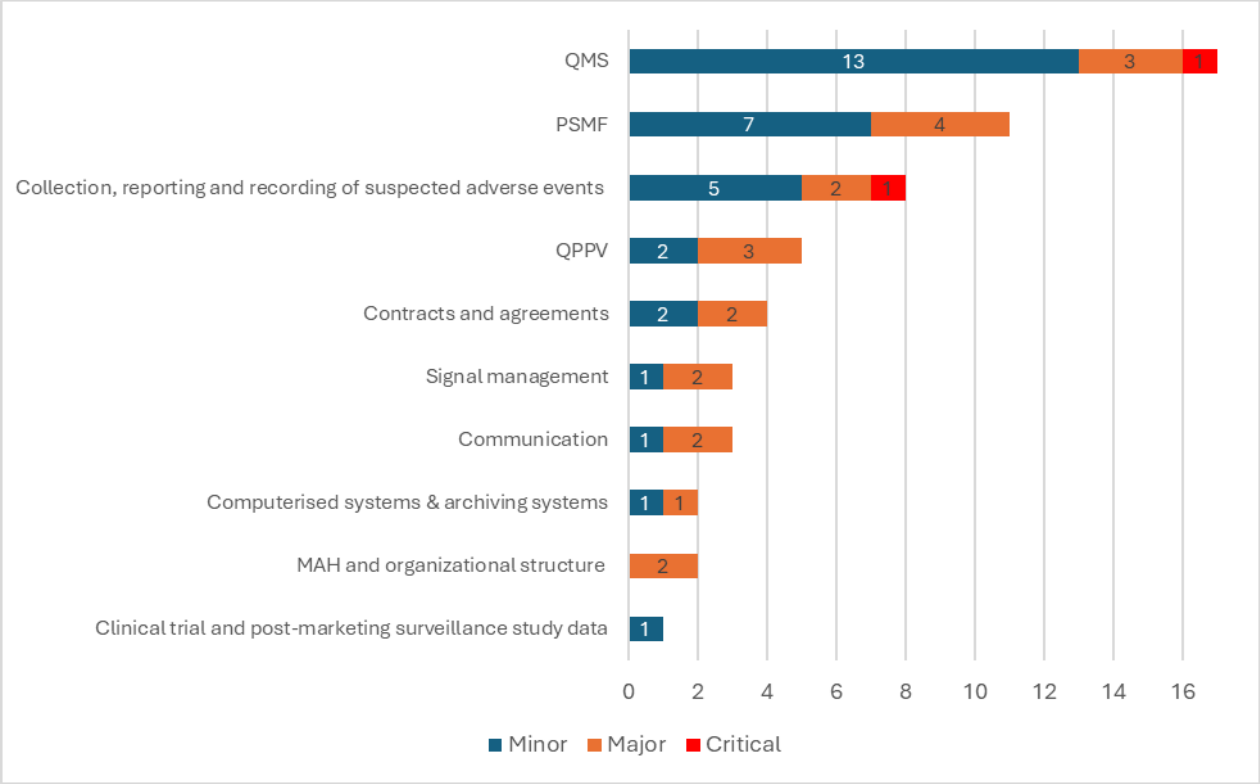
A total of 56 deficiencies, comprising 2 (3.57%) critical, 21 major (37.50%) and 33 minor (58.93%) findings were recorded for the CVMP requested veterinary medicines pharmacovigilance inspections conducted in 2023 (period covered from 01/01/2023 until 31/12/2023).

The main findings observed during inspections conducted in the 2023 are detailed in Figure 2 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 2023 were the following:

- Quality Management System (QMS).
- Pharmacovigilance System Master File (PSMF).
- Collection, reporting and recording of suspected adverse events.

Figure 2 - Number of findings related to the main categories graded as critical, major, and minor for CVMP requested inspections conducted in 2023



In 2023, a total of 17 findings in the Quality Management System (QMS) were detected. One was classified as a critical finding related to the document management system. Three were classified as major findings related to audit and CAPA process, training, and written instructions (SOPs, manuals, etc.). The remaining 13 were classified as minor findings, related to written instructions (SOPs, manuals, etc.), audit and CAPA process, KPIs, training and the document management system.

4. Harmonisation topics

4.1. Human pharmacovigilance legislation

To support further harmonisation for the mutual recognition of pharmacovigilance inspections within the Union and in connection with human medicinal products, in 2023 the group was involved in the drafting of the:

- Q&A on Day zero for ICSRs described in the medical literature.

4.2. Implementation of the new veterinary pharmacovigilance legislation

To support the implementation of the new pharmacovigilance legislation and in connection with veterinary medicinal products in 2023 the group continued the work on the following Union procedure:

- Union procedure on coordination of veterinary pharmacovigilance inspections (published).

The group was involved in the drafting of the:

- Q&A on the meaning of the terms "unresolved" and "outstanding" in Article 8(3), Article 22(2)(e)(vi) and Article 22(3)(d)(ii) of the Commission Implementing Regulation (EU) 2021/1281

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 development of the Module in IRIS to collect the outcome of the inspections has been completed.

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 conducted in 2023; 3 inspections were joint inspections involving more than one MS (see Table 1 in Section 3).

From the total of 7 CVMP pharmacovigilance site inspections conducted in 2023; 1 inspection was a joint inspection involving more than one MS (see Table 2 in Section 3).

4.4. Training and development

A hybrid Pharmacovigilance Inspectors' Working Group training course took place, from 07 to 08 December 2023. The training organisation was supported by the programme committee (Germany [BVL and PEI], Belgium (FAMHP), Sweden (Swedish Medical Products Agency). Inspectors and assessors of both, veterinary and human units of Member States (Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Hungary, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Norway, Poland, Portugal, Slovenia, Spain, Sweden) as well as inspectors, assessors/experts from non-EU countries (Australia, Bosnia and Herzegovina, Canada,

Chile, Moldova, Republic of El Salvador, Republic of Korea, Republic of North Macedonia, Switzerland, Turkey, Uganda, UK, Ukraine, 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:
  - Inspections of computerised systems and Artificial Intelligence.
  - Power BI for faster inspection preparation and better results.
- The following topics were presented and/or discussed in the human medicinal products related workshops:
  - AE reporting in clinical studies: ADR reporting to EVPM *vs* EVCTM; GVP *vs.* GCP inspections.
  - safety variations.
  - EudraVigilance Data Analysis System (EVDAS) for quality and compliance.
  - safety database validation.
  - soft skills.
  - harmonisation in grading of findings.
- The following topics were presented and/or discussed in the veterinary medicinal products related workshops:
  - Inspections under the New Veterinary Regulation.
  - overarching communication plan.
  - veterinary IT systems and reports.
  - data quality/accuracy of adverse event reports.
  - signal detection.
  - safety database validation.
  - soft skills.

- harmonisation in grading of findings.

4.5. Medicinal products for human use

- The PhV IWG has prepared and is maintaining the 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 2023, discussions on the following topics took place:
  - Revision of the PhV IWG Work plan for 2021-2024.
  - 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.
  - Use of the AI in the process of monitoring scientific medical literature.
  - risk-based inspection planning.
  - queries on guidance/legislation interpretation.
  - PIC/S activities in the field of PhV inspections.

4.6. Medicinal products for veterinary use

- The PhV IWG has prepared and is maintaining the 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 2023, discussions on the following topics took place:
  - Revision of the PhV IWG Work plan for 2021-2024
  - Regulation (EU) 2019/6 on veterinary medicinal products, corresponding implementing and delegated acts and guidance, as applicable.
  - 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.
  - PIC/S activities in the field of PhV inspections.

5. Liaison with other groups

5.1. Interaction with the PRAC

- The PhV IWG interacted with assessors on topics related to
  - Issues identified during periodic safety update report single assessment (PSUSA) procedures for risk assessment and follow up, as necessary.
  - preparation and maintenance of the risk-based programme for routine pharmacovigilance inspections of MAHs connected with human CAPs.

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, corresponding implementing and delegated acts and guidance, as applicable.
  - 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.

5.3. Communication with the public and external bodies

Delegates from the PhV IWG have participated and/or given presentations on behalf of the group in different European conferences and meetings covering different topics of public interest:

- PhV WP Interested Parties meeting, EMA, Amsterdam 27 September 2023.
- Medicine for Europe Webinar - Pharmacovigilance: system efficiency enabling patient safety EudraVigilance, (02 October 2023).
- EudraVigilance and Signal Management Information Day, EMA, Amsterdam 21 November 2023.
- Expert Working Group (EV-EWG) on an *ad hoc* basis as additional domain experts on pharmacovigilance areas of common interest to the PhV IWG and EV-EWG.
- PIC/S meetings: GVP Best Practices and Artificial Intelligence-Machine Learning Working Groups.