



Pharmacovigilance Inspection Metrics Report

April 2015 - March 2016

Introduction

During the period 01 April 2015 to 31 March 2016, the GPvP Inspectorate conducted 34 inspections of Marketing Authorisation Holders (MAHs) and one inspection of a pharmacovigilance service provider. Of these:

- 8 inspections were of MAHs who had not previously undergone an MHRA GPvP inspection.
- 7 inspections were routine re-inspections.
- 19 inspections were triggered due to critical findings identified at previous inspections or in response to a specific issue.¹
- 1 inspection was requested by the European Committee for Medicinal Products for Human Use (CHMP).
- Of the 35 inspections conducted, 15 were performed to fulfil the EMA programme of inspections relating to centrally authorised products.

This report contains data relating to all 35 inspections conducted during the period.

The table below illustrates the type of MAHs inspected during this period:

	Innovative Pharma	Generics	Other ²
Number of MAHs inspected	18	15	2

Findings identified during inspections were graded as 'Critical', 'Major' or 'Minor'; the definitions for which are included in Appendix 1.

A total of 11 Critical, 94 Major and 111 Minor findings were identified during this period.

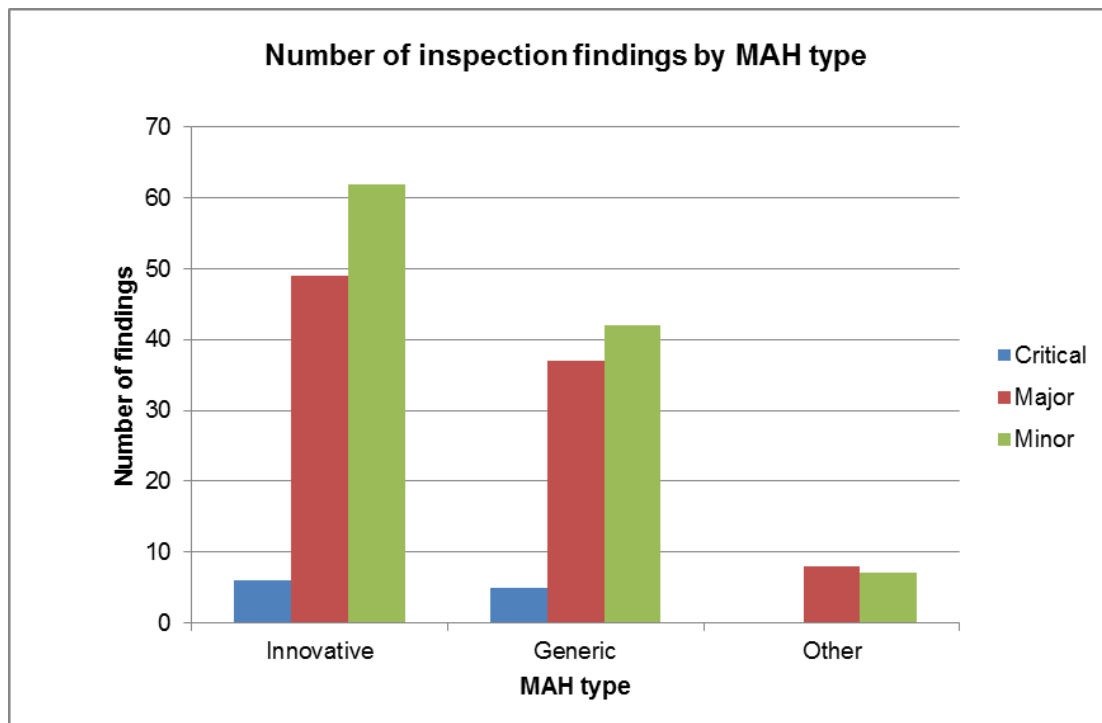
¹ The majority of these inspections were triggered due to critical findings identified at previous inspections.

² Companies included in 'other' category include for example those marketing mature/established, orphan, niche or herbal products, or pharmacovigilance service providers.

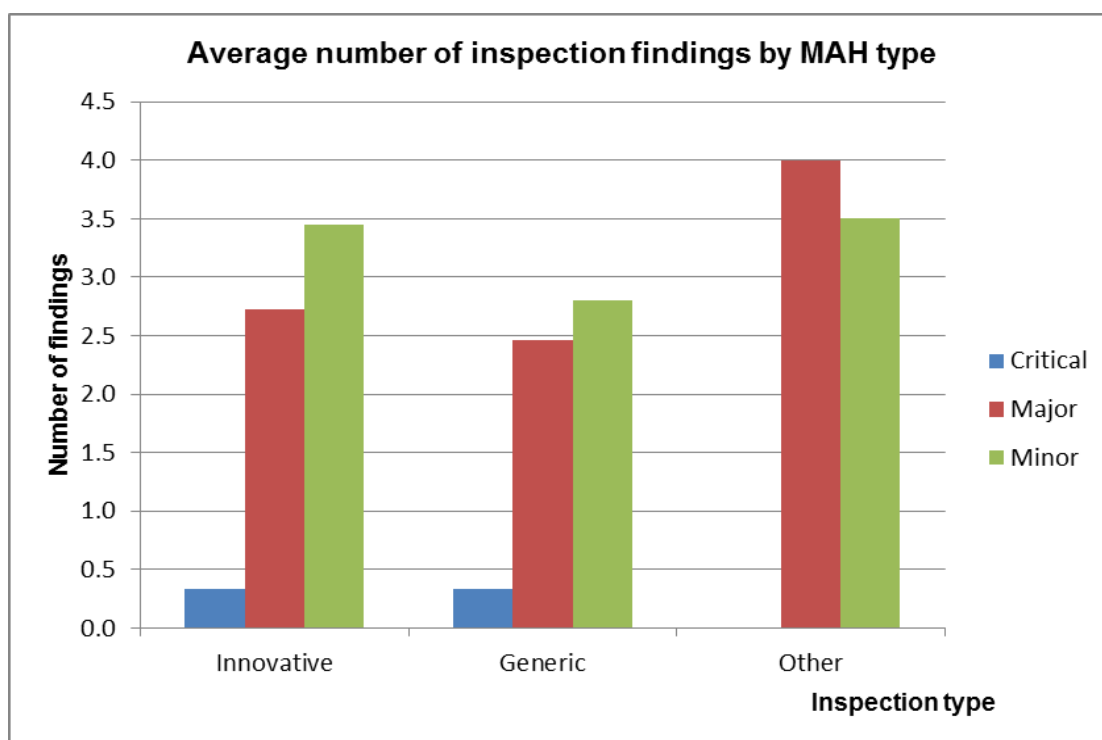


Inspection Findings by MAH and inspection type

The graph below displays the number of inspection findings for each type of MAH inspected:

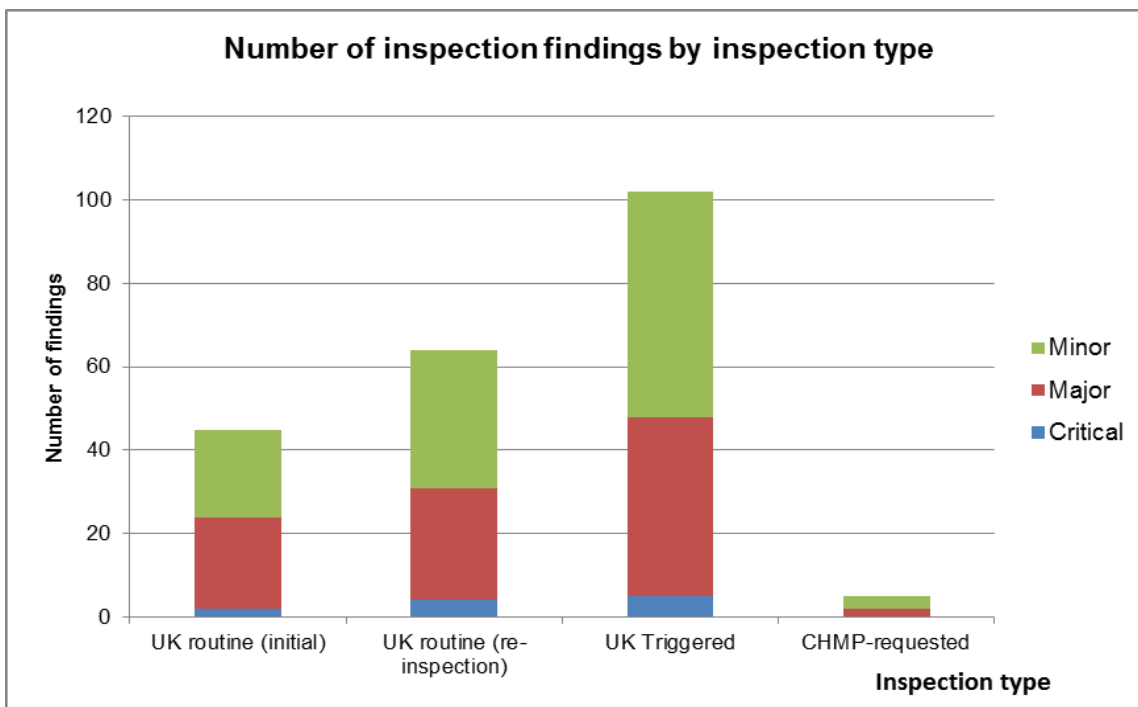


During this reporting period the average number of findings per inspection has been calculated as 0.3 Critical findings, 2.7 Major findings and 3.2 Minor findings. The graph below displays this information based on MAH type:

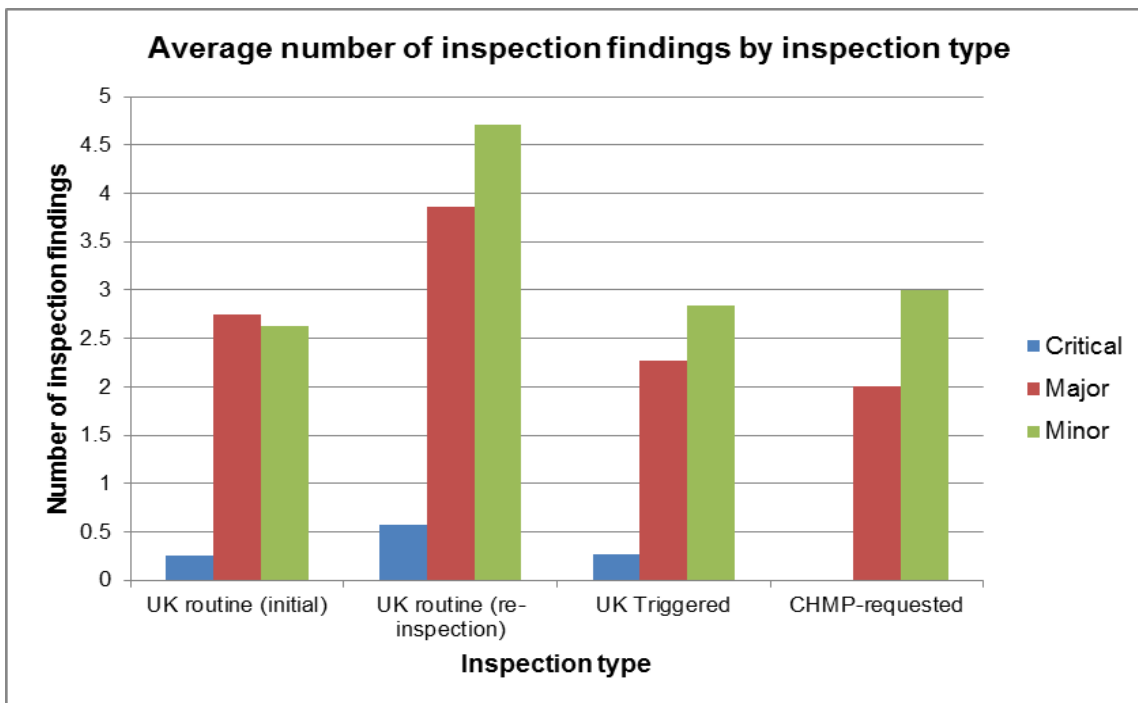




The number of inspection findings based on the inspection type is displayed below. Definitions of the inspection type are included in Appendix II:



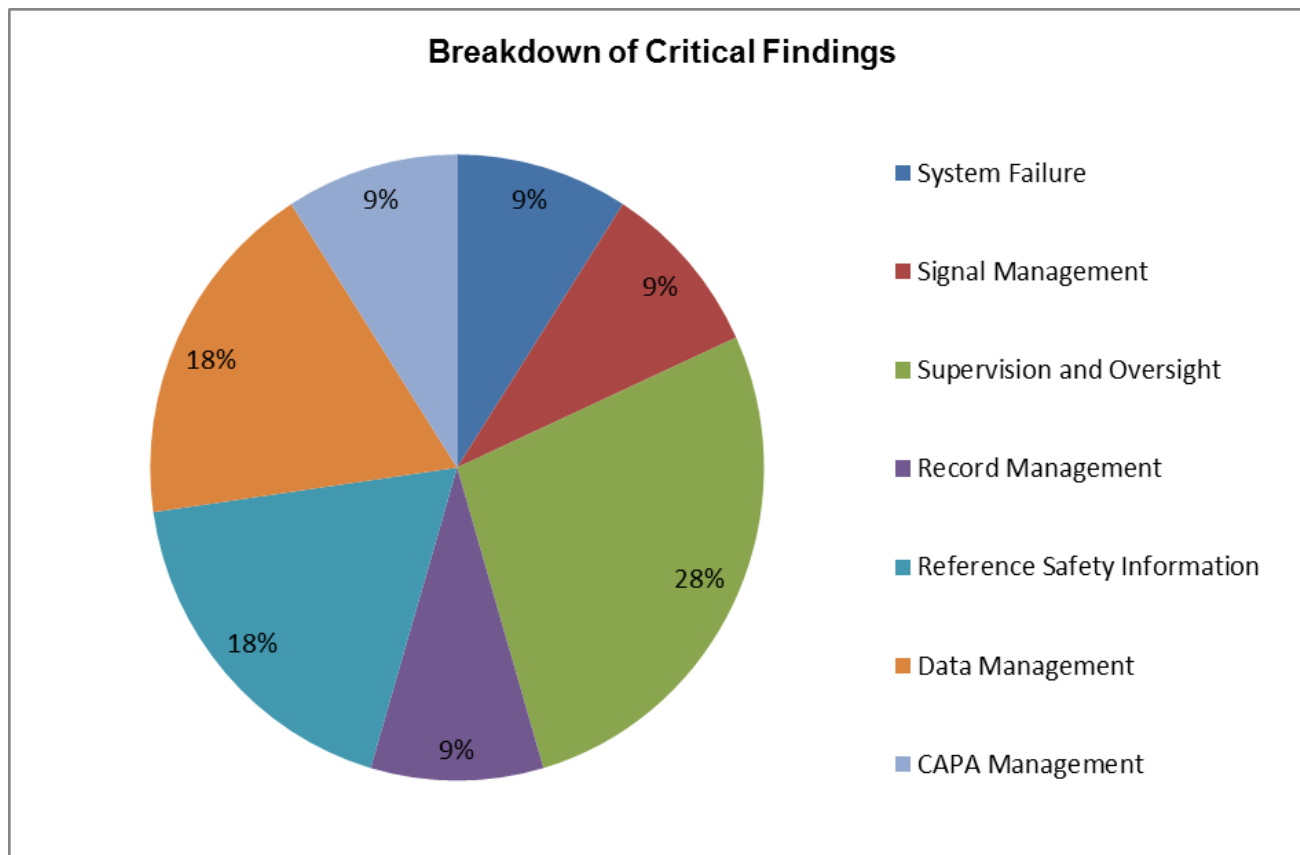
The average number of findings reported by inspection type is displayed in the graph below:





Critical Findings

The 11 Critical findings reported were identified during 6 of the 35 inspections that were performed. The graph below details the topic areas where Critical findings were identified.



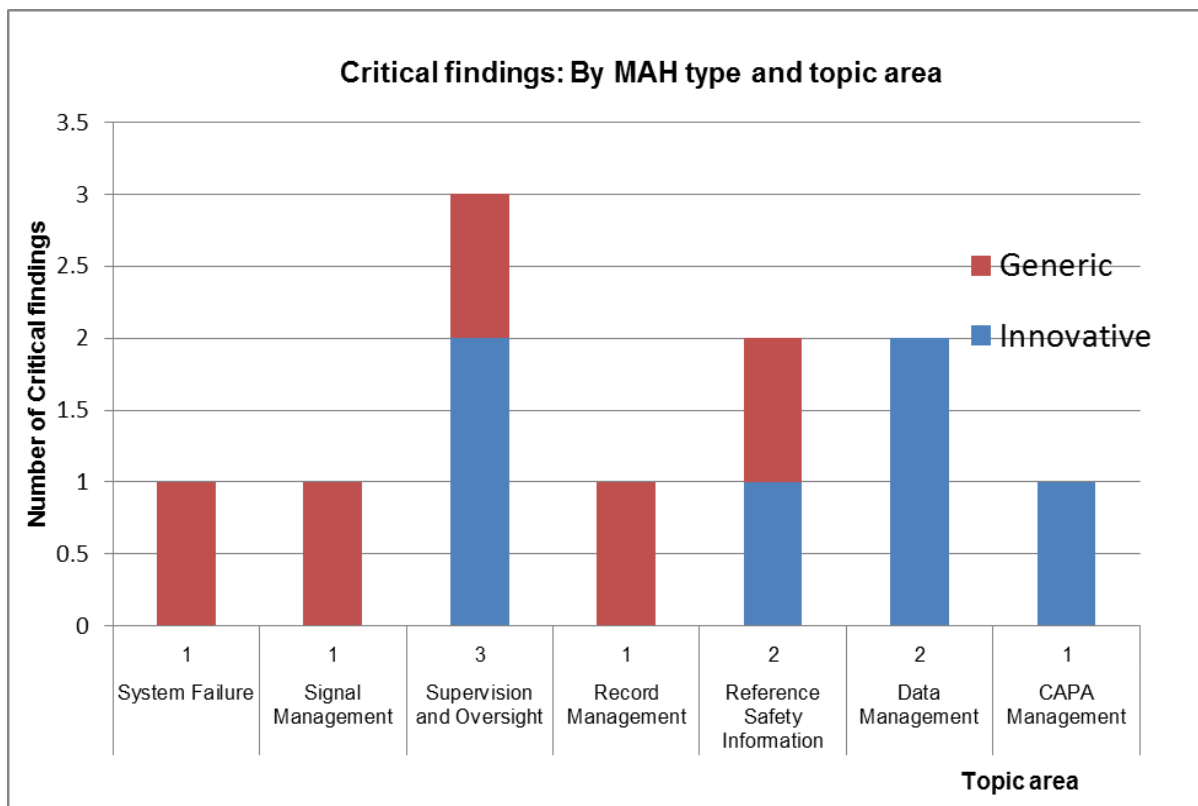
The largest proportion of Critical findings reported was in relation to supervision and oversight of the pharmacovigilance system, representing 28% of all Critical findings identified. This included issues in relation to provision of complete and accurate information to national competent authorities and inspectors, maintenance of the PSMF and QPPV/ MAH oversight of the pharmacovigilance system.

Critical deficiencies associated with the management of reference safety information and safety data management represented the next largest proportion, each representing 18% of all Critical findings identified.

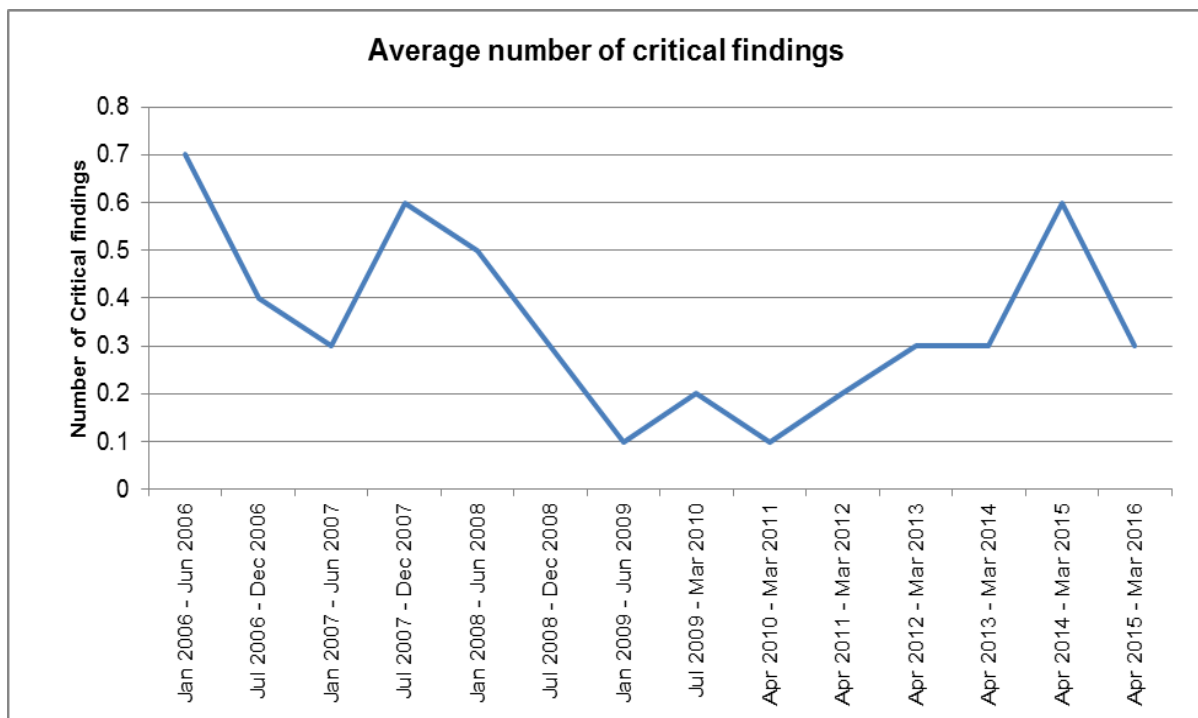
A single Critical finding was identified in each of the following areas: record management, management of Corrective and Preventative Actions (CAPA), signal management and failure to establish a global pharmacovigilance system.



The graph below displays the number of Critical findings identified by MAH type, broken down into topic area.



The graph below displays the average number of Critical findings identified per inspection over time:

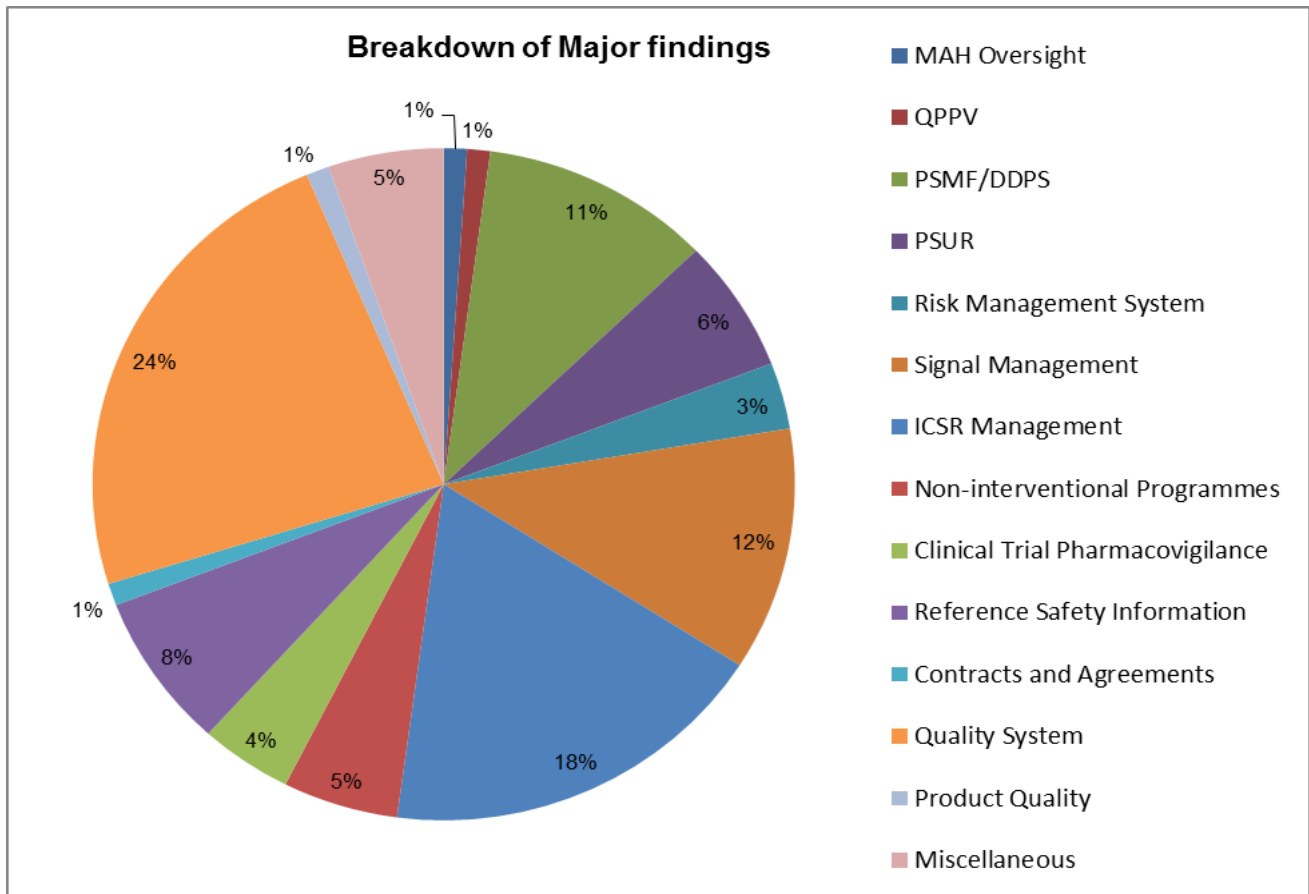




Major Findings

94 Major findings were identified across 29 of the inspections performed in this reporting period.

The graph below displays the distribution of Major findings by topic area:



Major findings were identified across 14 topic areas, as detailed in the graph above. The largest proportion of Major findings was identified in relation to the quality management system, which included findings in relation to auditing of the pharmacovigilance system, CAPA management, procedural documentation and overall quality system failures. These findings represented 24% of all Major findings identified.

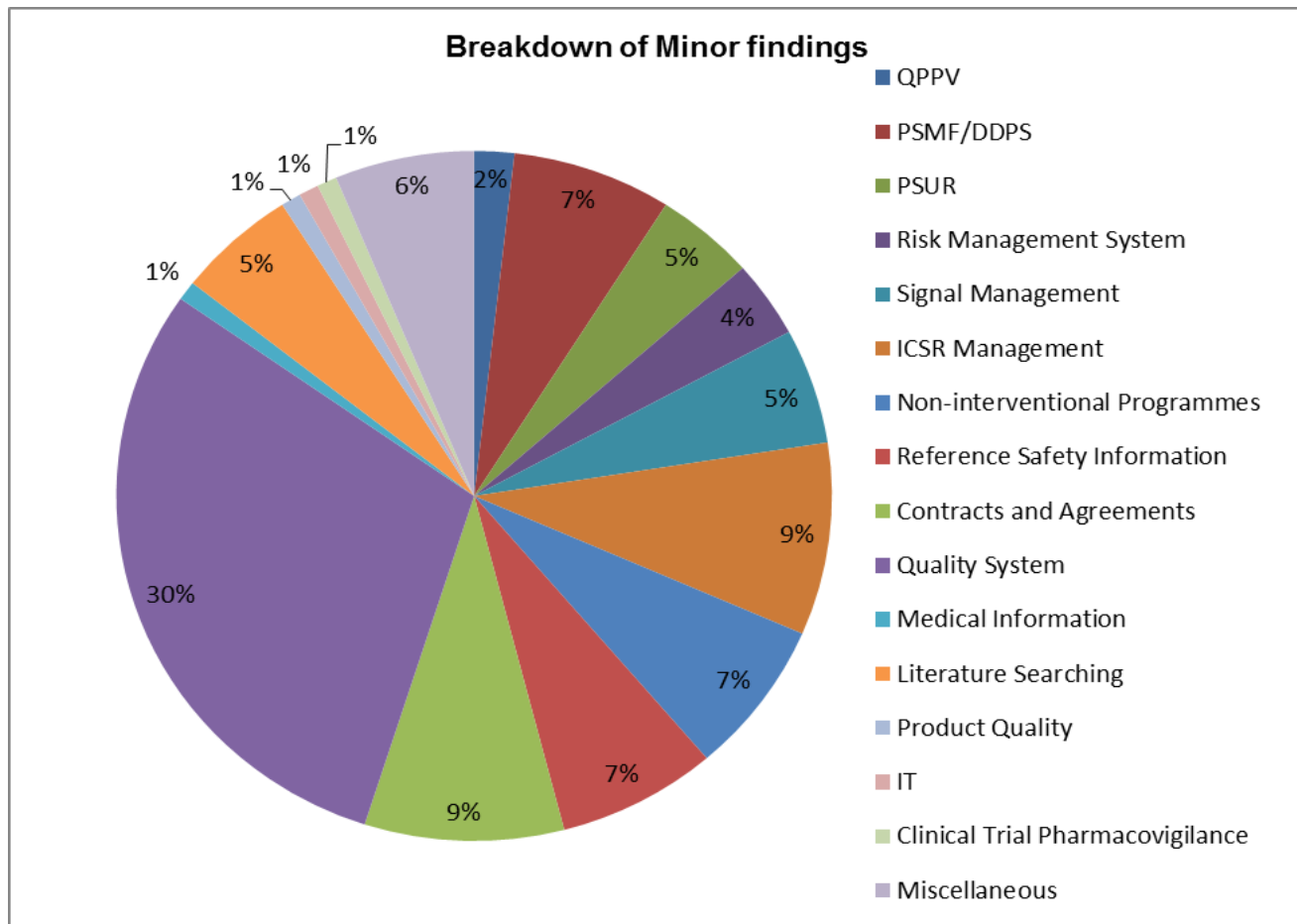
Major deficiencies associated with ICSR management and signal management represented the next largest proportion, representing 18% and 12% of all Major findings respectively. These three most common topic areas where Major findings were identified (quality system, ICSR management and signal management) represented in excess of 50% of all Major findings identified.

Miscellaneous findings included failures in the collection and collation of adverse drug reaction data and issues with submission of regulatory information to EMA.



Minor Findings

111 Minor findings were identified during the reporting period. The graph below displays the distribution of Minor findings by topic area:

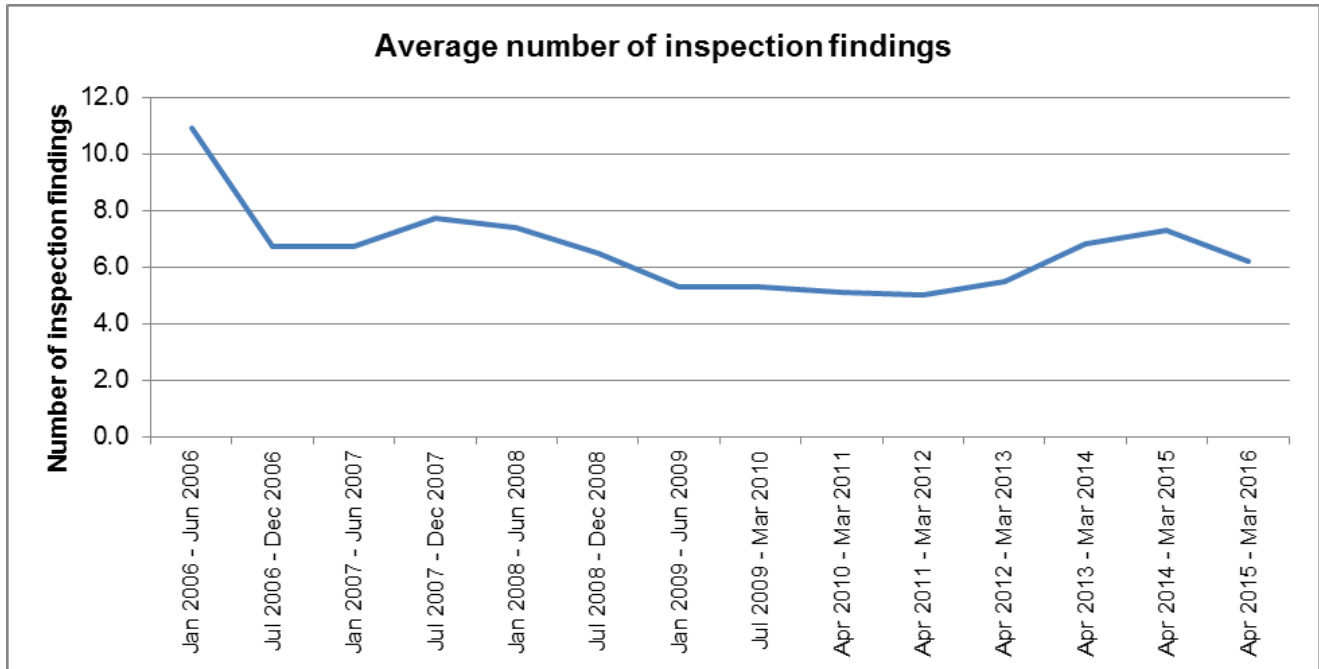


Minor findings were reported across 16 topic areas. The findings classified as miscellaneous referred to issues with the collection and collation of adverse drug reaction data, CAPA management and data migration.



Average number of inspection findings over time

The graph below displays the average number of inspection findings identified over time:



The average number of findings identified in this reporting period has decreased from the last period.



Conclusions

In the period April 2015 to March 2016, the MHRA conducted a total of 35 pharmacovigilance inspections. Approximately 23% of these inspections were of MAHs that had not previously undergone a MHRA pharmacovigilance inspection. The largest proportion of inspections was triggered due to critical findings identified at previous inspections or in response to a specific issue (54%).

The number of Critical findings identified during this reporting period had significantly decreased from the previous period, with 11 Critical findings reported versus 27 in the previous period. It is acknowledged that the total number of inspections performed had decreased by 27% from the previous period; however the reduction in critical findings indicates that significant issues identified at previous inspections were found to have been largely resolved during re-inspection.

The largest proportion of Critical findings was in relation to the supervision and oversight of the pharmacovigilance system, representing 28% of all reported Critical findings. These findings included issues with the provision of complete and accurate information to national competent authorities, maintenance of the PSMF and QPPV/ MAH oversight of the pharmacovigilance system.

Critical deficiencies associated with safety data management and the management of reference safety information represented the next largest proportion, each representing 18% of all Critical findings identified. Critical findings associated with data management included issues with collation and integrity of the global safety dataset, ICSR handling and safety database validation, configuration and control. Critical findings associated with reference safety information were again characterised by failures and significant delays to submit safety variations to update the safety sections of SPCs and PILs.

The number of overall Major findings had decreased from the previous period by approximately 44%. Additionally, the number of Critical and Major findings reported in association with signal management had significantly decreased from the previous period by approximately 64%. The largest proportion of Major findings was identified in relation to the quality system underpinning pharmacovigilance activities, which included findings in relation to auditing of the pharmacovigilance system, CAPA management, procedural documentation and overall quality system failures.

Overall the topic areas representing the largest proportion of inspection findings in this period are associated with the quality system, safety data management, signal management and maintenance of the PSMF. It is worth noting that there may be some variability in the assignment of a topic heading to specific findings, based on the information available at the time of the inspection. For example, where there is evidence that pharmacovigilance deficiencies are the direct result of data management issues, consequently the finding will be classified as such. Alternatively, the finding may be classified to reflect the symptom of the issue(s), for example under a heading of signal management or aggregate reports.

GPvP Inspectorate, August 2016



Appendix I – Inspection finding definitions

Critical: a deficiency in pharmacovigilance systems, practices or processes that adversely affects the rights, safety or well-being of patients or that poses a potential risk to public health or that represents a serious violation of applicable legislation and guidelines.

Major: a deficiency in pharmacovigilance systems, practices or processes that could potentially adversely affect the rights, safety or well-being of patients or that could potentially pose a risk to public health or that represents a violation of applicable legislation and guidelines.

Minor: a deficiency in pharmacovigilance systems, practices or processes that would not be expected to adversely affect the rights, safety or well-being of patients.



Appendix II – Inspection type definitions

UK routine inspection (initial) – this comprises inspections performed according to the national inspection programme and where it is the first MHRA pharmacovigilance inspection of the MAH.

UK routine inspection (re-inspection) – this comprises routine re-inspections of MAHs under the national inspection programme.

UK triggered - these inspections are performed under the national inspection programme and are triggered by either previous critical findings, requests from other MHRA divisions or as a result of other intelligence.

CHMP triggered – inspections requested by the CHMP in response to a specific trigger.