Pharmacovigilance Inspection Metrics Report

April 2011 to March 2012

During the period 1st April 2011 to 31st March 2012 the pharmacovigilance inspectorate conducted 81 inspections of Marketing Authorisation Holders (MAHs). Of these, 38 inspections were of MAHs who have not undergone an MHRA pharmacovigilance inspection before, 33 inspections were routine re-inspections and 10 inspections were triggered due to critical findings identified at previous inspections or in response to a specific issue. There were no CHMP-requested inspections. 10 inspections were performed to fulfil the EMA programme of inspections relating to centrally authorised products. At the time of writing, specific data regarding inspection findings relating to 80 inspections were available for analysis and inclusion in this report.

The type of companies inspected during the period is presented in the table below.

	Innovative Pharma	Generics	Other[1]
Number of MAHs inspected	25	32	24

Findings identified during inspections are graded as either critical, major or other, the definitions for which are available on the MHRA website:

A total of 19 critical, 219 major and 165 other findings were identified during this period.

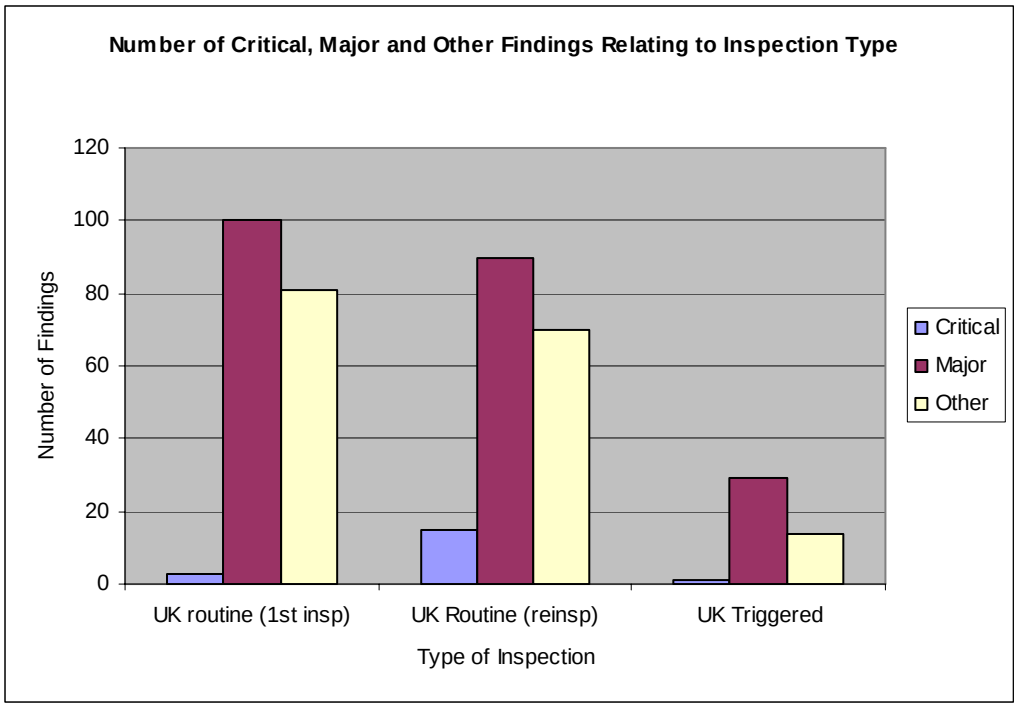
In terms of types of inspections, the following categories have been used:

- UK routine inspection (1st inspection) – 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.

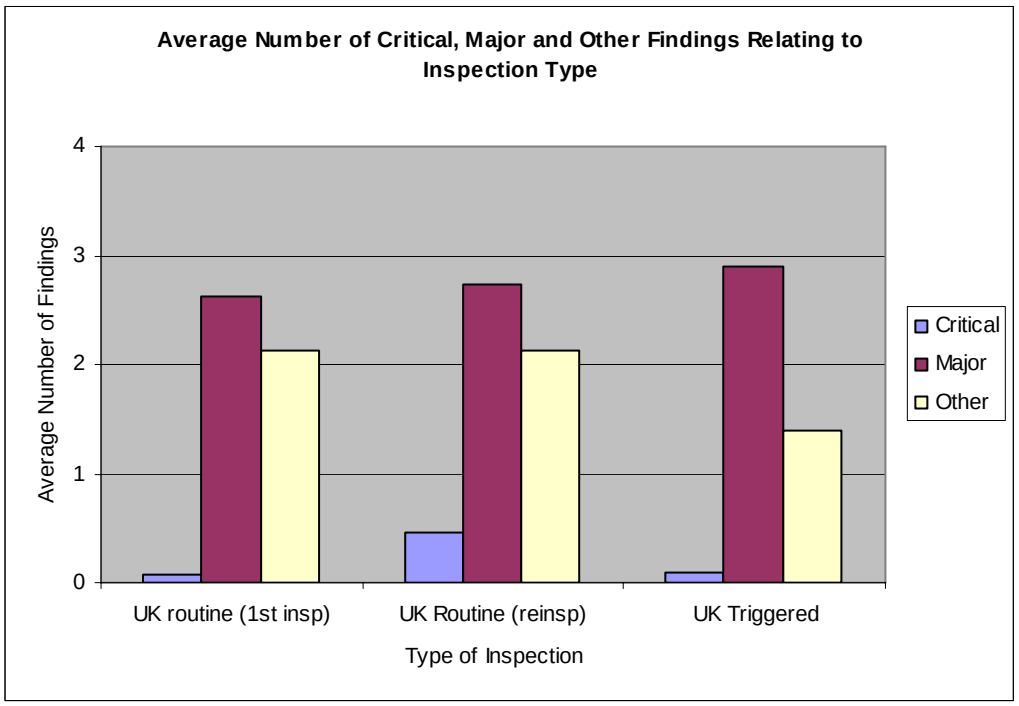
[1] Companies included in 'other' category include for example those marketing mature/established, orphan, niche or herbal products.

Type of inspection

A breakdown of the number of critical, major and other findings for each type of inspection is shown below:

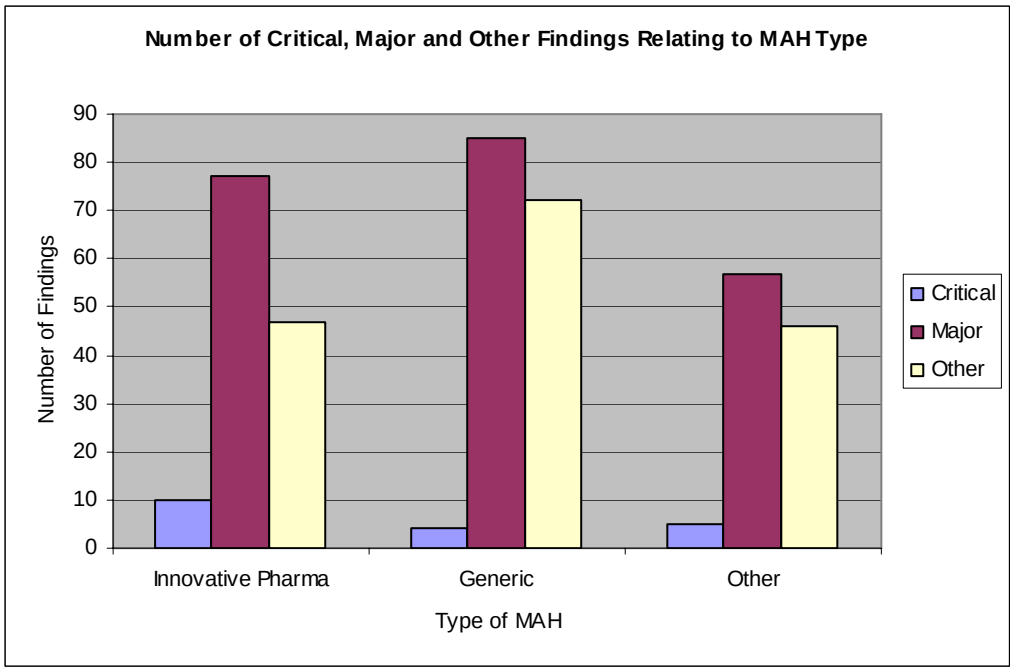


The information shown above can also be represented as the average number of findings for each type of inspection.

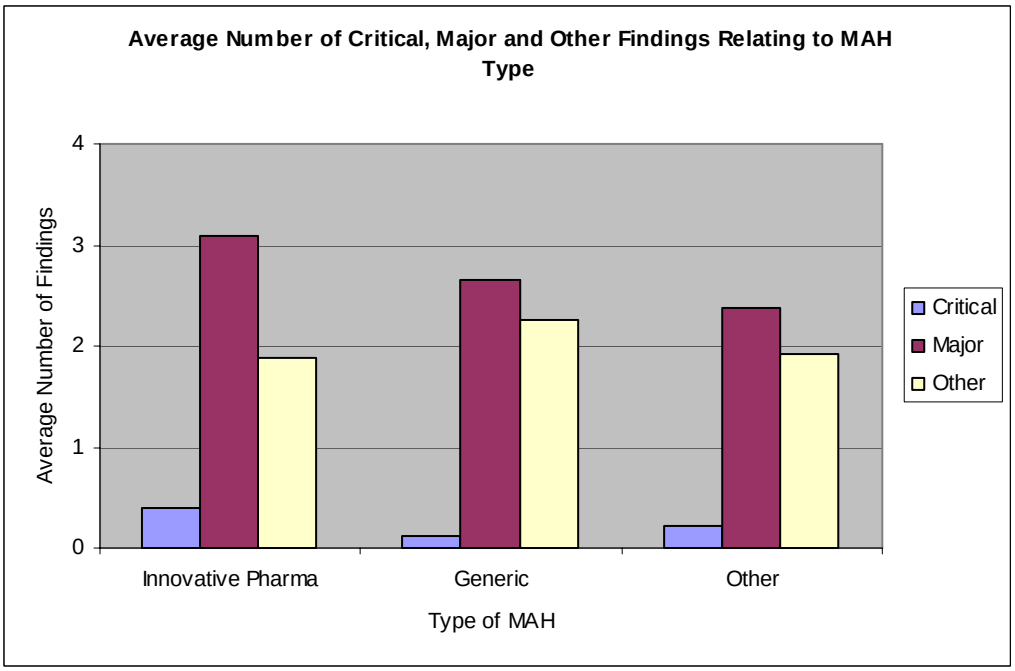


Type of MAH

A breakdown of the number of each grading of finding for each type of MAH is given below:



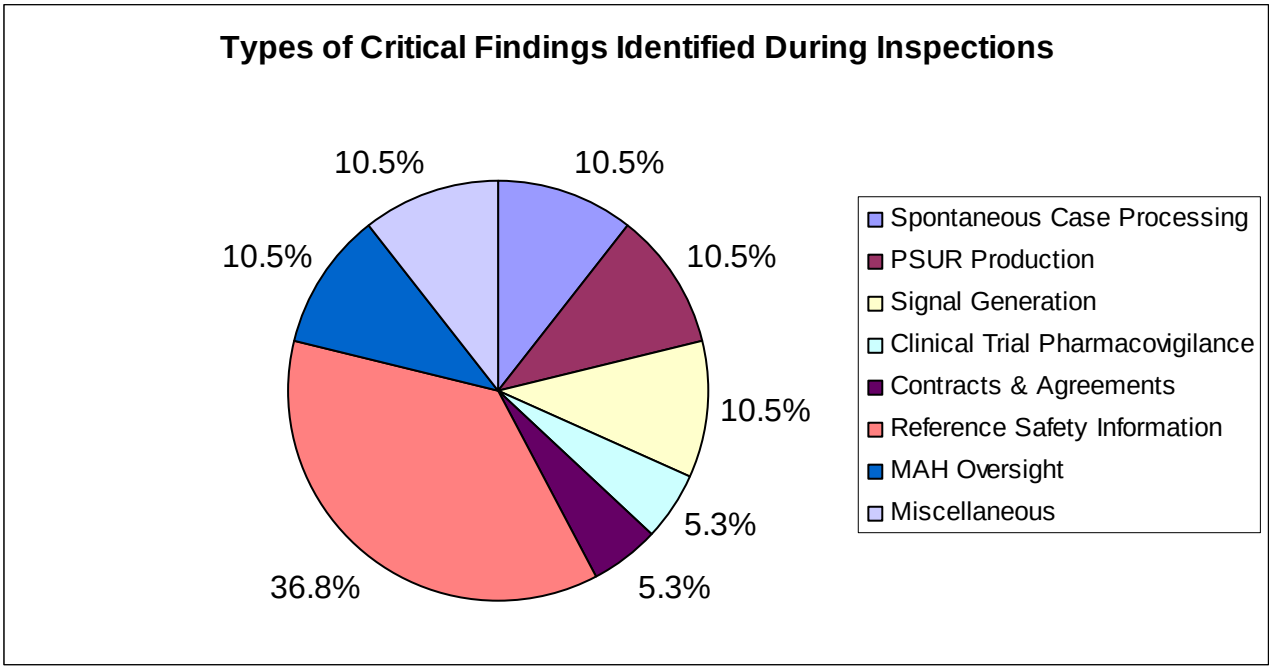
Similarly, this can be represented as the average number of findings for each type of MAH:



Critical findings

As stated previously, there were a total of 19 critical findings during this period, identified during 14 of the 80 total inspections that were performed.

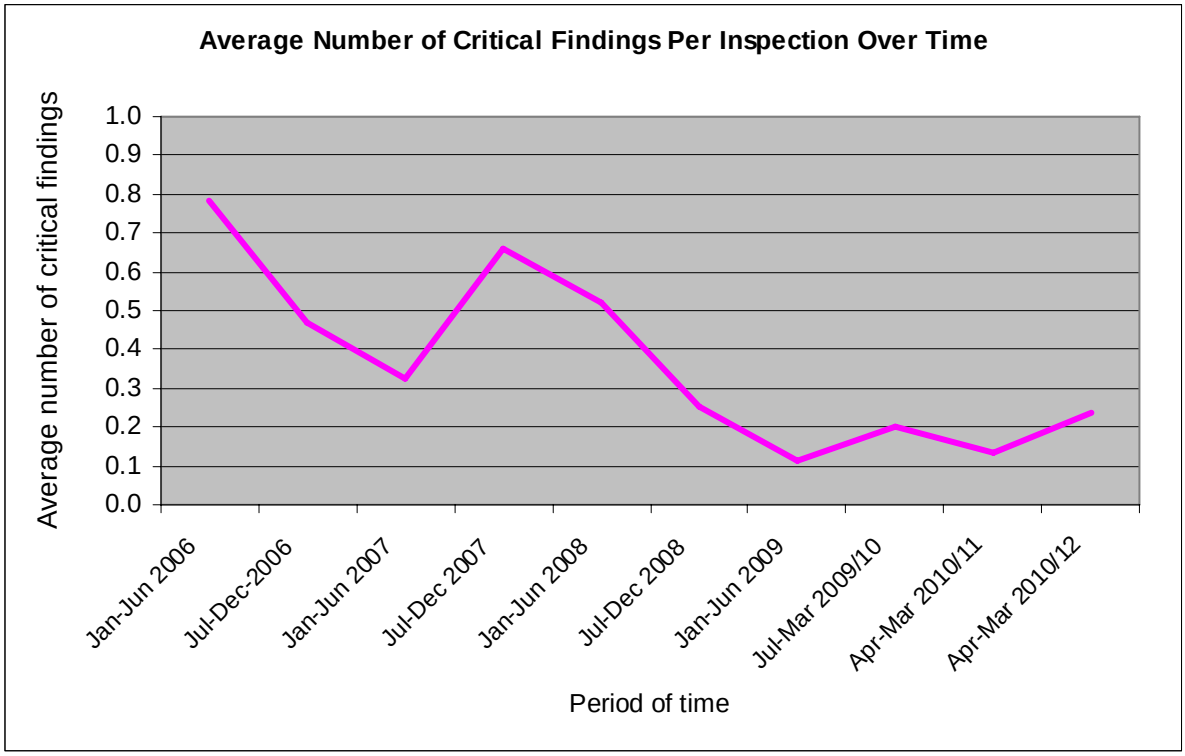
The breakdown of critical findings by type for the current period is given below. The miscellaneous finding related to management of non-interventional programmes (including patient support programmes and market research).



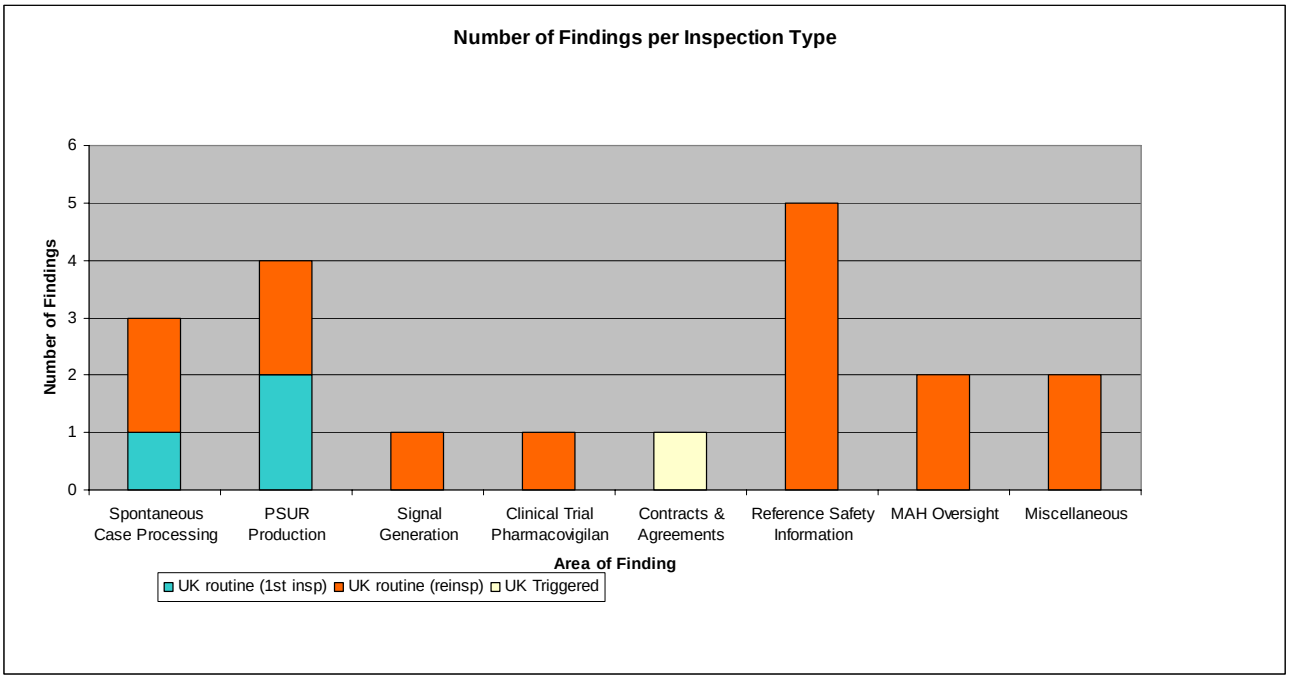
It can be seen that the majority of critical findings related to control and maintenance of reference safety information (such as summaries or product characteristics (SPCs), patient information leaflets (PILs), investigator brochures, company core safety information).

There were no critical findings relating to overall system failures, which were seen more frequently in the first few years following implementation of the statutory programme of pharmacovigilance inspections. However, critical findings relating to MAH oversight have features similar to overall system failures, in that typically the deficiencies relating to MAH oversight encompass multiple aspects of the system e.g. collection and collation of data, contracts and agreements, procedural documentation, training, CAPA management.

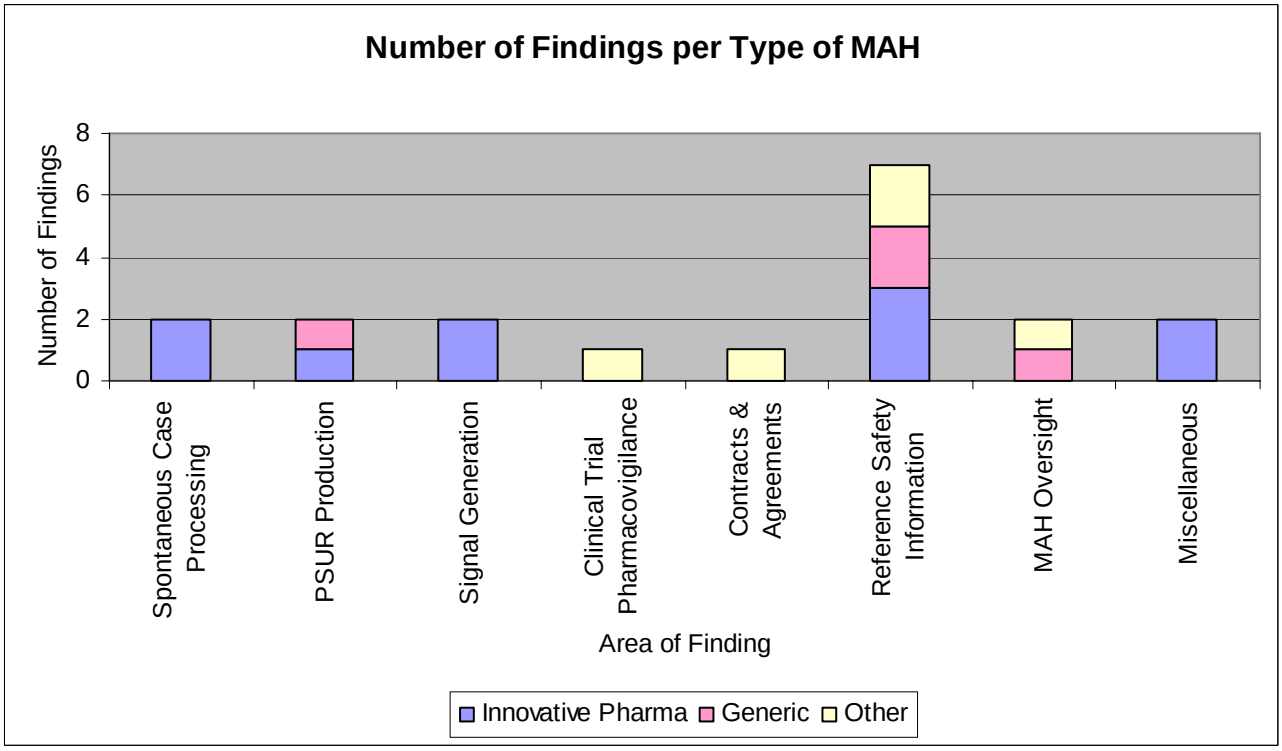
The graph below shows that over time, the average number of critical findings per inspection has generally decreased since Jul-Dec 2007 but has started to rise again throughout the current period, having declined the previous year.



The graph below illustrates the areas in which critical findings were identified compared to the different types of inspection:



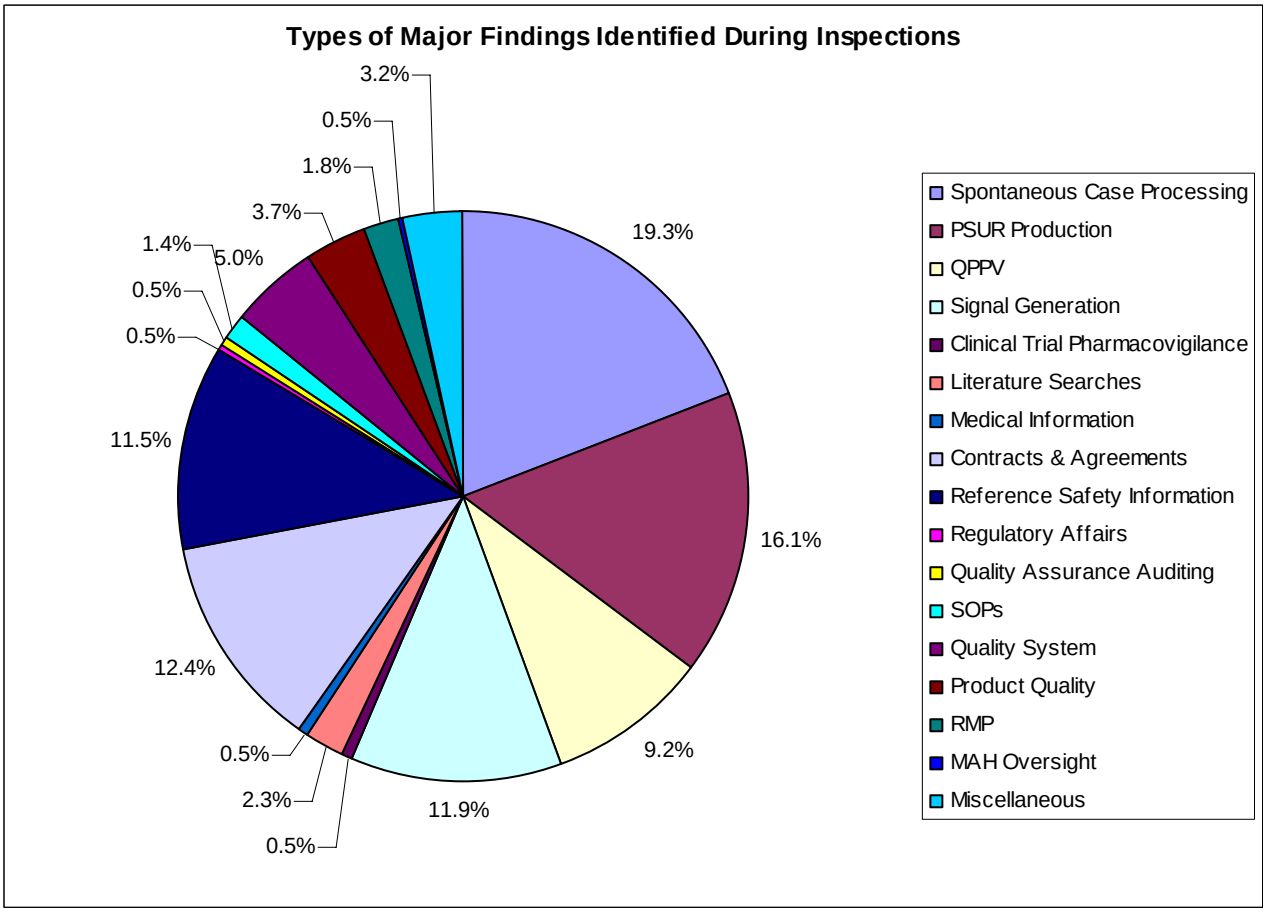
The graph below illustrates the areas in which critical findings were identified compared to the different types of MAHs:



Major Findings

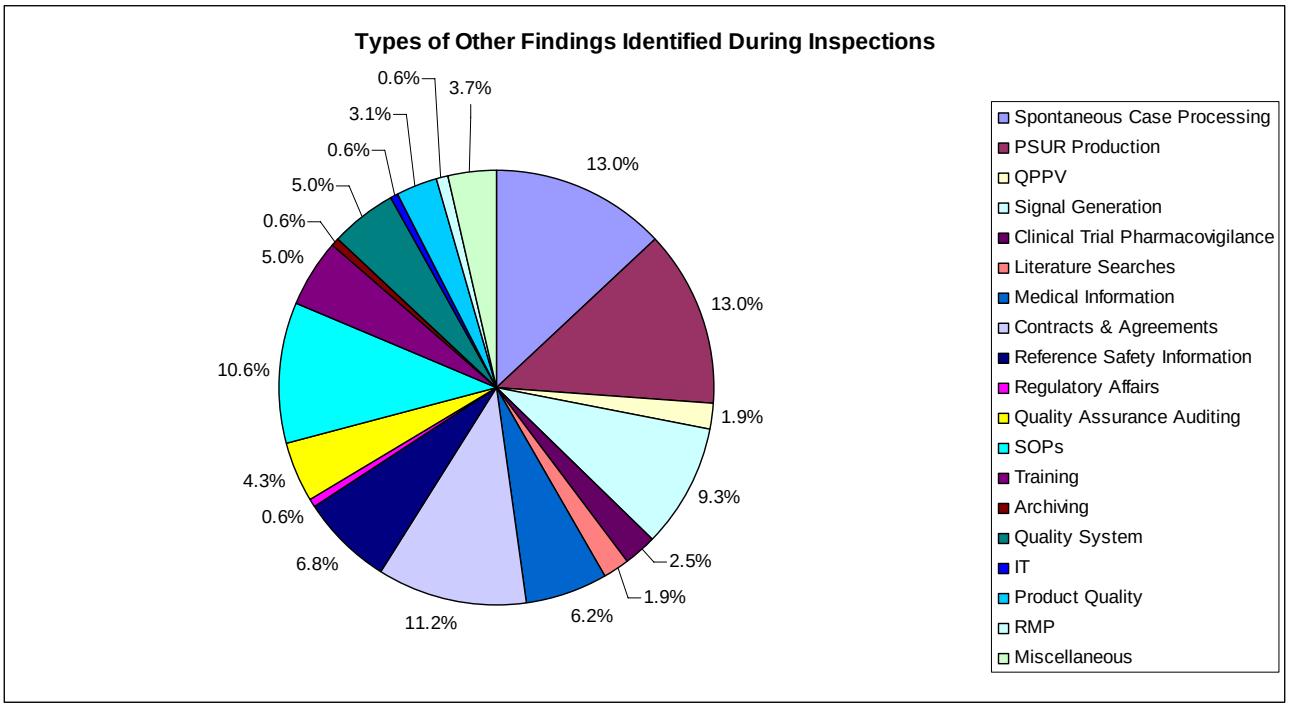
There were a total of 219 major findings identified during the period. Although major findings were identified in 17 different categories, spontaneous case processing, PSUR production, ongoing safety evaluation (signal generation), contracts and agreements and reference safety information accounted for 71.2% of the total number.

Miscellaneous findings included issues such as management of pharmacovigilance data (including that from patient support programmes), inability to report cases electronically, failure to comply with corrective and preventative actions arising from inspections and deficiencies in follow-up of pregnancy cases.

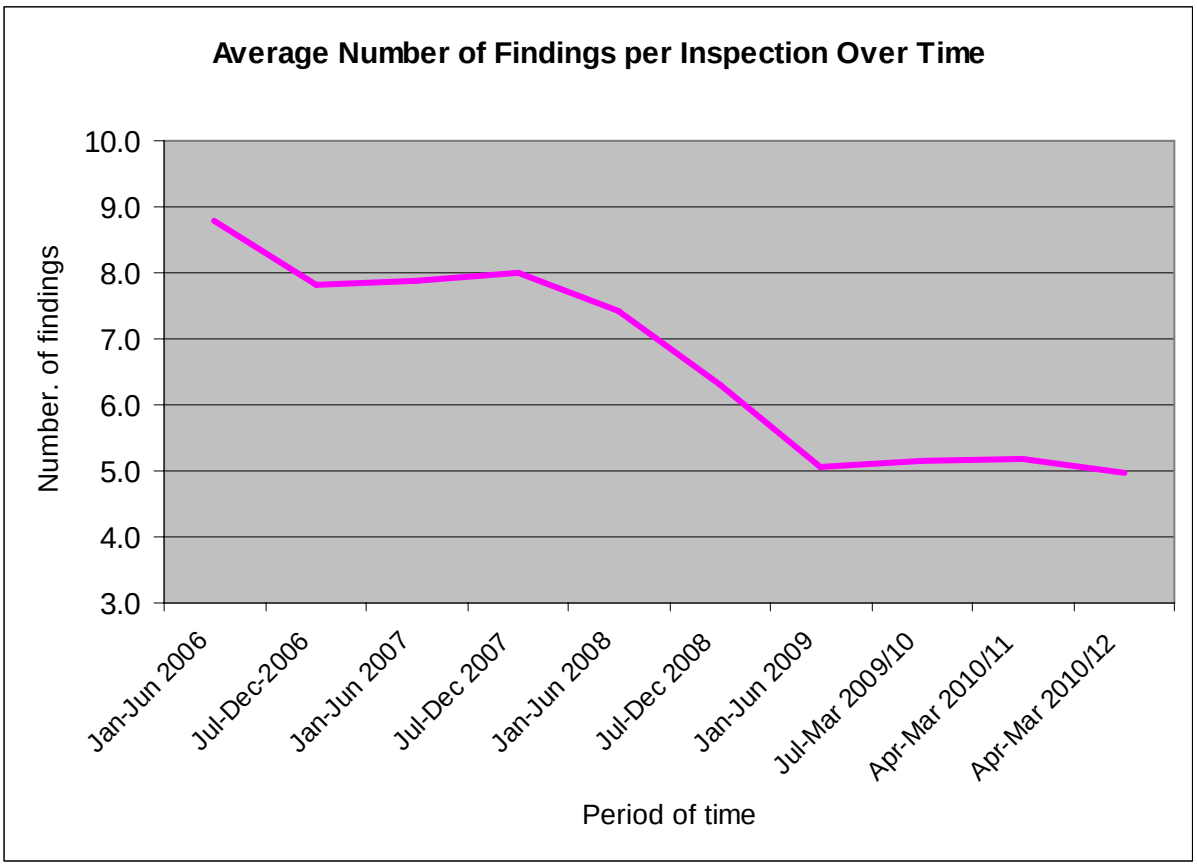


Other findings

165 findings were graded as other during this period and findings were identified in all areas of inspections. A breakdown of the types of other findings is presented below:



The graph below shows the average number of total findings (critical, major and other) identified per inspection.



Conclusions

During the current reporting period average number of findings has decreased slightly compared to the previous reporting period. Overall, the average number of findings identified at inspections has decreased significantly since 2006.

Of the nineteen critical findings identified during the period, three were identified during inspections of MAHs who have not previously undergone an MHRA pharmacovigilance inspection compared to fifteen from routine re-inspections and one from a triggered inspection. Ten of the critical findings were identified during inspections of MAHs classified as Innovative compared to four during inspections of MAHs classified as Generic and five classified as Other.

As per previous inspection reports, a large number of critical and major findings were identified in the areas of case processing, PSURs, ongoing safety evaluation (signal generation), contracts and agreements and reference safety information. Findings relating to reference safety information include failure of MAHs to ensure that the safety information in SPCs and PILs is up-to-date, that safety variations are submitted in a timely manner and that approved product information is made available to manufacturing sites; in many cases

these findings have led to significant post inspection actions. Additional areas in which findings are being reported more frequently than previously are handling of data from patient support programmes and MAH oversight.

Of note, with the implementation of the new pharmacovigilance legislation in July 2012, revisions to the manner in which MHRA categorises and groups findings may occur in the future. Information about the new pharmacovigilance legislation is available on the MHRA website:
http://www.mhra.gov.uk/Howweregulate/Medicines/Pharmacovigilancelegislation/index.htm