الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

Mid-annual PV Inspection Report 2023

1st Jan 2023 until 30st Jun 2023

Table of Contents

Introduction

During the period 01 Jan 2023 to 30 Jun 2023, the National pharmacovigilance center (NPC) in Saudi Food & Drug Authority (SFDA) conducted 30 inspections of MAHs—four MAHs requested to postpone their inspections due to different acceptable reasons. These inspections aimed to examine compliance with existing Saudi pharmacovigilance regulations and guidelines. MAHs were selected for inspection using the risk-based methodology. This risk-based methodology follows GVP Module III and considers multiple factors as follows:

- 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 contains data relating to 12 routine and for cause inspections conducted from 01 Jan 2023 to 30 Jun 2023. Information on types of inspection and inspection findings have been examined, including analysis of specific topics where the inspection team found the highest number of findings among the visits.

The inspection types identified that used by the inspection team in Appendix I. The inspection findings identified as critical, major, or minor, the definitions for which are included in Appendix II.

Overview

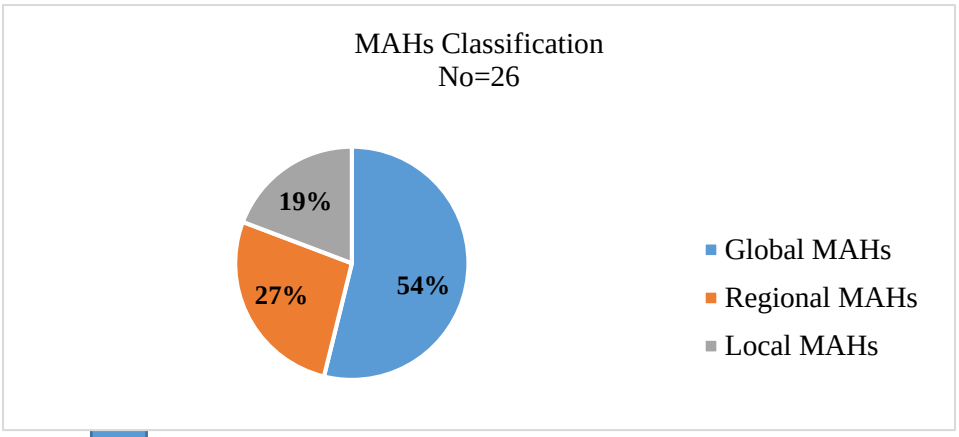
In the reported period, the inspection team conducted:

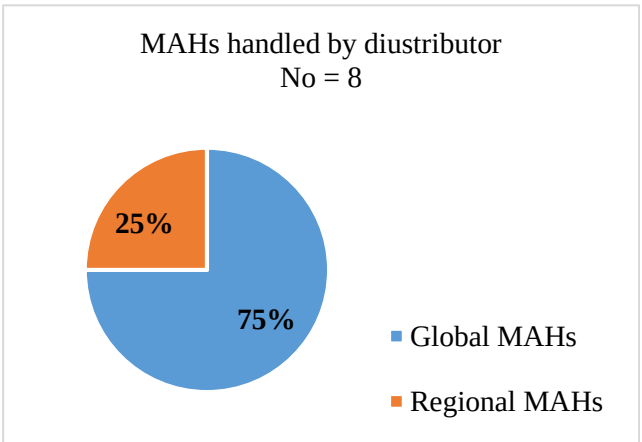
- ✓ 8 routine inspection.
- ✓ 4 Trigger Inspection.
- ✓ 14 Re-inspection (One Remote Re-inspection).

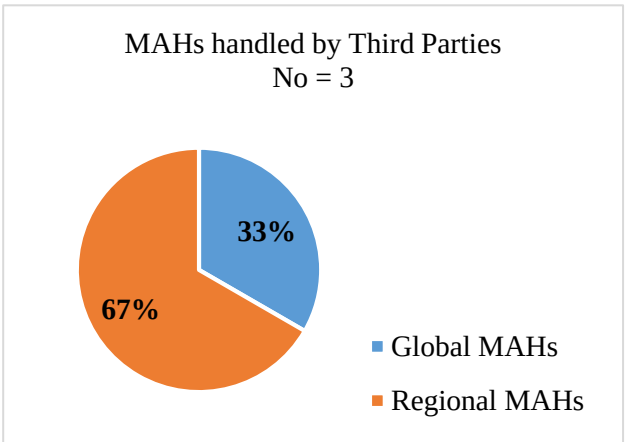
Inspection results

I. Routine inspection results

MAHs Classification :

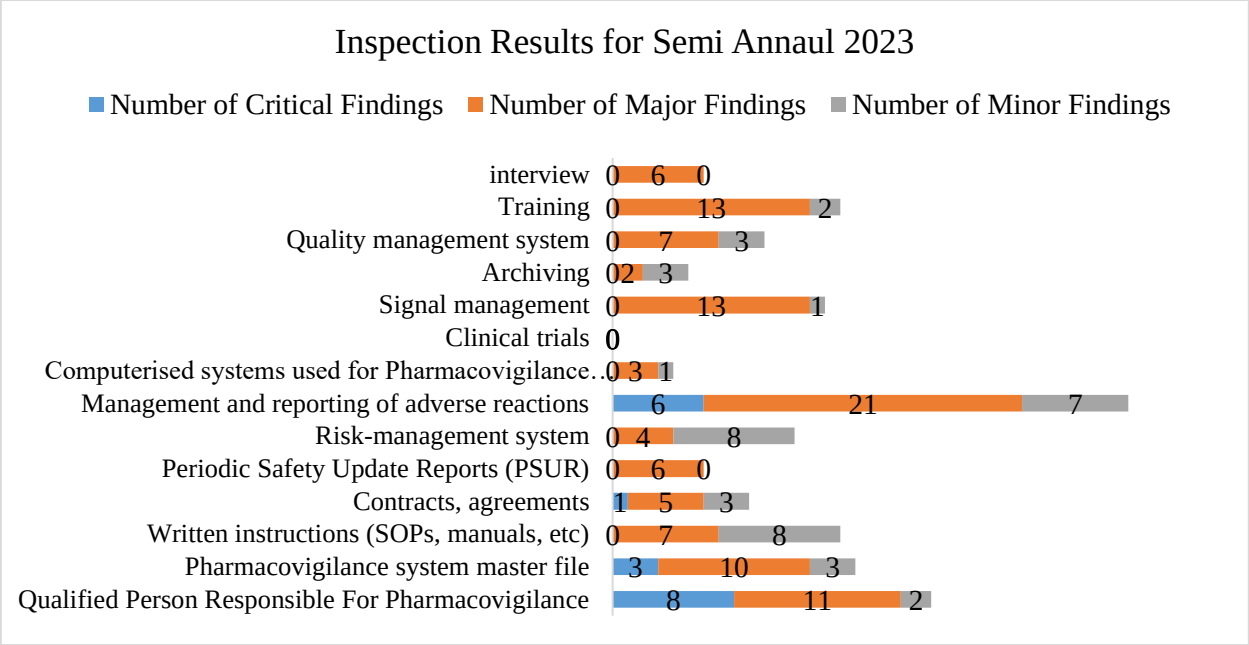






The inspection team conducted 14 inspections on Global MAHs and 7 inspections on regional MAHs and 5 inspections on local MAHs were out of 14 inspection visits, 8 MAHs were handled by local distributors and 3 MAHs were handled by third parties.

Inspection results:



The total observations in the inspected MAHs were 167 findings:

- ✓ 18 Critical findings.
- ✓ 108 Major Findings.
- ✓ 41 Minor findings.

All data were collected as described in the bellow table:

Topic Areas	Critical Findings	Major Findings	Minor Findings
Qualified Person Responsible For Pharmacovigilance	8	11	2
Pharmacovigilance system master file	3	10	3
Written instructions (SOPs, manuals, etc)	0	7	8
Contracts, agreements	1	5	3
Periodic Safety Update Reports (PSUR)	0	6	0
Risk-management system	0	4	8
Management and reporting of adverse reactions	6	21	7

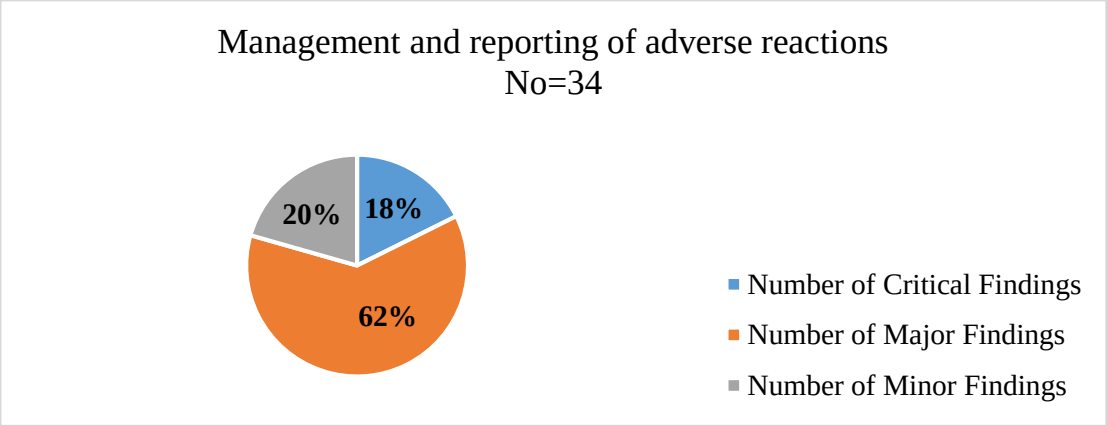
Computerized systems used for Pharmacovigilance activities	0	3	1
Clinical trials	0	0	0
Signal management	0	13	1
Archiving	0	2	3
Quality management system	0	7	3
Training	0	13	2
Interview	0	6	0

The highest proportion of overall findings were observed in Management and reporting of adverse reactions followed by Qualified person responsible for Pharmacovigilance (QPPV), Pharmacovigilance system master file (PSMF).

Common areas of findings:

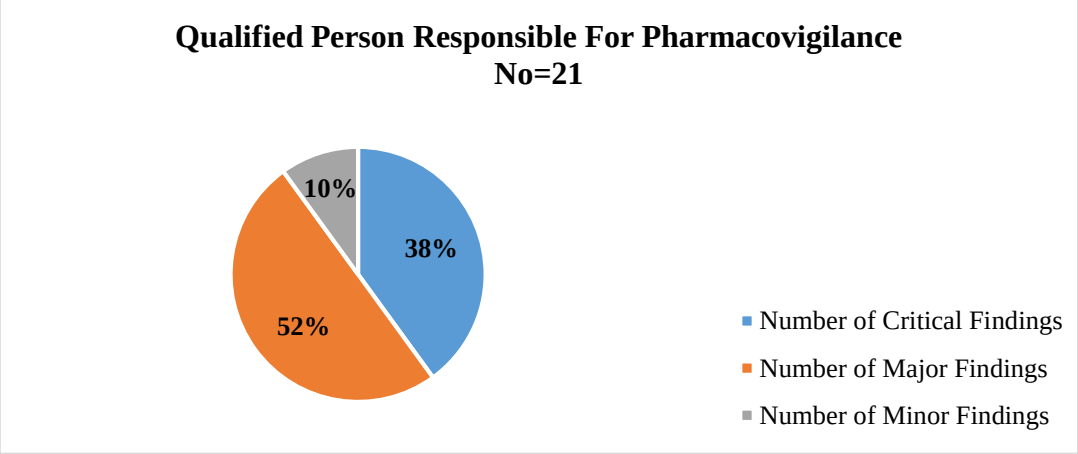
i. Management and reporting of adverse reactions

This area represented the highest proportion (20.4 %) of all findings.



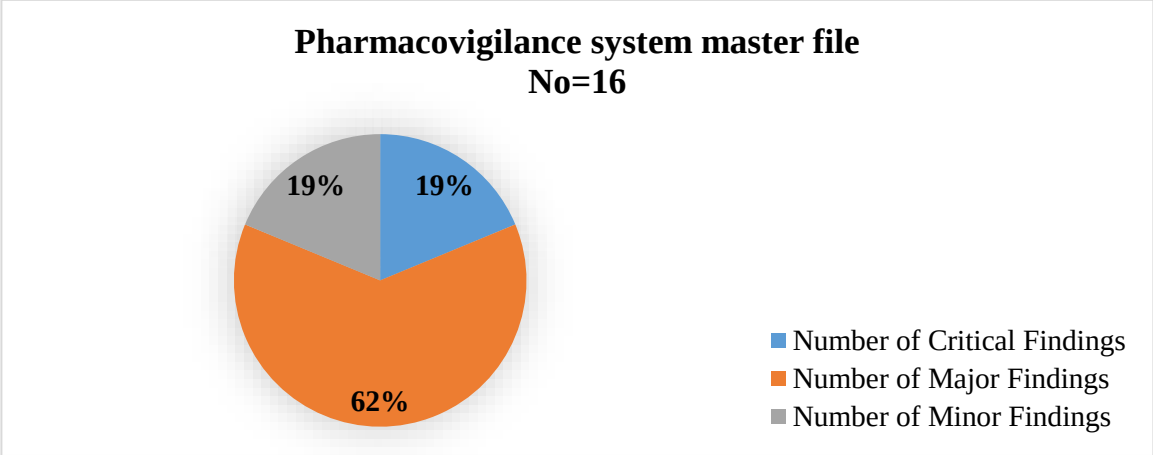
ii. Qualified Person Responsible For Pharmacovigilance

This area represented the (12.6%) of all findings.



iii. Pharmacovigilance system master file

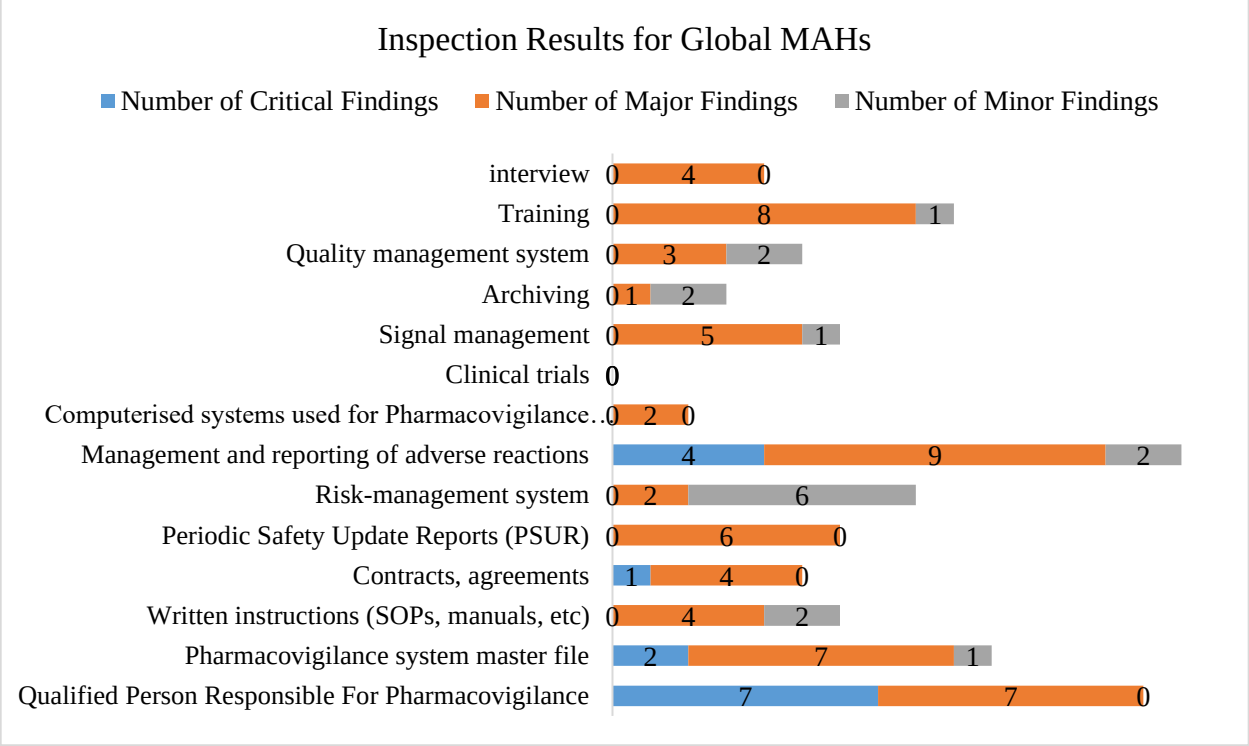
This area represented the (9.6 %) of all findings.



Global Pharmaceutical Companies

The inspection team conducted 14 inspection on Global MAHs were out of 14 MAHs, 6 MAHs were handled by local distributors and one MAH was handled by third parties.

Inspection results:



The total observations in the inspected MAHs were 93 findings:

- ✓ 14 Critical findings.
- ✓ 62 Major Findings.
- ✓ 17 Minor findings.

All data were collected from Global MAHs as described in the bellow table:

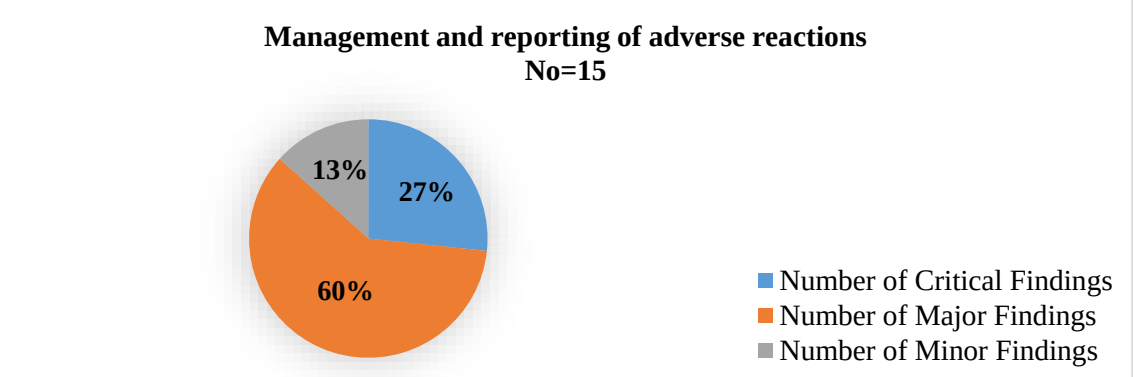
Topic Areas	Critical Findings	Major Findings	Minor Findings
Qualified Person Responsible For Pharmacovigilance	7	7	0
Pharmacovigilance system master file	2	7	1
Written instructions (SOPs, manuals, etc)	0	4	2
Contracts, agreements	1	4	0
Periodic Safety Update Reports (PSUR)	0	6	0
Risk-management system	0	2	6
Management and reporting of adverse reactions	4	9	2
Computerized systems used for Pharmacovigilance activities	0	2	0
Clinical trials	0	0	0
Signal management	0	5	1
Archiving	0	1	2
Quality management system	0	3	2
Training	0	8	1
Interview	0	4	0

The highest proportion findings from global MAHs were observed in Management and reporting of adverse reactions followed by qualified person responsible for Pharmacovigilance (QPPV), Pharmacovigilance system master file (PSMF).

Common areas of findings:

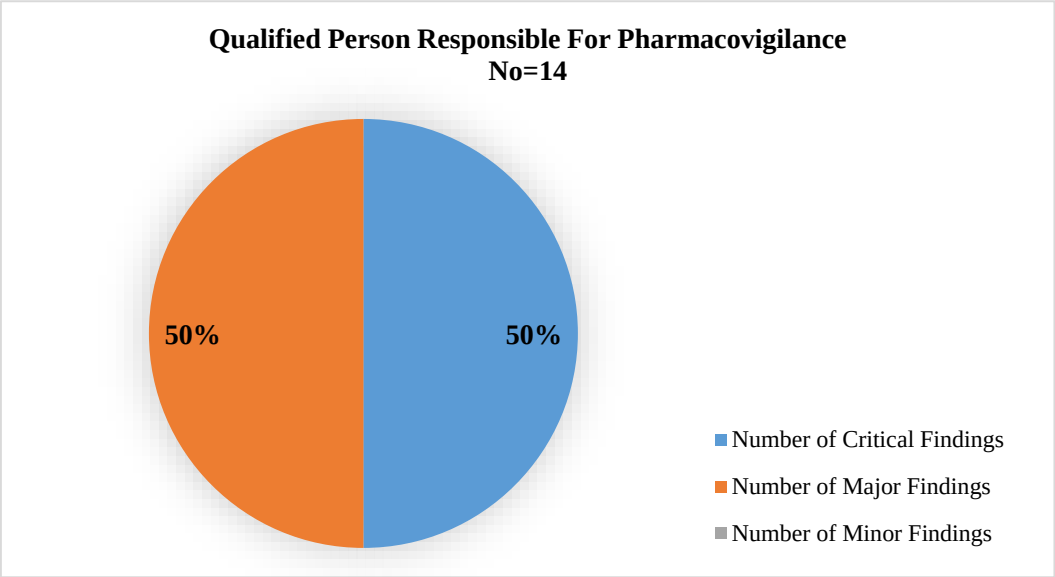
i. Management and reporting of adverse reactions

This area represented the highest proportion (16.1 %) of all findings.



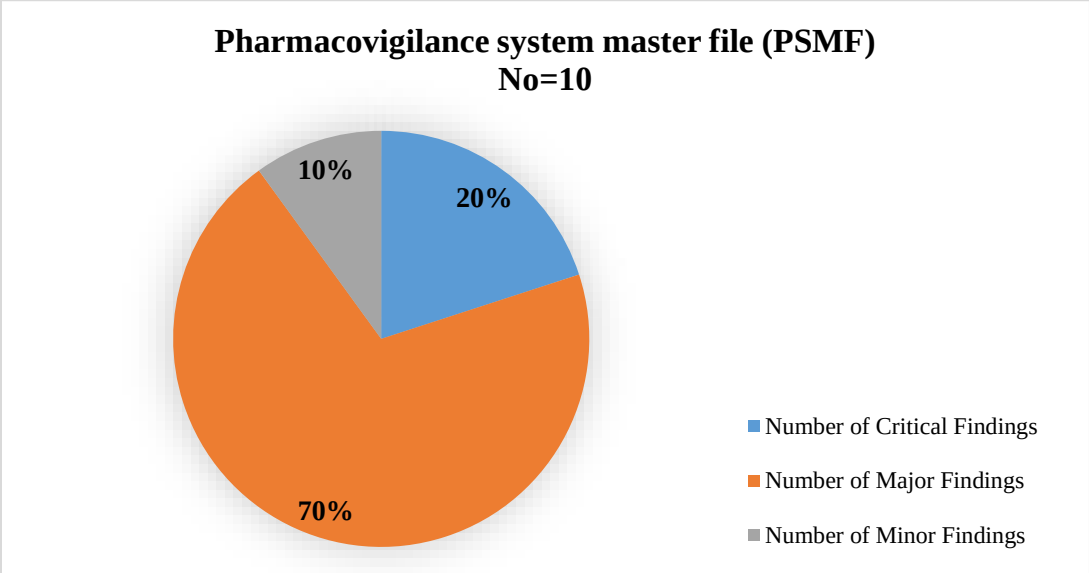
ii. Qualified Person Responsible For Pharmacovigilance

This area represented the (15.1%) of all findings.



iii. Pharmacovigilance system master file (PSMF)

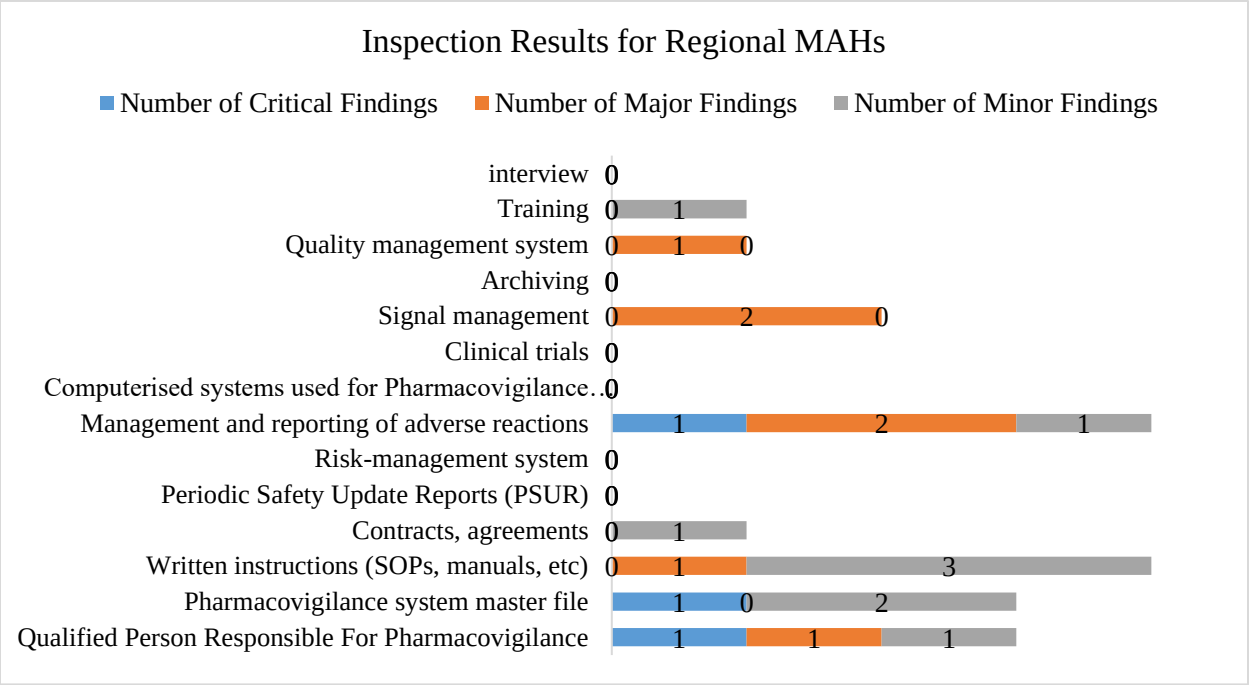
This area represented the (11.5 %) of all findings.



Regional Pharmaceutical Companies

The inspection team conducted 7 inspection on regional MAHs were out of 7 MAHs, 2 MAHs were handled by local distributors and 2 MAHs were handled by third parties.

Inspection results:



The total observations in the inspected MAHs were 19 findings:

- ✓ 3 Critical findings.
- ✓ 7 Major Findings.
- ✓ 9 Minor findings.

All data were collected from regional MAHs as described in the bellow table:

Topic Areas	Critical Findings	Major Findings	Minor Findings
Qualified Person Responsible For Pharmacovigilance	1	1	1

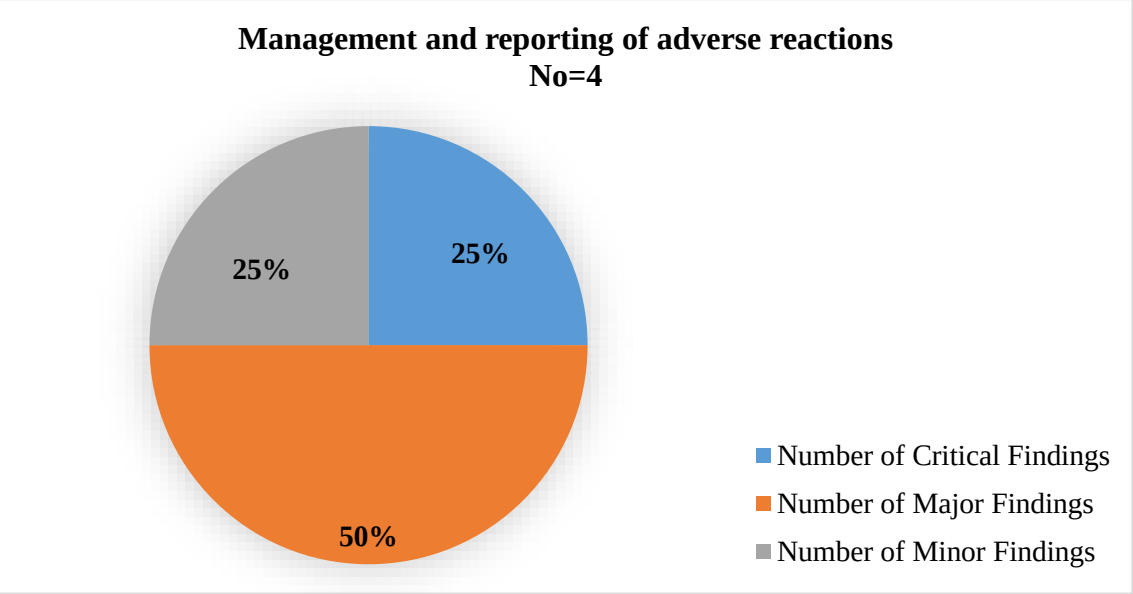
Pharmacovigilance system master file	1	0	2
Written instructions (SOPs, manuals, etc)	0	1	3
Contracts, agreements	0	0	1
Periodic Safety Update Reports (PSUR)	0	0	0
Risk-management system	0	0	0
Management and reporting of adverse reactions	1	2	1
Computerized systems used for Pharmacovigilance activities	0	0	0
Clinical trials	0	0	0
Signal management	0	2	0
Archiving	0	0	0
Quality management system	0	1	0
Training	0	0	1
Interview	0	0	0

The highest proportion findings from regional MAHs were observed in Management and reporting of adverse reactions followed by written instructions (SOPs, manuals), Qualified Person Responsible for Pharmacovigilance, and Pharmacovigilance system master file (PSMF).

Common areas of findings:

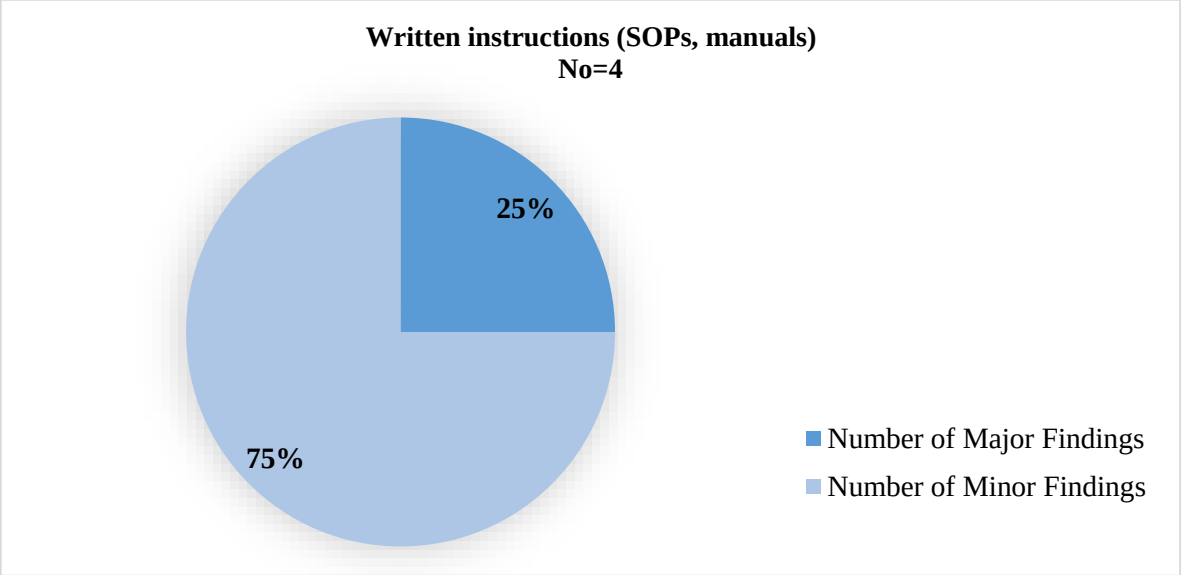
i. Management and reporting of adverse reactions

This area represented the highest proportion (21.1%) of all findings.



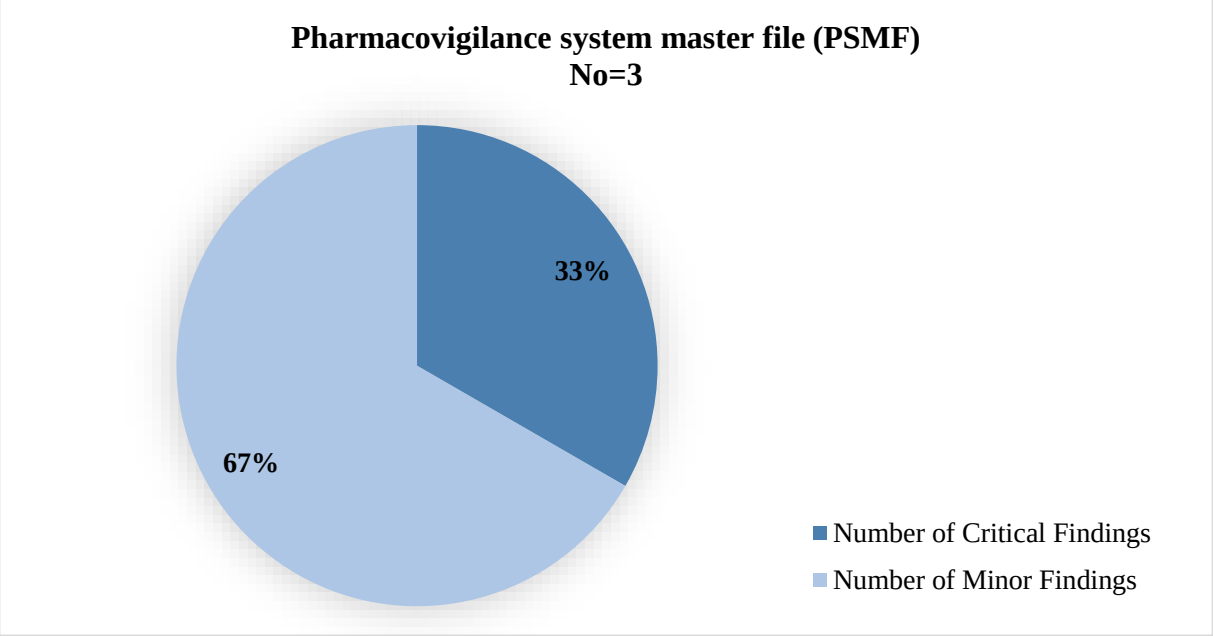
ii. Written instructions (SOPs, manuals).

This area represented the (21.1 %) of all findings.

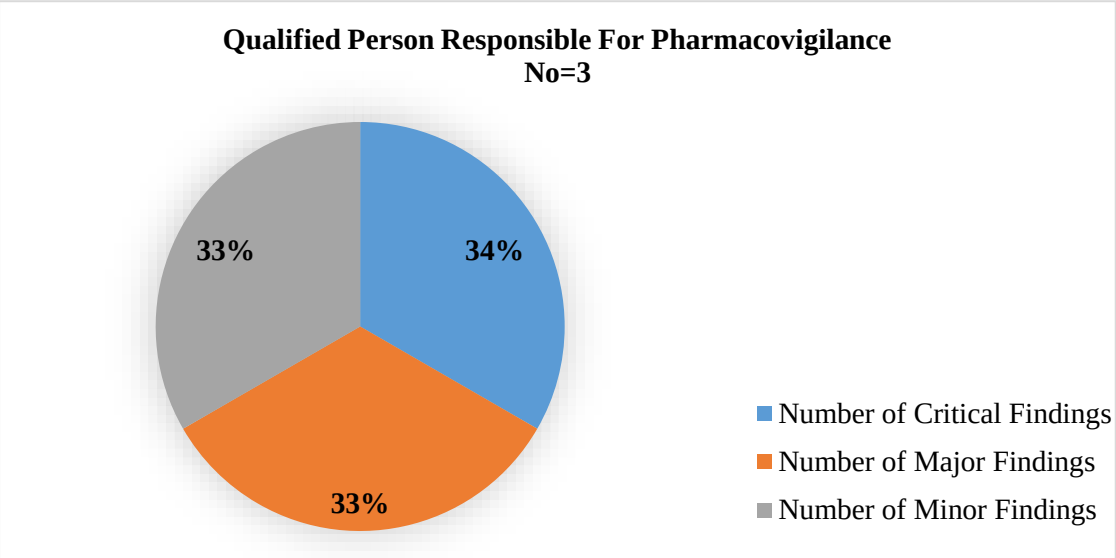


iii. Pharmacovigilance system master file (PSMF).

This area represented the (15.8 %) of all findings.



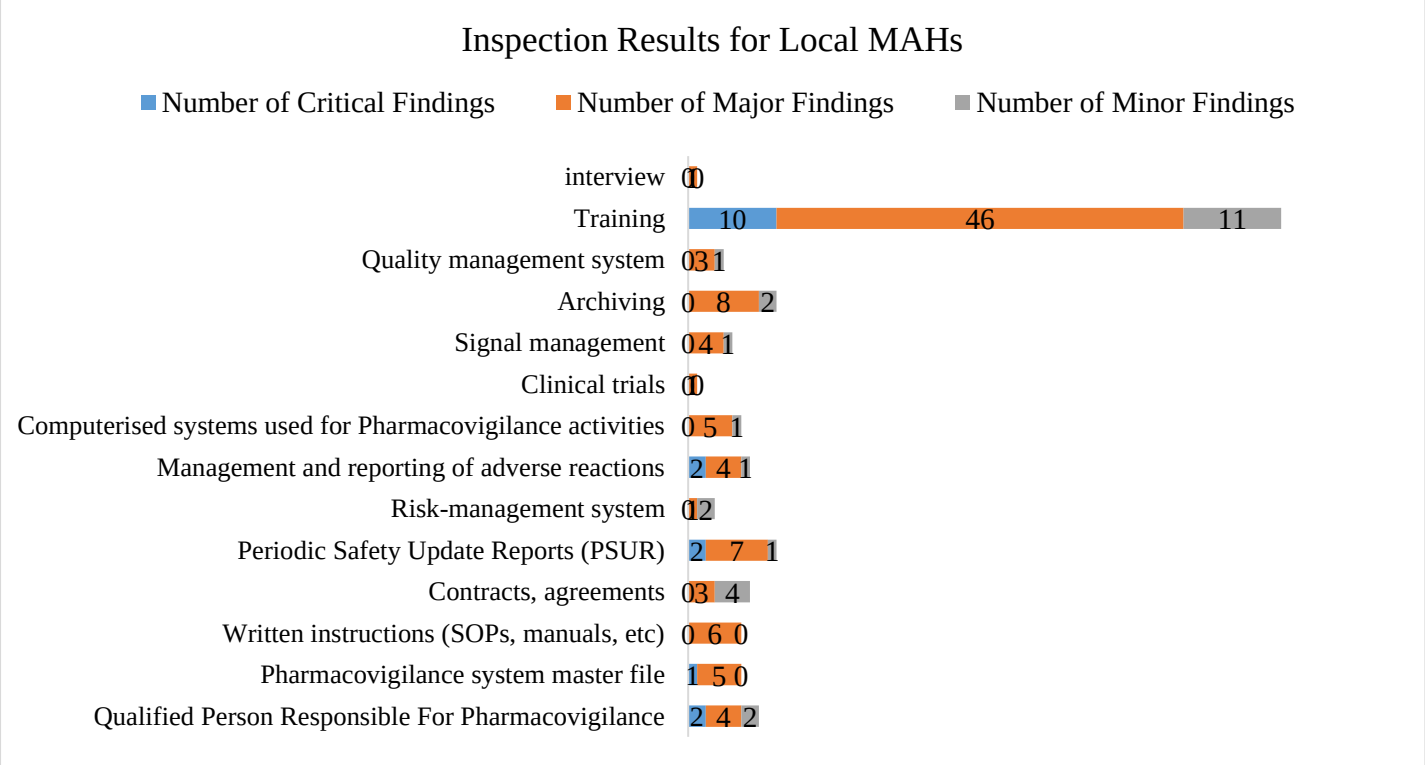
iv. Qualified Person Responsible For Pharmacovigilance
This area represented the (15.8 %) of all findings.



Local Pharmaceutical Companies.

The inspection team conducted 5 inspection visits on local Pharmaceutical companies.

Inspection results:



The total observations in the inspected MAHs were 55 findings:

- ✓ 1 Critical findings.
- ✓ 39 Major Findings.
- ✓ 15 Minor findings.

All data were collected from local MAHs as described in the bellow table:

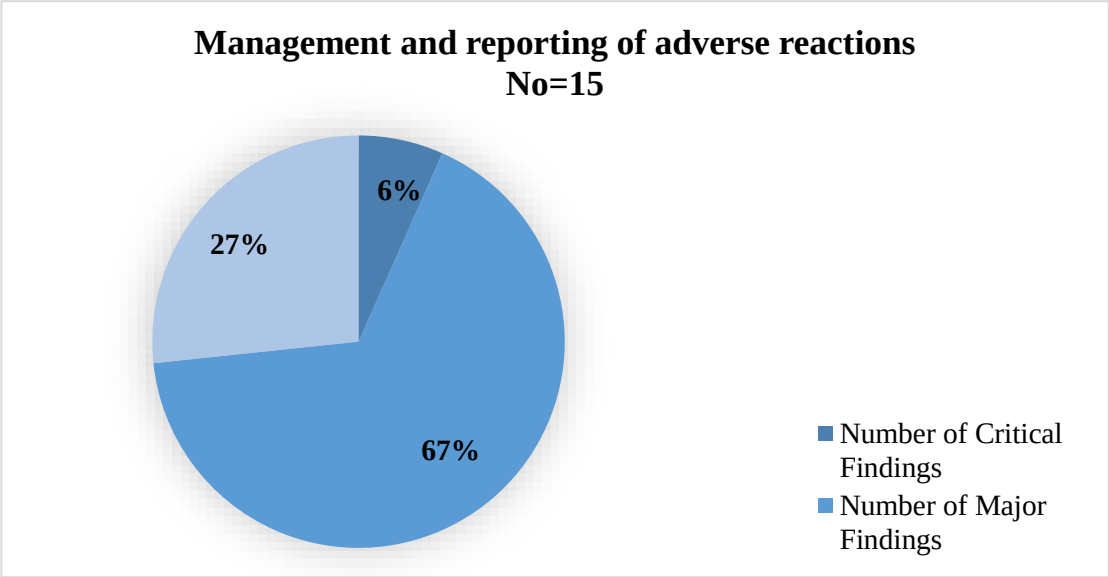
Topic Areas	Critical Findings	Major Findings	Minor Findings
Qualified Person Responsible For Pharmacovigilance	0	3	1
Pharmacovigilance system master file	0	3	0
Written instructions (SOPs, manuals, etc)	0	2	3
Contracts, agreements	0	1	2
Periodic Safety Update Reports (PSUR)	0	0	0
Risk-management system	0	2	2
Management and reporting of adverse reactions	1	10	4
Computerized systems used for Pharmacovigilance activities	0	1	1
Clinical trials	0	0	0
Signal management	0	6	0
Archiving	0	1	1
Quality management system	0	3	1
Training	0	5	0
Interview	0	2	0

The highest proportion findings from regional MAHs were observed in Management and reporting of adverse reactions followed by written instructions (SOPs, manuals), Signal management system, written instructions (SOPs, manuals), and Pharmacovigilance Training.

Common areas of findings:

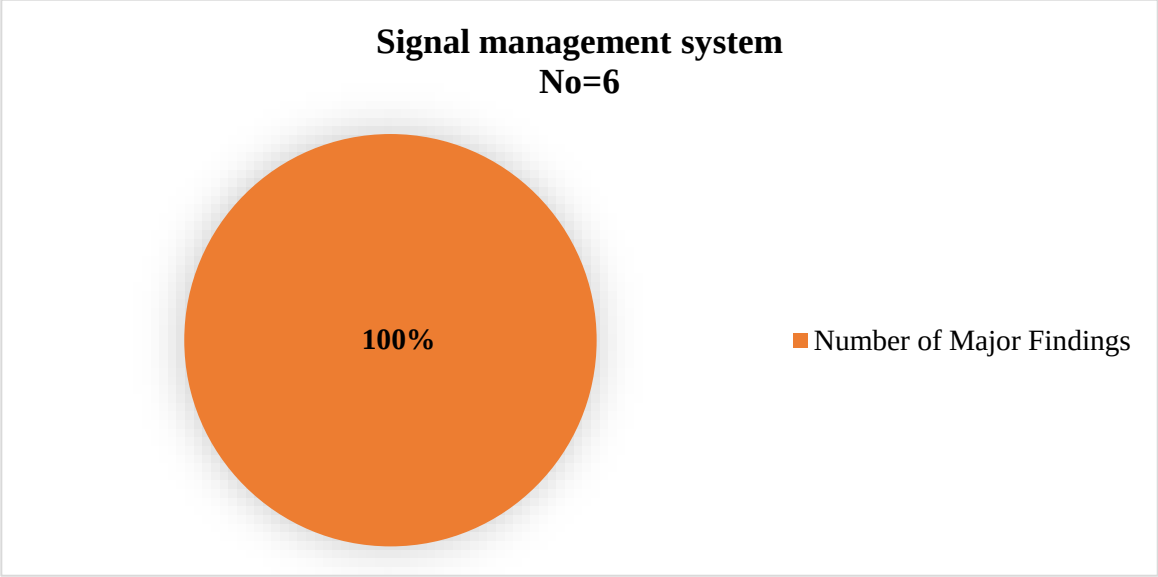
i. Management and reporting of adverse reactions

This area represented the highest proportion (27.3%) of all findings.



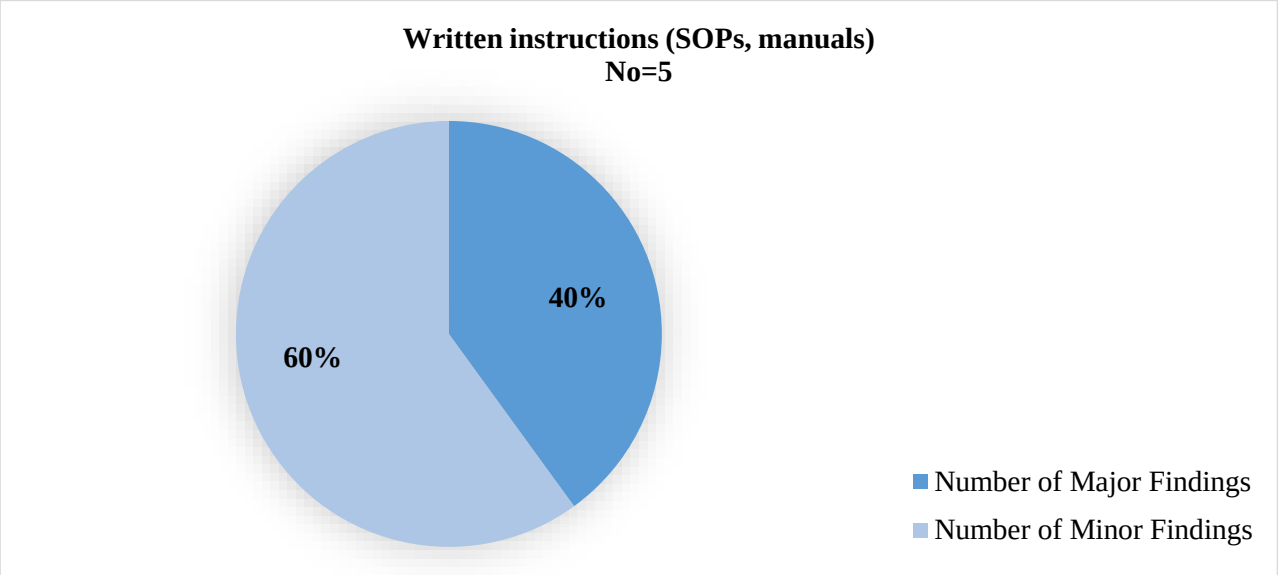
ii. Signal management system.

This area represented the highest proportion (10.9%) of all findings.



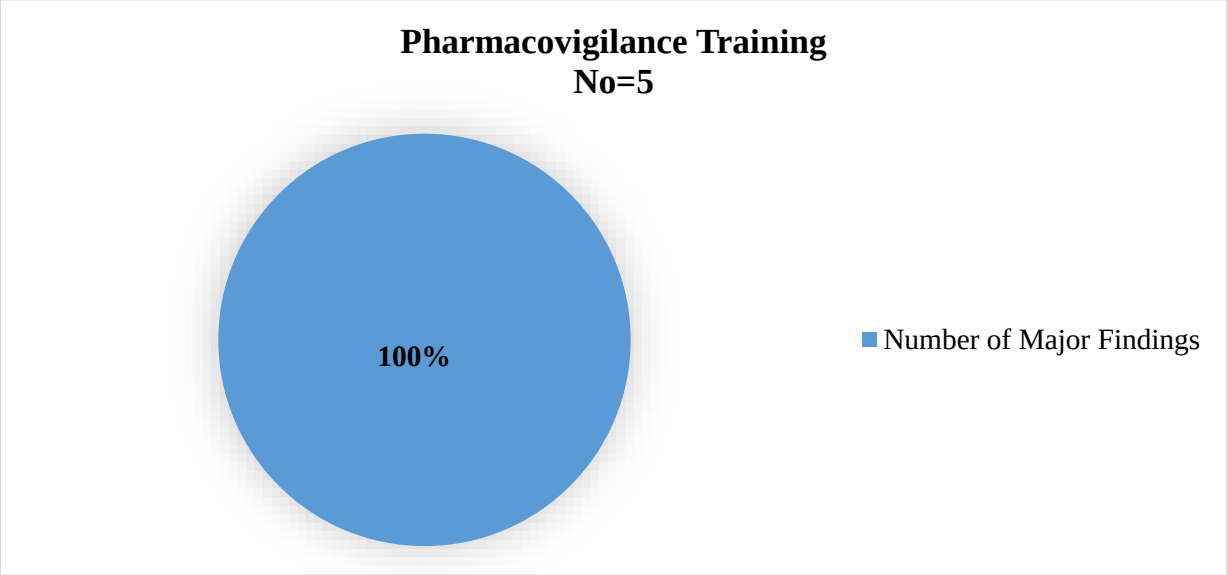
iii. Written instructions (SOPs, manuals, etc)

This area represented the highest proportion (9.1%) of all findings.



iv. Pharmacovigilance Training

This area represented the highest proportion (9.1%) of all findings.



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