الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

Mid-annual PV Inspection Report 2024

1st Jan 2023 until 30st Jun 2024

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Introduction

From January 1, 2024 to June 30, 2024, the National Pharmacovigilance Center (NPC) of the Saudi Food & Drug Authority (SFDA) conducted 25 inspections of Marketing Authorization Holders (MAHs). Out of those, four MAHs requested to postpone their inspections due to acceptable reasons, and one inspection was cancelled because the Qualified Person for Pharmacovigilance (QPPV) did not show up on time.

The purpose of these inspections was to evaluate the MAHs' compliance with existing Saudi pharmacovigilance regulations and guidelines. The MAHs were selected for inspection using a risk-based methodology, which follows the guidance in GVP Module III. This methodology considers factors such as:

- Product-specific risks (e.g., new active substances or new biological products)
- The complexity of the pharmacovigilance system
- The complexity and size of the organizations 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 contains data related to 4 routine inspections, 5 "for cause" inspections, and 12 re-inspections conducted from January 1, 2023 to June 30, 2023. The report examines the types of inspections performed and the inspection findings, including an analysis of the specific topics where the inspection team found the highest number of findings.

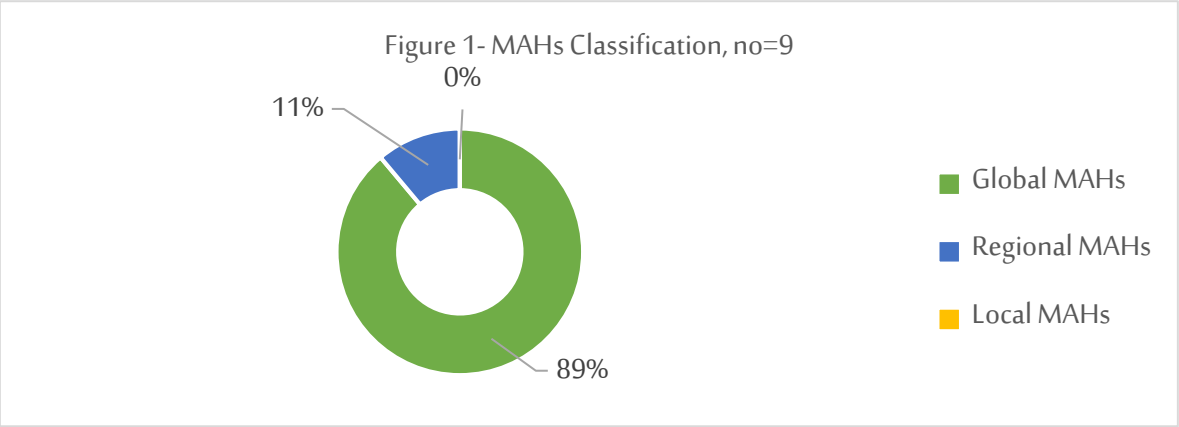
The inspection types used by the inspection team are listed in Appendix I. The definitions for critical, major, and minor inspection findings are included in Appendix II.

Overview

In the reported period, the inspection team conducted:

- ✓ 4 routine inspection.
- ✓ 5 for cause Inspection.
- ✓ 12 Re-inspection.

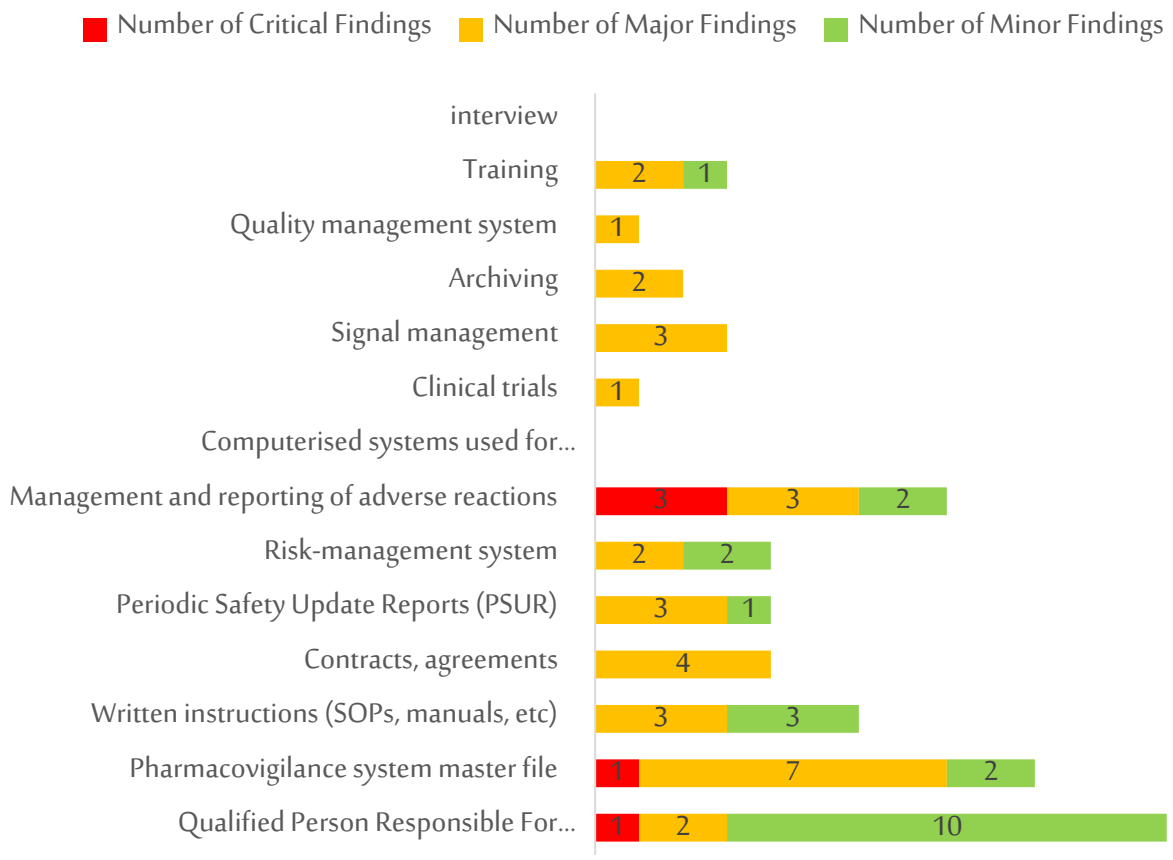
Inspection Results of Routine and for cause inspections



As the figure 1 demonstrated, Out of the 25 inspections conducted by the NPC from January 1, 2024 to June 30, 2024, 8 inspections were performed on global MAHs and 1 inspection was performed on a regional MAH, totaling 9 inspection visits. Additionally, 2 of the MAHs were handled by local distributors.

Inspection Results:

Figure 2- Inspection Results for Semi Annaul 2024



The total observations in the inspected MAHs were 59 findings:

- ✓ 5 Critical findings.
- ✓ 33 Major Findings.
- ✓ 21 Minor findings.

Table 1: Inspection Findings by Topic Area and Severity

Topic Areas	Critical Findings	Major Findings	Minor Findings
Qualified Person Responsible For Pharmacovigilance	1	2	10
Pharmacovigilance system master file	1	7	2
Written instructions (SOPs, manuals, etc)	0	3	3
Contracts, agreements	0	4	0
Periodic Safety Update Reports (PSUR)	0	3	1
Risk-management system	0	2	2
Management and reporting of adverse reactions	3	3	2
Computerized systems used for Pharmacovigilance activities	0	0	0
Clinical trials	0	1	0
Signal management	0	3	0
Archiving	0	2	0
Quality management system	0	1	0
Training	0	2	1
Interview	0	0	0

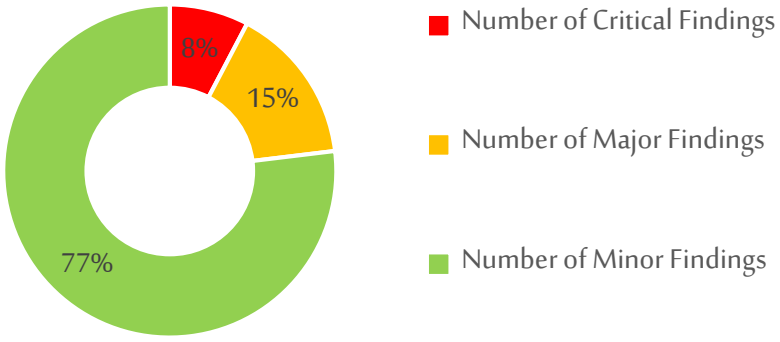
The table shows the number of critical, major, and minor inspection findings identified by the inspection team across various topic areas. The highest proportion of overall findings were observed in qualified person responsible for pharmacovigilance followed by pharmacovigilance system master file and management and reporting of adverse reactions.

Common Areas of Findings:

I. Qualified person responsible for pharmacovigilance

This area represented the highest proportion (22 %) of all findings.

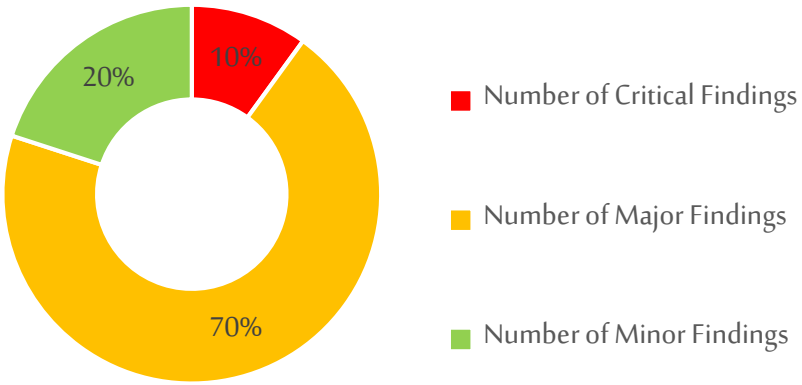
Figure 3- Qualified Person Responsible For Pharmacovigilance, no=13



II. Pharmacovigilance system master file

This area represented the (16.9%) of all findings.

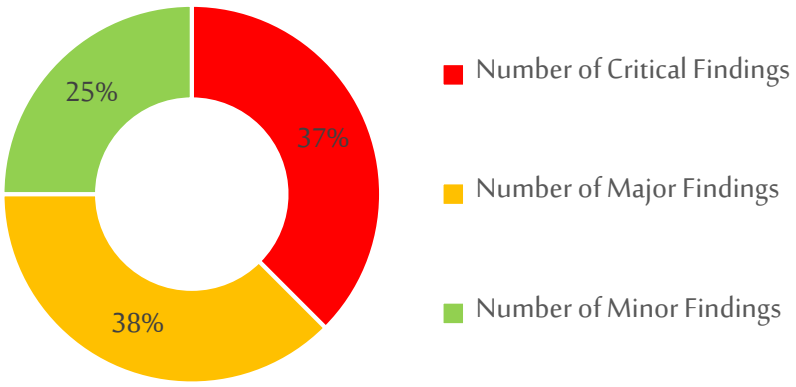
Figure 4- Pharmacovigilance system master file, no=10



III. Management and reporting of adverse reactions

This area represented the (13.6 %) of all findings.

Figure 4- Management and reporting of adverse reactions, no=8



Global Pharmaceutical Companies VS Regional Pharmaceutical Companies

During the reporting period from January 1, 2023 to June 30, 2023, the data collected during the inspection visits were captured at 8 global pharmaceutical companies. Additionally, there was 1 inspection visit conducted at a regional pharmaceutical company, but no findings were identified during that visit. Interestingly, the number of reported inspection findings was significantly decreased compared to the previous semi-annual report in 2023. This may be attributed to a few factors:

- Reduced number of inspection visits conducted: The report mentions 9 total inspection visits, which is lower than the previous period.
- Impact of MAH classification: The distribution of global versus regional MAHs inspected may have played a role, as the regional MAH visit did not identify any findings.
- Impact of previous inspection visits and educational workshops: The report suggests that the educational workshops regularly conducted by the inspection team may have contributed to the decrease in findings, as regulated entities better understood and addressed the previously identified issues.

Re-Inspection Outcomes

Out of the 12 re-inspection visits conducted during the reporting period from January 1, 2023 to June 30, 2023, the following was observed:

- 4 of the inspected MAHs were able to resolve the previously identified findings and were deemed compliant during the re-inspection.
- 3 of the inspected MAHs were given another chance to complete the required actions and address the outstanding issues. This was due to the inspection team observing significant improvements and changes made by these MAHs during the re-inspection visit.
- However, 5 of the inspected MAH files were escalated and put on the legal track. This was due to the unsatisfactory performance demonstrated by these MAHs during the re-inspection visit, as they were unable to close out their Corrective and Preventative Actions (CAPAs) as proposed.

Summary

The inspection team conducted 4 routine inspections, 5 for-cause inspections, and 12 re-inspections during the reported period. Of the 25 total inspections, 9 were performed on marketing authorization holders (MAHs), with 8 being global MAHs and 1 being a regional MAH.

The 9 MAH inspections resulted in a total of 59 findings: 5 critical, 33 major, and 21 minor. The highest proportion of findings were in the areas of qualified person responsible for pharmacovigilance (22%), pharmacovigilance system master file (16.9%), and management and reporting of adverse reactions (13.6%).

Compared to the previous semi-annual report, the number of reported inspection findings decreased, which may be attributed to factors like reduced inspections, the impact of MAH classification, and the effectiveness of the inspection team's educational workshops.

Of the 12 re-inspections conducted, 4 MAHs were able to resolve previously identified issues and were deemed compliant, 3 were given another chance to address outstanding items, and 5 were escalated to the legal track due to unsatisfactory performance.

Appendix I: Inspection 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 programs. 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- authorization inspections

Pre-authorization pharmacovigilance inspections are inspections performed before a marketing authorization 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 authorization application. Pre-authorization inspections are not mandatory, but may be requested in specific circumstances.

Principles and procedures for requesting pre-authorization inspections should be developed to avoid performing unnecessary inspections which may delay the granting of a marketing authorization.

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 authorization holder or firms employed by the marketing authorization 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 authorization holder.

Re-inspections

A re-inspection may be conducted on a routine basis as part of a routine inspection program. Risk factors will be assessed in order to priorities 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 finding

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 V: 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 Sub-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