Pharmacovigilance Inspection Metrics Report

April 2013 - March 2014

Introduction

During the period 01 April 2013 to 31 March 2014, the Pharmacovigilance inspectorate conducted 56 inspections of Marketing Authorisation Holders (MAHs). Of these:

- 14 inspections were of MAHs who had not previously undergone an MHRA GPvP inspection
- 28 inspections were routine re-inspections
- 12 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)
- 19 inspections were performed to fulfil the EMA programme of inspections relating to centrally authorised products.

This report contains data relating to all 56 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	30	22	4

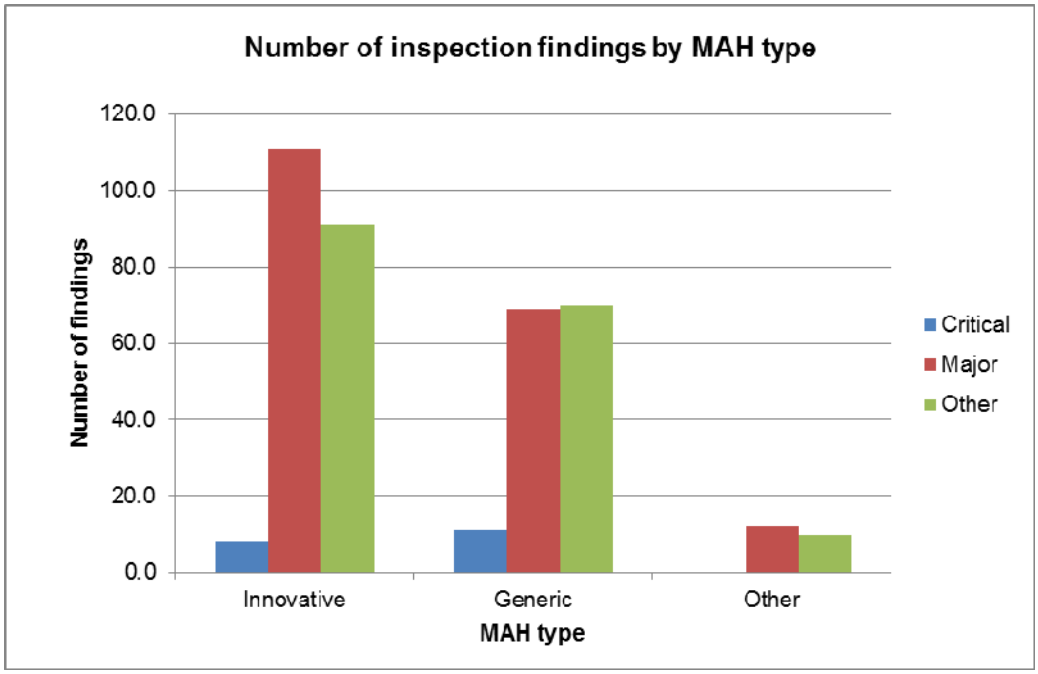
Findings identified during inspections were graded as 'Critical', 'Major' or 'Other'; the definitions for which are included in Appendix 1.

A total of 19 Critical, 192 Major and 172 Other findings were identified during this period.

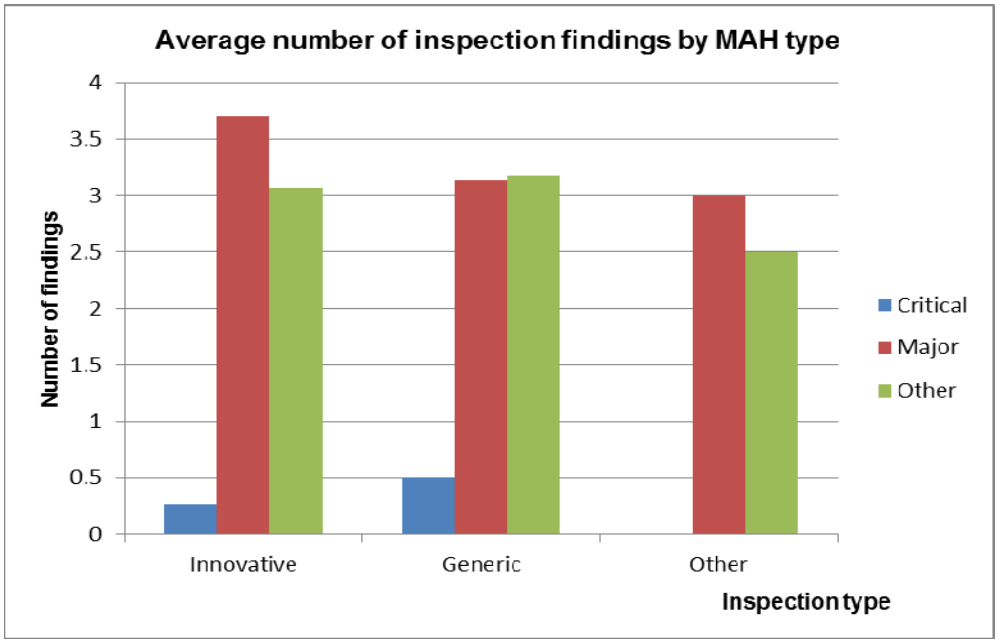
[1] Examples of MAH companies classified as 'other' include those marketing mature/established, orphan, niche or herbal products.

Inspection Findings by MAH and inspection type

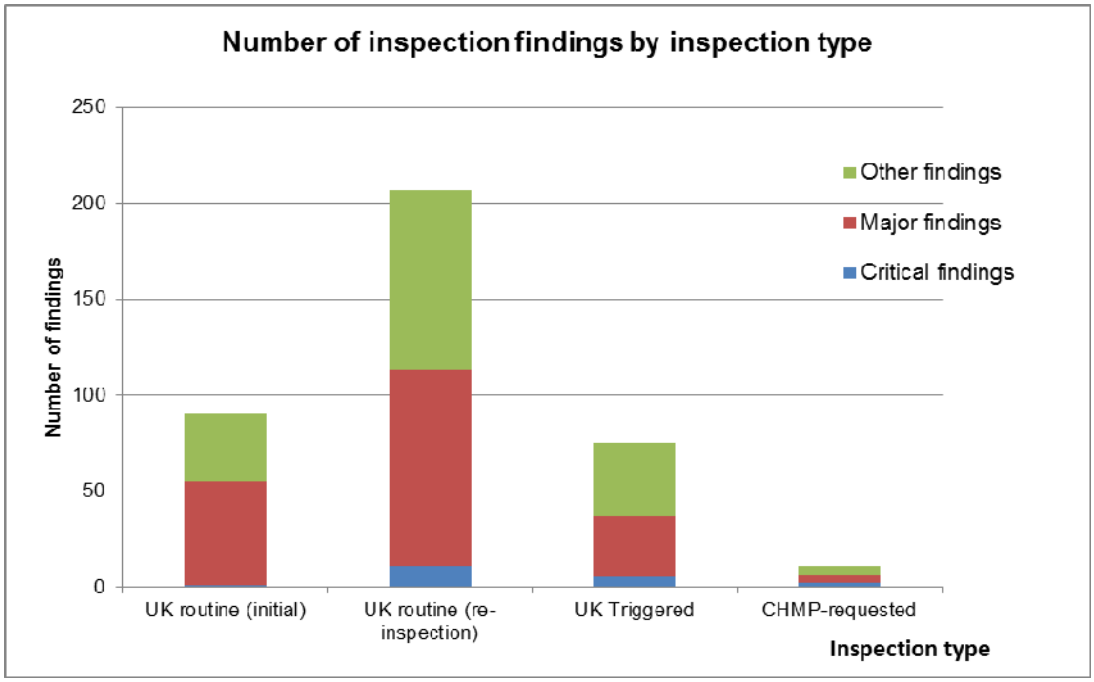
The graph below displays the number of inspection findings for each type of MAH inspected:



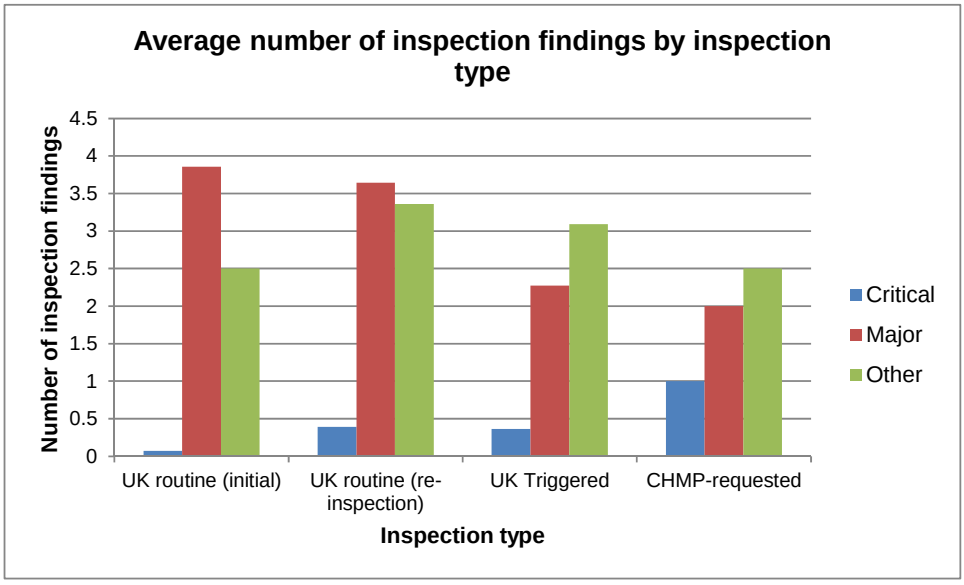
During this reporting period the average number of findings per inspection has been calculated as 0.3 Critical findings, 3.4 Major findings and 3 Other findings. The graph below displays this information based on MAH type:



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

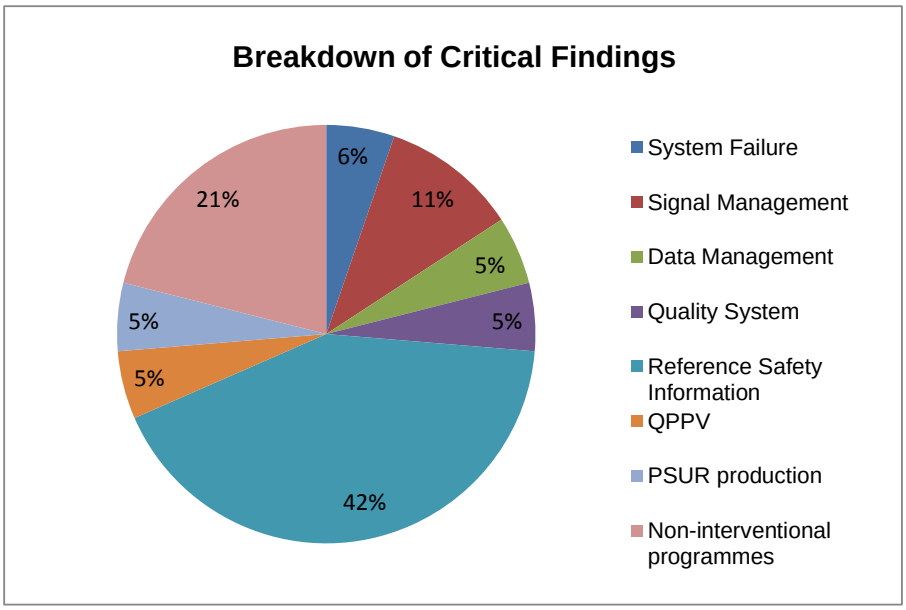


The average number of findings reported by inspection type is displayed in the graph below:



Critical Findings

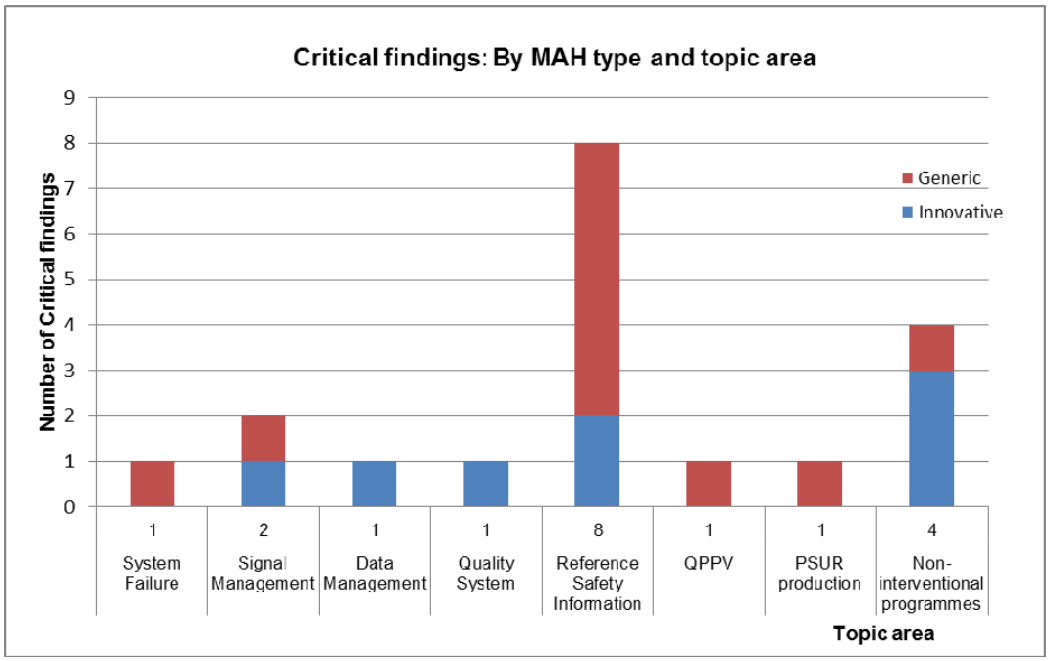
The 19 Critical findings reported were identified during 16 of the 56 inspections that were performed. The graph below details the topic areas where Critical findings were identified.



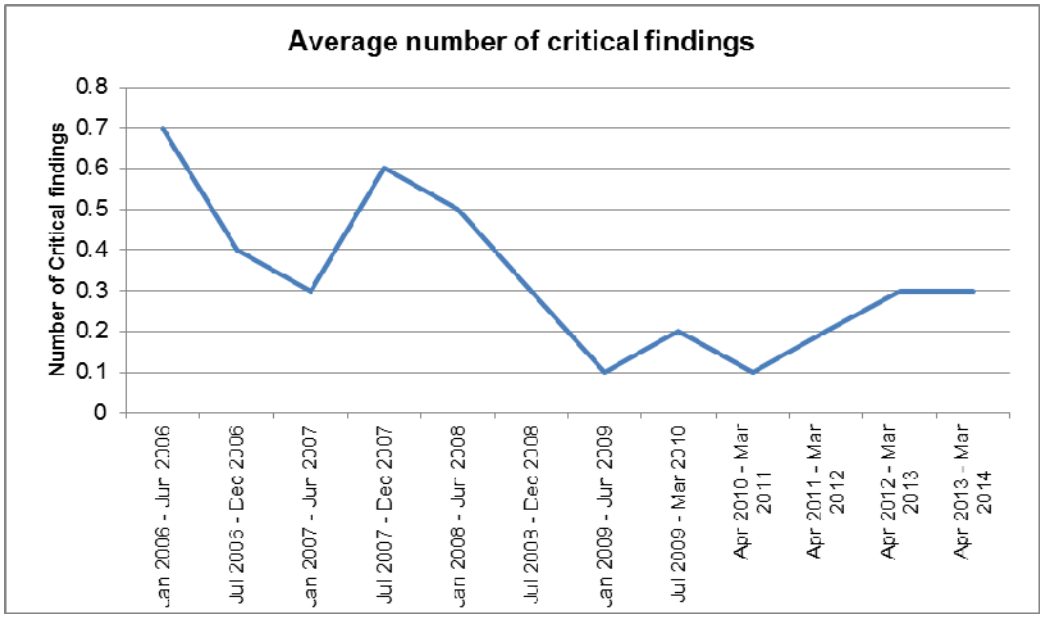
The majority of Critical findings were reported in relation to the maintenance of reference safety information, representing 42% of all Critical findings identified. This is consistent with the metrics from the previous reporting period where the largest proportion of Critical findings were reported in relation to activities concerning reference safety information. In this reporting period, Critical deficiencies associated with non-interventional programmes represented the next largest proportion of findings identified (21% of all Critical findings).

Further Critical findings were identified in relation to signal management, with a single Critical finding identified in each of the following areas: complete system failure, pharmacovigilance quality management system, roles and responsibilities of the EU-QPPV, PSURs and ICSR data management.

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



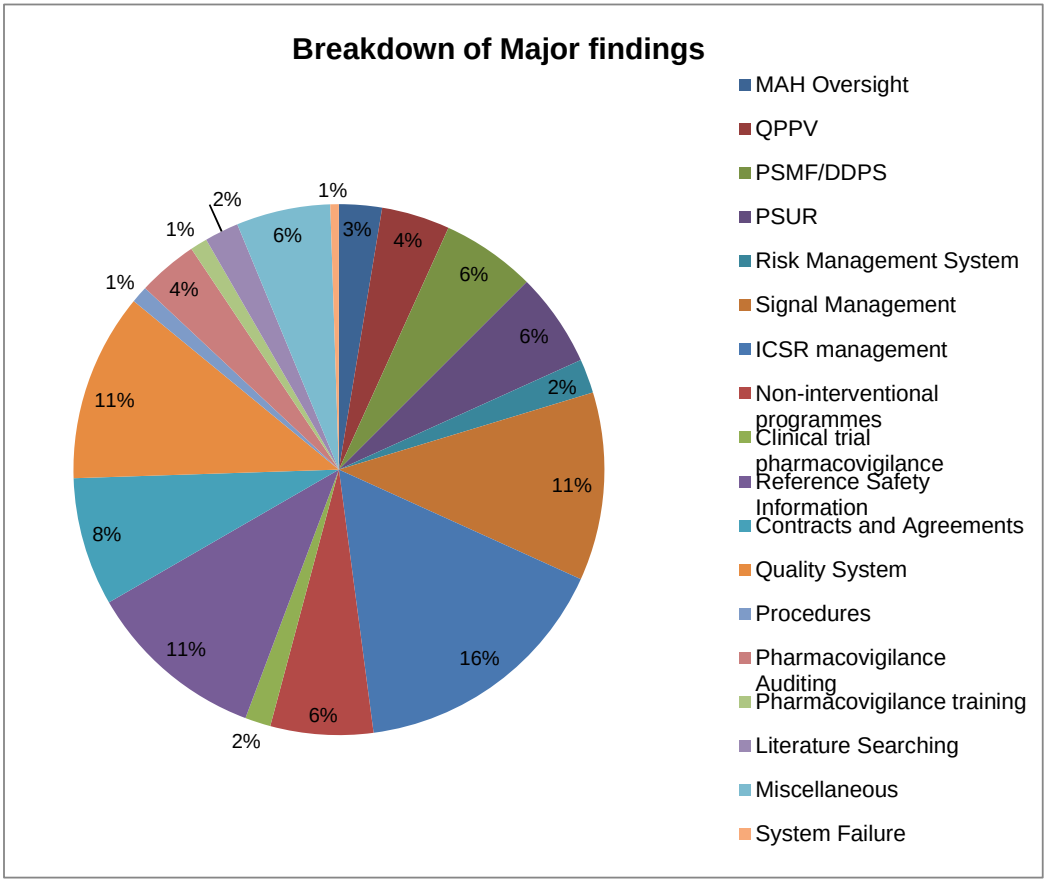
The graph below displays the average number of Critical findings identified per inspection over time:



Major Findings

192 Major findings were identified across 56 of the inspections performed in this reporting period.

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

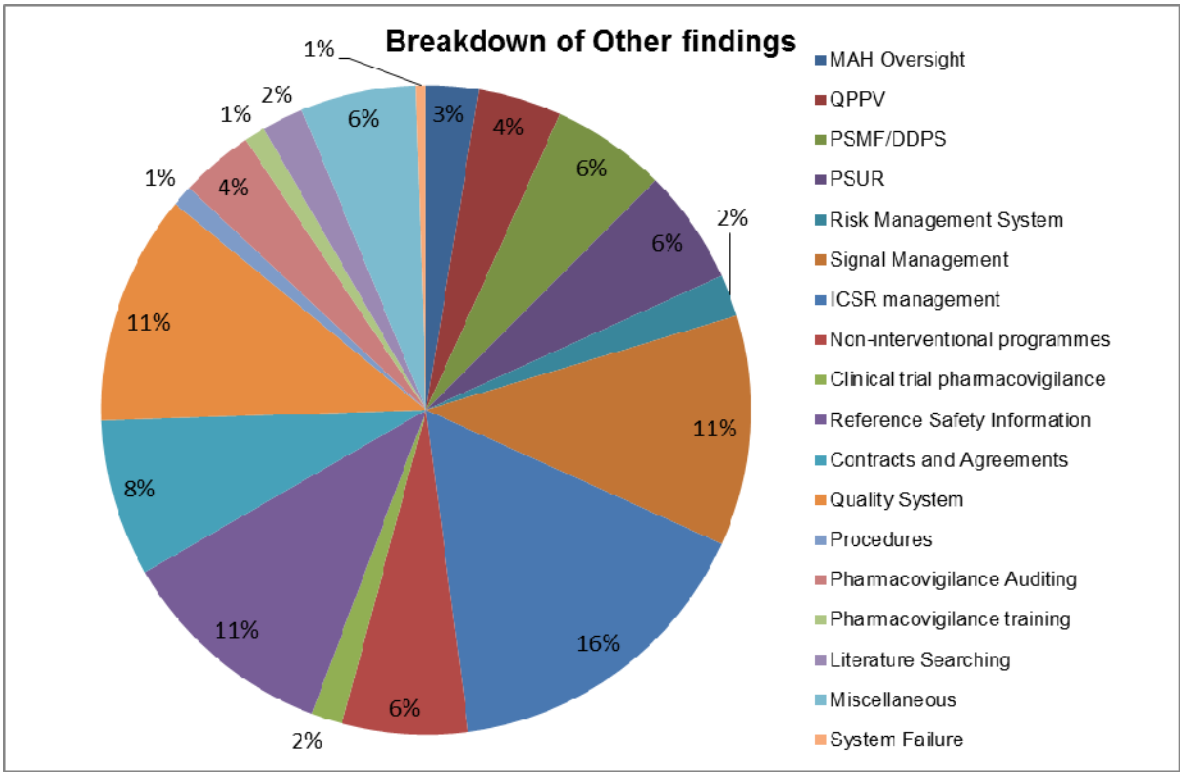


Major findings were identified across 18 topic areas, detailed in the graph above. The largest proportion of Major findings were identified in relation to spontaneous case processing, representing 16% of all Major findings identified. The four most common topic areas where Major findings were identified (spontaneous case processing, signal management, quality systems and reference safety information) represented in excess of 50% of all Major findings identified.

Miscellaneous findings included deficiencies such as the management of Corrective and Preventative Actions (CAPA), failures in the collection and collation of ADR data and the management and collection of data from Non-Interventional Studies.

Other Findings

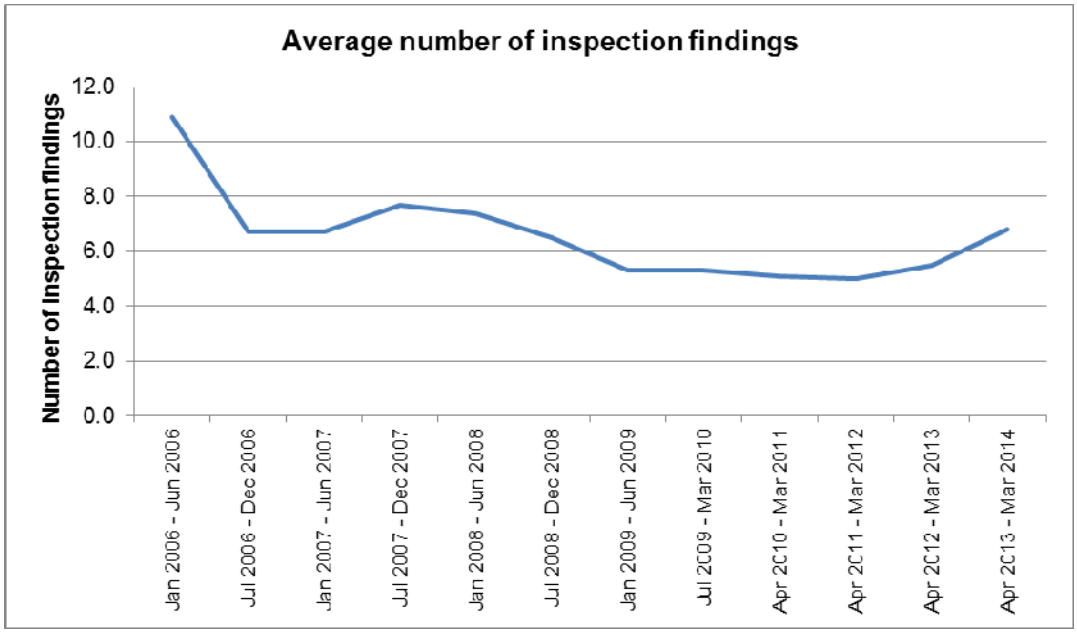
172 Other findings were identified during the reporting period. The graph below displays the distribution of Other findings by topic area:



Other findings were reported across 18 topic areas. The findings classified as miscellaneous referred to those relating to 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 increased from the last period, and indicates a steady increase since 2011, with a sharper increase in 2013/2014.

Conclusions

In the period April 2013 to March 2014, the MHRA conducted a total of 56 pharmacovigilance inspections. Approximately 21% of these inspections were of MAHs that had not previously undergone a MHRA pharmacovigilance inspection. The largest proportion of inspections were 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 was slightly higher than the previous period, reporting 19 Critical findings versus 18 in the previous period. The largest proportion of Critical findings remained in the topic area of reference safety information, representing 42% 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 an increase in the number of Critical findings associated with non-interventional programmes were identified. Of these three Critical findings, two were in association with failures to ensure collection of safety information from patient support programmes that had been identified at previous inspections and not appropriately resolved by the time of re-inspection. Failures to appropriately resolve deficiencies reported at previous inspections and failures to implement agreed corrective and preventative actions (CAPA) were reported more frequently compared with previous reporting periods.

In this reporting period the impact of the revised pharmacovigilance legislation became more apparent. In areas where the legislation and guidance has been strengthened, an increased number of inspection findings have been reported. Such examples include an increased number of findings across the Quality Management System (QMS), incorporating pharmacovigilance auditing, training and procedures, representing a 66% increase in the average number of QMS findings identified. Similarly the introduction of the Pharmacovigilance Master File has continued to generate an increased number of inspection findings. Finally a number of findings were reported in association with deficiencies in the collection of data from non-interventional studies, resulting from changes in the data collection requirements introduced in the reviewed legislation.

Nevertheless, 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, February 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.

Other: 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.