Pharmacovigilance Inspection Metrics Report for year 2023

Table of content:

1. Introduction:

Since 2015, PVGA had been conducting desk review of Companies' Pharmacovigilance systems that involve reviewing compliance documents for example PSMF document submitted by organizations, instead of going on-site for an inspection.

Starting March 2020, the EDA started onsite Pharmacovigilance inspections.

The purpose of these inspections was to examine compliance with currently applicable Egypt pharmacovigilance regulations and guidelines.

PV systems are selected for inspection using a risk-based methodology which is aligned with the principles outlined in Good Vigilance Practice (GVP) Chapter III and considers the critical pharmacovigilance processes outlined in GVP Chapter I.

This report contains data relating to all 18 inspections conducted during the 2023. Information on the types of inspection, inspection findings over time and the data from each inspection arm have been examined.

Findings identified during inspections were graded as critical, major or minor; the definitions for which are included in Appendix I. The topics under which findings can be categorized are explained in Appendix II.

A list of abbreviations used throughout this report is provided in Appendix III.

2. Inspection model and review of findings

- System and product-related inspections Pharmacovigilance system inspections are designed to review the procedures, systems, personnel, and facilities in place and determine their compliance with regulatory pharmacovigilance obligations. As part of this review, product specific examples may be used to demonstrate the operation of the pharmacovigilance system. Product-related pharmacovigilance inspections are primarily focused on product-related pharmacovigilance issues, including product-specific activities and documentation, rather than a general system review. Some aspects of the general system may still be examined as part of a product-related inspection (e.g. the system used for that product).

- Routine and "for cause" pharmacovigilance 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 shall 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. 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 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.

- Post-authorization inspections are inspections performed after a marketing authorization is granted and are intended to examine whether the marketing authorization holder complies with its pharmacovigilance obligations. They can be any of the types mentioned above.

- 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).

- 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 prioritize 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.

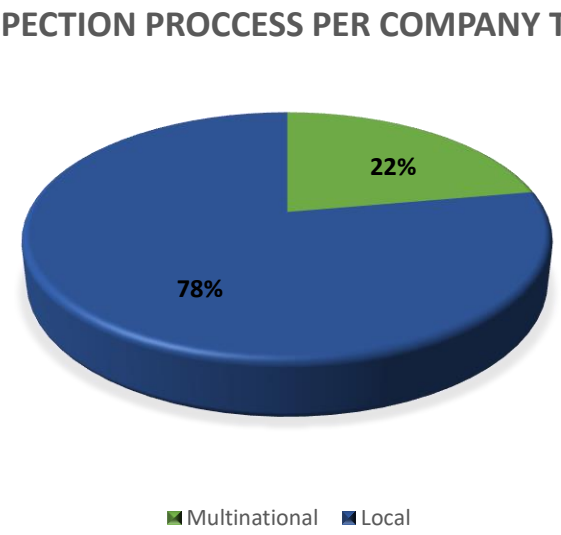
- Remote inspections

  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.

3. Overview of inspections conducted

There were 14 inspections of local organization,4 inspections of multinational organizations,

Figure 1: provides inspections conducted per company type.



Of the 18 inspections conducted on 2023, 1 inspection was triggered for its PV performance and commitment, and 17 were scheduled and conducted in accordance with the routine national inspection schedule.

Figure 2-provides a breakdown of the number of inspections conducted by inspection type.

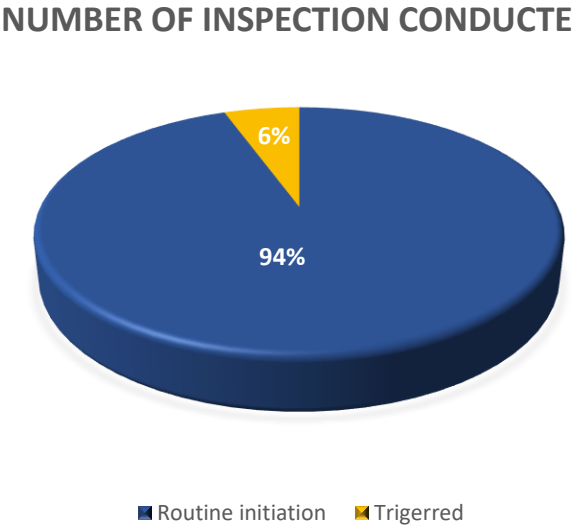
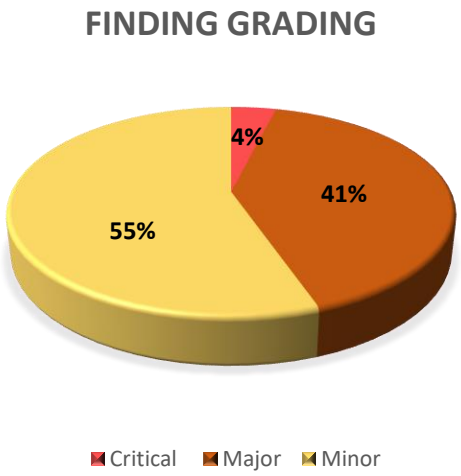


Figure 3- Number and distribution of critical findings across topics over years



- The implementation of GVP – Egypt obligations regarding different PV activities the topic for which the largest number of critical findings has been reported overall.
  Then we got in 2nd order Agreements/contract & SDEAs/ Safety Data Migration.

- The implementation of GVP – Egypt obligations regarding different PV activities the topic for which the largest number of Major findings has been reported overall, then we got in 2nd order QMS.

- The Archiving and documentation process the topic for which the largest number of Minor findings has been reported overall, then we got in 2nd PV staff

Figure 4- Number of inspection findings by inspection type

A total of 4 critical, 42 major and 57 minor findings were identified during this reporting period

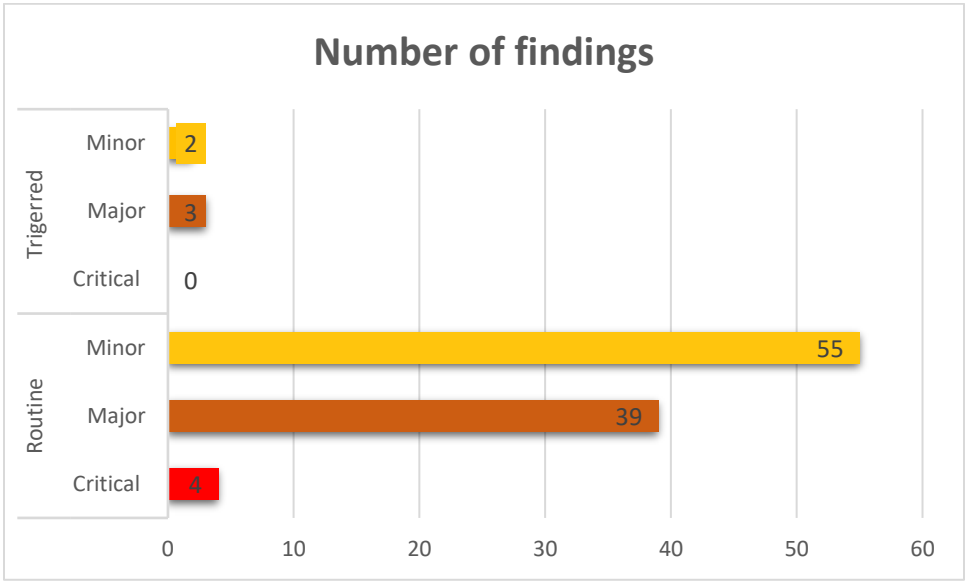


Figure 4 provides a breakdown of inspection findings reported in 2023 by topic area. For the purposes of this report, findings have been grouped by overarching topics across the pharmacovigilance system. The nature of findings covered by each topic is provided in Appendix II.

The highest proportion of finding regardless of grading were related to the implementation of GVP – Egypt obligations regarding different PV activities, 100 % (18 PV system out of 18 PV one had been inspected). Alike, was the finding relating to Quality Management System with 100% (18 PV system out of 18 PV one had been inspected).

Figure 5- Findings by topic area

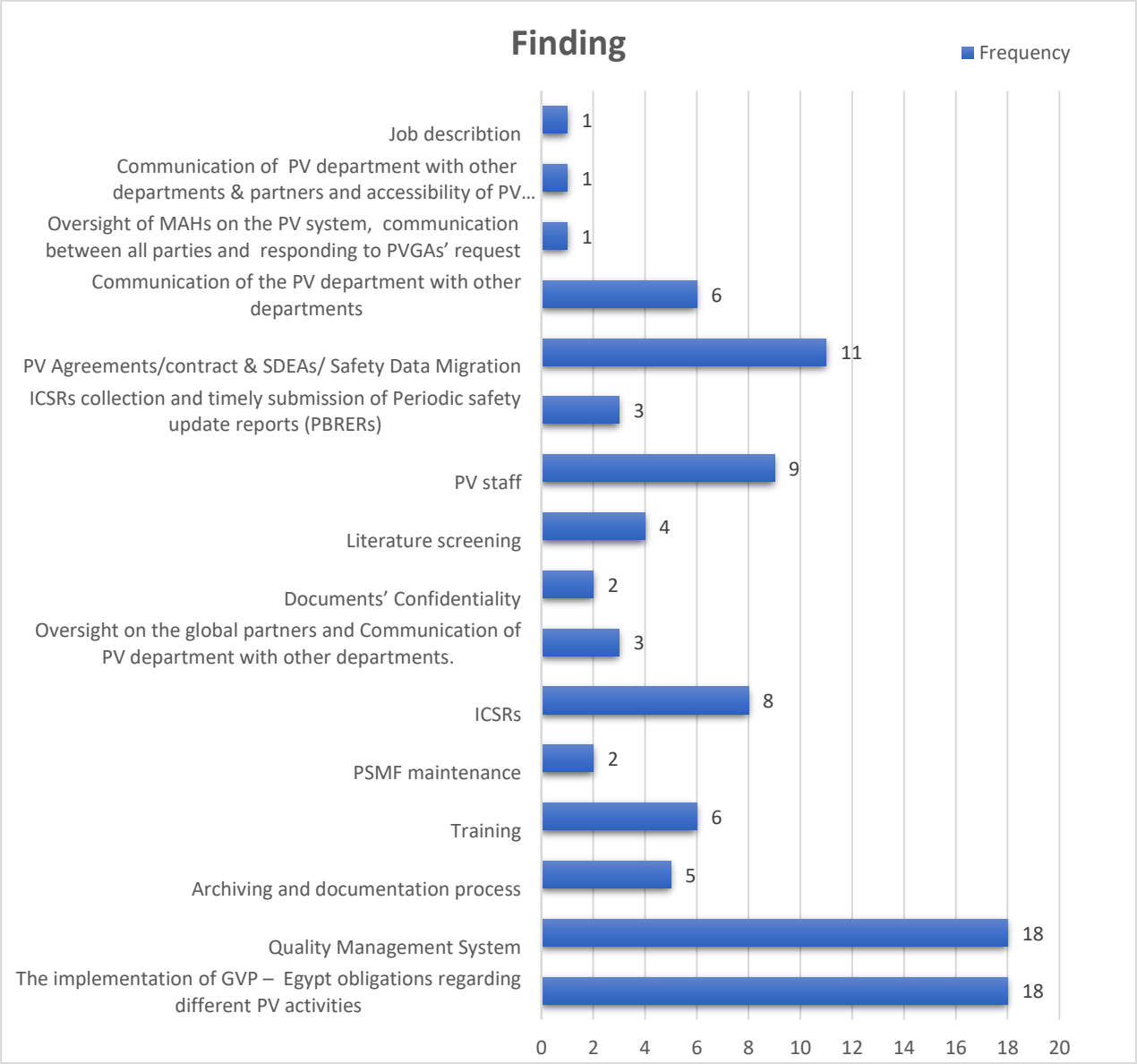


Figure 6 – Breakdown of inspections findings per grading

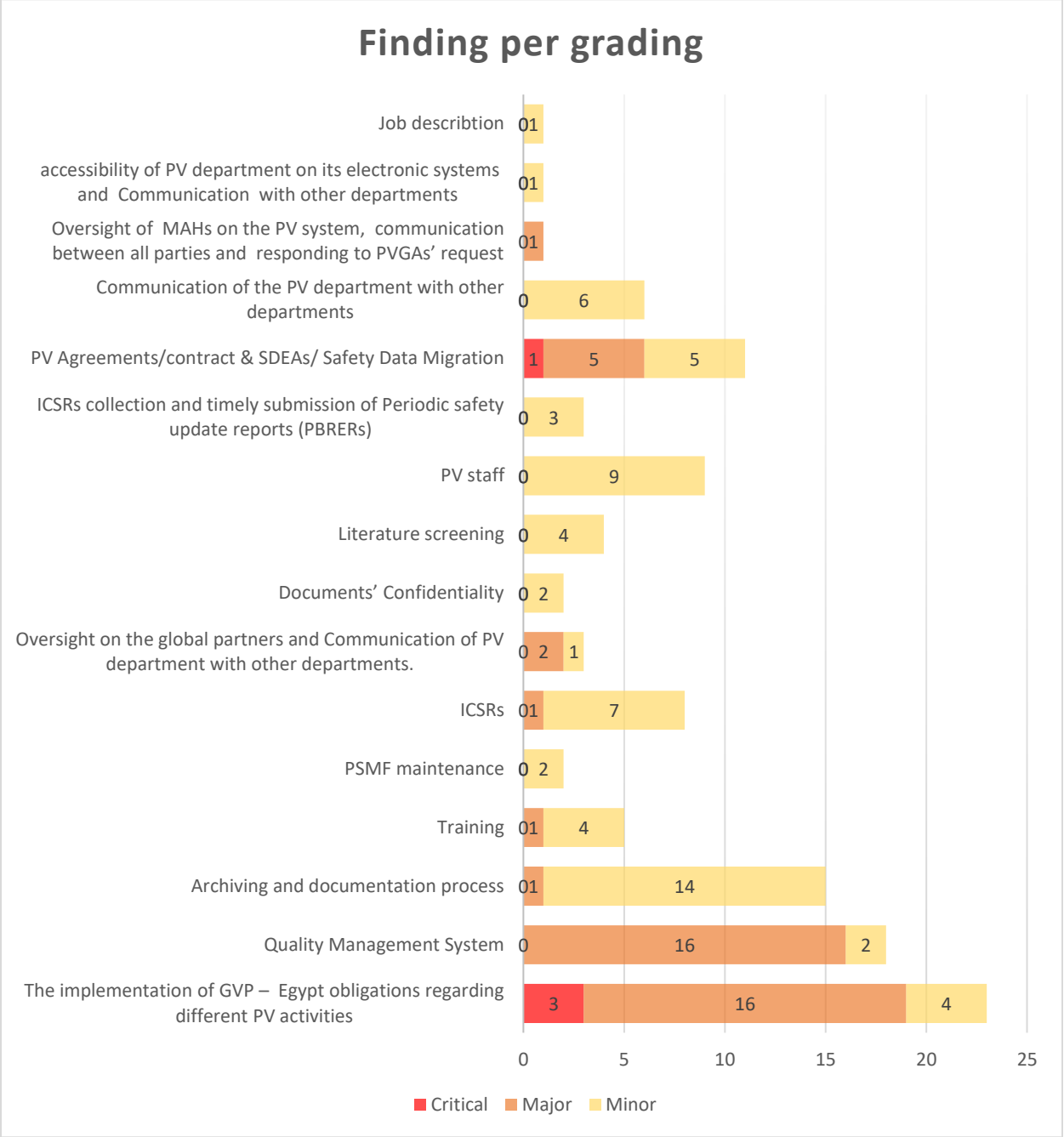


Figure 7 – Number of major findings per each MAH during 2023

Upon analyzing the findings, it has become evident that the number of critical findings is significantly lower when compared to the major and minor findings. Given this disparity, it is currently more worthwhile to focus on breaking down the data for the major and minor findings, as they represent a higher volume and may provide more actionable insights for immediate attention and resolution.

While the critical findings remain important, the volume of major and minor findings warrants a more detailed analysis at this stage. This approach will ensure that resources are allocated efficiently, and that any potential issues within the major and minor categories are addressed proactively before they escalate

During this reporting period, the number of major findings per inspection varied, ranging from zero to four. Considering that, one inspection did not raise any major findings at all, Out of the eighteen inspections conducted in 2023.

The number of minor findings per inspection varied, ranging from one to five.

A visual representation of the distribution of major findings across inspections can be seen in Figure 7

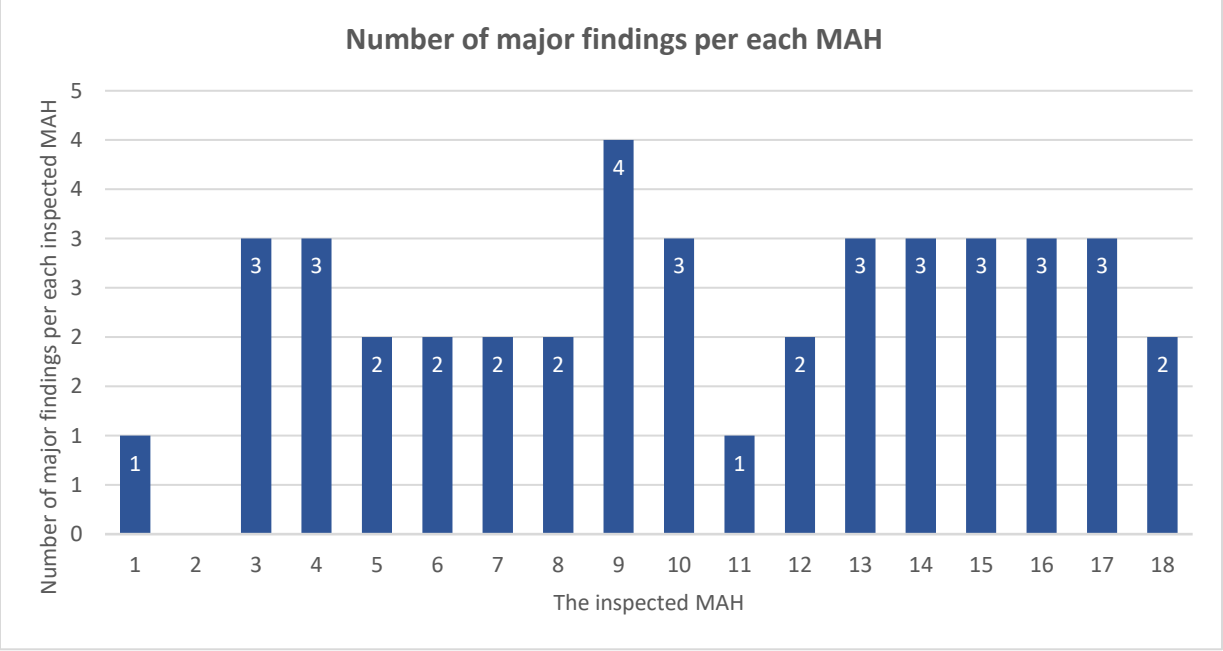


Figure 8- Breakdown of the major finding area of the implementation of GVP – Egypt obligations regarding different PV activities on 2023

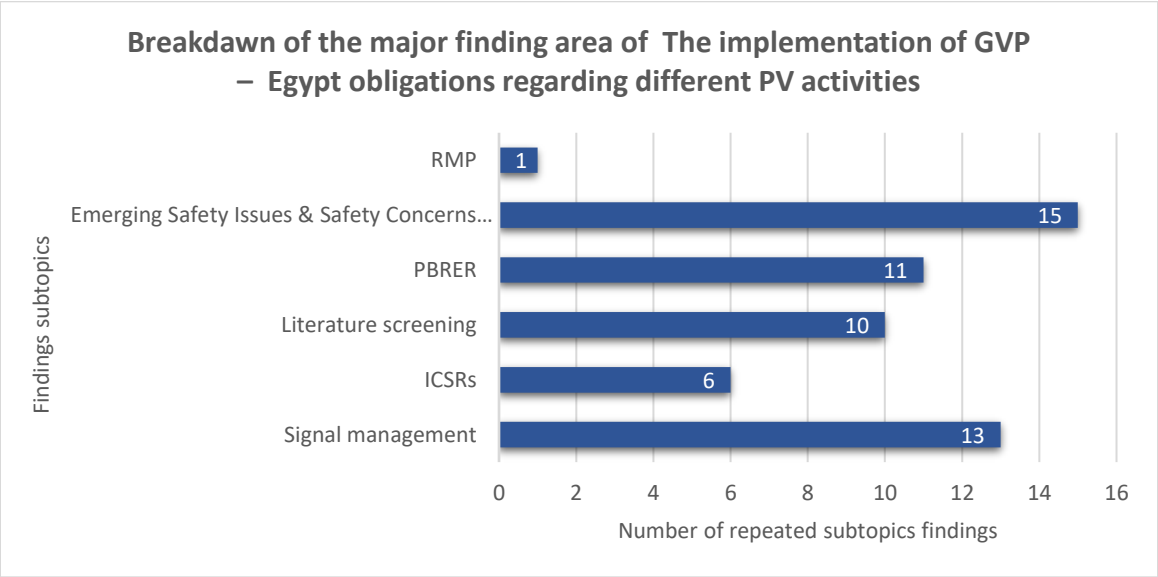


Figure 9- Breakdown of the major finding area of Quality Management System on 2023

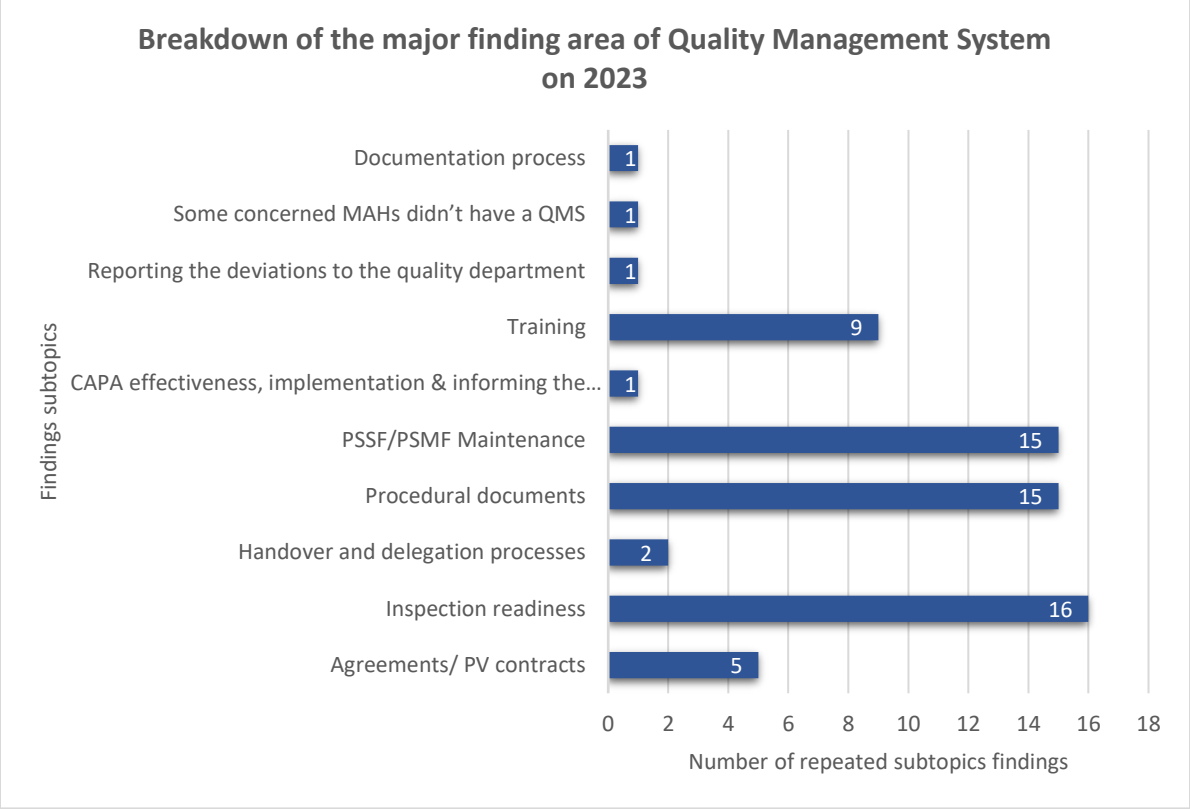


Figure 10 – Number of minor findings per each MAH during 2023

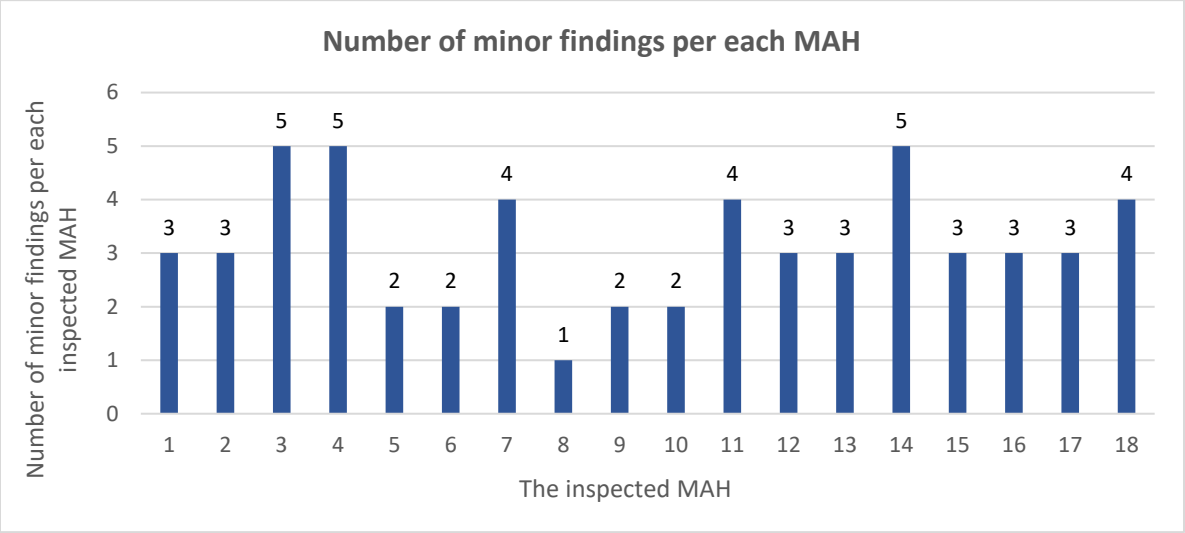
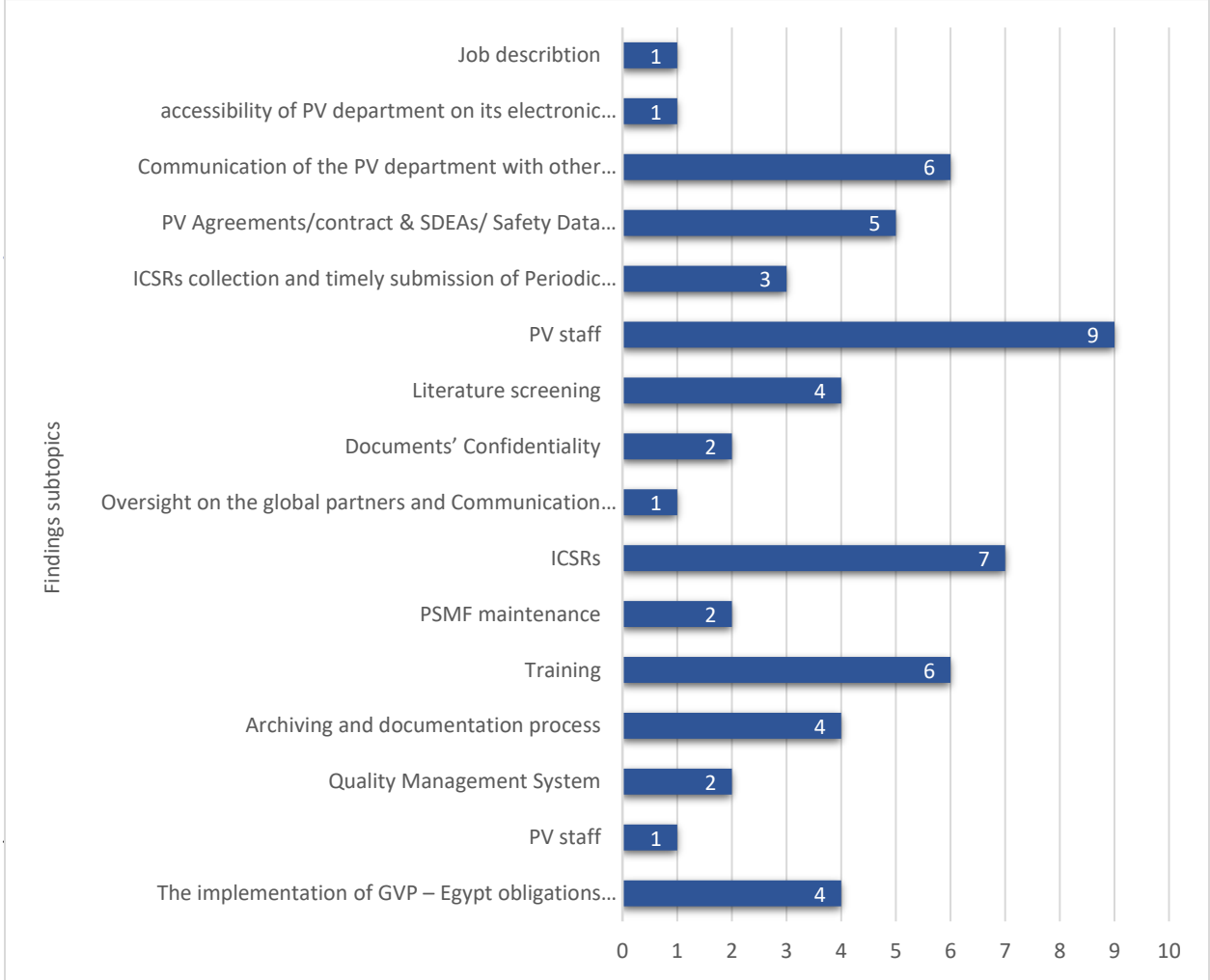
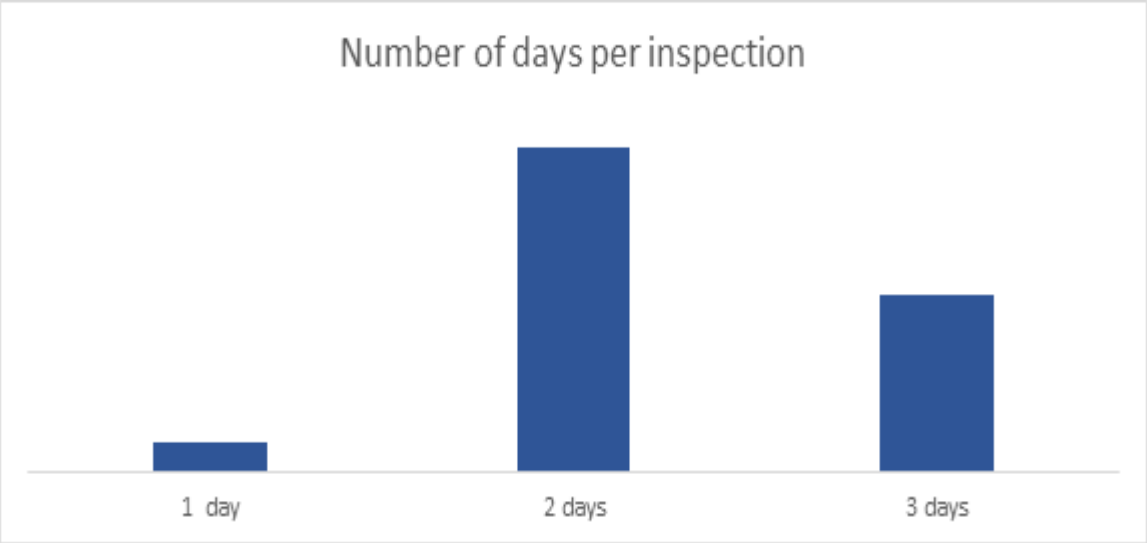


Figure 11 – Breakdown of the minor findings on 2023



5. Inspections over time

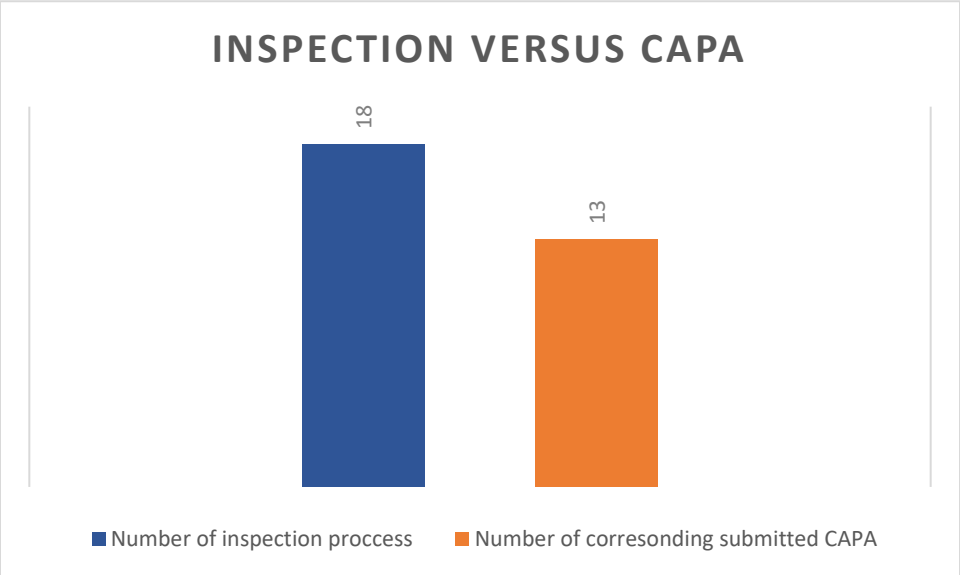
Figure 12- Number of inspections against the mean number of inspection days per inspection



The duration of the inspection process is determined by the identified risks, in accordance with the risk-based criteria

6. Inspections vs corrective and preventive actions (CAPA)

Figure 13- Number of inspections process against number of corresponding submitted CAPA



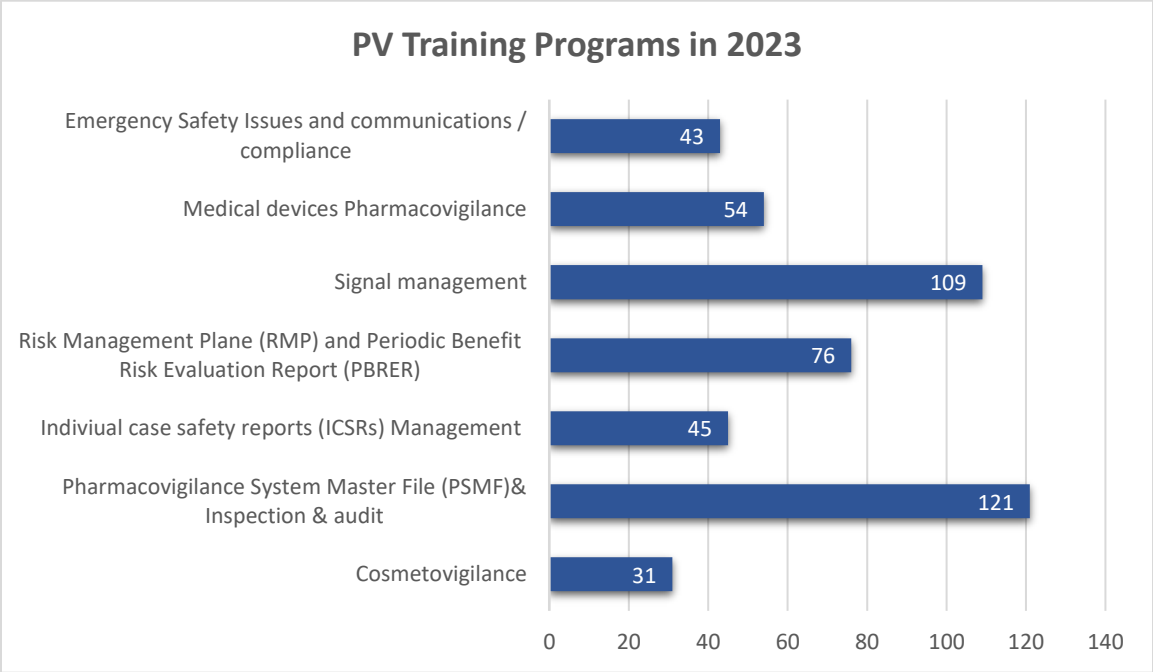
7. PV Training program in 2023

Pharmacovigilance training impact to PV compliance

PVGA provides this training to assist Marketing Authorization Holders (MAHs) in fulfilling their pharmacovigilance (PV) compliance obligations. When it comes to PV inspections, comprehensive training ensures that staff fully understand their roles and the procedures necessary to maintain compliance with both local and international regulations, helping to minimize the risk of non-compliance.

Well-trained staff are better equipped to identify systemic issues, resolve them quickly, and take preventive measures to enhance the overall safety profile of the products. This helps drive continuous improvements in the PV system and lowers the likelihood of regulatory findings.

Figure 14- number of PV training programs with respect to number to trainee



Appendix I – Inspection finding definitions

- Critical 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. It may include a pattern of deviations classified as major. It also includes the engaging in fraud, misrepresentation or falsification of data.

- Major 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. It may include a pattern of deviations classified as minor.

- Minor 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. A deficiency may be minor either because it is judged as minor or because there is insufficient information to classify it as major or critical.

Appendix II – Categorization of findings

Topic Area	Subtopic of the reported findings
The implementation of GVP – Egypt obligations regarding different PV activities	Signal management
	ICSRs
	Literature screening
	PBRER
	PV system (nomination)
	Emerging Safety Issues & Safety Concerns communications
	Safety variations
	RMP
Quality Management System	Agreements/ PV contracts
	Inspection readiness
	Handover and delegation processes
	Procedural documents
	PSSF/PSMF Maintenance
	CAPA effectiveness, implementation and informing the quality departments with deviations
	Training
	Reporting the deviations to the quality department
	Some concerned MAHs didn't have a QMS
	Documentation process

Appendix III – Abbreviations

PVGA: Pharmacovigilance general administration

EDA: Egyptian drug authority

GVP: Good Pharmacovigilance practice

PBRER: Periodic benefit risk evaluation report

PSMF: Pharmacovigilance system master file

PSSF: Pharmacovigilance sub-system master file

QMS: Quality management system

CAPA: Corrective and preventive action

PV: Pharmacovigilance

MAH: marketing authorization holder