Report to the European Commission on Pharmacovigilance audits carried out in The Medicines and Healthcare products Regulatory Agency of the United Kingdom: September 2019 to September 2021

1. INTRODUCTION

This report provides an overview of the audit activities conducted from September 2019 to September 2021 by the internal auditors of the Medicines and Healthcare products Regulatory Agency (MHRA) and the Quality Standards Manager of the MHRA's Vigilance and Risk Management of Medicines Division (VRMM).

2. DEVELOPMENTS IN THE PHARMACOVIGILANCE SYSTEM SINCE THE LAST REPORT

There are significant changes to the pharmacovigilance system since the last report with respect to EU exit, responding to the coronavirus pandemic and the MHRA governance review.

EU Exit

The United Kingdom (UK) left the European Union (EU) on 31st January 2020 and entered into a transition period immediately thereafter, which ended on 31st December 2020. Under the terms of the EU Withdrawal Agreement, the provisions of European Union law concerning medicines regulation continued to apply in the UK during the transition period. Preparations for the UK exit from the EU required new legislation, new regulatory processes, the development of IT systems and publishing detailed guidance on the regulatory framework for the conduct of pharmacovigilance by the licensing authority and UK marketing authorisation holders following the transition period.

The MHRA retains responsibility for pharmacovigilance across the UK from 1st January 2021. There are differences in the requirements for medicinal products placed on the market in the UK with respect to Great Britain (GB) and Northern Ireland (NI). From 1st January 2021 under the terms of the Protocol on Ireland/Northern Ireland, medicinal products licensed for sale or supply in Northern Ireland must continue to conform to applicable European Union law.

The Human Medicines Regulations 2012 (HMR) as amended requires that the licensing authority must perform a regular audit of its pharmacovigilance system relating to medicinal products for sale or supply in Great Britain and in Northern Ireland. The results of the pharmacovigilance audits for medicinal products for sale or supply in Northern Ireland must be reported to the European Commission no later than 21st September 2021 and every two years thereafter.

The EU guidelines on good pharmacovigilance practices (GVP) modules remain in force however a statutory guidance note on the 'exceptions and modifications to the EU guidance on good pharmacovigilance practices that apply to UK marketing authorisation holders and the licensing authority' has been published.

Responding to the coronavirus pandemic

The MHRA has played a key role in tackling the coronavirus pandemic, approving the emergency-use authorisations and marketing authorisations for COVID-19 vaccines and therapeutics. Changes in regulatory requirements and comprehensive planning activities were undertaken in relation to the COVID-19 vaccination campaign, including technology improvements and resources.

Following government advice in 2020, there was a move under national lockdown from a predominately office-based to a predominately home-based working model. The VRMM

Division has operated the principles of its business continuity plan since December 2020, due to the impact of the COVID-19 pandemic and vaccine surveillance activities. The GPvP Inspectorate has implemented a risk-based strategy for inspections of holders of emergency-use authorisations/ marketing authorisations for COVID-19 vaccines and therapeutics.

Governance review

The MHRA governance structure was reviewed in 2020 to make recommendations for changes to the existing governance structures to improve decision-making, organisational management, control and accountability across the organisation. The MHRA has made changes to improve the Board, Executive and operational level governance and operational control. The Unitary Board comprising the Chair, Non-Executive Directors, Chief Executive and Chief Officers is primarily responsible for advising on strategic development and providing assurance on the MHRA's performance in the delivery of its statutory duties. The Executive Committee (ExCo) comprising the Chief Executive and Chief Officers takes overall responsibility for the delivery of the objectives including all financial, policy, operational and resource management issues. The ExCo are also responsible for ensuring that the requirements of the quality management system (QMS) are implemented and maintained.

3. INTERNAL AUDIT ACTIVITY FOR THE PERIOD UNDER REVIEW

3.1 RISK ASSESSMENT

A risk assessment exercise was conducted in order to determine the pharmacovigilance system audit priorities for the period under review. The final audit strategy was prepared based on this risk assessment and was approved by the MHRA Chief Executive Officer (CEO) on 27th July 2021.

The following audits of the pharmacovigilance system were conducted during the period under review however the final audit reports have not been issued:

- VRMM 02 2021 on Collection, management and reporting of suspected adverse reactions to medicinal products and communicating information on suspected adverse reactions.
- VRMM 03 2021 on Safety communication.
- IES 2021 10 on Suspected falsified/counterfeit medicines.

The process for 'risk management systems combined with tools, educational materials and effectiveness measurement for risk minimisation' was assigned a medium risk rating in 2021 by the MHRA. The internal audit VRMM 01 2021 on 'risk management systems combined with tools, educational materials and effectiveness measurement for risk minimisation' was scheduled to take place in May 2021. The VRMM Senior Management Team paused the internal audit VRMM 01 2021 as the Division is operating in Business Continuity mode due to the COVID-19 surveillance activities.

3.2 SUMMARY OF THE AUDITS FOR THE PERIOD UNDER REVIEW

3.2.1 AUDIT ASSIGNMENTS FOR THE PERIOD UNDER REVIEW

All audits listed were performed in line with the guidance provided in the GVP Module IV Pharmacovigilance audits.

Audit No	Audit title	Date of audit report
VRMM 06 2019	Safety communication	4th October 2019
VRMM 10 2019	Assessment of periodic safety update reports	24th January 2020
VRMM 12 2019	Assessment of centralised, mutual recognition and national renewal applications	23rd April 2020
VRMM 01 2020	Signal management	30th June 2020
VRMM 02 2020	Management, reporting and communicating information on suspected adverse reactions to medicinal products	7th August 2020
VRMM 03 2020	Safety communication	15th July 2020
VRMM 04 2020	Post authorisation safety studies	1st December 2020
VRMM 05 2020	Signal management	12th May 2021
VRMM 04 2021	Additional monitoring	9th July 2021

3.2.2 SAFETY COMMUNICATION VRMM 06 2019

3.2.2.1 Objective and scope

To assess compliance with the documented pharmacovigilance system, applicable legislation and GVP guidelines, the MHRA quality management system and ISO 9001:2015.

The scope of the audit is to ensure that safety communication activities operate in accordance with procedures.

3.2.2.2 Audit body

The audit was conducted by an internal auditor with the support of the Quality Standards Manager for the Vigilance and Risk Management of Medicines Division.

3.2.2.3 Opinion

Processes and activities were compliant with the documented pharmacovigilance system, applicable legislation and GVP guidelines, the MHRA quality management system and ISO 9001:2015. No non-conformities were identified, however there were some suggestions to improve the system.

3.2.3 ASSESSMENT OF PERIODIC SAFETY UPDATE REPORTS VRMM 10 2019

3.2.3.1 Objective and scope

To assess compliance with the documented pharmacovigilance system, applicable legislation and GVP guidelines, the MHRA quality management system and ISO 9001:2015.

The scope of the audit is to ensure that the assessment of periodic safety update reports operate in accordance with procedures.

3.2.3.2 Audit body

The audit was conducted by an internal auditor with the support of the Quality Standards Manager for the Vigilance and Risk Management of Medicines Division.

3.2.3.3 Opinion

Processes and activities were compliant with the documented pharmacovigilance system, applicable legislation and GVP guidelines, the MHRA quality management system and ISO 9001:2015. There was one minor non-conformity. Corrective action has been satisfactorily completed.

3.2.4 ASSESSMENT OF CENTRALISED, MUTUAL RECOGNITION AND NATIONAL RENEWAL APPLICATIONS VRMM 12 2019

3.2.4.1 Objective and scope

To assess compliance with the documented pharmacovigilance system, applicable legislation and GVP guidelines, the MHRA quality management system and ISO 9001:2015.

The scope of the audit is to ensure that the assessment of renewal applications operate in accordance with procedures.

3.2.4.2 Audit body

The audit was conducted by an internal auditor with the support of the Quality Standards Manager for the Vigilance and Risk Management of Medicines Division.

3.2.4.3 Opinion

Processes and activities were compliant with the documented pharmacovigilance system, applicable legislation and GVP guidelines, the MHRA quality management system and ISO 9001:2015. No non-conformities were identified, however there were some suggestions for improvement.

3.2.5 SIGNAL MANAGEMENT VRMM 01 2020

3.2.5.1 Objective and scope

To assess compliance with the documented pharmacovigilance system, applicable legislation and GVP guidelines, the MHRA quality management system and ISO 9001:2015.

The scope of the audit is to ensure that signal management activities operate in accordance with procedures.

3.2.5.2 Audit body

The audit was conducted by an internal auditor with the support of the Quality Standards Manager for the Vigilance and Risk Management of Medicines Division.

3.2.5.3 Opinion

Processes and activities were compliant with the documented pharmacovigilance system, applicable legislation and GVP guidelines, the MHRA quality management system and ISO 9001:2015. No non-conformities were identified, however there were some suggestions for improvement.

3.2.6 MANAGEMENT, REPORTING AND COMMUNICATING INFORMATION ON SUSPECTED ADVERSE REACTIONS TO MEDICINAL PRODUCTS VRMM 02 2020

3.2.6.1 Objective and scope

To assess compliance with the documented pharmacovigilance system, applicable legislation and GVP guidelines, the MHRA quality management system and ISO 9001:2015.

The scope of the audit is to ensure that management, reporting and communicating information on suspected adverse reactions to medicinal products operate in accordance with procedures.

3.2.6.2 Audit body

The audit was conducted by an internal auditor with the support of the Quality Standards Manager for the Vigilance and Risk Management of Medicines Division.

3.2.6.3 Opinion

Processes and activities were compliant with the documented pharmacovigilance system, applicable legislation and GVP guidelines, the MHRA quality management system and ISO 9001:2015. No non-conformities were identified, however there were some suggestions for improvement.

3.2.7 SAFETY COMMUNICATION VRMM 03 2020

3.2.7.1 Objective and scope

To assess compliance with the documented pharmacovigilance system, applicable legislation and GVP guidelines, the MHRA quality management system and ISO 9001:2015.

The scope of the audit is to ensure that safety communication activities operate in accordance with procedures.

3.2.7.2 Audit body

The audit was conducted by an internal auditor with the support of the Quality Standards Manager for the Vigilance and Risk Management of Medicines Division.

3.2.7.3 Opinion

Processes and activities were compliant with the documented pharmacovigilance system, applicable legislation and GVP guidelines, the MHRA quality management system and ISO 9001:2015. No non-conformities were identified.

3.2.8 POST AUTHORISATION SAFETY STUDIES VRMM 04 2020

3.2.8.1 Objective and scope

To assess compliance with the documented pharmacovigilance system, applicable legislation and GVP guidelines, the MHRA quality management system and ISO 9001:2015.

The scope of the audit is to ensure that post authorisation safety studies activities operate in accordance with procedures.

3.2.8.2 Audit body

The audit was conducted by an internal auditor with the support of the Quality Standards Manager for the Vigilance and Risk Management of Medicines Division.

3.2.8.3 Opinion

Processes and activities were compliant with the documented pharmacovigilance system, applicable legislation and GVP guidelines, the MHRA quality management system and ISO 9001:2015. No non-conformities were identified. A preventative action was raised.

3.2.9 SIGNAL MANAGEMENT VRMM 05 2020

3.2.9.1 Objective and scope

To assess compliance with the documented pharmacovigilance system, applicable legislation and GVP guidelines, the MHRA quality management system and ISO 9001:2015.

The scope of the audit is to ensure that signal management activities operate in accordance with procedures.

3.2.9.2 Audit body

The audit was conducted by an internal auditor with the support of the Quality Standards Manager for the Vigilance and Risk Management of Medicines Division.

3.2.9.3 Opinion

Processes and activities were compliant with the documented pharmacovigilance system, applicable legislation and GVP guidelines, the MHRA quality management system and ISO 9001:2015. Two minor non-conformities were identified and there

were some suggestions for improvement. Corrective action has been satisfactorily completed.

3.2.10 ADDITIONAL MONITORING VRMM 04 2021

3.2.10.1 Objective and scope

To assess compliance with the documented pharmacovigilance system, applicable legislation and GVP guidelines, the MHRA quality management system and ISO 9001:2015.

The scope of the audit is to ensure that additional monitoring activities operate in accordance with procedures.

3.2.10.2 Audit body

The audit was conducted by an internal auditor with the support of the Quality Standards Manager for the Vigilance and Risk Management of Medicines Division.

3.2.10.3 Opinion

Processes and activities were compliant with the documented pharmacovigilance system, applicable legislation and GVP guidelines, the MHRA quality management system and ISO 9001:2015. One minor non-conformity was identified and there were some suggestions for improvement.

3.2.2.4 Audit outcomes and actions

There are no audit outcomes which were reported and rated as ‘Critical’ and as ‘Major’.

Audit No	Find No	Audit outcomes description	Grading	Action short description	Action end date	Comments on status of actions	Type of follow-up required
Not applicable							

3.2.2.5 Summary of action plan for current reporting period

Not applicable.

For action from audit outcome graded as:	Total	Number implemented	Number not implemented	
			Not started	In progress
Critical	Not applicable			
Major	Not applicable			
Total	Not applicable			

4. FOLLOW-UP

4.1 SUMMARY OF ACTION PLANS FROM PRIOR BIENNIAL REPORTS

Not applicable.

For action from audit outcome graded as:	Total	Number implemented	Number not implemented	
			Not started	In progress
Critical	Not applicable			
Major	Not applicable			
Total	Not applicable			

4.2 OUTSTANDING ISSUES FROM PRIOR BIENNIAL REPORTS

There are no outstanding issues from prior biennial reports.

5. DECLARATION

The MHRA Chief Executive confirms that this report contains a complete account of all pharmacovigilance system audit activities performed in the period under review to fulfil the obligations of this organisation under Directive 2001/83/EC.

Jane M. Rawe

30 September 2021

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Head of the National Competent Authority **Date**