الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

Pharmacovigilance Inspections Report

1st Jan 2023 to 31st Dec 2023

Contents

1 Introduction

Between January 1, 2023, and December 31, 2023, the National Pharmacovigilance Center (NPC) in the Saudi Food and Drug Authority (SFDA) carried out a total of twenty-two inspections of Marketing Authorization Holders (MAHs). The primary objective of these inspections was to assess and ensure compliance with the pharmacovigilance regulations and guidelines in Saudi Arabia. The selection of MAHs for inspection was based on a risk-based methodology, which followed the principles outlined in GVP Module III and took into account several factors, including:

- Product-specific risks (e.g., new active substances or new biological products)
- The complexity of the pharmacovigilance system,
- The complexity and size of the organization(s) involved in the pharmacovigilance system, including service providers and the number of products
- The compliance and inspection history of an organization
- The reporting rate of the MAHs.

This report provides data on a total of sixteen routine inspections and six inspections conducted for cause during the same period. It also includes information on the types of inspections carried out and the findings of these inspections. The report specifically analyzes the areas where the inspection team identified the highest number of findings across the visits.

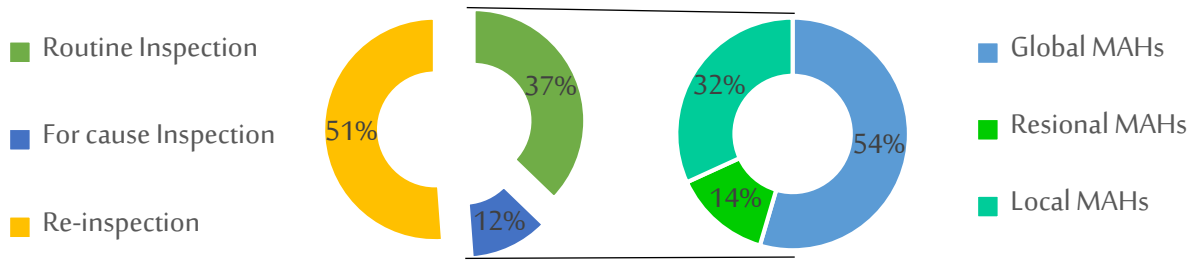
The appendix (Appendix I) contains the identified inspection types used by the inspection team, while the definitions for critical, major, and minor findings are provided in Appendix II

2 Overview of Inspection Department activities

In 2023, out of the twenty-two inspections conducted, five inspections of Marketing Authorization Holders (MAHs) were postponed and rescheduled for a later time due to specific circumstances related to the inspected MAHs. Additionally, six inspections were triggered by the NPC departments based on the performance of the MAHs. Among the for-cause inspections, one inspection case was referred to the legal department to initiate necessary action against the MAH due to their compliance history in SFDA inspection data. Out of the twenty-two routine and for-cause inspections, twelve global MAHs, three regional MAHs, and seven local MAHs. Furthermore, out of the twenty-two inspections, nine MAHs were inspected through local distributors.

During the same period, an additional twenty-two re-inspections were conducted. One of these re-inspections was rescheduled for a later time, and two inspection cases were referred to the legal department due to significant malpractice in implementing pharmacovigilance.

Figure 1 - The distrubution of inspections conducted by type during 2023



In the case of a non-compliant Marketing Authorization Holder (MAH), the inspection team provides two inspection attempts to address the observations and rectify the non-compliance. If the MAH remains non-compliant during these attempts and continues to be non-compliant during the third and final inspection, the inspection team prepares a special report and submits it to the Drug & Medical Devices Inspection department in the middle region. This department is responsible for taking the necessary action.

The Inspection department has the authority to suspend the activities of the non-compliant MAH and impose penalties based on the severity of the non-compliance until the compliance matter is resolved.

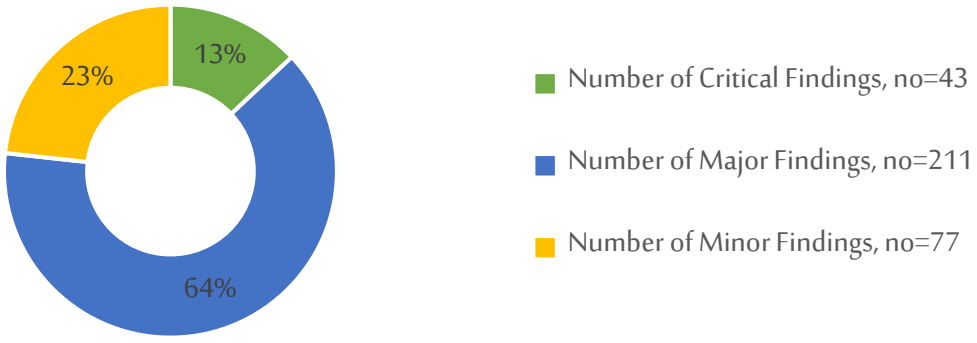
On January 2023, the Saudi Food and Drug Authority (SFDA) introduced new good pharmacovigilance guideline update. This update brought about significant changes in the reporting time frame and the classification of reports. These changes had an impact on the compliance of MAHs during 2023.

3 Summary of findings during the reported period

During the reporting period of 2023, a total of forty-three critical findings, two hundred-eleven major findings, and seventy-seven minor findings were identified. It is important to note that a reported finding can often encompass multiple instances of non-compliance, as per the requirements of Saudi Good Pharmacovigilance Practices (GVP) or the cumulative impact on pharmacovigilance.

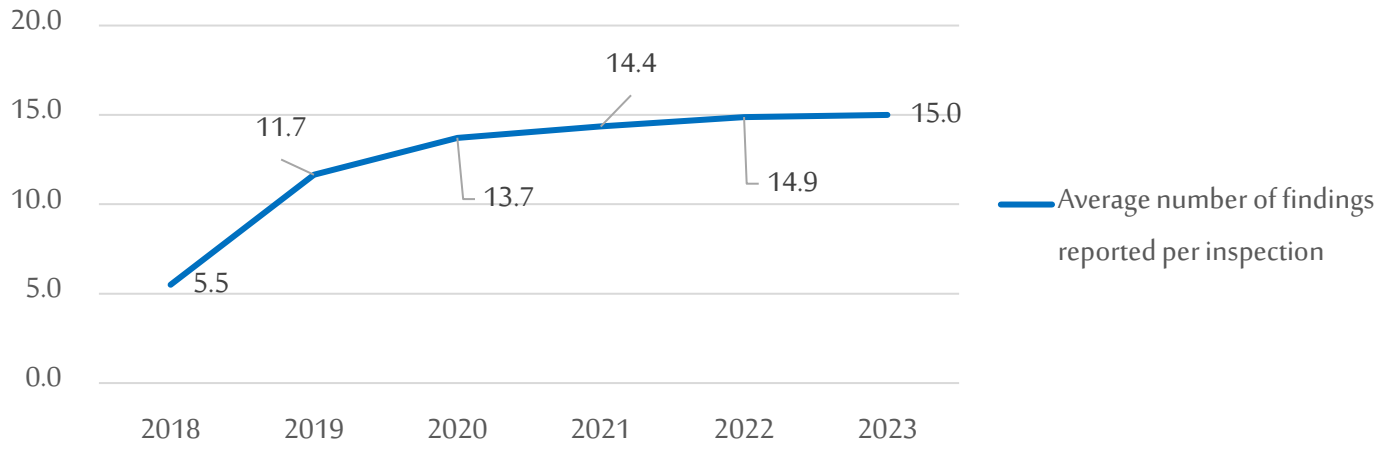
Among the inspections conducted, there were instances where a targeted scope was applied. These inspections, known as "Trigger inspections" focused on a specific technical area and were initiated by the NPC departments. The purpose of these inspections was to review the overall system within that particular area of focus.

Figure 2 - Number of over all inspection findings for Routine initial and for cause inspections



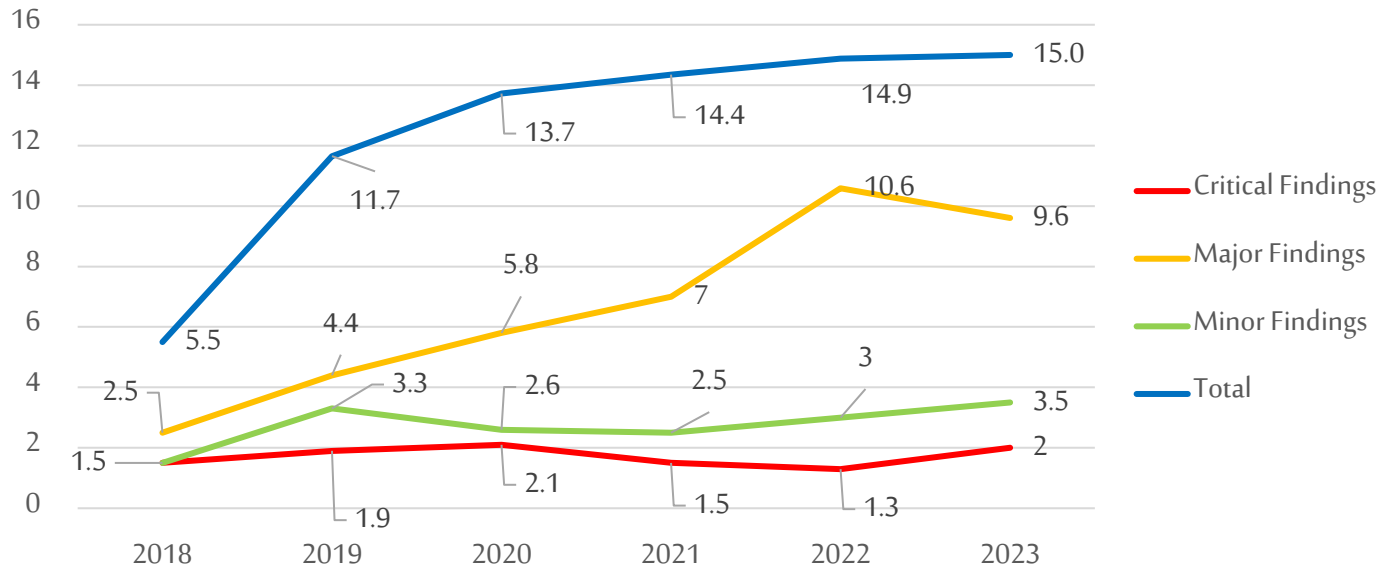
Compared to the previous reporting periods, the average number of findings per inspection (irrespective of grading) was almost stable. The average number of findings reported per inspection in 2023 was increased from 14.9 to 15 (0.67% increased), as demonstrated in Figure 3 below.

Figure 3 - Average number of findings reported per inspection over time



A review of the average findings reported each year by grading was completed and is presented in Figure 4.

Figure 4 - Average Number of Findings by Grading Reported Per Inspection Over Time

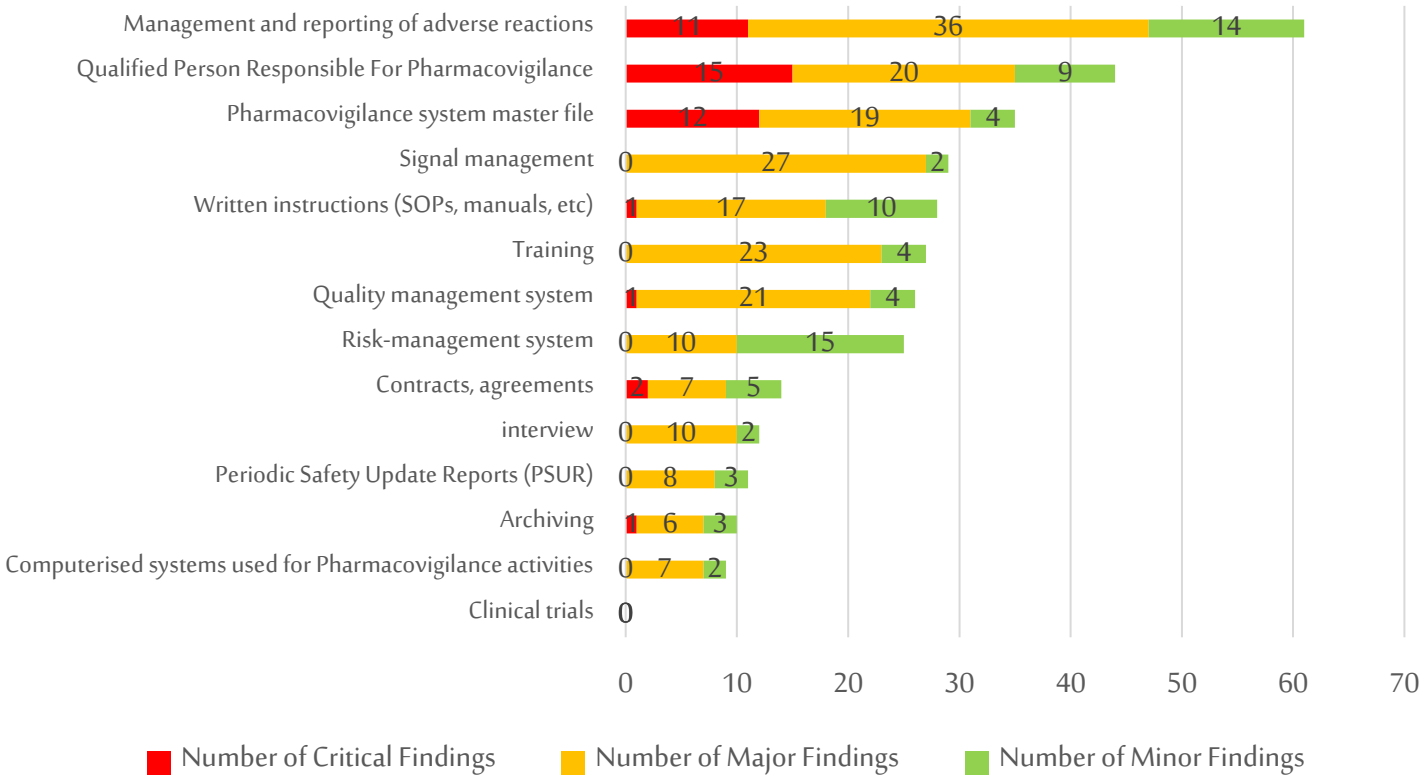


Over the years, the average number of critical findings per inspection has remained relatively stable, ranging from 3 to 3.5 reported findings. However, there has been a decrease in the average number of major findings reported per inspection.

The fluctuation in findings over time can be attributed to several factors. One significant factor is the introduction of a new update to the Saudi Good Pharmacovigilance Practices (GVP) in January 2023. This update may have required some time for Marketing Authorization Holders (MAHs) in Saudi Arabia to properly adapt and implement the changes, leading to variations in the findings observed during this period. It was noted in the previous year that certain Marketing Authorization Holders (MAHs) inspected were being operated by local distributors who lacked sufficient data safety exchange agreements. These agreements failed to encompass all the essential activities that should be carried out within Saudi Arabia. This discrepancy might have contributed to the findings identified during the inspections. This issue has been addressed in the updated guideline, which now emphasizes the requirement for MAHs to submit a preapproval request before registering distributors as Qualified Persons for Pharmacovigilance (QPPV) of the MAH. This measure aims to ensure that the necessary activities are adequately covered and addressed in the data safety exchange agreements.

The average number of minor findings reported per inspection has increased, while there has been a decrease in the average number of major findings. This suggests a positive shift in the attitude and practice of

Figure 5 - Findings by topic area for 2023



pharmacovigilance, indicating a greater focus on addressing major issues and improving overall compliance.

When analyzing the inspection findings according to specific topic areas, Figure 5 shows that the highest proportion of findings, regardless of their grading, was related to the Management of adverse drug reactions, accounting for 18.4% or 61 out of 331 reported findings. Following closely was the qualified person responsible for pharmacovigilance, which accounted for 13.3% (44 out of 331) of all findings. The Pharmacovigilance system master file was the third highest topic, representing 10.6% (35 out of 331) of the total findings. It is worth noting that these three topics also had a significant proportion of findings in the year 2022, indicating their ongoing importance and potential areas for improvement in pharmacovigilance practices.

4 Critical findings

4.1 Critical findings reported during 2023

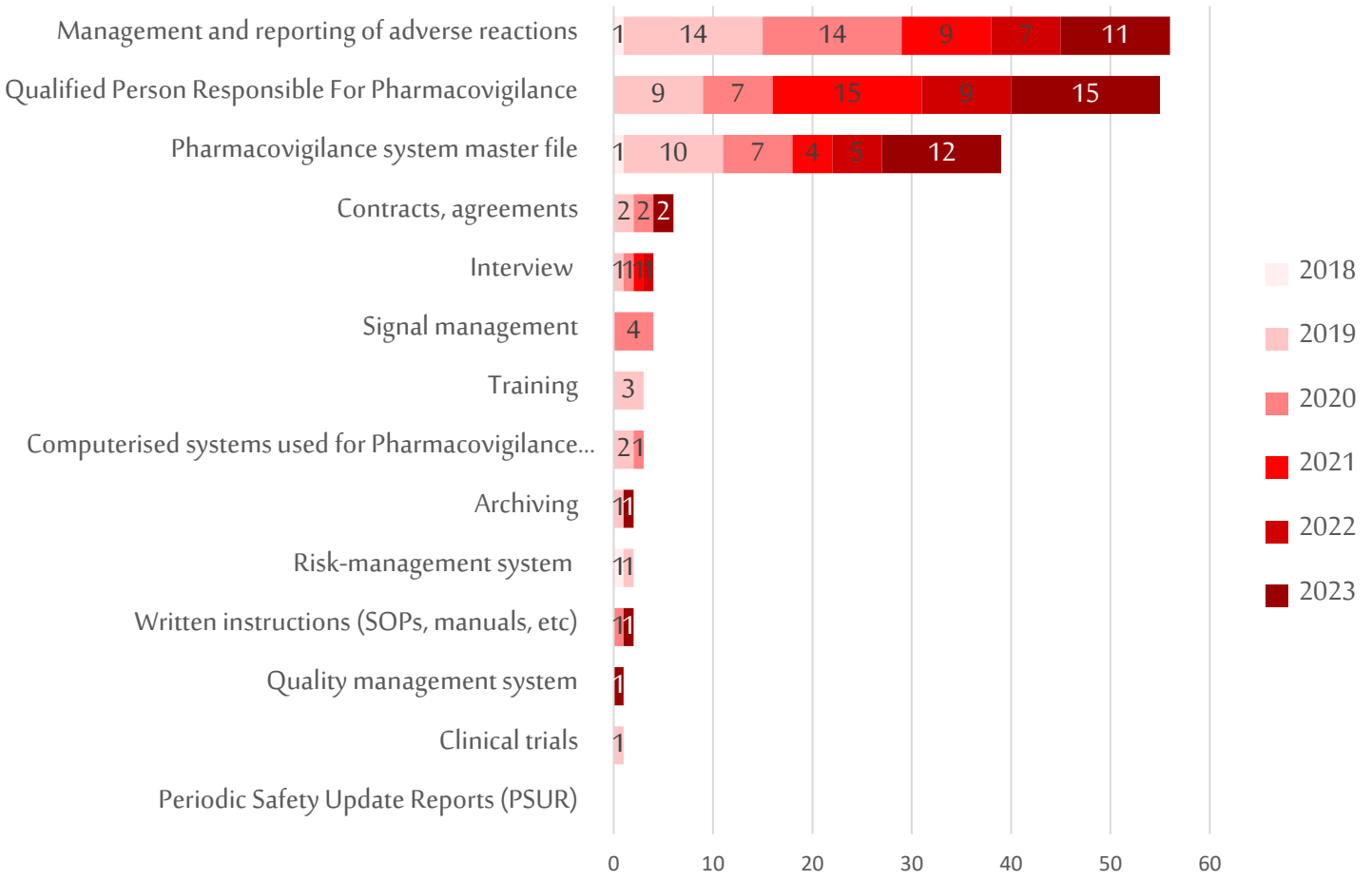
Forty-three critical findings were identified from nine inspections in 2023. The average of reporting finding per inspection was approximately two critical findings reported. All forty-three critical findings were in the area of Qualified Person Responsible for Pharmacovigilance, Pharmacovigilance system master file, Management and reporting of adverse reactions, contracts and agreements, written instructions (SOPs, manuals, etc.), archiving and quality management system.

4.2 Distribution of critical findings over time

From November 2018 to December 31, 2023, a total of 178 critical findings were reported. In the current reporting period of 2023, 43 critical findings were identified from 15 out of 22 inspections. This represents an increase compared to the previous four reporting periods.

Figure 6 illustrates the number and distribution of critical inspection findings across different inspection topics since November 2018. The findings have been grouped under overarching topics that encompass various aspects of the pharmacovigilance system. For more detailed information about the specific nature of the findings covered by each topic, please refer to Appendix III.

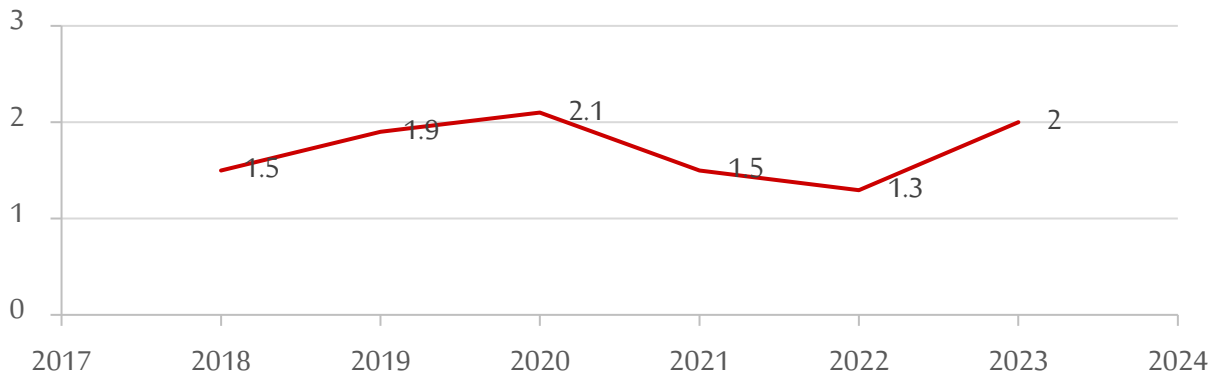
Figure 6 - Number and distribution of critical findings across topics since 2018 until 2023



The management and reporting of adverse reactions continue to be the topic with the highest number of critical findings reported over the time. In 2023, eleven critical findings were specifically related to the data collection methods in this area. Another topic that consistently yields critical findings is the qualified person responsible for Pharmacovigilance, with fifteen critical findings reported during 2023. Similarly, the pharmacovigilance system master file has historically been an area with frequent critical findings, and twelve critical findings were reported in this area during 2023. In addition, for this reporting period, critical findings were uniquely reported against the topics of contracts and agreements, archiving, and quality management system. These findings highlight specific areas of concern within these topics and were observed in multiple years, indicating a need for focused attention and improvement in these areas.

On average, there were approximately two critical findings reported per inspection, indicating an increase of 53.8% compared to the previous reporting period. This change in the number of critical findings may be attributed to the release of the updated Saudi Good Pharmacovigilance Practices (GVP) early in 2023. The updated GVP specifically addressed the quality aspect in pharmacovigilance. Notable changes in the updated GVP included modifications to the qualifications of the Qualified Person for Pharmacovigilance (QPPV) and their deputy, adjustments to pharmacovigilance task timeframes, transforming certain tasks from reporting to implementation, and a thorough review of contracts related to pharmacovigilance activities. The aim of these changes was to ensure that the contracts adequately covered all the required tasks to be carried out by the local QPPV. These updates in the Saudi GVP likely contributed to the increase in critical findings, as they emphasized the importance of maintaining high-quality standards in pharmacovigilance practices.

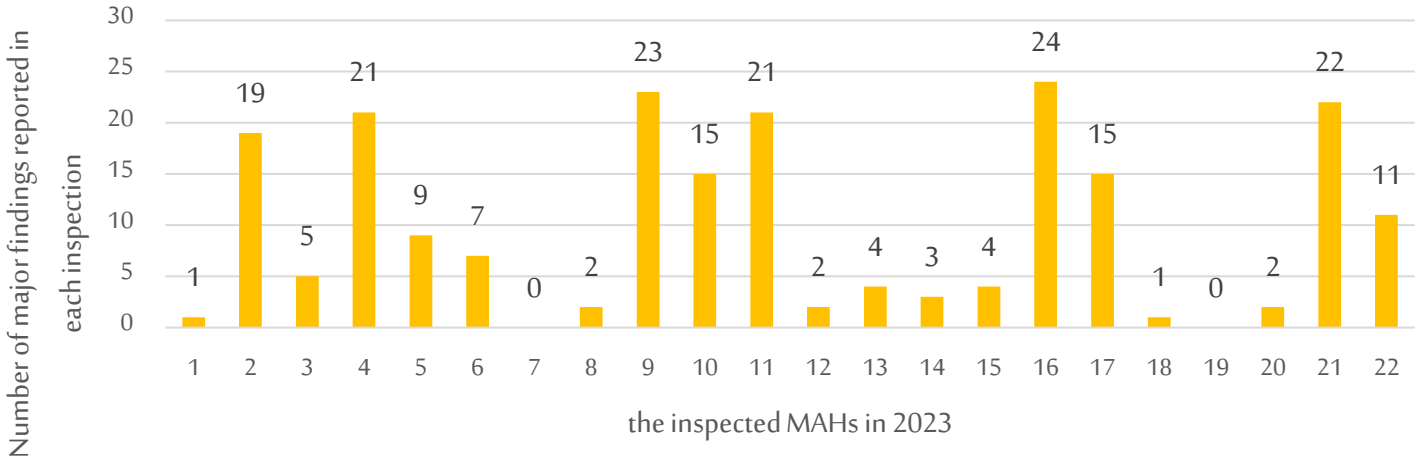
Figure 7 - Average Number of Critical Finding Per Reported Inspection Over Time



5 Major findings

During this reporting period, the number of major findings per inspection varied, ranging from zero to twenty-four. Interestingly, two inspections did not raise any major findings at all. Out of the twenty-two inspections conducted in 2023, the average number of major findings per inspection was 9.6. A visual representation of the distribution of major findings across inspections can be seen in Figure 8.

Figure 8 - Number of major findings reported by the number of inspections in 2023



In total, there were two hundred eleven major findings identified in 2023. These findings have been categorized under overarching topics that encompass various aspects of the pharmacovigilance system. For more detailed information about the specific nature of the findings covered by each topic, please refer to Appendix II.

Figure 9 - Percentage of major findings reported for each topic area during 2023

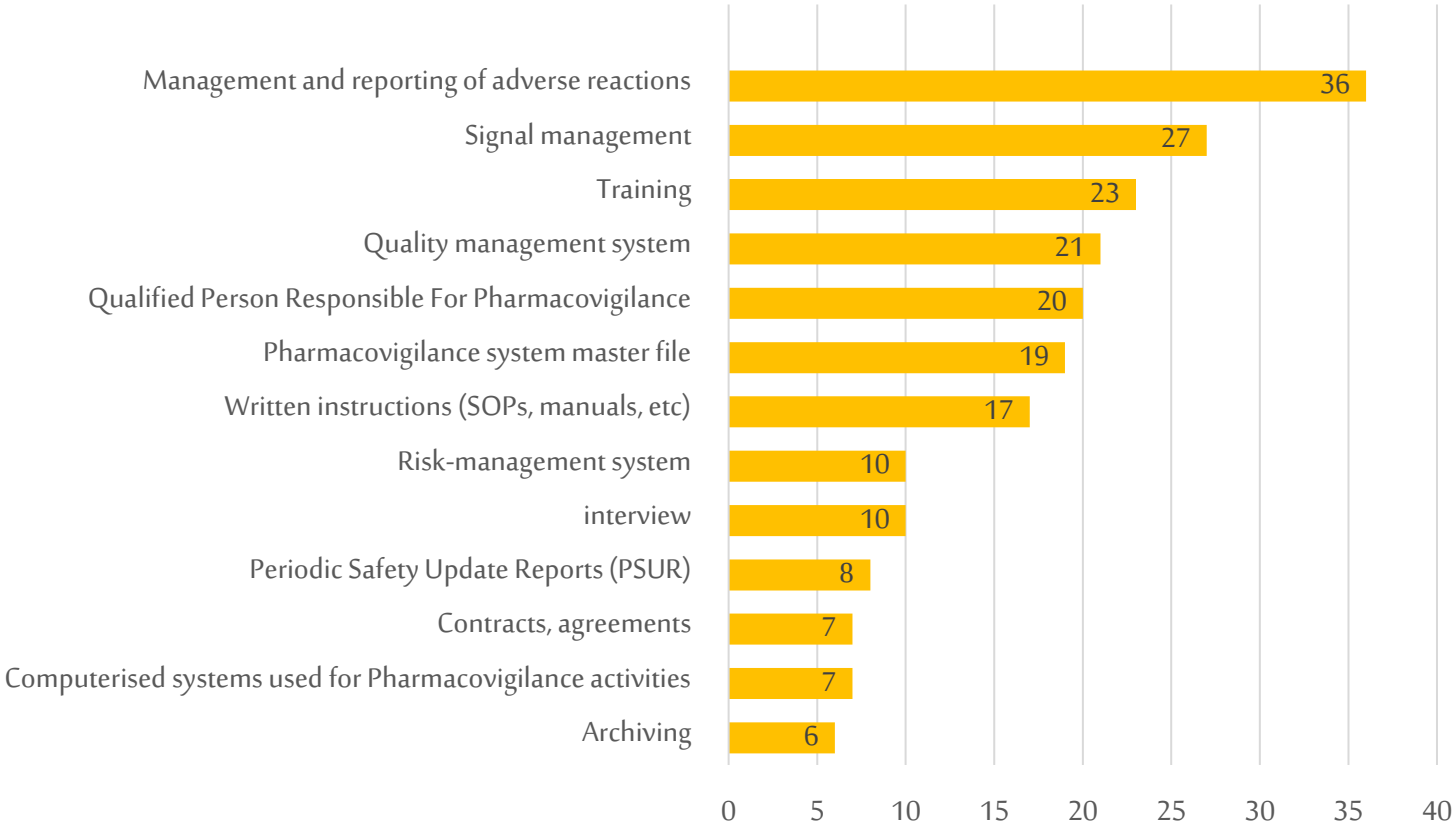


Figure 9 illustrates the distribution of major findings across different topics, revealing the following insights:

- Management and reporting adverse reactions: This topic accounted for the highest proportion of major findings, with 36 reported findings, representing 17.1% of the total. It emphasizes the importance of effectively managing and reporting adverse reactions associated with medications. Proper monitoring, documentation, and reporting of potential risks or adverse effects are crucial in ensuring patient safety.
- Signal management: Following closely, this topic consisted of 27 major findings, representing 12.8% of the total. Signal management involves the detection, evaluation, and management of signals or potential safety concerns related to medications. The findings in this area may highlight deficiencies or gaps in the signal management process, warranting attention and improvement.
- Training: The topic of training accounted for 23 major findings, comprising 10.9% of the total. It underscores the significance of providing adequate training to personnel involved in

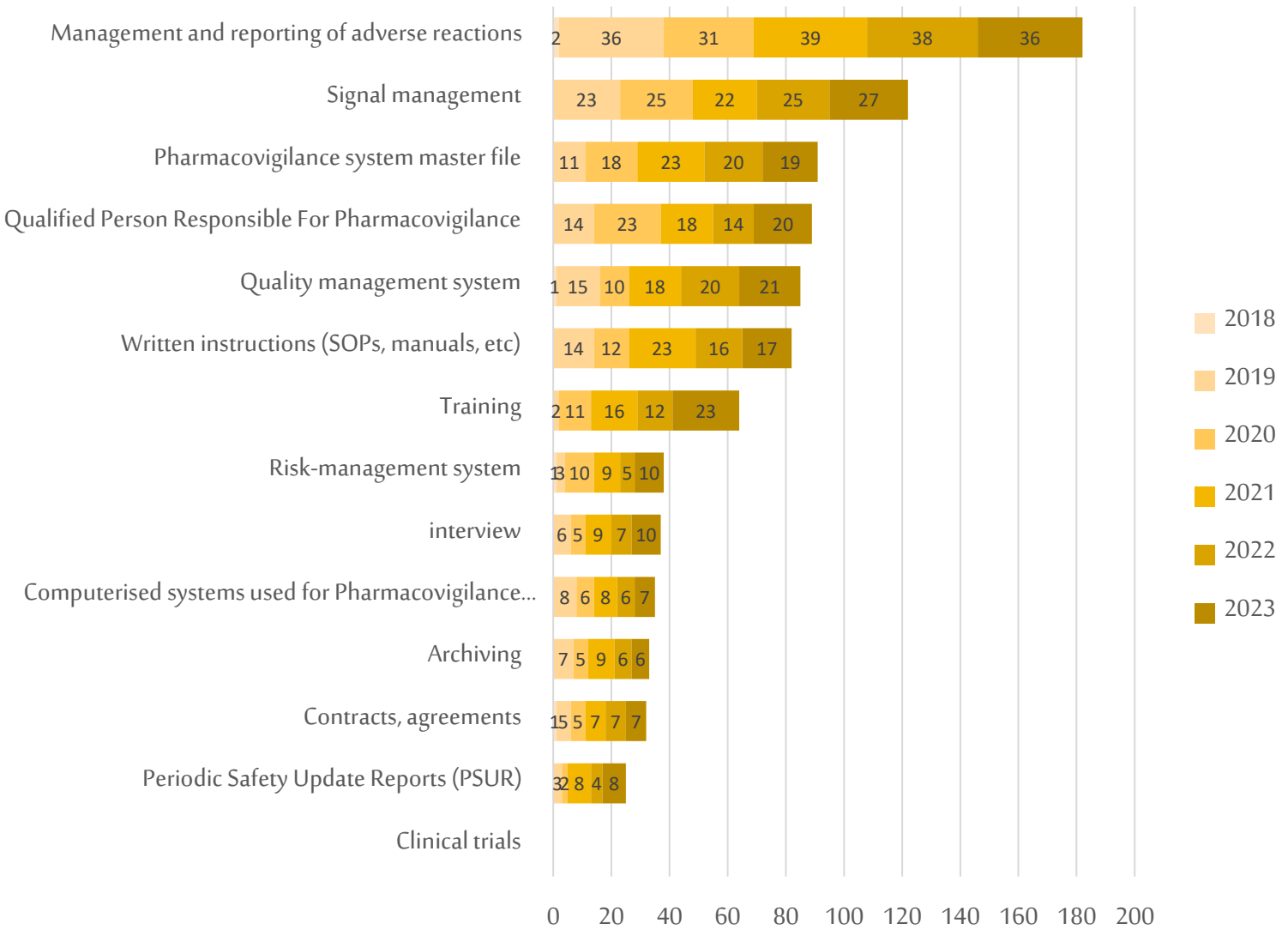
pharmacovigilance activities. The findings in this area may relate to deficiencies in training programs, insufficient documentation, or a lack of available training resources and attendees knowledge evaluation.

- Quality management system: With 21 major findings, representing 10% of the total, the topic of quality management system focuses on establishing and maintaining robust quality management practices within pharmacovigilance operations. Findings in this area may encompass issues related to quality control, documentation practices, or adherence to standard operating procedures.
- Qualified Person Responsible for Pharmacovigilance: This topic accounted for 20 major findings, representing 9.5% of the total. The QPPV plays a crucial role in overseeing pharmacovigilance activities. The findings in this area may pertain to deficiencies in the qualifications or responsibilities of the QPPV or issues related to their overall performance and the delegation process during the QPPV absence.
- Pharmacovigilance system master file: With 19 major findings, representing 9% of the total, this topic focuses on the pharmacovigilance system master file, which is a comprehensive document that outlines the pharmacovigilance system in place. The findings in this area may highlight deficiencies or gaps in the documentation, organization, or maintenance of the master file.
- Written instructions (SOPs, manuals, etc.): This topic accounted for 17 major findings, representing 8.1% of the total. Properly documented written instructions, including standard operating procedures (SOPs) and manuals, are essential for ensuring consistency and compliance in pharmacovigilance practices. The findings in this area may involve deficiencies in the development, implementation, or adherence to written instructions.

Addressing these major findings in the areas of management and reporting adverse reactions, signal management, training, quality management system, qualified person responsible for pharmacovigilance, pharmacovigilance system master file, and written instructions (SOPs, manuals, etc.) is crucial for enhancing

pharmacovigilance practices, ensuring patient safety, and maintaining compliance with regulatory requirements.

Figure 10 - Number and distribution of major findings across topics over time since 2018 until 2023



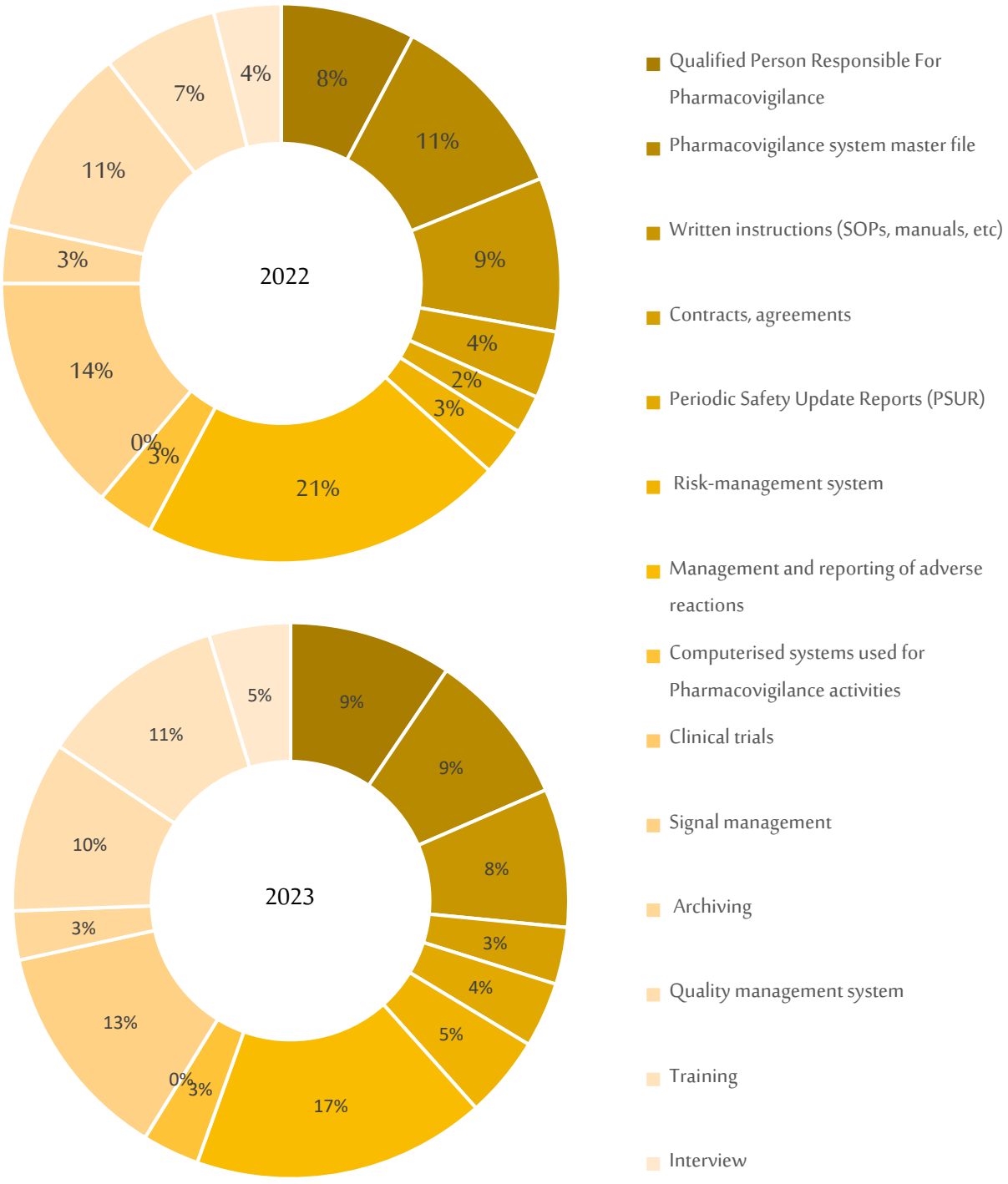
From November 2018 to December 31, 2023, a total of 915 major findings were reported, representing an approximate 30% in overall increase. For the current reporting period, 211 major findings were identified from 20 out of 22 inspections. The distribution of major inspection findings across various inspection topics since November 2018 is depicted in Figure 10. This figure provides a visual representation of the number and distribution of major findings across different inspection topics over the specified time frame. The reporting

and analysis of major findings play a crucial role in improving pharmacovigilance practices, strengthening regulatory compliance, and safeguarding public health. By addressing these findings, organizations can enhance their pharmacovigilance systems, mitigate risks, and ensure the safe and effective use of medications.

When comparing the previous reporting periods from 2022 to 2023, the distribution of major findings across different topics exhibited fluctuations, with the topics maintaining a relatively similar ratio. Notably, the topic of Management and reporting of adverse reaction findings experienced a decrease of 19% in its overall proportion of findings compared to the previous period. Specifically, the proportion of Management and reporting of adverse reaction findings decreased from 21% in 2021 to 17% in 2023, as illustrated in Figure 11 below. This decrease recorded a reduction that was slightly lower than the decrease observed in 2021, which amounted to 19% of total finding.

During this reporting period, another topic that experienced a decrease in the proportion of major findings compared to the previous period was signal management, which decreased from 14% to 13%. Additionally, the majority of inspection topics saw a decrease in the proportion of findings. However, two specific areas showed significant increases in the proportion of major findings. The topic of Qualified Person Responsible for Pharmacovigilance saw an increase from 8% to 9%, while the topic of training witnessed a notable rise from 7% to 11%. These findings indicate shifts in the distribution of major findings across different areas of focus, highlighting the importance of QPPV and training in the pharmacovigilance process.

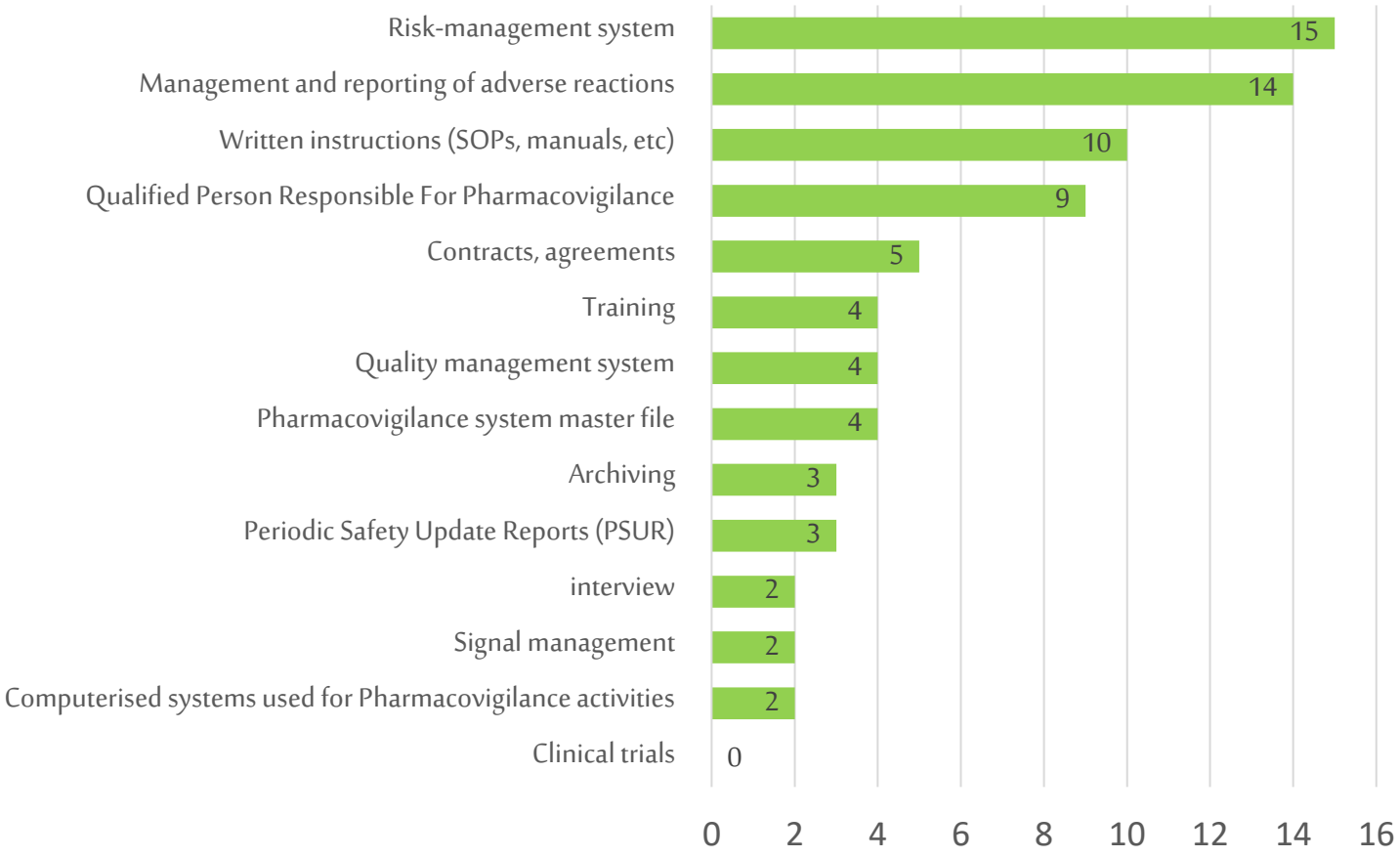
Figure 11 – Percentage change in the major findings between inspection findings from 2022 to 2023 by topic area



6 Minor findings

In 2023, a total of seventy-seven minor findings were identified. Interestingly, this aligns with the occurrence value reported in 2019, indicating a return to a similar level of findings compared to the previous reporting period. Figure 12 provides an overview of the proportion of minor findings categorized by topic area for the reporting period in 2023. This visualization helps to illustrate the distribution and relative significance of minor findings across different areas of focus during that specific period.

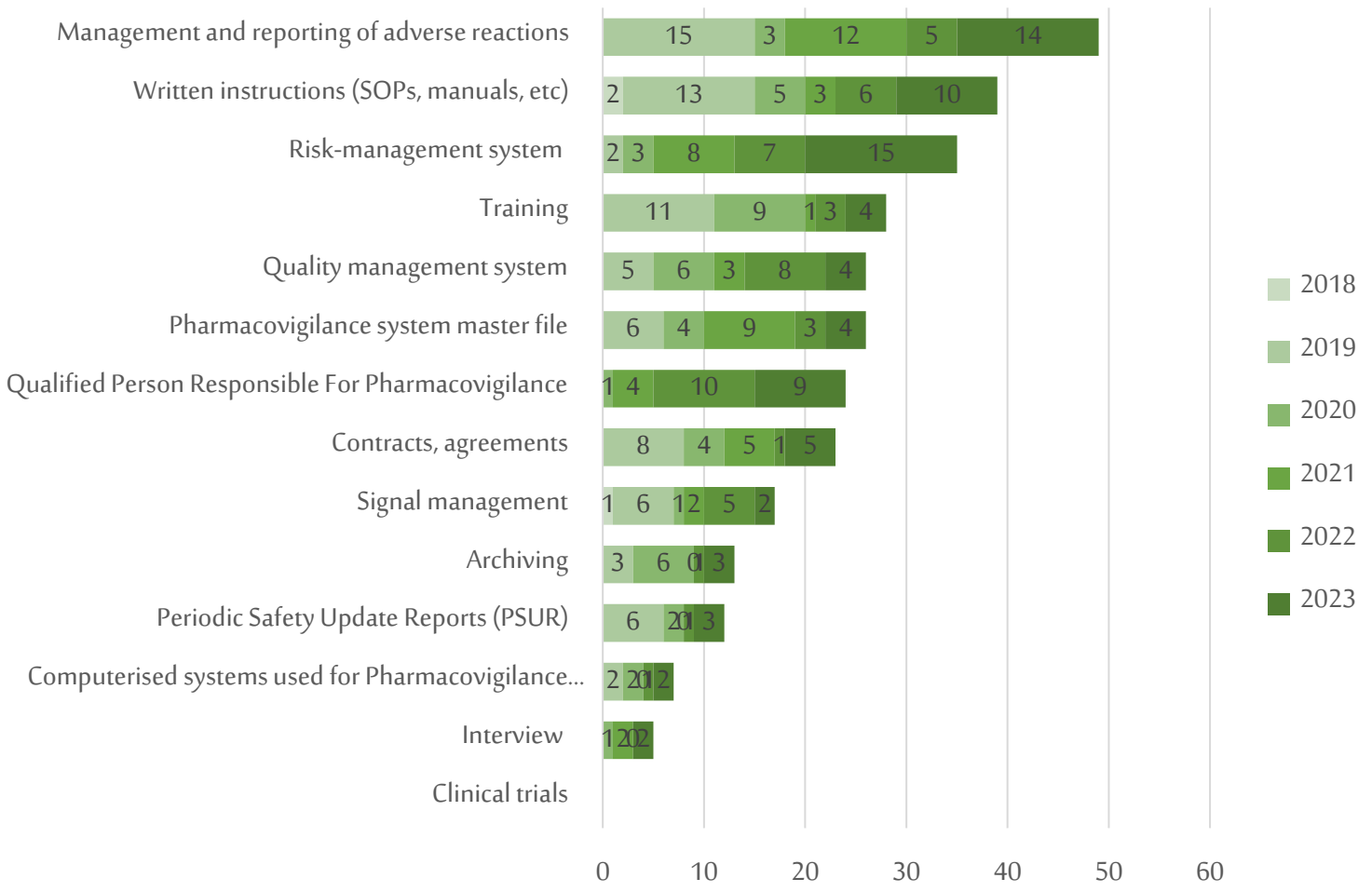
Figure 12 - Proportion of minor findings reported for each topic area in 2023



Among the minor findings, the highest proportion was attributed to non-compliances in the risk-management system. Following closely were findings related to the management and reporting of adverse reactions, written instructions (SOPs, manuals, etc.), the qualified person responsible for pharmacovigilance, as well as contracts and agreements. These areas accounted for a significant portion of the minor findings, indicating potential

areas for improvement in terms of compliance, documentation, and the overall effectiveness of risk management practices within the pharmacovigilance system.

Figure 13 - Number and distribution of minor findings across topics since 2018 until 2023



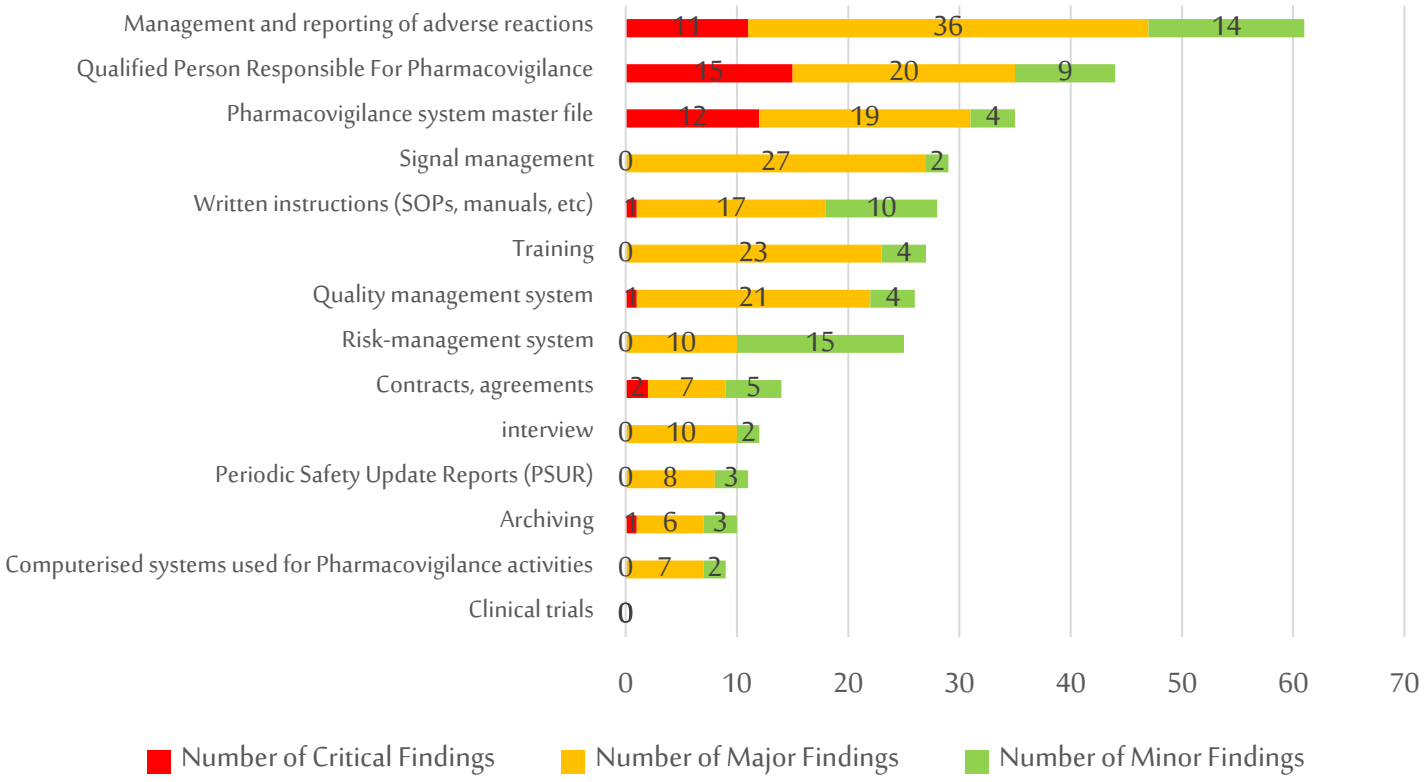
In 2023, the topics of management and reporting of adverse reactions, written instructions (SOPs, manuals, etc.), and risk management observed a higher proportion of minor findings compared to 2022. This suggests that there were more identified areas for improvement or non-compliances in these specific areas during the reporting period of 2023.

On the other hand, the topics of the interview of inspected MAH's medical representatives and computerized systems used for pharmacovigilance activities had a lower proportion of minor findings raised in 2023. This implies that fewer areas of concern or non-compliances were identified within these specific topics during the reporting period of 2023, indicating a relatively better performance or adherence to requirements in these areas compared to the previous year.

7 Focus topics

In the reporting period, irrespective of the grading of the findings, the topic with the highest number of all findings was the management and reporting of adverse reactions. This was followed by the qualified person responsible for pharmacovigilance and then the pharmacovigilance system master file. These areas accounted for the largest number of identified findings, indicating their significance in terms of potential improvements,

Figure 5 - Findings by topic area for 2023



compliance, and overall effectiveness in the pharmacovigilance system.

7.1 Management and reporting of adverse reactions

For the past two reporting periods, the management and reporting of adverse reactions has consistently remained the topic with the highest number of findings. In the current reporting period, it accounted for 61 out of 331 findings, constituting approximately 18.4% of all findings. These findings were reported from 18 out of the 22 inspections conducted.

Figure 14 - Breakdown of Management and reporting of adverse reactions findings in 2023

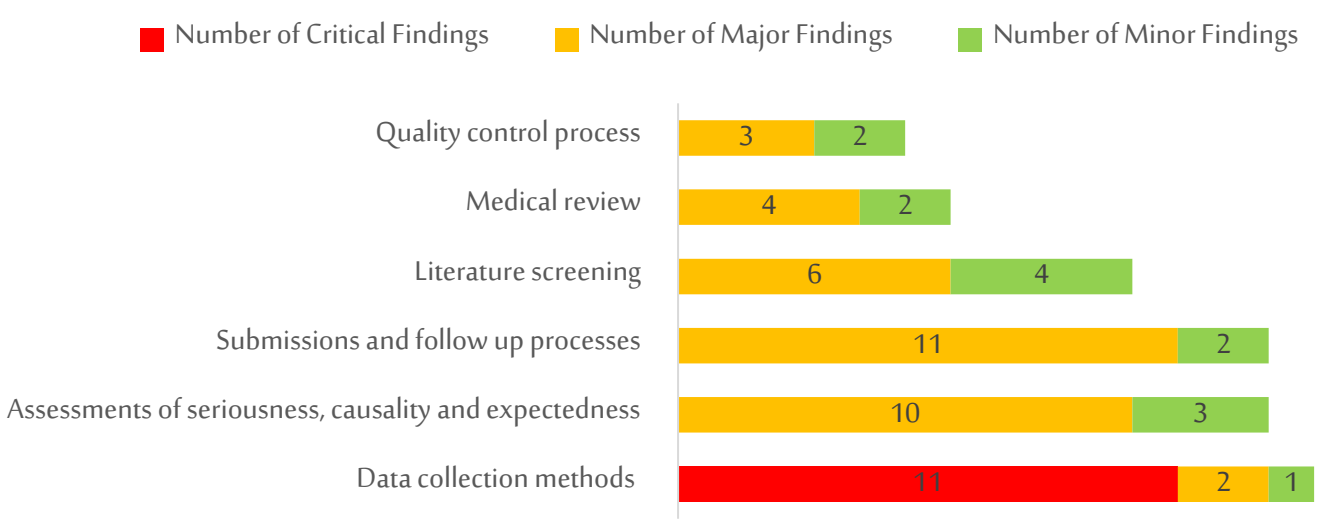


Figure 14 provides a breakdown of the 61 findings within the management and reporting of adverse reactions topic, categorizing them by sub-topic. This breakdown helps to identify specific areas or sub-topics within the broader topic where the findings were concentrated. By analyzing this breakdown, it becomes possible to identify patterns, trends, or specific areas that require attention or improvement in the management and reporting of adverse reactions.

The consistent high number of findings in this area highlights the importance of robust and effective systems for managing and reporting adverse reactions. Addressing these findings and implementing appropriate measures can enhance patient safety and contribute to the overall improvement of pharmacovigilance practices.

The majority of findings in the area of management and reporting of adverse reactions were associated with failures in the data collection method. Specifically, there were 14 findings related to limited channels used to receive adverse drug event reports. The most common non-compliance issues in this area included:

- Absence of a phone number or Arabic website for the public to report adverse events.
- Lack of a system to document and process locally received cases.
- Inability of the local Qualified Person Responsible for Pharmacovigilance (QPPV) to access the Marketing Authorization Holder (MAH) database to handle local Individual Case Safety Reports (ICSRs).
- Inability of the local QPPV to access Saudi market medical representatives to collect adverse event reports.
- Lack of a database or excel sheet for documenting local cases.
- Presence of the Saudi Arabia webpage in the global drop list.
- Lack of connection between the available website and important pharmacovigilance links.
- Outdated information on the website for the public to report adverse events.

The second-largest number of findings in the management and reporting of adverse reactions sub-topic were related to failures in assessing the seriousness, causality, and expectedness of reported adverse events. There were 13 findings in this area, with the most common non-compliance issues being the exclusion of the local QPPV from these processes or their lack of awareness regarding the processes.

Additionally, there were nine findings concerning the submissions and follow-up processes in the management and reporting of adverse reactions. The most common non-compliance issues in this area included:

- Lack of updating the local Standard Operating Procedure (SOP) with new regulations for reporting local ICSRs and quality reports.
- Absence of an SOP or specific requirements for submissions and follow-ups.
- Lack of awareness by the local QPPV regarding ICSRs submission timeframes and follow-up criteria.
- Furthermore, there were ten findings related to literature screening. The most common non-compliance issues observed in this area were:

- Failure to conduct literature screening of local journals in Saudi Arabia.
- Absence of a defined timeframe for conducting literature screening, as well as inadequate documentation of previous attempts.
- Lack of involvement from both the global team and the local QPPV in the literature screening process.
- Absence of an SOP describing the local literature screening process (including periodicity, documentation, and involvement of the local QPPV).
- Absence of an SOP describing the process of handling the vendor responsible for literature screening (including periodicity, reconciliation with the MAH, and auditing capacity by the MAH).
- Inconsistency between provided SOPs and actual practices.
- Failure of the inspected MAH to perform literature screening as required in the SOP and safety agreement.
- Lack of periodic reconciliation with the global team on literature screening outcomes.
- Performance of literature screening of local journals by the local QPPV without any proofing.

Additionally, there were four findings related to medical review activities. The most common non-compliance issues observed in this area were:

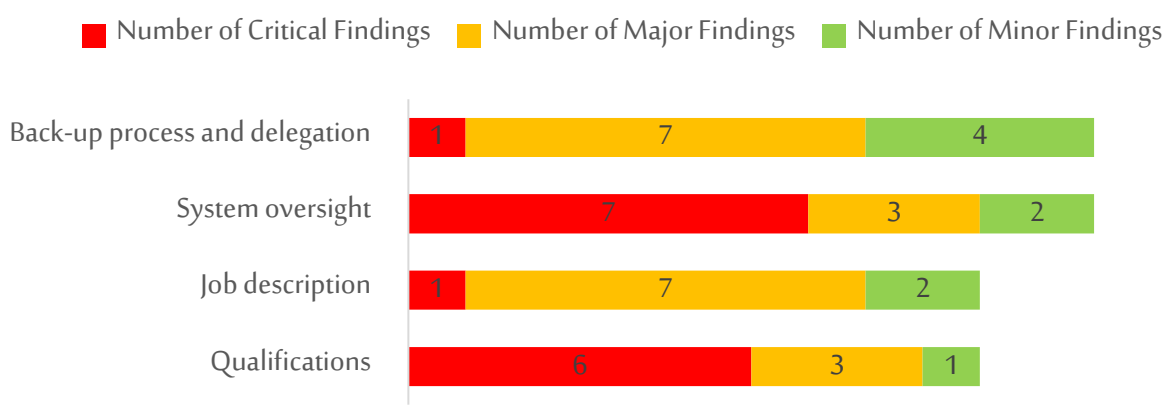
- Absence of an SOP for medical review activities.
- Lack of medical review for the provided local ICSRs.
- Lack of awareness by the local QPPV regarding ICSRs submission timeframes and follow-up criteria.

Lastly, there were four findings related to the quality control process. The most common non-compliance issues observed in this area were the absence of an SOP for the quality control process or lack of awareness regarding the process.

7.2 Qualified person responsible for pharmacovigilance

In 2023, the QPPV subject accounted for the second-largest percentage of all reported findings. Specifically, 44 out of 331 findings, which constituted 13% of the total, were related to this topic. These findings were obtained from inspections conducted in 15 out of the 22 locations. For a detailed breakdown of the 44 findings within the QPPV topic, please refer to Figure 15.

Figure 15 - Breakdown of Qualified person responsible for pharmacovigilance findings in 2023



The backup process and delegation emerged as the sub-topic with the highest number of findings for QPPV, totaling 12. It was closely followed by 12 findings related to System oversight of the local QPPV, and 10 findings associated with the job description of the local QPPV. These sub-topics encompassed critical, major, and minor findings.

The most common non-compliance observed in the backup process and delegation sub-topic were as follows:

- Absence of a clear, written backup and delegation standard operating procedure (SOP) or process.
- Inadequate documentation and implementation of the backup and delegation process.

In the System oversight sub-topic, a common non-compliance was the lack of awareness or involvement of the local QPPV in the implemented pharmacovigilance (PV) activities or delegated responsibilities, both locally and globally.

Regarding the job description of the local QPPV sub-topic, the most prevalent non-compliance issues were:

- Absence of a job description specifically outlining the handling of local pharmacovigilance activities.
- Failure of the local QPPV to sign the provided job description.
- Lack of clarity regarding the responsibilities of the local QPPV in the provided job description.
- Inadequate implementation of the available job description.
- Omission of certain responsibilities of the local QPPV in the provided job description.

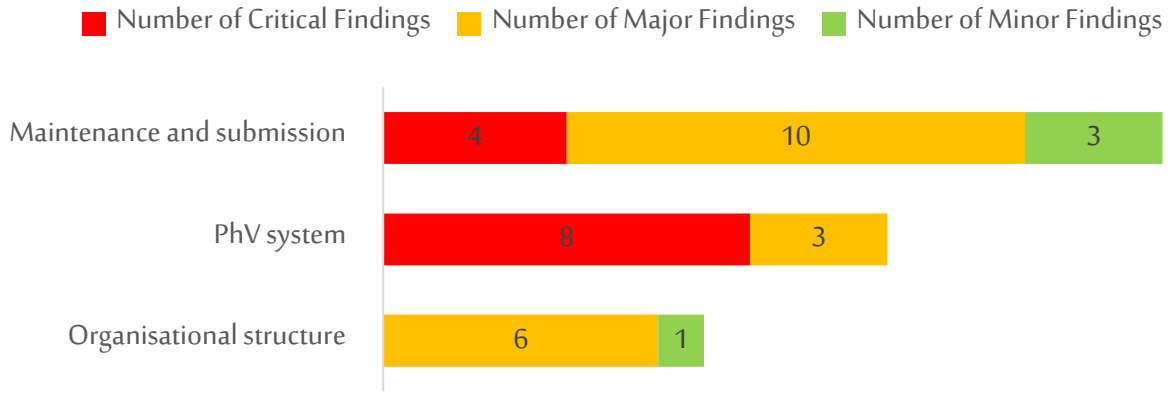
Lastly, the common non-compliance observed in the qualifications of the local QPPV sub-topic were:

- The local QPPV not dedicating full-time to handling pharmacovigilance activities.
- Inspection being conducted by a Deputy-QPPV, with no presence of a local QPPV in the Marketing Authorization Holder (MAH).
- Failure of the MAH to assign a local QPPV.
- Lack of awareness by the local QPPV about the requirements mentioned in the Saudi GVP guideline.

7.3 The pharmacovigilance system master file

In 2023, the pharmacovigilance system master file (PSMF) accounted for the third-largest proportion of reported findings. Specifically, out of the total 331 findings, 35 findings were related to this topic, comprising 10.6% of all findings. These findings were reported from 17 out of the 22 inspections conducted. For a detailed breakdown of the 35 findings within the PSMF topic, please refer to Figure 16.

Figure 16 - Breakdown of The Pharmacovigilance system master file findings in 2023



Among the sub-topics of the pharmacovigilance system master file (PSMF), Maintenance and submission had the highest number of findings, totaling 17. It was followed by 11 findings related to the pharmacovigilance system and 7 findings associated with the organizational structure. These sub-topics encompassed critical, major, and minor findings.

The most common non-compliances observed in the Maintenance and submission sub-topic were as follows:

- Incompatibility of the provided PSMF/PSSF with the required template mentioned in the Saudi GVP guidelines.
- Lack of standard operating procedures (SOPs) describing the preparation, maintenance, and updating frequency of the local PSMF/PSSF.
- Limited accessibility of the local QPPV to the MAH PSMF.
- Absence of the PSMF/PSSF document in the inspected MAH.
- Lack of clarity regarding the authorizing party and required signatories in the provided document.
- Failure to provide both PSMF/PSSF when required.
- Limited access for the local QPPV to the updated PSMF unless requested by the SFDA.
- Generalized language in the PSSF, failing to reflect harmonization between the regional team and the local QPPV.
- Availability of an outdated PSMF with gaps in information.

In the pharmacovigilance system sub-topic, the common non-compliances observed were:

- Limited awareness or knowledge of the pharmacovigilance system in the MAH's global office and/or restricted access for the local QPPV.
- Absence of an electronic system for handling PV activities.

Lastly, in the organizational structure sub-topic, the common non-compliances observed were:

- Inadequate presentation of the actual practice and relationship between the local QPPV and the global team.
- The organizational structure being in draft form and not authorized by the MAH.

8 Engaging the stakeholders in Saudi GVP update

In 2023, the inspection team organized three workshops for all QPPVs and their deputies. The purpose of these workshops was to discuss the updated Saudi GPV (Good Pharmacovigilance Practices) released in January 2023. During these workshops, the new timeframes for pharmacovigilance activities and the new legislations mentioned in the guidelines were disclosed. Representatives from the National Pharmacovigilance Center (NPC) were present to provide information about the updates in each department and to address any questions or concerns raised by the attendees based on their experiences. To assess the impact of these sessions on the attendees' overall knowledge, the NPC prepared pre and post assessments. These assessments aimed to evaluate the attendees' understanding of the discussed topics before and after the workshops.

Furthermore, the NPC conducted a satisfaction survey to gather feedback from the attendees regarding the provided sessions. The survey also aimed to gather attendees' expectations for future events of a similar nature, allowing them to express their preferences and suggestions.

9 Summary

In 2023, the Inspection Department conducted a total of 22 inspections, including routine and for-cause inspections. Out of these inspections, five were postponed and rescheduled, and six for-cause inspections were initiated by NPC departments. One inspection case was referred to the legal department for necessary action against an MAH with a history of non-compliance.

During the reporting period, a total of 43 critical findings, 211 major findings, and 77 minor findings were identified. The average number of findings per inspection remained stable compared to previous periods, with an average of 15 findings per inspection in 2023. The average number of major findings decreased, indicating a positive shift in pharmacovigilance practices. The areas with the highest proportion of findings were the management of adverse drug reactions, the qualified person responsible for pharmacovigilance, and the pharmacovigilance system master file.

In terms of major findings, the management and reporting of adverse reactions accounted for the highest proportion, representing 17.1% of the total major findings. This was followed by signal management (12.8%), training (10.9%), quality management system (10%), and the role of the Qualified Person Responsible for Pharmacovigilance (QPPV) (9.5%). Other significant findings were related to the pharmacovigilance system master file and written instructions (SOPs, manuals, etc.). Among the minor findings, a total of 77 were identified in 2023. The highest proportion of minor findings was related to non-compliance in the risk management system, followed by the management and reporting of adverse reactions, written instructions, the QPPV, and contracts and agreements. Compared to the previous year, there was a higher proportion of minor findings in the topics of management and reporting of adverse reactions, written instructions, and risk management, suggesting more areas for improvement or non-compliance in these specific areas. However, the topics of interviews of inspected MAH's medical representatives and computerized systems used for pharmacovigilance activities had a lower proportion of minor findings.

In addition to inspections and findings, the introduction of a new pharmacovigilance guideline in January 2023 had a significant impact on MAHs' compliance throughout the year. A workshops were organized in 2023 for QPPVs and their deputies to discuss the updated Saudi GVP. These workshops provided information on new timeframes for pharmacovigilance activities and new legislation. Pre and post assessments were conducted to

evaluate the attendees' understanding, and a satisfaction survey gathered feedback and expectations for future events.

Appendix I: Inspection type definitions

**excerpt from page 100-105 of the Guideline on Good Pharmacovigilance Practices (GVP) (Version 2.0, September 2015).*

Routine inspections

Routine pharmacovigilance inspections are inspections scheduled in advance as part of inspection programes. There is no specific trigger to initiate these inspections, although a risk-based approach to optimize supervisory activities should be implemented. These inspections are usually system inspections but one or more specific products may be selected as examples to verify the implementation of the system and to provide practical evidence of its functioning and compliance. Particular concerns, e.g. raised by assessors, may also be included in the scope of a routine inspection, in order to investigate the specific issues.

'For cause' inspections

For-cause pharmacovigilance inspections are undertaken when a trigger is recognized, and an inspection is considered an appropriate way to examine the issues. For-cause inspections are more likely to focus on specific pharmacovigilance processes or to include an examination of identified compliance issues and their impact for a specific product. However, full system inspections may also be performed resulting from a trigger.

Pre-authorisation inspections

Pre-authorisation pharmacovigilance inspections are inspections performed before a marketing authorisation is granted. These inspections are conducted with the intent of examining the existing or proposed pharmacovigilance system as it has been described by the applicant in support of the marketing authorisation application. Pre-authorisation inspections are not mandatory, but may be requested in specific circumstances. Principles and procedures for requesting pre-authorisation inspections should be developed to avoid performing unnecessary inspections which may delay the granting of a marketing authorisation.

Announced and unannounced inspections

It is anticipated that the majority of inspections will be announced i.e. notified in advance to the inspected party, to ensure the availability of relevant individuals for the inspection. However, on occasion, it may be appropriate to conduct unannounced inspections or to announce an inspection at short notice (e.g. when the announcement could compromise the objectives of the inspection or when the inspection is conducted in a short timeframe due to urgent safety reasons).

Remote inspections

These are pharmacovigilance inspections performed by inspectors remote from the premises of the marketing authorisation holder or firms employed by the marketing authorisation holder. Communication mechanisms such as the internet or telephone may be used in the conduct of the inspection. This approach may also be taken where there are logistical challenges to an on-site inspection during exceptional circumstances (e.g. a pandemic outbreak or travel restrictions). Such approaches are taken at the discretion of the inspectors and in agreement with the body commissioning the inspection. The logistical aspects of the remote inspection should be considered following liaison with the marketing authorisation holder.

Re-inspections

A re-inspection may be conducted on a routine basis as part of a routine inspection programme. Risk factors will be assessed in order to prioritise re-inspections. Early re-inspection may take place where significant non-compliance has been identified and where it is necessary to verify actions taken to address findings and to evaluate ongoing compliance with the obligations, including evaluation of changes in the pharmacovigilance system. Early re-inspection may also be appropriate when it is known from a previous inspection that the inspected party had failed to implement appropriately corrective and preventive actions in response to an earlier inspection.

Appendix II: Inspection finding definitions

**excerpt from page 127-128 of the Guideline on Good Pharmacovigilance Practices (GVP) (Version 2.0, September 2015).*

Critical deficiency: Is a fundamental weakness in one or more pharmacovigilance processes or practices that adversely affects the whole pharmacovigilance system and/or the rights, safety or well-being of patients, or that poses a potential risk to public health and/or represents a serious violation of applicable regulatory requirements.

Major deficiency: Is a significant weakness in one or more pharmacovigilance processes or practices, or a fundamental weakness in part of one or more pharmacovigilance processes or practices that is detrimental to the whole process and/or could potentially adversely affect the rights, safety or well-being of patients and/or could potentially pose a risk to public health and/or represents a violation of applicable regulatory requirements which is however not considered serious.

Minor deficiency: Is a weakness in the part of one or more pharmacovigilance processes or practices that is not expected to adversely affect the whole pharmacovigilance system or process and/or the rights, safety or well-being of patients.

Deficiencies are classified by the assessed risk level and may vary depending on the nature of medicine. In some circumstances, an otherwise major deficiency may be categorized as critical. A deficiency reported after a previous inspection and not corrected may be given higher classification.

Appendix III: Categorization of findings

Table 2: Topics and sub-topics of inspection findings

Topic area	**Sub-topic of reported findings**
Qualified Person Responsible For Pharmacovigilance	Qualifications
	Job description
	System oversight
	Back-up process and delegation
Pharmacovigilance system master file	Organizational structure
	Pharmacovigilance system
	Maintenance and submission
Written instructions (SOPs, manuals, etc.)	Procedures
	Manuals
	Process for SOP training
Contracts, agreements	Contracts
	Agreements
Periodic Safety Update Reports (PSUR)	PSUR scheduling
	Format and content
	Quality control of PSURs
	Timeliness of submission
	Assessment report comments
Risk-management system	Risk-management plan format and content
	Compliance with risk minimization measures which are beyond routine Pharmacovigilance
Management and reporting of adverse reactions	Data collection methods
	Assessments of seriousness, causality and expectedness
	Medical review

	Quality control process
	Submissions and follow up processes
	Literature screening
Computerized systems used for Pharmacovigilance activities	Backup and disaster recovery process
Clinical trials	Adverse event reporting from clinical trials
	Consistency between the Investigator's Brochure and SPC when marketed products are used in CT
Signal management	Dataset used for conducting signal detection (inclusion of information from all relevant sources)
	Periodicity of data review
	Signal validation process
Archiving	Archiving facilities
Quality management system	Quality system and compliance management
	Facilities and equipment for pharmacovigilance
	Audit (internal- and external) and Corrective and Preventive Actions process
Training	Available trainings
	Evaluation of training
	Maintenance of training records
Interview	MAH employees interview

Appendix IV – Abbreviations

ADR	Adverse Drug Reaction
AE	Adverse Event
aRMM	Additional Risk Minimisation Measure
CAPA	Corrective and Preventative Action
GVP	Good Pharmacovigilance Practice
ICSR	Individual Case Safety Report
MAH	Marketing Authorisation Holder
NPC	National Pharmacovigilance Center
PSMF	Pharmacovigilance System Master File
PSSF	Pharmacovigilance Sut-System File
PSUR	Periodic Safety Update Report
PV	Pharmacovigilance
QPPV	Qualified Person responsible for Pharmacovigilance
RMP	Risk Management Plan
SFDA	Saudi Food & Drug Authority
SOP	Standard Operation Procedures