Medicines & Healthcare products Regulatory Agency

MHRA Regulating Medicines and Medical Devices

Pharmacovigilance Inspection Metrics Report

April 2014 - March 2015

Introduction

During the period 01 April 2014 to 31 March 2015, the GPvP Inspectorate conducted 47 inspections of Marketing Authorisation Holders (MAHs) and one inspection of a pharmacovigilance service provider. Of these:

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

This report contains data relating to all 48 inspections conducted during the period.

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

	Innovative Pharma	Generics	Other[1]
Number of MAHs inspected	25	20	2

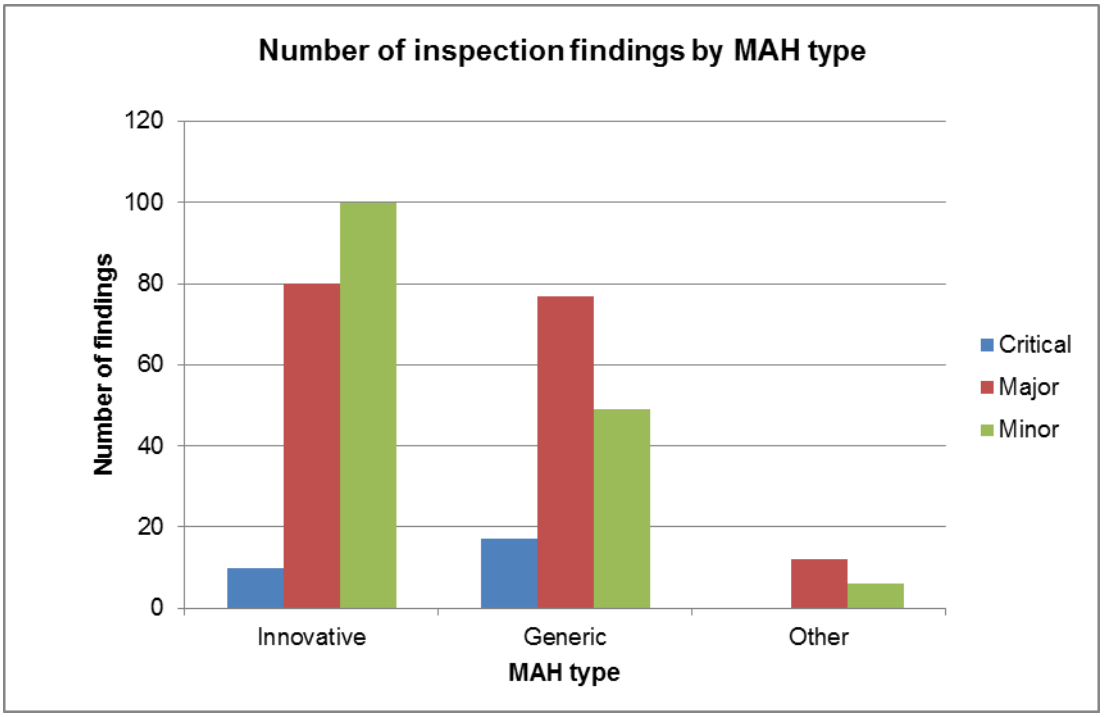
Findings identified during inspections were graded as 'Critical', 'Major' or 'Minor'; the definitions for which are included in Appendix 1.

A total of 27 Critical, 169 Major and 155 Minor findings were identified during this period.

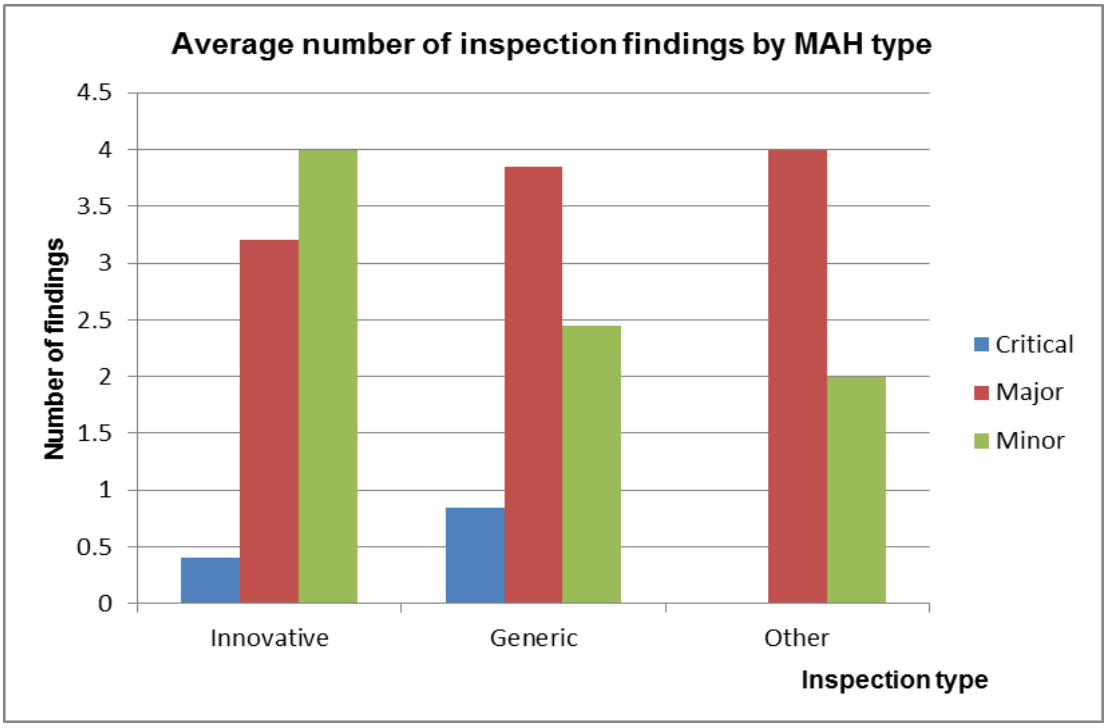
[1] Companies included in 'other' category include for example those marketing mature/established, orphan, niche or herbal products.

Inspection Findings by MAH and inspection type

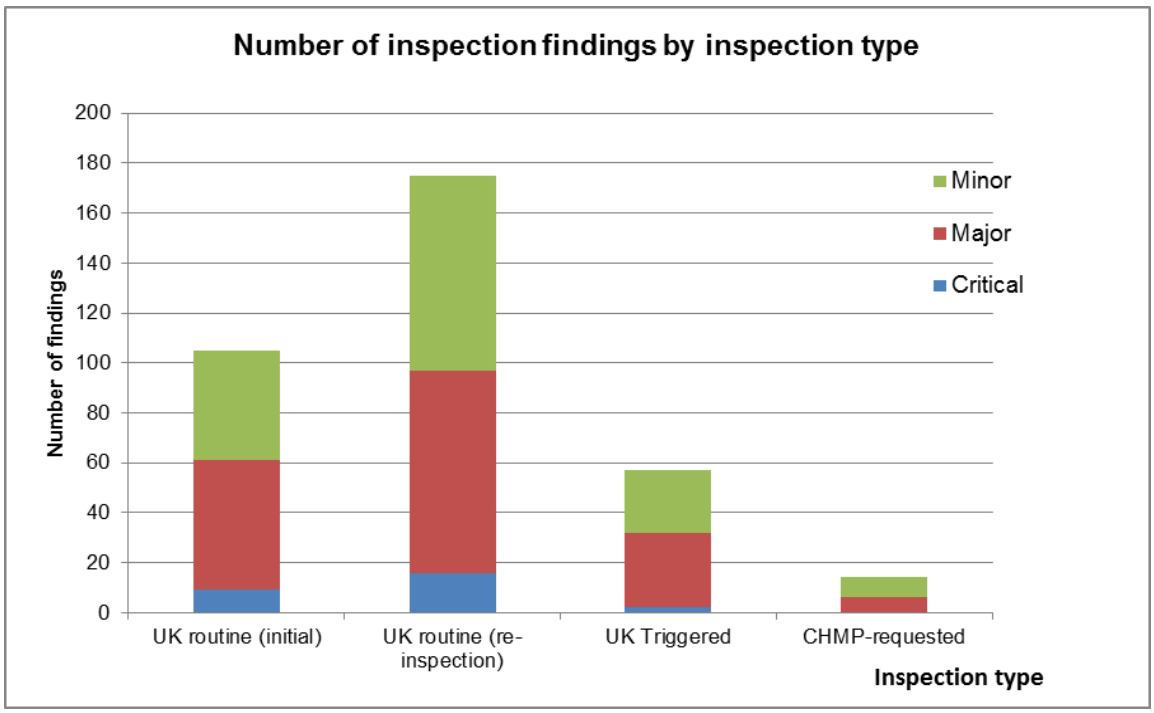
The graph below displays the number of inspection findings for each type of MAH inspected:



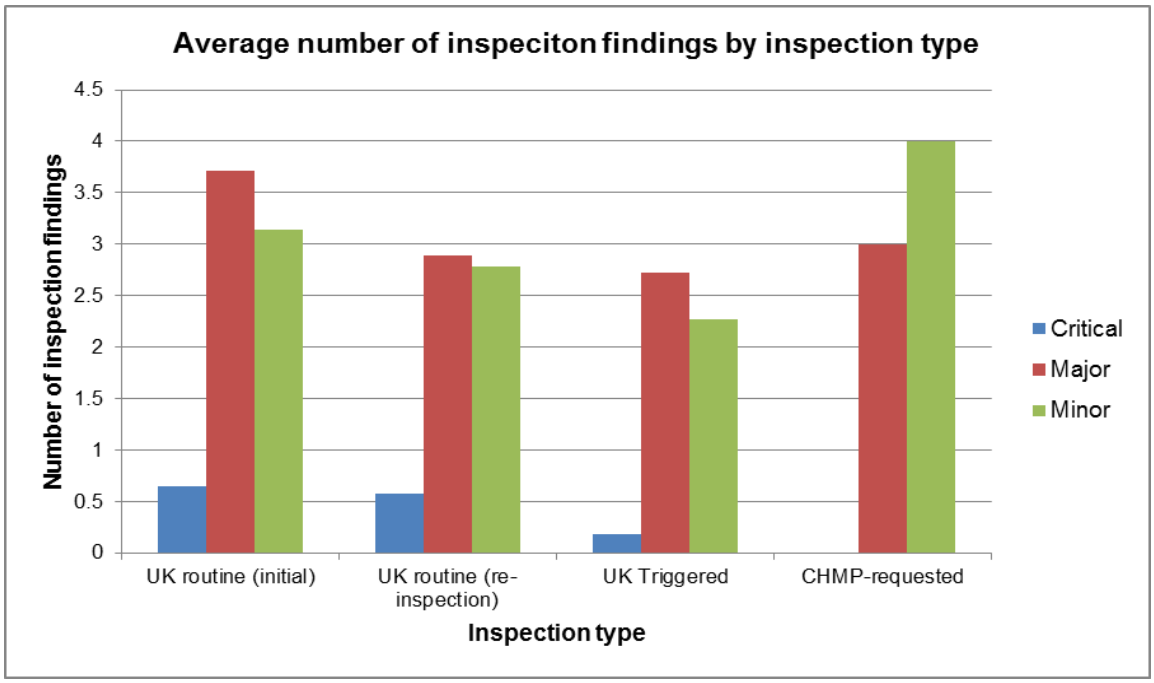
During this reporting period the average number of findings per inspection has been calculated as 0.6 Critical findings, 3.5 Major findings and 3.2 Minor findings. The graph below displays this information based on MAH type:



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

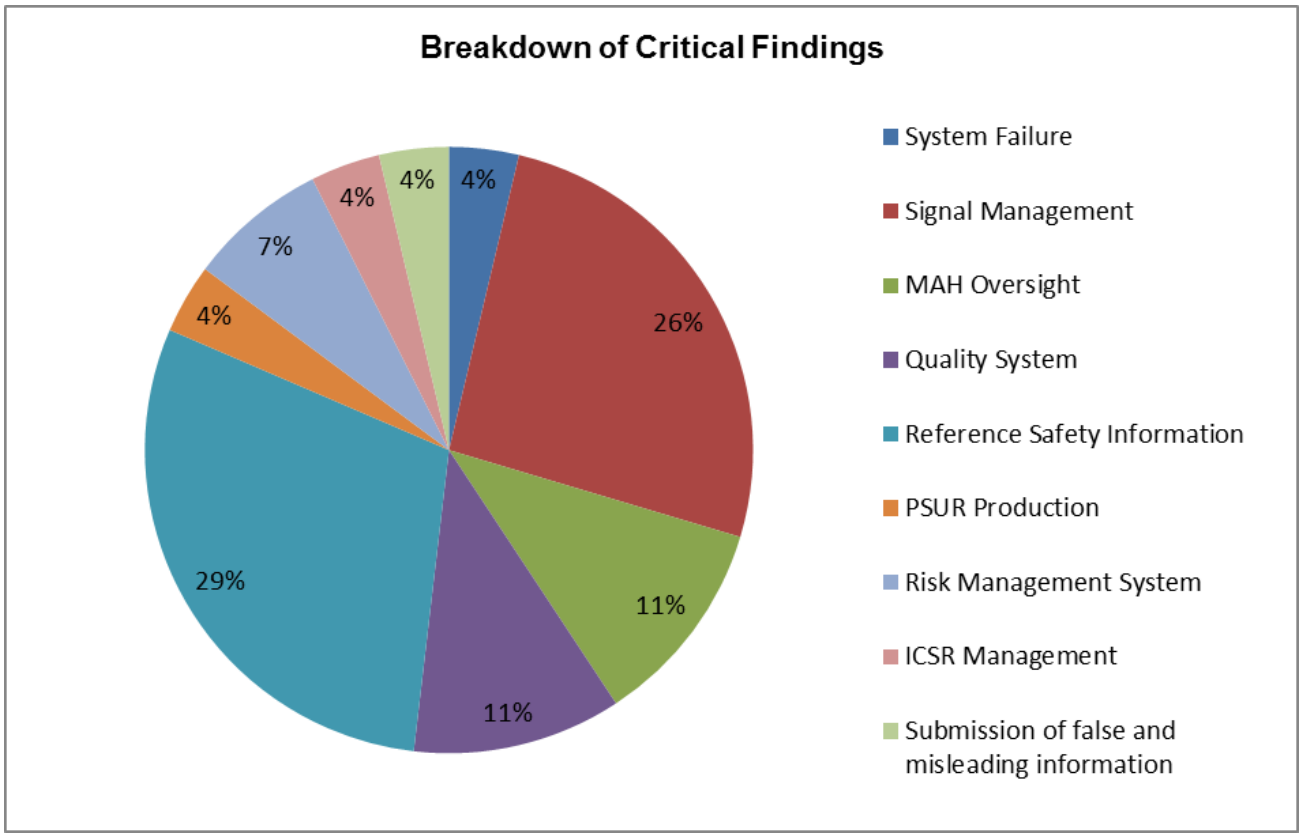


The average number of findings reported by inspection type is displayed in the graph below:



Critical Findings

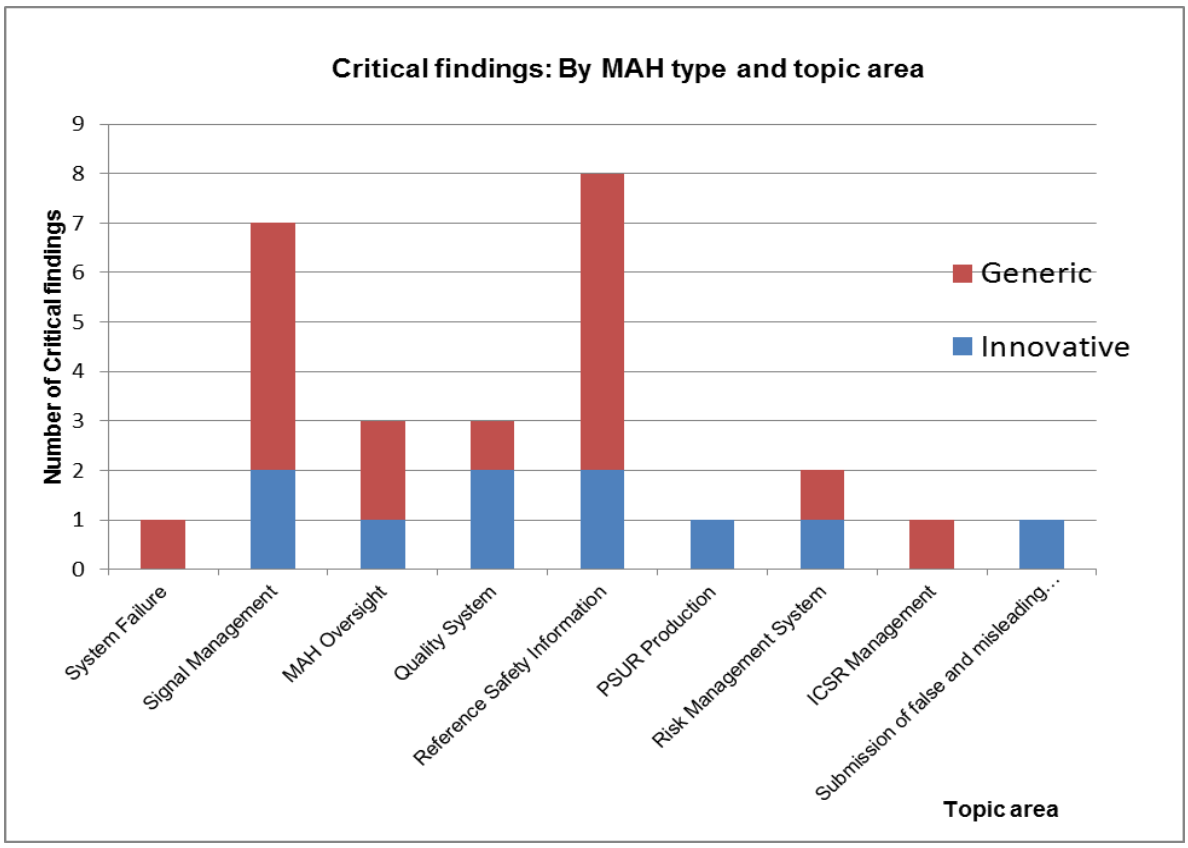
The 27 Critical findings reported were identified during 17 of the 48 inspections that were performed. The graph below details the topic areas where Critical findings were identified.



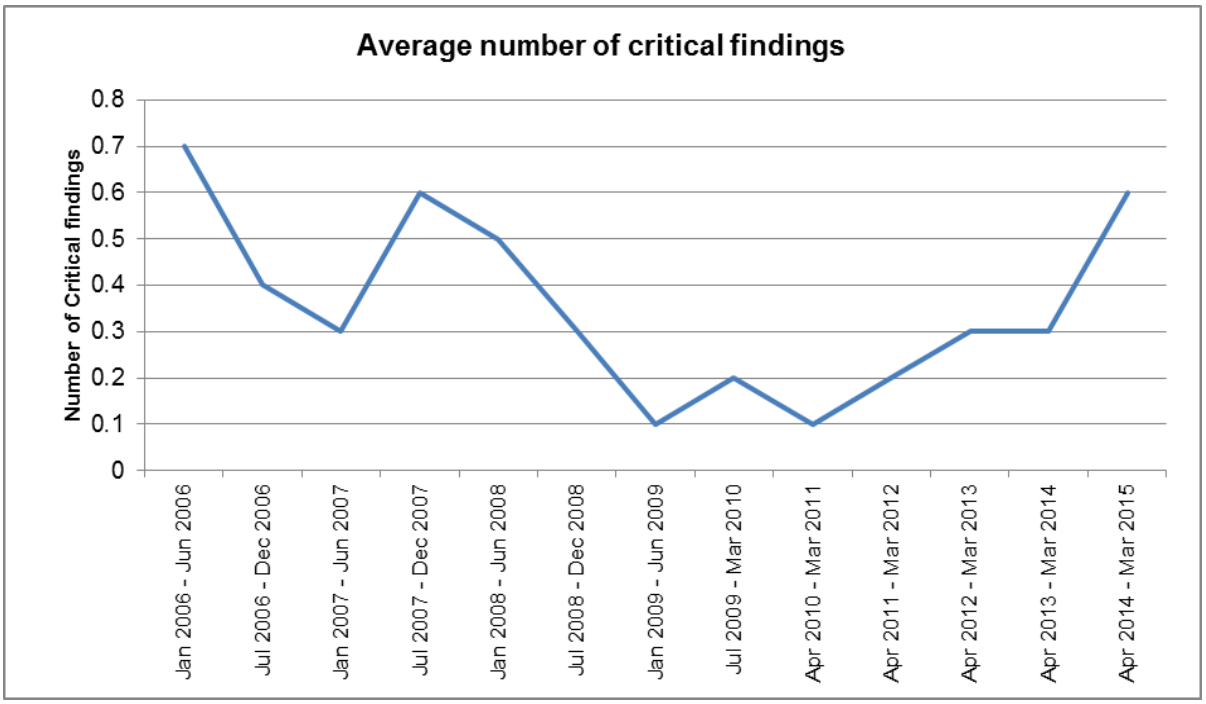
The majority of Critical findings were reported in relation to the maintenance of reference safety information, representing 29% of all Critical findings identified. This is consistent with the metrics from the previous reporting period where the largest proportion of Critical findings was reported in relation to activities concerning reference safety information. In this reporting period, Critical deficiencies associated with signal management represented the next largest proportion of findings identified (26% of all Critical findings).

Further Critical findings were identified in relation to MAH oversight of the pharmacovigilance system, pharmacovigilance quality management system and risk management system. A single Critical finding was identified in each of the following areas: complete system failure, PSURs, case processing and submission of false and misleading information to the EMA. There were no Critical findings in relation to non-interventional programmes compared to four reported during the April 2013 – March 2014 period.

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



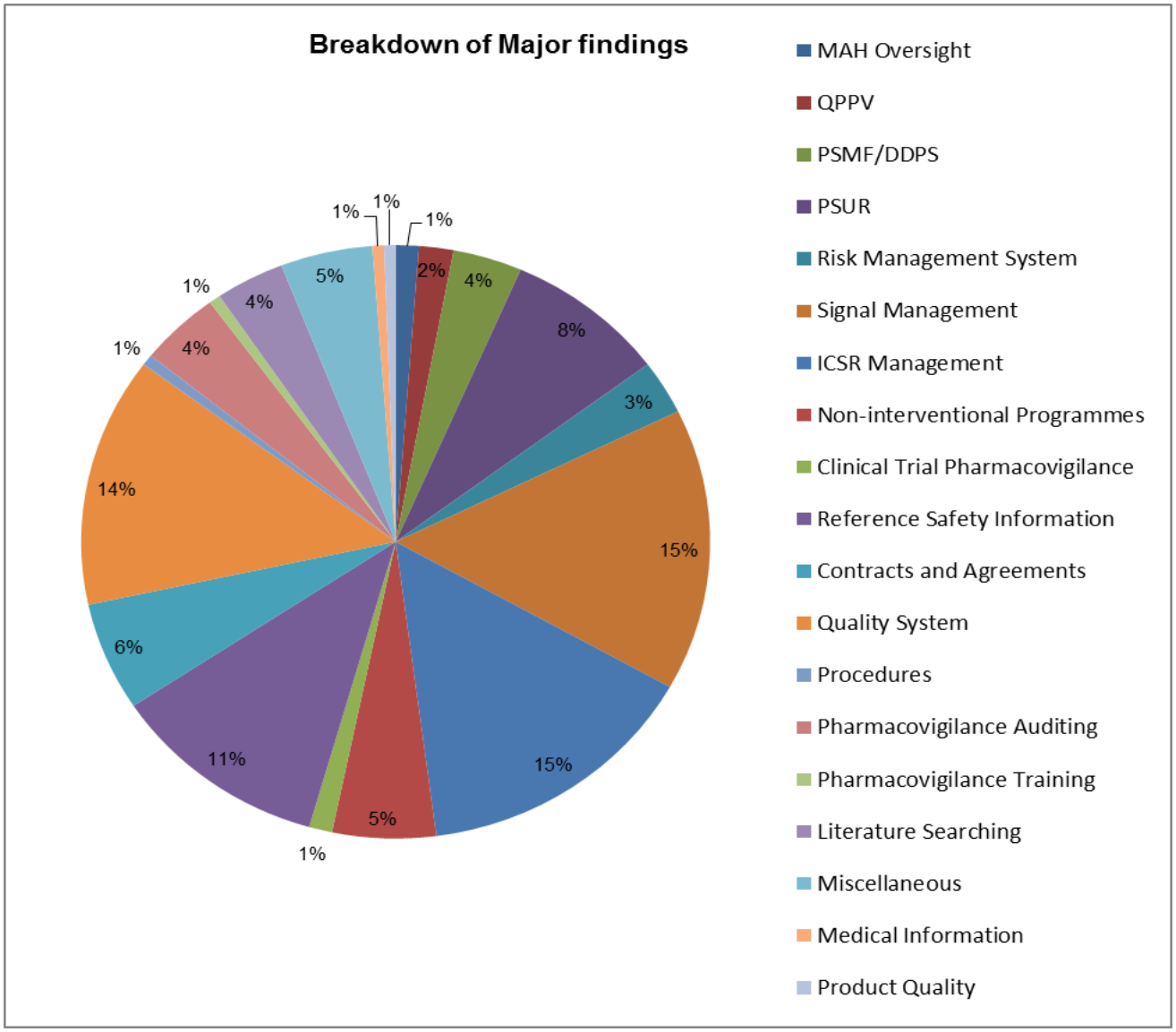
The graph below displays the average number of Critical findings identified per inspection over time:



Major Findings

169 Major findings were identified across 47 of the inspections performed in this reporting period.

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

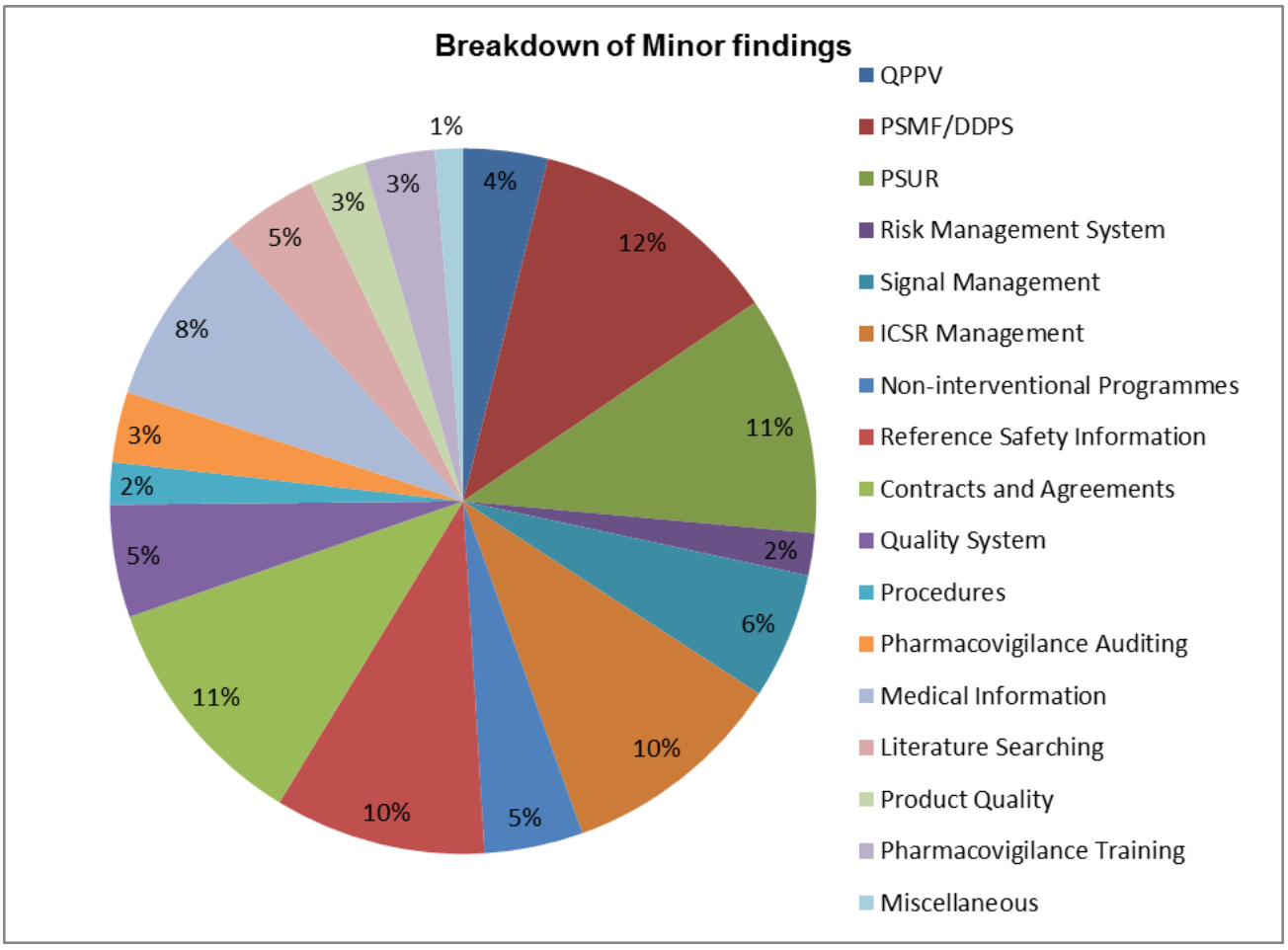


Major findings were identified across 19 topic areas, detailed in the graph above. The largest proportion of Major findings was identified in relation to signal management and ICSR management, each representing 15% of all Major findings identified. The four most common topic areas where Major findings were identified (signal management, ICSR management, quality systems and reference safety information) represented in excess of 50% of all Major findings identified.

Miscellaneous findings included deficiencies in the management of Corrective and Preventative Actions (CAPA), failures in the collection and collation of ADR data and issues with data migration and/or integrity.

Minor Findings

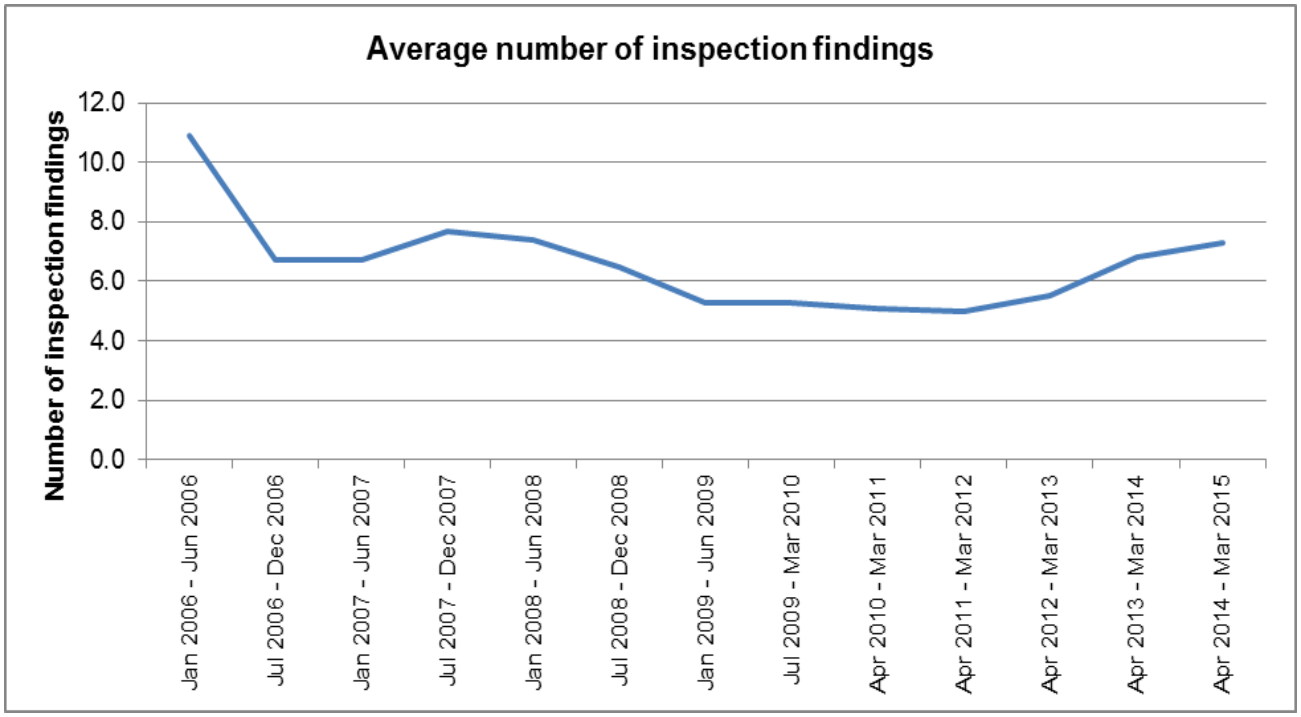
155 Minor findings were identified during the reporting period. The graph below displays the distribution of Minor findings by topic area:



Minor findings were reported across 17 topic areas. The findings classified as miscellaneous referred to issues with data migration and due diligence activities following product acquisition.

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 increased from the last period and indicates a steady increase since 2011.

Conclusions

In the period April 2014 to March 2015, the MHRA conducted a total of 48 pharmacovigilance inspections. Approximately 29% of these inspections were of MAHs that had not previously undergone a MHRA pharmacovigilance inspection. The largest proportion of inspections was performed as routine re-inspections (i.e. of MAHs who had previously undergone a pharmacovigilance inspection).

The number of Critical findings identified during this reporting period had increased from the previous period, with 27 Critical findings reported versus 19 in the previous period. The largest proportion of Critical findings remained in the topic area of reference safety information, representing 29% of all reported Critical findings. 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.

In this reporting period a sharp increase in the number of Critical findings associated with signal management was identified. Seven Critical findings were reported and these were associated with failures to conduct signal detection activities, failures to incorporate all available data into signal detection activities, significant delays in completing signal evaluation and failures to address previously reported major inspection findings, resulting in an escalation of the issue (persistent non-compliance). In some instances the persistent non-compliance had had a measurable impact, i.e. subsequent completion of signal detection activities had resulted in new signals being identified and updates to product information.

The number of Major findings associated with the Pharmacovigilance Master File has decreased from the previous period by approximately 45%. Additionally, the number of Critical and Major findings reported in association with deficiencies in the collection of data from non-interventional programmes has decreased from the previous period. The topic areas representing the largest proportions of inspection findings remain associated with key pharmacovigilance activities and outputs such as ICSR management, signal management and reference safety information.

GPvP Inspectorate, October 2015

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.