Medicines & Healthcare products Regulatory Agency

PHARMACOVIGILANCE INSPECTION REPORT

Pharmacovigilance System Name: Organon & Co

MHRA Inspection Number: Insp GPvP 25/36429846-0001

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Table of Contents

ABBREVIATIONS

ADR	Adverse Drug Reaction
AE	Adverse Event
CAPA	Corrective and Preventative Action
CCDS	Company Core Data Sheet
CHMP	Committee for Medicinal Products for Human Use
DCP	Decentralised Procedure
EMA	European Medicines Agency
EU	European Union
GVP	Good Vigilance Practice
HCP	Healthcare Professional
ICH	International Conference on Harmonisation
ICSR	Individual Case Safety Report
MAH	Marketing Authorisation Holder
MedDRA	Medical Dictionary for Regulatory Activities
MRP	Mutual Recognition Procedure
PIL	Patient Information Leaflet
PRAC	Pharmacovigilance Risk Assessment Committee
PSMF	Pharmacovigilance System Master File
PSUR	Periodic Safety Update Report
PV	Pharmacovigilance
PVA	Pharmacovigilance Agreements
QPPV	Qualified Person responsible for Pharmacovigilance
SDEA	Safety Data Exchange Agreement
SmPC	EU Summary of Product Characteristics
SOP	Standard Operating Procedure
UK	United Kingdom

SECTION A: INSPECTION REPORT SUMMARY

Inspection type:	Statutory National Inspection
System(s) inspected:	Organon Pharma (UK) Limited UK PSMF No: [redacted]
Site(s) of inspection:	Organon Pharma (UK) Limited, 145 City Road, London, EC1V 1AZ, United Kingdom
Main site contact:	[redacted] Associate Director Research & Development Quality & Compliance Operations [redacted]
Date(s) of inspection:	11-14 March 2025, onsite, with one remote inspector.
Lead Inspector:	[redacted]
Accompanying Inspector(s):	[redacted] (MHRA, remote), [redacted] (MHRA, remote observer), [redacted] Health Canada, observer), [redacted] (URPL, observer)
Previous inspection date(s):	16-19 February 2004
Purpose of inspection:	Inspection of pharmacovigilance systems to review compliance with UK and requirements.
Products selected to provide system examples:	As part of the general systems review, specific ADR reports were examined for [redacted] and [redacted]
Name and location of UK QPPV:	[redacted] Email [redacted]
Global PV database (in use at the time of the inspection):	[redacted] released on 03-Nov-2024, version [redacted] commercial off the shelf product, the [redacted] which is based on [redacted] platform).
Key service provider(s):	Pharmacovigilance services provided by TCS, IQVIA, PPD and RxLogix. Medical information services provided by ProPharma in the UK.
Inspection finding summary:	3 Major findings 8 Minor findings
Date of first issue of report to MAH:	22 May 2025
Deadline for submission of responses by MAH:	27 June 2025 Follow-up 1: 06 October 2025
Date(s) of receipt of responses from MAH:	27 June 2025 Follow-up 1: 04 October 2025
Date of final version of report:	31 October 2025
Report author:	[redacted] GPvP Inspector [redacted] Head of GPvP

SECTION B: BACKGROUND AND SCOPE

B.1 Background information

Organon & Co., Inc. (hereafter 'Organon') was selected for routine inspection as part of the MHRA's statutory, national pharmacovigilance inspection programme. The purpose of the inspection was to review compliance with currently applicable UK and pharmacovigilance regulations and guidelines. In particular, reference was made to The Human Medicines Regulations 2012 as amended, Commission Implementing Regulation (EU) No 520/2012 and the EU good pharmacovigilance practices (GVP) Modules as modified by the guidance note 'Exceptions and modifications to the EU GVP that apply to UK MAHs and the licensing authority'.

A list of reference texts is provided at Appendix I.

Organon is a global specialty pharma company focusing on Women's Health medicines and medical devices as well as established brands. The organisation is headquartered in Jersey City, USA and has local affiliates (local commercial organisations) in 62 countries and collaborations in more than 80 countries through business partner commercial agreements. Organon Pharma (UK) Limited was the MAH of UK licences under the inspected pharmacovigilance system. At the time of the inspection, Organon held [redacted] UK product licences, [redacted] of which were classified as a Category 1 product under the Windsor Framework.

Organon was spun out of Merck & Co. (MSD) and became a publicly traded company on 3 June 2021. The global safety database was [redacted] based on the [redacted] went live on 23 February 2021 with the most recent version of [redacted], version [redacted] being released on 03 November 2024.

Third party vendors were involved in the following pharmacovigilance activities:

- TCS: data entry of cases that meet the criteria for entry into [redacted] Medical Review; global literature search; aggregate safety report writing.
- IQVIA: monitors Company owned social media and third-party social media; ICSR processing in Japan; provides patient exposure data for aggregate reports.
- PPD: performs follow-up activities for all US cases; intake of adverse events and product quality complaint information in the US.
- ProPharma Group: medical information services in UK/Ireland.
- Freyr: management of the company core data sheet and local label approvals globally.
- RxLogix: development, configuration and operationalisation of safety applications including [redacted] and [redacted]
- Tepsivo: local and global literature screening.

B.2 Scope of the inspection

The inspection included a review of the global pharmacovigilance systems and was performed at Organon Pharma (UK) Limited offices in London, UK, and remotely via videoconference for one inspector. Personnel from Organon attended the London site in order to participate in the inspection. Additionally, personnel from Organon and vendors participated via remote videoconference.

The inspection was performed using interviews and document review (including outputs from the global safety database and listings of medical information enquiries and product

complaints). The systems reviewed during the inspection are highlighted in the Pharmacovigilance Inspection Plan (attached as Appendix II).

PSURs and Quality Management Systems were not reviewed in detail and it is recommended that these areas are subject to closer review during a subsequent pharmacovigilance inspection.

B.3 Documents submitted prior to the inspection

The company submitted a PSMF ([redacted] version [redacted] dated 24 January 2024) to assist with inspection planning and preparation. Specific additional documents were also requested by the inspection team and provided by the company prior to the inspection. The details of the pre-inspection document requests is contained within the pre-inspection list of document requests on the inspection[redacted] document request tracker.

B.4 Conduct of the inspection

In general, the inspection was performed in accordance with the Inspection Plan. Amendments to the Inspection Plan that occurred during the inspection are highlighted using italic text in Appendix II.

The inspection was not completed during the onsite days (11-14 March 2025) and an interim closing meeting was held at the Organon Pharma (UK) Limited offices in London, UK, on 14 March 2025 to summarise the inspection status and to provide preliminary feedback regarding the inspection findings. The inspection was concluded via office-based document review, and a close-out email was sent to the company on 31 March 2025 summarising an additional major finding.

A list of the personnel who attended the closing meeting is contained in the Closing Meeting Attendance Record, which will be archived together with the inspection notes, a list of the documents requested during the inspection and the inspection report.

SECTION C: INSPECTION FINDINGS

C.1 Summary of significant changes and action taken since the last inspection

The Organon PV system was independently established at the legal separation of Organon from Merck & Co. (MSD) on 2 June 2021. More recently, the following changes had occurred:

- as of 01 February 2025, [redacted] was appointed as the UK QPPV
- Tepsivo was the new vendor for literature screening, replacing the previous vendors (Freyr and Vitrana) since 1 November 2024 and 1 January 2025, for local and global literature screening, respectively.
- Organon had initiated in September 2023 work to improve the audit and risk assessment process. Key milestones included:
    - September 2023: Initiation of the project and engagement of an external consultant to assess the existing audit management process.
    - June 2024: The risk assessment was completed, incorporating initial feedback from the consultant. A comprehensive audit plan for the entire year of 2024 was issued.
    - June – December 2024: Continuous improvements were made to address identified gaps in the assessment process. New risk factors were introduced to ensure better granulation of the audit targets, and the audit universe was redefined. By January 2025, the revised methodology was documented in work instruction [redacted] *Risk Methodologies for Audit Planning*, which became effective on 07 March 2025.

At the time of inspection conduct, Organon was undergoing a restructuring process whereby the Affiliate Pharmacovigilance, which was within the Global Regulatory Affairs department (RA/aPV group), would be integrated into the Global Pharmacovigilance (GPV) department. The Company was working to finalize the organisational design for these functions by the end of Q1 2025.

C.2 Definitions of inspection finding gradings

Critical (CR): 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 (MA): 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 (MI): a deficiency in pharmacovigilance systems, practices or processes that would not be expected to adversely affect the rights, safety or well-being of patients.

Comment: the observations might lead to suggestions on how to improve quality or reduce the potential for a deviation to occur in the future.

The factual matter contained in the Inspection Report relates only to those things that the inspection team saw and heard during the inspection process. The inspection report is not to be taken as implying a satisfactory state of affairs in documentation, premises, equipment, personnel or procedures not examined during the inspection.

Findings from any inspection that covers Category 2 products which are graded as critical or major will be shared with the EMA, EU competent authorities and the European Commission.

C.3 Guidance for responding to inspection findings

Responses to inspection findings should be clear, concise and include proposed actions to address both the identified deficiency and the root cause of the deficiency. Consideration should also be given to identifying and preventing other potential similar deficiencies within the pharmacovigilance system.

Responses should be entered directly into the table(s) in section C.4. The following text is intended as guidance when considering the information that should be entered into each of the fields within the table(s). 'Not applicable' should be entered into the relevant field if the requested information is not appropriate for the finding in question.

Root Cause Analysis Identify the root cause(s) which, if adequately addressed, will prevent recurrence of the deficiency. There may be more than one root cause for any given deficiency.
Further Assessment Assess the extent to which the deficiency exists within the pharmacovigilance system and what impact it may have for all products. Where applicable, describe what further assessment has been performed or may be required to fully evaluate the impact of the deficiency e.g. retrospective analysis of data may be required to fully assess the impact.
Corrective Action(s) Detail the action(s) taken / proposed to correct the identified deficiency.
Preventative Action(s) Detail the action(s) taken / proposed to eliminate the root cause of the deficiency, in order to prevent recurrence. Action(s) to identify and prevent other potential similar deficiencies should also be considered.
Deliverable(s) Detail the specific outputs from the proposed / completed corrective and preventative action(s). For example, updated procedure/work instruction, record of re-training, IT solution.
Due Date(s) Specify the actual / proposed date(s) for completion of each action. Indicate when an action is completed.

Further information relating to inspection responses can be found under 'Inspection outcomes' at: https://www.gov.uk/guidance/good-pharmacovigilance-practice-gpvp

C.4 Inspection findings

C.4.1 Critical findings

No critical findings were identified from the review of pharmacovigilance processes, procedures and documents performed during this inspection.

C.4.2 Major findings

MA.1 Maintenance of Reference Safety Information

Requirements:

The Human Medicines Regulations 2012 (Statutory Instrument 2012 No. 1916), Part 5, regulation 76

The Human Medicines Regulations 2012 (Statutory Instrument 2012 No. 1916), Schedule 12A, Part 3, paragraph 11(1)(e)(f)(g)

Commission Implementing Regulation (EU) No. 520/2012, Article 11(1)(e)(f)(g)

Commission Regulation (EC) No 1234/2008, Article 24(1)

Guidelines on the details of the various categories of variations, on the operation of the procedures laid down in Chapters II, IIa, III and IV of Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products and on the documentation to be submitted pursuant to those procedures
"*2.1.1. Submission of Type IA notifications*
Minor variations of Type IA do not require prior examination by the authorities before they can be implemented by the holder."

Section 2.1.1 (Type IA notification), section 2.2.1 (Type IB notification), section 2.3.1 (Type II variation) outlining the requirement to provide mock-ups or specimens to reference member state and licensing authority for variations affecting the labelling and package leaflet.

MHRA published guidance: Medicines: packaging, labelling and patient information **(07 March 2024)**
"*For a single MA, all label, leaflet and label-leaflet mock-ups must be submitted as a set of consolidated PDF documents. For a single product there could be 3 documents containing either all of the labels, all of the leaflets or all of the label-leaflets for all pack sizes and presentations of the product.*"

CMDh/132/2009 (Rev.63, October 2024) Q&A - List for the submission of variations for human medicinal products according to Commission Regulation (EC) 1234/2008
"5.2. What is meant by "implementation" for Type IA variations?
Answer: […] For product information, it is when the Company internally approves the revised product information. The revised product information should normally be used in the next packaging run."

GVP Module I – Pharmacovigilance systems and their quality systems (as modified by the Exceptions and modifications to the EU guidance on good pharmacovigilance practices that apply to UK marketing authorisation holders and the licensing authority):
I.B.4. Overall quality objectives for pharmacovigilance
"*The overall quality objectives of a pharmacovigilance system are: […]*

- *promoting the safe and effective use of medicinal products, in particular through providing timely information about the safety of medicinal products to patients, healthcare professionals and the public;*"

When new information about the benefits and risks of a product become available it is often appropriate to make changes to reference safety information documents, such as SmPCs, and PILs, so that healthcare professionals and patients are able to use the medicinal product correctly on the basis of full and comprehensive information.

The following findings were noted in relation to control and maintenance of reference safety information:

Finding MA.1 a)

There was a delay of more than one year in updating the product information for [redacted] and [redacted] containing products with PRAC recommended wording regarding the signal of [redacted] with [redacted] due to the untimely management of safety variations.

The PRAC recommendation ([redacted] was published on [redacted] and required update of SmPC section 4.4 and 4.8, and PIL section 2 and 4 within two months of the publication date. Organon accordingly submitted a bulk Type IB variation[1] on 05 April 2023 for all UK-authorised products containing [redacted] and [redacted]. However, a 'Notification with Grounds' letter sent to the MAH from the MHRA on 20 July 2023 queried the changes made to the product information and the MAH was requested to provide the mock-ups that had been missing from the submitted variation documentation. Following this, there were delays of eight months by the MAH following the actions advised by the MHRA, which included but were not limited to the submission of mock-ups, and ultimately the variation was rejected by the MHRA on 18 June 2024.

The MAH resubmitted the update as Type IB variations on 02 July 2024, which was subsequently approved on [redacted] As a result of the incomplete data initially presented to the MHRA, and the delayed actions taken by the MAH, there were significant delays in updating the product information and making new safety information available to patients and healthcare professionals.

While five out of the eleven affected Organon product licences were not marketed at the time of the inspection ([redacted] and all licenses for [redacted] the remaining six licenses for [redacted] and [redacted] were, however, marketed.

This finding was graded as major as the affected products were prescription-only medicines and therefore made available to patients under the supervision of an HCP.

[1] Variations submitted on 05 April 2023: [redacted]

[2] Variations submitted on 02 July 2024: [redacted]

Root Cause Analysis
[redacted]

Further Assessment
[redacted]

Corrective Action(s)
[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

Preventative Action(s)
[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

[redacted]

Finding	**MA.1 b)**

Several examples of delayed implementation of updated of product information were identified. The impacted products were prescription-only medicines, and thereby only available to patients under HCP supervision.

For three products [redacted] product packs containing a superseded PIL version were QP certified for up to 3.5 months beyond the six-month timeframe to implement the updated PIL version.

i. [redacted]
The Type IB variation submitted via worksharing procedure [redacted] to update SmPC sections 4.3-4.5, and 4.8, and PIL sections 2 and 4 in line with the outcome of procedure [redacted] received Reference Member State (RMS) approval on [redacted]. The superseded PIL version should therefore not have been used after [redacted] however, the following two batches were QP-certified with superseded artwork:

Batch number	Expiry date	Batch size	QP certification date	Days > six-month implementation due date
[redacted]	[redacted]	[redacted]	[redacted]	7 days
				104 days

Changes to the product information related to the changed frequency of the ADR [redacted] in addition to changes to reflect the drug-drug interaction with [redacted]

ii. [redacted]
The Type IB variation submitted via worksharing procedure [redacted] to update SmPC section 4.4 and 4.8 and PIL sections 2 and 4 in line with the outcome of procedure [redacted] received RMS approval on [redacted]. Batch [redacted] containing the superseded PIL version was QP-certified on [redacted] 23 days beyond the six-month implementation

timeframe.

iii. [redacted]
The national Type IA_{IN} variation was submitted to the MHRA on 01 September 2023 to update section 4.8 of the SmPC and section 4 of the package leaflet in line with the outcome of procedure [redacted] Batch [redacted] containing the superseded PIL version was QP-certified on [redacted] 17 days beyond the expected six-month implementation timeframe.

As the impacted batch for [redacted] had not yet expired, the MAH was instructed after the inspection to contact the MHRA Defective Medicines Report Centre (DMRC) to determine any actions required. The MAH contacted DMRC on 03 April 2025.

Root Cause Analysis

[redacted]

Further Assessment

[redacted]

[redacted]

Corrective Action(s)
[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

Preventative Action(s)
[redacted]

Deliverable(s)	**Due Date(s)**
[redacted]	

Finding MA.1 c)
The updated product information (SmPC and PIL) for two products was uploaded to the electronic medicines compendium (emc) with delays of up to approximately five months. i. [redacted] – refer to finding MA.1 a) i. for full variation details The updated PIL and SmPC were uploaded to the emc on [redacted], almost five months beyond the expected implementation timeframe following RMS approval on [redacted] ii. [redacted] - refer to finding MA.1 a) iii. for full variation details The updated PIL and SmPC were uploaded to the emc on [redacted] 34 days beyond the expected implementation timeframe following submission of the Type IA_{IN} variation on [redacted]

Root Cause Analysis
[redacted]

Further Assessment
[redacted]

[redacted]

Corrective Action(s)
[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

Preventative Action(s)
[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

Finding MA.1 d)
The MAH applied an incorrect approach to the management of Type IA_{IN} variations submitted under as a UK national procedure. Organon explained during the inspection that the updated product information would be implemented and disseminated following 'approval' from the MHRA, which was also reflected in procedure [redacted] (revision [redacted] effective 15 March 2021). The SOP described the actions taken by the UK regulatory affairs team in relation to updated product information "upon receipt of MHRA or EMA approval". Findings MA.1 b), point iii and MA.1 c), point ii related to a safety update submitted via a Type IA_{IN} variation, and the described delays in implementing the updated product information may have been due to the incorrect calculation of day 0 for implementation based on Organon's document process. Type IA variations are known as 'do and tell'. In accordance with European and MHRA guidance, Type IA variations in relation to product information should be implemented (i.e. the company should internally approve the revised product information) prior to submission of the variation to the UK. The variation should be submitted within two weeks of the change being implemented. Therefore, implementation timeframes should commence no later than the date of submission of the variation to the MHRA. MHRA expectations include: • upload to the electronic medicines compendium (emc) and dissemination to relevant stakeholders within 10 days of the submission; • updated PIL to be included within the next batch production run, but no later than six months following the submission date. It is understood that some European Competent Authorities would like reference member state (RMS) approval to be given prior to implementation, therefore for products under EU MRP, DCP or worksharing processes, it is acceptable to the MHRA if implementation timeframes begin from RMS approval date.
Root Cause Analysis
[redacted]
Further Assessment
[redacted]

[redacted]

Corrective Action(s)
[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

Preventative Action(s)
[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

MA.2 Management and Reporting of Adverse Reactions

Requirements:

The Human Medicines Regulations 2012 (Statutory Instrument 2012 No. 1916), Schedule 12A, Part 6, Paragraph 20(1), (2), (4)(d)(e)(n)

Commission Implementing Regulation (EU) No. 520/2012, Chapter V, Article 28(1), (3)(d)(e)(n)

GVP Module VI – Collection, management and submission of reports of suspected adverse reactions to medicinal products (Rev 2) (as modified by the Exceptions and modifications to the EU guidance on good pharmacovigilance practices that apply to UK marketing authorisation holders and the licensing authority)
VI.B.2. Validation of reports
"*Only valid ICSRs qualify for submission. In accordance with ICH-E2D (see GVP Annex IV), all reports of suspected adverse reactions should be validated before submitting them to the competent authorities to make sure that the minimum criteria are included in the reports.*"

VI.B.5. Quality management
"*[…] marketing authorisation holders should have a quality management system in place to ensure compliance with the necessary quality standards at every stage of case documentation, such as […] data transfer*".

"*Clear written standard operating procedures should guarantee that the roles and responsibilities and the required tasks are clear to all parties involved and that there is provision for proper control and, when needed, change of the system.*"

Finding MA.2 a)

An incorrect listedness assessment against the CCDS was recorded in the safety database for approximately 2,600 cases.

During the inspection, it was identified that listedness against the CCDS was incorrectly captured in the safety database as unlisted for the following cases containing the drug-event pair of [redacted] (Product family [redacted] and [redacted] (MedDRA PT):

[redacted]

On further investigation by the MAH it was found that the incorrect assessment was related to the migration of Japanese cases from the MAH's separate internal [redacted] database into the main [redacted] database, which was completed in September 2023.

During the migration, cases that existed in both the Global and Japanese systems had local data merged into the remaining case. This included the listedness assessments that are stored at the license level. Japanese cases had a world product licence ("XA") where assessment against CCDS was always assessed as "Unknown". During the data migration "Unknown" assessment against CCDS mapped to "Unlisted". When assessment against CCDS was outputted in line listings the most conservative case for all licenses was used,

even if the assessment against other licences, for example EU and GB licences, was “Listed”.

The MAH stated that their initial investigation, performed as a result of the deficiency being identified during the inspection, had identified approximately 2,600 affected cases and that once full analysis was complete, they would develop, validate and implement a correction to set the affected Japan cases to the correct value.

It is noted that listedness per the Company Core Data Sheet (CCDS) impacted several key areas within the Organon pharmacovigilance system including signal detection, case processing, regulatory reporting timelines, risk management and aggregate reporting.

Root Cause Analysis

[redacted]

Further Assessment

[redacted]

Corrective Action(s)

[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

Preventative Action(s)

[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

Finding MA.2 b)

Ten ICSRs were submitted to the MHRA despite not meeting the minimum criteria to qualify as valid ICSR requiring regulatory reporting:

Case #	MAH comments on why the case non-valid	When was the case declared invalid?
[redacted]	Cases were received via social media and considered to be non-valid due to not having a contactable reporter.	Cases were considered invalid from the initial report.
[redacted]	Non-valid cases due to multiple indistinguishable patients.	Cases were considered invalid from the initial report.

The cases were marked for non-submission to MHRA in the safety database, but due to a field entry error made by the submission team during the submission step, reports were generated and inadvertently expedited to the MHRA. The MAH stated that they will carry out further evaluation and correct any impacted cases.

Root Cause Analysis

[redacted]

Further Assessment

[redacted]

Corrective Action(s)

[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

Preventative Action(s)

[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

Finding MA.2 c)

Four ICSRs were identified where the initial case was correctly submitted to the MHRA but when follow-up indicated that the case was no longer valid, no notification of downgrading was sent to the MHRA:

Case #	MAH comments on why the cases non-valid	When was the case declared invalid?
[redacted]	Case was initially considered valid, but it was determined to be non-valid upon follow-up indicating that the information was received via social media and there was no contactable reporter.	Case was determined to be non-valid upon follow-up received on 17 August 2022.
[redacted]	Case was previously considered as valid, but upon receipt of a clarification response, it was determined that the case was non-valid due to multiple indistinguishable patients.	Case was determined to be non-valid upon follow-up received on 25 October 2022.
[redacted]	Literature case was previously considered valid, but it was determined to be non-valid after it was determined to be not related to the company product.	Case was determined to be non-valid upon follow-up received on, March 28th, 2023.
[redacted]	Case was previously considered as valid, but upon receipt of a clarification response it was determined that there were no patient identifiers, hence, case was deemed non-valid.	Case was determined to be non-valid upon follow-up received on, 08 June 2023.

Root Cause Analysis

[redacted]

Further Assessment

[redacted]

Corrective Action(s)

[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

Preventative Action(s)

[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

MA.3 Pharmacovigilance System Master File

Requirements:

The Human Medicines Regulations 2012 (Statutory Instrument 2012 No. 1916), Schedule 12A Part 1, Paragraph 1(1), 4(1)

Commission Implementing Regulation (EU) No. 520/2012, Chapter I, Article 1(1), 4(1)

GVP Module II – Pharmacovigilance system master file (Rev 2) (as modified by the Exceptions and modifications to the EU guidance on good pharmacovigilance practices that apply to UK marketing authorisation holders and the licensing authority)

"Holders of UK marketing authorisations must maintain a PSMF that describes the pharmacovigilance system that is applied to their UK authorised products and make this available upon request of the licensing authority."

II.B. Structures and processes
"The content of the PSMF should reflect global availability of safety information for medicinal products authorised in the UK, presenting information on the pharmacovigilance system applied at global, regional and local levels."

II.B.4. Information to be contained in the pharmacovigilance system master file
"The content of the PSMF should reflect the global availability of safety information for medicinal products authorised in the UK."

II.B.4.7. PSMF section on quality system - Auditing
"The list should describe the date(s) (of conduct and of report), scope and completion status of audits of service providers, specific pharmacovigilance activities or sites undertaking pharmacovigilance and their operational interfaces relevant to the fulfilment of the obligations in the Human Medicines Regulations 2012 […]."

Every MAH should establish a pharmacovigilance system to ensure the monitoring and supervision of one or more of its authorised medicinal products. Details of the system should be recorded in a PSMF, which should be permanently available for inspection. The following findings were noted in relation to the PSMF:

Finding MA.3 a)

The UK PSMF provided to the MHRA (version [redacted] effective 24 January 2025 and version [redacted] effective 03 February 2025) was not specific to UK authorised medicinal products.

i. Annex B1a *List of PV Contracts for Business Partner agreements in any territory where at least one product has an EEA and/or UK Market Authorisation (MA) and Organon is the Marketing Authorisation Holder (MAH) or both, Organon and the Partner, are the MAH in the EEA and/or UK* included non-UK authorised active substances such as [redacted] or various biosimilars in the list of products covered by a number of business partner agreements, e.g.:

- [redacted] (distribution agreement) [redacted]
- [redacted] distribution agreement [redacted]

ii. Annex B1c *List of PV Contracts for Medical Device Only Agreements* (version [redacted] dated 16 December 2024) was dedicated to distribution agreements relating to

medical devices in [redacted] and several [redacted].

iii. The C annexes included a number of studies and programmes that were not applicable to UK authorised products or active substances:

- Annex C04a *List of Market Research Programs* included market research programmes for the medical device [redacted] and for biosimilars (e.g. [redacted] not authorised to Organon in the UK.
- Annexes C05a *List of Local Data Generation* and C05b *List of Outcomes Research* included studies for the medical device [redacted] and non-UK authorised products such as [redacted]
- Annex C06 *List of Patient Support Programs (PSPs)* included numerous patient support programmes for biosimilars not authorised to Organon in the UK.

Root Cause Analysis

[redacted]

Further Assessment

[redacted]

Corrective Action(s)

[redacted]

[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

Preventative Action(s)

[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

Finding MA.3 b)

Annexes to the UK PSMF (version [redacted] effective 24 January 2025 and version [redacted] effective 03 February 2025) did not contain up-to-date and current information as the data lock point was between three and five months prior to the provision of the PSMF for the purposes of the inspection. For example:

- Annex C10 List of Social Media Programmes (version [redacted] dated 16 December 2024) had a data lock point of 31 October 2024, as a result the social media programmes [redacted] (launched on 09 December 2024) and [redacted] (launched on 23 December 2024) were not visible from the annex.

- Annex G2 List of Conducted and Completed Pharmacovigilance Audits for the Last Five-Year Period (version [redacted] dated 16 December 2024) had a data lock point of 08 November 2024, as a result the audit related to the signal management [redacted] conducted on 19-20 November 2024 was not visible from this annex.

Root Cause Analysis

[redacted]

[redacted]

Further Assessment
[redacted]

Corrective Action(s)
[redacted]

Deliverable(s)	**Due Date(s)**
[redacted]	

Preventative Action(s)
[redacted]

Deliverable(s)	**Due Date(s)**
[redacted]	

Finding MA.3 c)
The UK PSMF provided to the MHRA (version [redacted] effective 24 January 2025 and version [redacted] effective 03 February 2025) contained limited or missing information in some annexes. i. Annex B1a *List of PV Contracts for Business Partner agreements in any territory where at least one product has an EEA and/or UK Market Authorisation (MA) and Organon is the Marketing Authorisation Holder (MAH) or both, Organon and the Partner, are the MAH in the EEA and/or UK* (version [redacted] dated 16 December 2024) contained incomplete information with regards to the territories that were in scope of the licensing agreement with [redacted] for [redacted]. The products were licensed to [redacted] in [redacted] and [redacted] but the PSMF only listed Italy for [redacted] and only [redacted] and [redacted] for [redacted] ii. PSMF G.2 *List of Conducted and Completed Pharmacovigilance Audits for the Last Five-Year Period* (version [redacted] dated 16 December 2024) did not display the following information: • Name of the party details for business partner and vendor audits • Audit dates
Root Cause Analysis
[redacted]
Further Assessment
[redacted]
Corrective Action(s)
[redacted]

Deliverable(s)	**Due Date(s)**
[redacted]	

Preventative Action(s)
[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

C.4.3 Minor findings

MI.1 Contracts and Agreements

Finding MI.1 a)
The distribution agreement with [redacted] (effective 01 January 2023) did not include any provisions for pharmacovigilance audit for oversight of the distributor's adherence to the pharmacovigilance responsibilities outlined in Schedule 9 *Pharmacovigilance Agreement* of the agreement. It is noted that Appendix 1 to the Technical Quality Agreement (version [redacted] last signature dated 07 November 2024) included provisions for GMP and GDP audits, but there were no separate provisions for PV audits. The Pharmacovigilance Agreement did include a requirement for pharmacovigilance training of distributor staff and the right for Organon to request the corresponding training records. While wholesale distributors without a separate PVA, such as [redacted] were not included by default in Organon's risk assessment conducted for audit planning, Organon should have provisions in place to allow the audit of [redacted] if deemed necessary, to ensure that the partner is complying with the pharmacovigilance requirements stipulated in the distribution agreement. Evidence was seen by inspectors that an 'annual reminder' or 'yearly partner notification' was sent by the Local Pharmacovigilance Responsible since 2021 in accordance with [redacted] (revision [redacted], effective 31 January 2023). While the distributor had replied to all but the latest notification confirming that they had sent Organon all adverse event information, product quality complaints and other reportable information, there was no indication of the number of reports sent to Organon to allow for an independent verification by Organon of adherence to the pharmacovigilance requirements set out in the agreement.
Root Cause Analysis
[redacted]
Further Assessment
[redacted]
Corrective Action(s)

[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

Preventative Action(s)

[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

Finding MI.1 b)

The original PVA with [redacted] (dated 13 September 2019) did not include [redacted] as reportable safety information to Organon but was added as part of the creation of a standalone PVA (effective 18 January 2024).

Organon did not conduct any retrospective review with [redacted] to confirm whether [redacted] had received any such reports prior to January 2024 that had not been forwarded to Organon yet.

It is noted that reconciliation records between 2021 - 2023 indicated that the business partner had received very little safety information.

Root Cause Analysis

[redacted]

Further Assessment

[redacted]

Corrective Action(s)

[redacted]

[redacted]	

Preventative Action(s)
[redacted]

Deliverable(s)	**Due Date(s)**
[redacted]	

Finding MI.1 c)
Reconciliations were not carried out with the distributor [redacted] in accordance with the underlying commercial agreement (effective 09 December 2021). Section 3.5.7 of the agreement stipulated monthly reconciliations. In practice Organon followed the 'annual reminder' or 'yearly partner notification' process outlined in [redacted] (revision [redacted] effective 31 January 2023). In response to the reminders sent by Organon in October 2022, January 2024 and January 2025, [redacted] confirmed that no AE or PQC reports had been received in the preceding year.

Root Cause Analysis
[redacted]

Further Assessment
[redacted]

Corrective Action(s)
[redacted]

Deliverable(s)	**Due Date(s)**
[redacted]	

Preventative Action(s)

[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

Finding MI.1 d)
Incomplete information was included in the Distribution and Promotion Services Agreements between [redacted] and Organon: • Organon [redacted] (effective 08 May 2024): Annex A stated [redacted] as the active ingredient for the [redacted] products, whereas the product contained both [redacted] and [redacted] • Organon [redacted] (effective 08 May 2024: Annex A stated [redacted] as the active ingredient for the [redacted] product, whereas the product contained both [redacted] and [redacted] It is acknowledged that the complete active substances were listed in Appendix 2 of the supporting PVA (effective 03 July 2024).

[redacted]

Further Assessment

[redacted]

Corrective Action(s)

[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

Preventative Action(s)

[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

Finding MI.1 e)

The contract with the vendor [redacted] regarding market research programme [redacted] (lasted signed 31 Aug 2023) did not include Lack of Efficacy as reportable safety information. It is acknowledged that the term was included in the PV training materials provided to the vendor.
Root Cause Analysis
[redacted]
Further Assessment
[redacted]
Corrective Action(s)
[redacted]

Deliverable(s)	**Due Date(s)**
[redacted]	

Preventative Action(s)
[redacted]

Deliverable(s)	**Due Date(s)**
[redacted]	

MI.2 Signal Management

Finding MI.2 a)
Procedures relating to signal management activities lacked sufficient detail in order to reflect the extent to which quantitative review was incorporated into Organon's signal detection methodology. There were no defined thresholds documented in relation to the review of case counts/volume displayed within the aggregate event report (AER) outputs, nor was any other prescriptive instruction given to those responsible for signal detection on how to review the data quantitatively. As Organon received a large number of safety reports each year (e.g. >26,000 cases in 2024 and >29,000 cases in 2023), a purely qualitative approach to signal detection is not considered to be adequate. According to the company procedure [redacted] (revision [redacted] effective 17 February 2025), the [redacted] tool highlighted product-event combinations (PEC) that fulfilled certain qualitative criteria i.e. events with positive rechallenge, resulted in a fatal outcome, or were designated medical events (DMEs). Organon's Signal Management Team (SMT) was also responsible for manually reviewing the data in relation to product-specific topics of special interest, general topics of special interest (e.g. special situations), PECs marked as signal of disproportionate reporting and with changes during the period in eRMR reports downloaded from EVDAS and country-specific safety data, as required per local regulation(s). In addition, the SMT would manually review s*elected events based on scientific/medical judgement.* [redacted] included the following guidance for this review: *"The following information may be informative for selecting additional PECs: product's mode of action, case clustering or reporting frequency over time, known class effects, case counts and reporting frequencies for similar events, relative distribution of case counts by age, gender, lot number and/or country/region.* *Documentation of this review is tracked in the meeting minutes template provided in* [redacted] *for SMT and stored in the repository"* [underlined for emphasis]. Aggregate review reports for [redacted] (04 June 2023 to 03 June 2024) and [redacted] 03 June 2023 to 02 June 2024), alongside respective SMT meeting minutes were reviewed during inspection. Whilst evidence of quantitative review of auto-flagged/pre-defined product event combinations (PECs) was observed in signal detection outputs, it was not possible to verify from these outputs, nor the respective minutes, how the MAH had reviewed data quantitatively for PECs that did not meet the company's pre-defined criteria. Therefore, it could not be verified if Organon consistently reviewed detection datasets in a complete and quantitative manner. As a mitigating factor, the company performed quantitative analysis based on eRMR from EVDAS; however, it should be noted that not all MAH data may be submitted to the EMA (i.e. non-serious reports from outside of the EU/EEA, or ICSRs not meeting the minimum validation criteria), and therefore the quantitative methodology that was observed would not have considered the totality of safety information available to the MAH. Organon are reminded of the quality requirements outlined in GVP Module XI.B.5., describing the requirement for a clearly documented signal management system with clear and standardised tasks that is supported by detailed procedures.
Root Cause Analysis

[redacted]

Further Assessment
[redacted]

Corrective Action(s)
[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

[redacted]

Preventative Action(s)	
[redacted]	
Deliverable(s)	**Due Date(s)**
[redacted]	

Finding MI.2 b)
Discrepancies were identified with the data migrated from the legacy Signal Management system [redacted] to the [redacted] tool, which was implemented on 01 March 2021. For signal [redacted] the detection date was displayed as "23-Jan-2020", yet signal closure was indicated as "13-Dec-2019". Organon explained that the legacy system did not include a 'detected date' field and therefore was pulled from the signal creation date. The MAH confirmed that the actual detection date would be documented within the respective RMST minutes, and therefore this information was retrievable.
Root Cause Analysis
[redacted]
Further Assessment
[redacted]
Corrective Action(s)
[redacted]

[redacted]

Preventative Action(s)
[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

MI.3 Maintenance of Reference Safety Information

Finding MI.3 a) was downgraded and can be found in section C.4.4 Comments.

Finding MI.3 b)
In addition to finding MA.1 a), a further example was identified where Organon submitted a safety variation to the licensing authority for a marketed product without mock-ups being provided. [redacted] Type II variation [redacted] submitted on 27 October 2023 to update SmPC section 4.8 and the PIL, with [redacted] the PIL mock-up had not been provided in the submission package to the MHRA. It is acknowledged that this omission did not impact the timely conclusion of the initial variation; however, a follow-up submission including the mock-up was provided to MHRA afterwards, which required additional processing by the MHRA.
Root Cause Analysis
[redacted]
Further Assessment
[redacted]
Corrective Action(s)
[redacted]

Deliverable(s)	**Due Date(s)**
[redacted]	

Preventative Action(s)
[redacted]

Deliverable(s)	**Due Date(s)**
[redacted]	

MI.4 Auditing of the Pharmacovigilance System

Finding MI.4 a)
The UK QPPV did not receive the reports of the following audits: • [redacted] UK affiliate audit, conducted 17-18 November 2022, report issued on 12 January 2023 • [redacted] regarding contractual agreements, conducted 26-27 March 2024, report issued on 09 April 2024. Organon also confirmed that prior to revision [redacted] of [redacted] (effective 22 April 2022), there was no procedural requirement to share the audit report with the QPPV. Instead, reports were required to be distributed to "relevant Process Owner(s), Quality and Compliance, relevant local management, Quality and Compliance Head, and identified functional area stakeholders". Per GVP Module IV, section IV.C.1.1.1., the QPPV should receive pharmacovigilance audit reports.
Root Cause Analysis
[redacted]
Further Assessment
[redacted]
Corrective Action(s)
[redacted]

Deliverable(s)	**Due Date(s)**
[redacted]	

Preventative Action(s)
[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

Finding MI.4 b)

The following deficiencies were identified with regards to Organon's pharmacovigilance audit programme:

i. There was no documented audit strategy in place prior to the Strategic Pharmacovigilance (PV) Audit Plan 2025-2029 (signed 04 February 2025).

SOP [redacted] (revision [redacted] effective 25 October 2021 – 07 August 2024) stated that a "*risk-based strategic plan (Audit Strategy) will be developed taking into consideration the risks inherent to critical business activities and/or systems such that the audit conduct, timing, and management is fit for purpose. The Audit Strategy will describe the applicable audit universe and the methodology used for selecting auditees. The Audit Strategy will be used to develop the Annual Audit Plan, which will encompass two (2) years.*" However, no audit strategy had been put in place during that time.

ii. [redacted] programmes were not considered as part of the pharmacovigilance audit universe until the updated work instruction [redacted] (revision [redacted]) became effective on 07 March 2025.

This finding was graded as minor since Organon had conducted work since September 2023 to improve the audit and risk assessment process (refer to section C.1). In addition, evidence was seen on inspection that Organon had prepared tactical audit plans for 2023, 2024 and 2025 despite the lack of an overarching audit strategy.

Root Cause Analysis

[redacted]

Further Assessment

[redacted]

Corrective Action(s)

[redacted]

[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

Preventative Action(s)
[redacted]
[redacted]

MI.5 Management and Reporting of Adverse Reactions

Finding MI.5 a)

Errors were identified with the completion of the field "Observe Study Type" in the safety database:

i. Four examples were seen where Observe Study Type was NA (blank) when it should have been "Other Studies". All the cases were considered non-valid for expedite reporting and originated in market research or other solicited sources.

- [redacted] Case Type: Report From Study, Non-serious, Study ID [redacted]
- [redacted] Case Type: Report From Study, Non-serious, Study ID [redacted]
- [redacted] Type: Report From Study, Non-serious, Study ID [redacted]
- [redacted] Case Type: Report From Study, Non-serious, Study ID [redacted]

ii. Thirteen cases were incorrectly classified with the Observe Study Type of "Clinical Trial" when they should have been classified as "Other Studies".

- *Study ID:* [redacted] *(Non-serious, Case Report Type: Literature Study, Non-serious)*: [redacted]
- *Study ID:* [redacted] *(Non-serious, Case Report Type: Literature Study, Non-serious):*
- *Study ID:* [redacted] *(Non-serious, Case Report Type: Literature Study, Non-serious)*: [redacted]

The [redacted] field Observe Study Type (OST) was used to differentiate between sub-types of studies which had an Organon study configuration. The OST "Clinical Trial" was used for interventional clinical trials including company sponsored, investigator initiated, or business partner sponsored studies. The OST "Individual Patient Use" was used for Temporary Use Authorization or Pre-License Patient Access Programs (PLPA) and the OST "Other Studies" was used to denote non-interventional trials and reports from solicited sources such as but not limited to company registries, patient support programs, and market research programs. The MAH stated that the field was used in regulatory submissions, signal detection and risk management and aggregate reporting and data analysis.

Root Cause Analysis

[redacted]

[redacted]

Further Assessment
[redacted]

Corrective Action(s)
[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

[redacted]

Preventative Action(s)
[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

Finding MI.5 b)
One example was observed of a spontaneous case which was mistakenly classified as "Solicited" in the [redacted] Case Classification Field according to [redacted] (revision [redacted] effective 08 July 2024), section 13.2 General Information, page 190. Case [redacted] was received from Health Canada. It was initially reported as case type "Report From Study", with [redacted] and was processed as study report by adding the classification as "Solicited". In a subsequent FU report the report type was stated as spontaneous and the case processing coordinators changed the report type to "Spontaneous". However, case processing personnel omitted to remove the case classification "Solicited" which was added during initial version when the case was considered a study report. The Case Classification field in [redacted] provided a further sub-division of case type and was used for case identification and data querying but did not impact reportability.
Root Cause Analysis
[redacted]
Further Assessment
[redacted]
Corrective Action(s)
[redacted]

Deliverable(s)	**Due Date(s)**
[redacted]	

Preventative Action(s)
[redacted]

Deliverable(s)	**Due Date(s)**
[redacted]	

MI.6 Provision of Information to Enable Supervision by the Licensing Authority

Finding MI.6 a)

The listings provided to inspectors presenting information on the submission, approval (as applicable) and implementation of safety variations (PILs into products packs) displayed erroneous data.

i. For Type II variation [redacted] ([redacted]), batch packing records indicated that the last batch [redacted] containing the superseded PIL version (component code [redacted]) was QP-certified on 15 December 2023. However, the listing presented to inspectors indicated that the QP certification date for the last batch [redacted] containing a superseded PIL version [redacted] was 02 July 2024.

ii. For Type II variation [redacted] [redacted]), the RMS approval was received on [redacted] yet according to the safety variation listings the date of approval was 11 July 2024. The MAH stated that 11 July 2024 reflected the date of receiving approval from the MHRA; however, the letter received from the MHRA on 11 July 2024 clearly stated the approval date as [redacted]

Based on the implementation data provided in the listings, the discrepancy with respect to the approval data did not have an impact to the timeliness of artwork implementation, therefore this has been captured as minor documentation finding only.

Root Cause Analysis

[redacted]

Further Assessment

[redacted]

[redacted]

Corrective Action(s)
[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

Preventative Action(s)
[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

MI.7 Quality Management System

Finding MI.7 a)
Quality Issue [redacted] was opened on 25 March 2024 due to multiple deficiencies relating to the [redacted] partnership, including lack of reconciliation; however, no retrospective reconciliation was conducted with the vendor [redacted] after it was identified that reconciliations had not been carried out since the agreement start date. The Master Services Agreement became effective on 31 March 2023 and the first reconciliation was conducted in October 2024, leaving a period of 1.5 years that was not covered by any reconciliation. [redacted] supported Organon with regulatory affairs activities.
Root Cause Analysis
[redacted]
Further Assessment
[redacted]
Corrective Action(s)
[redacted]

Deliverable(s)	**Due Date(s)**
[redacted]	

Preventative Action(s)
[redacted]

Deliverable(s)	**Due Date(s)**
[redacted]	

MI.8 Medical Information

Finding MI.8 a)
An adverse event relating to the continued use of [redacted] after its expiry date received via Medical Information on 01 December 2023 ([redacted]) was not sent to pharmacovigilance as the notification e-mail, drafted in the [redacted] system, was not sent in error.
Root Cause Analysis
[redacted]
Further Assessment
[redacted]

Corrective Action(s)	
[redacted]	
Deliverable(s)	**Due Date(s)**
[redacted]	
Preventative Action(s)	
[redacted]	
Deliverable(s)	**Due Date(s)**
[redacted]	

C.4.4 Comments

1. SOP [redacted] (revision [redacted] effective 11 October 2022) referred to the responsibilities of the EU QPPV but did not specifically refer to the UK QPPV.

2. [redacted] (revision [redacted] effective 30 May 2024) referred to the EU QPPV but did not specifically refer to the UK QPPV.

3.

Note: strikethrough text indicates text that has been removed.

~~**Finding MI.3 a)**~~

Organon did not conservatively consider the implementation of two PSUSA procedure outcomes into the product information of specific product licences that contained active substances covered by the respective PSUSA.

i. On [redacted], the PRAC recommended that product information of products containing [redacted] should be updated to reflect [redacted] Updated wording was provided for SmPC section 4.6 and PIL section 2. MAHs were expected to submit their variations by [redacted]

   Organon held UK licences for [redacted]

   Organon did not proceed to update the product information based on review of available data and concluded at the signal management meeting dated 26 September 2024 that there was no evidence of increased risk during pregnancy, and that the existing product information contained the necessary details regarding use during pregnancy. Of note the current wording in section 4.6 of the SmPCs regarding use during pregnancy was specifically in relation to the [redacted] of the products. ~~Therefore, to reflect the information in relation to [redacted] wording should be introduced to align with the PRAC recommendation.~~ It is acknowledged that the PRAC recommendation was split into three categories depending on the product formulation and application route but may not cover all types of [redacted] on the market. To determine the appropriate application of the recommendations, the MAH is encouraged to reach out to MHRA assessors to discuss a suitable approach.

ii. On [redacted] the outcome for procedure [redacted] concerning [redacted] was published, which required revision of SmPC section 4.4, 4.5 and 4.8, and PIL section 2 and 4 to include information regarding [redacted] Submission of the safety variation to relevant health authorities was expected by [redacted]

   Organon held four UK licences of [redacted]

   As warnings regarding [redacted] were already present in the [redacted] product information, the company's Signal Management Team (SMT) concluded on 29 August 2024 that no further assessment was required of this topic, which the MHRA agrees with. However, the SMT also decided that no further assessment was required regarding [redacted] since the data received by the company since the previous signal assessment was not considered to be significant enough. Consequently, the [redacted] product information was not updated with these new ADRs.

The MAH is reminded of their obligation to ensure that product information remains up-to-date and consistent with available scientific knowledge, including signals that may apply to a whole class of medicinal products. It is noted that the PRAC assessment report stated that [redacted] may be a class effect of [redacted] In the event of uncertainty, the MAH is encouraged to consult with MHRA assessors.

It is acknowledged that currently the [redacted] products were not currently marketed, and therefore there is limited impact to patients; however, the company should ensure that product information is appropriately up to date at the time of placing the product onto the UK market.

Post-inspection requests:

a) Pertaining to point i. and ii: Organon are requested to contact the MHRA Safety and Surveillance unit to agree to which extent the above safety wording should be implemented in the product information of affected Organon UK authorised medicinal products.

b) Pertaining to point ii: Organon are requested to include in their responses to the inspection report to which extent implementation of procedure [redacted] outcome had been considered for other [redacted] combination products, e.g. [redacted] at the time of publication.

Root Cause Analysis

[redacted]

Further Assessment

[redacted]

Corrective Action(s)

[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

Preventative Action(s)

[redacted]

Deliverable(s)	Due Date(s)
[redacted]	

[redacted]

SECTION D: CONCLUSIONS AND RECOMMENDATIONS

D.1 Conclusions

The factual matter contained in the Inspection Report relates only to those things that the inspection team saw and heard during the inspection process. The Inspection Report is not to be taken as implying a satisfactory state of affairs in documentation, premises, equipment, personnel or procedures not examined during the inspection. It is recommended that you review whether the inspection findings also apply to areas not examined during the inspection and take appropriate action, as necessary.

The responses to the inspection findings, which include proposed corrective and preventative actions, do appear to adequately address the issues identified. No additional responses are required at this time. When the company has adequately implemented the proposed corrective and preventative actions, the pharmacovigilance system will be considered to be in general compliance with applicable legislation.

D.2 Recommendations

The Lead Inspector has recommended that the next MHRA inspection is performed as part of the routine risk-based national inspection programme.

APPENDIX I REFERENCE TEXTS

- The Human Medicines Regulations 2012 (Statutory Instrument 2012 No. 1916).
- Commission Implementing Regulation (EU) No 520/2012.
- Guideline on good pharmacovigilance practices (GVP).
- Exceptions and modifications to the EU guidance on good pharmacovigilance practices that apply to UK marketing authorisation holders and the licensing authority.
- EMA/CHMP/ICH/287/1995: ICH guideline E2B (R3) on electronic transmission of individual case safety reports (ICSRs) - data elements and message specification - implementation guide.
- CPMP/ICH/3945/03: ICH guideline E2D “Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting”.

APPENDIX II PHARMACOVIGILANCE INSPECTION PLAN

MHRA INSPECTION NUMBER	Insp GPvP 25/36429846-0001	**DATES**	11-14 March 2025
PHARMACOVIGILANCE INSPECTION OF	Organon Pharma (UK) Limited	**START TIME**	08:45 arrival for 09:15 start (Day 1), 09:00 (Day 2-4)
LOCATION	Days 1 to 4: Onsite at Organon Pharma (UK) Limited, 145 City Road, London, EC1V 1AZ	**INSPECTION TEAM**	[redacted] (Inspection Lead), [redacted] (MHRA, remote), [redacted] (MHRA, remote observer), [redacted] (Health Canada, observer), [redacted] (URPL, observer)

This inspection will primarily focus on a review of the following topics:

- Collection and collation of pharmacovigilance data
- Management and reporting of ADRs
- Signal management
- Risk management

The inspection plan below outlines the topics for which specific sessions are requested to orientate inspectors around the systems and processes in place. Demonstration of live systems such as the safety database or systems used in the activities under review may also be requested. Please ensure that subject matters experts are available and indicate any times personnel may be unavailable below.

Additional ad hoc discussions with company personnel may also be required. The inspectors will liaise with the designated inspection host to arrange ad hoc discussions as needed.

The remainder of the inspection will consist of document review. Document requests will be submitted throughout the course of the inspection.

All times are GMT.

N.B. The Inspection Plan may be subject to change before and during the inspection.

Day 1: 11 March 2025		
Session	**Time**	**Attendees/interviewees (*Presenters)**
Opening meeting Led by [redacted] **Agenda:** • Introductions • Review of inspection logistics and inspection plan • **Company Presentation.** The MAH is requested to provide an overview of the company's PV system and the quality system (to last no longer than 20 minutes). Please highlight any relevant ongoing remediation work on the PV system and any significant recent or upcoming changes to the pharmacovigilance system.	09:15 – 10:00	Attendee(s): [redacted] - Head of Global QPPV Office/ QPPV UK [redacted] - Local PV Responsible [redacted] - Head of Quality & Compliance Operations [redacted] - Local RA Responsible [redacted] - Cluster Director [redacted] - Chief Safety Office/Head of Global PV
Session 1 - Collection and collation of pharmacovigilance data Led by [redacted] Including but not limited to: • Solicited sources • SDEAs • Oversight of medical information and product complaints quality and compliance Please prepare a short (c. 10 mins) presentation on solicited sources and SDEAs to share during this session.	10:30 – 12:00	Interviewee(s): [redacted] - Local PV Responsible [redacted] - Global Business Partners Agreements [redacted] - Global PV Agreements [redacted] – Global Designated Point of Contact Lead [redacted] – UK Designated Point of Contact Responsible
Lunch	12:00 – 13:00	

Session 2 - Management and reporting of ADRs Led by [redacted] Including but not limited to: • Data entry, coding, and reporting of ICSRs • Follow-up activities • Quality and oversight • Database migration Please prepare a short (c. 10 mins) presentation on the migration of data to share during this session. Please have the safety database available for presenting in case of questions during this session. A break will be offered midway through the session.	14:00 – 16:00	Interviewee(s): [redacted] - Local PV Responsible [redacted] Case Processing, Global PV Process and Standards [redacted] [redacted] – Safety Database & Related Systems/Global PV Systems
Document review	16:00 – 17:30	Inspectors only

Day 2: 12 March 2025

Session	***Time***	***Attendees/interviewees***
Document review	09:00 – 11:00	Inspectors only
Session 3 – Signal management Led by [redacted] Including but not limited to: • Signal detection, validation, evaluation and tracking • Detection of relevant safety updates • Submission of safety variations Please prepare a short (c. 10 mins) presentation on signal management to share during this session. Please have [redacted] tool available in case of a request for a demonstration during this session. A break will be offered midway through the session.	11:00 – 13:00	Interviewee(s): [redacted] - Local PV Responsible [redacted] - Local RA Responsible [redacted] - Safety Signal Detection, Global PV [redacted] - PV Signal tool demon
Lunch	13:00 – 14:00	
Ad-hoc session.[redacted] Demo	*14:00 – 15:00*	[redacted] *- Local PV Responsible* [redacted] *- Back-up for local PVR*
Ad-hoc session: Reconciliations with business partners & [redacted] *demo*	*15:30 - 16:00*	[redacted] *- Global Business Partners Agreements* [redacted] *– Global Pharmacovigilance Licensing* [redacted] *- Local PV Responsible,* [redacted] *- Head of Global QPPV Office/ QPPV UK*

Ad-hoc session: DPOC activities	*16:00 - 16:30*	[redacted] – *Global Designated Point of Contact Lead* [redacted] – *UK Designated Point of Contact Responsible* [redacted] – *DPOC vendor process assurance*

Day 3: 13 March 2025		
Session	***Time***	***Attendees/interviewees***
Document review	09:00 – 17:30	Inspectors only
Lunch	*12:00 – 13:00*	
Session 4 - Risk management Led by [redacted] Including but not limited to: • Implementation of additional risk minimisation measures Please prepare a short (c. 10 mins) presentation on this topic to share during the session.	14:00 – 15:00	Interviewee(s): [redacted] - Local PV Responsible [redacted] - Local RA Responsible [redacted] - Risk Management and Risk Minimization, Global PV
Ad-hoc session: Patient Assistance Programmes/ Unregistered product supply	*15:00 - 15:15*	[redacted] – *Director Family Planning Access Supply* [redacted] *- Head of Quality & Compliance Operations* [redacted] *- Local PV Responsible*
Ad-hoc session: Audits	*15:15 - 15:45*	[redacted] - [redacted] [redacted] *- Head of Quality & Compliance Operations* [redacted] *- Local PV Responsible*
Ad-hoc session: Signal detection strategy	*16:15 - 16:40*	[redacted] *- Safety Signal Detection, Global PV* [redacted] *- Local RA Responsible* [redacted] *- Safety Database & Related Systems/Global PV Systems* [redacted] *- PV Signal, Global PV Business Systems*

		Oversight [redacted] *- Head of Global QPPV Office/ QPPV* *Uk* [redacted] *- Head of Quality & Compliance Operations*

Day 4: 14 March 2025		
Session	***Time***	***Attendees/interviewees***
Document review	09:00 onward	Inspectors only
Ad-hoc session: PSMF	*11:30 - 11:45*	[redacted] – *PSMF QPPV Office* [redacted] [redacted] *- Head of Global QPPV Office/ QPPV UK* [redacted] *- Head of Quality & Compliance Operations*
Lunch	12:00 – 13:00	
Ad-hoc session: Product family in [redacted]	*13:30 - 13:55*	[redacted] *- Case Processing, Global PV Process and Standards* [redacted] *- Safety Database & Related Systems/Global PV System,* [redacted] *- Head of Global QPPV Office/ QPPV UK* [redacted] *- Head of Quality & Compliance Operations*
Closing meeting Verbal feedback will be provided from the inspection. All relevant personnel are welcome to attend the closing meeting.	16:30-17:00	Attendee(s): [redacted] - Chief Safety Office/Head of Global PV [redacted] - Head of Global QPPV Office/ QPPV UK [redacted] - Head of Quality & Compliance Operations [redacted] - Local PV Responsible [redacted] - Local RA Responsible [redacted] - Cluster Director [redacted] - Safety Signal Detection, Global PV [redacted] - Safety Database & Related Systems/Global PV Systems [redacted] Global Business Partners Agreements [redacted] – Global Pharmacovigilance Licensing [redacted] – PSMF Global QPPV Office [redacted] – PSMF Global QPPV Office

		[redacted] – PV Regional Lead EMEA [redacted] – PV Unit Lead Central Northern Europe-Italy [redacted] – Assoc. Director Quality & Compliance [redacted] – Assoc. VP Quality & Compliance Lead [redacted] – Director Quality & Compliance [redacted] – Global PV Operations [redacted] – Assoc. VP Drug Safety Head of Pharmacovigilance Operations [redacted] – Deputy EUQPPV

A designated contact point should be provided who can assist with any questions from inspectors or arrange ad hoc discussions between inspectors and subject matter experts if required. Please also list the inspection host, if different.

Designated contact point/inspection host and contact details:

Name: [redacted]
Job title: Associate Director Research & Development Quality & Compliance Operations
Email: [redacted]
Phone: [redacted]