Medicines & Healthcare products
Regulatory Agency

PHARMACOVIGILANCE
INSPECTION REPORT

Pharmacovigilance System Name: Bayer

MHRA Inspection Number: Insp GPvP 10/16303918-0005

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Table of Contents

ABBREVIATIONS

ADR	Adverse Drug Reaction
AE	Adverse Event
CAPA	Corrective and Preventative Action
CHMP	Committee for Medicinal Products for Human Use
EMA	European Medicines Agency
EU	European Union
GVP	Good Vigilance Practice
HCP	Healthcare Professional
ICSR	Individual Case Safety Report
MAA	Marketing Authorisation Application
MAH	Marketing Authorisation Holder
MedDRA	Medical Dictionary for Regulatory Activities
PSMF	Pharmacovigilance System Master File
PSUR	Periodic Safety Update Report
PV	Pharmacovigilance
QPPV	Qualified Person responsible for Pharmacovigilance
RMP	Risk Management Plan
SOP	Standard Operating Procedure
UK	United Kingdom

SECTION A: INSPECTION REPORT SUMMARY

Inspection type:	Statutory National Inspection
System(s) inspected:	Bayer [redacted]
Site(s) of inspection:	Bayer Inc 2920 Matheson Blvd E Mississauga, ON L4W 5R6 Canada
Main site contact:	[redacted] UK QPPV [redacted]
Date(s) of inspection:	17 November 2025: remote inspection (0.5 day) 18 – 21 November 2025: onsite inspection w/c 24 November 2025: remote post-inspection actions (0.5 day)
Lead Inspectors:	[redacted]
Accompanying Inspector(s):	[redacted]
Previous inspection date(s):	Previous MHRA GPvP inspections of Bayer were conducted on the following dates: • 02 – 05 March 2021 • 3 – 6 September 2019 (Bayer), 25 October 2019 [redacted] 11 – 12 November 2019 [redacted] • 19 – 23 March 2018 (Bayer Pharma and Consumer Health) • 6 – 8 October 2009 (Bayer Pharma) • 2 – 5 November 2009 (Bayer Consumer Health) • 10 – 13 March 2008 (Bayer Pharma)
Purpose of inspection:	Inspection of pharmacovigilance systems to review compliance with UK and EU requirements.
Products selected to provide system examples:	As part of the general systems review, specific ADR reports were reviewed for [redacted] Specific signal reports were examined for [redacted]
Name and location of UK QPPV:	[redacted] Bayer plc 400 South Oak Way Reading RG2 6AD United Kingdom Contact details as above.

Global PV database (in use at the time of the inspection):	[redacted] (commercially available)
Key service provider(s):	Pharmacovigilance services provided by Tata Consultancy Services.
Inspection finding summary:	2 Major findings 5 Minor findings
Date of first issue of report to MAH:	19 December 2025
Deadline for submission of responses by MAH:	Initial: 06 February 2026 Follow-up 1: 13 March 2026
Date(s) of receipt of responses from MAH:	Initial: 06 February 2026 Follow-up 1: 13 March 2026 and 17 March 2026
Date of final version of report:	17 March 2026
Report author:	[redacted]

SECTION B: BACKGROUND AND SCOPE

B.1 Background information

The Bayer group of companies (hereafter 'Bayer') was selected for joint inspection by the MHRA and Health Canada as part of a pilot GPvP joint inspections programme. The inspection planning, preparation and conduct was performed jointly with Health Canada inspectors. However, the inspection findings issued by Health Canada have been reported within a separate Health Canada Inspection Report.

The purpose of the inspection was to review compliance with currently applicable UK and EU 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'. In addition, reference was made to the Canadian pharmacovigilance regulations as described in the Health Canada Inspection Report.

A list of reference texts is provided at Appendix I.

Bayer is a multinational pharmaceutical company with pharmacovigilance activities being conducted globally at eight global PV centres (US, Brazil, UK, Germany, Switzerland, China and Japan) and three regional centres (Hungary, China and India).

Bayer operates three divisions, two of which relate to medicinal products – Pharmaceuticals and Consumer Health. The Pharmaceuticals division includes several therapeutic areas, including women's health, oncology, radiology, ophthalmology and cardiology. The Consumer Health division covers non-prescription medicines in the areas of allergy, dermatology, pain and cardiovascular risk prevention, and digestive health among others.

Bayer plc, headquartered in Reading, UK, is the UK MAH for 118 product licences across the Pharmaceuticals and Consumer Health divisions. 41 of these product licences were classified as Category 1 under the Windsor Framework.

Tata Consultancy Services (TCS) acts as Bayer's main PV service provider, predominantly responsible for ICSR collation and management as well as risk management activities.

B.2 Scope of the inspection

The inspection included a review of the global pharmacovigilance systems and was performed at Bayer's offices in Mississauga, Ontario, Canada. Personnel from Bayer Canada, Bayer UK and Global PV for Pharmaceuticals and Consumer Health attended the Mississauga site in order to participate in the inspection. Where personnel were not available in person, teleconferences were held.

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).

The collation and writing of Periodic Safety Update Reports 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] dated 31 August 2025) 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.

B.4 Conduct of the inspection

In general, the inspection was performed in accordance with the Inspection Plan. Minor amendments to the Inspection Plan and additional interview sessions that occurred during the inspection are highlighted using italic text in Appendix II.

The inspection included a scheduled office-based 0.5 inspection day, which was held on 17 November 2025 to review the pre-inspection documents. A further 0.5 inspection day was conducted by MHRA inspectors remotely in the week of 24 November 2025 to conclude document review and hold one clarification call with Bayer personnel via videoconference.

A wrap up meeting was held to review the inspection findings at Bayer Inc, Mississauga on 21 November 2025 and an exit meeting is due to be held on 15 December 2025. This is in line with Health Canada procedures.

A list of the personnel who attended the exit 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

Since the previous inspection in 2021 the company had made the following changes to the pharmacovigilance system:

- In April 2022, the UK QPPV changed from [redacted]
- In May 2023, the reporting line of PV Country Heads changed from local Medical Affairs to PV Regional Heads.
- In May 2024, the Global Head of PV was replaced by three pharmacovigilance capability clusters: PV Regions, Benefit Risk Management, and QPPV and PV Operations.
- With regards to Artificial Intelligence applications, Bayer had introduced two systems based on machine learning and natural language processing:
    - [redacted] was launched on 29 November 2022 to analyse free-text data from source systems to detect AEs and Product Technical Complaints with human oversight on its findings.
    - [redacted] was launched on 26 August 2025 to assist users by suggesting MedDRA codes for reported events in [redacted] The final responsibility of event coding remained with the [redacted] user.

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 products authorised in respect of Northern Ireland 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 Management and Reporting of Adverse Reactions

Requirements: **The Human Medicines Regulations 2012 (Statutory Instrument 2012 No. 1916)** Part 11 Pharmacovigilance, Regulation 188(1)

Finding MA.1 a)
The global safety database expedited reporting rules for foreign (serious) and UK (serious and non-serious) cases had been incorrectly configured in [redacted] to exclude cases identified by the EMA Medical Literature Monitoring (MLM) service. As a result, 5,664 serious cases identified by the EMA MLM service had not been submitted to the MHRA since 01 January 2021, 776 of which were assessed as life-threatening or fatal. At the time of the inspection, out of the 48 Bayer UK authorised active substances, 20 were monitored by the EMA MLM service. The percentage of Bayer products falling under EMA MLM service review was therefore 41.67%. The MAH is reminded that, following exit of the UK from the EU, the MHRA have no longer access to EMA MLM cases and therefore these cases need to be submitted to 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]	

MA.2 Quality Management System

Requirements:

The Human Medicines Regulations 2012 (Statutory Instrument 2012 No. 1916)

- Part 11 Pharmacovigilance, Regulation 184(1)(c)
- Schedule 12A, Part 2, Paragraph 8(3)(d) and Part 3, Paragraph 13(3)(a)

Commission Implementing Regulation (EU) No 520/2012

- Article 8(3)(d)
- Article 13(2)

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.6. Responsibilities for the quality system within an organisation
"*For the purpose of a systematic approach towards quality in accordance with the quality cycle (see I.B.3.), managerial staff (i.e. staff with management responsibilities) in any organisation should be responsible for: […]*

- *identifying and investigating concerns arising within an organisation regarding suspected non-adherence to the requirements of the quality and pharmacovigilance systems and taking corrective, preventive and escalation action as necessary*"

GVP Module IV – Pharmacovigilance audits (Rev 1) (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)
IV.B.2.4. Actions based on audit outcomes and follow-up of audits
"*Upper management and those charged with governance, should ensure that effective action is implemented to address the audit findings. The implementation of agreed actions should be monitored in a systematic way, and the progress of implementation should be communicated on a periodic basis proportionate to the planned actions to upper management.*"

Finding MA.2 a)

Deficiencies were identified with the timely and adequate documentation as well as the management of UK-specific CAPA, which stemmed from an internal audit of Bayer Canada conducted in September 2024.

During the audit, issue [redacted] was identified whereby ICSRs had not been submitted to Health Canada as required due to cross-reporting requirements having been set up incorrectly. As issue [redacted] was assessed as potentially systemic, CAPA [redacted] was opened on 22 February 2025 to determine the impact on other country specific reporting rules. The review was conducted between 26 February and 04 August 2025, the date on which it was identified that the reporting of non-UK ICSRs to the MHRA was also affected. In total 564 cases relating to [redacted] were identified by Bayer which had not been reported to the MHRA.

i. An inadequate corrective action was taken whereby Bayer decided that ICSRs that had not been reported to the MHRA due to the issue described above would only be retrospectively submitted as expedited reports if received after the last PSUR Data Lock Point (DLP) and therefore had not already been included in a PSUR.

   Consequently, Bayer determined that only 57 out of the 564 ICSRs met those criteria

and qualified for separate submission to the MHRA. The submission of the 57 ICSRs was due to be completed by 31 December 2025. This approach resulted in 507 cases not being scheduled for reporting to the MHRA as ICSRs, of which four were non-serious and 450 serious, including two fatal and eleven life-threatening cases. Bayer explained in a document request during the inspection that this approach was followed since the concerned products had been on the market for an extended period and possessed a well-established safety profile. The cases of concern were included in the pertinent PSURs, which did not raise any safety issues. Given the long-term experience with these products and the evaluations carried out in the relevant PSURs, evaluation and inclusion of ICSRs in these PSURs was deemed sufficient by Bayer.

The MAH is reminded that when regulatory underreporting is identified, the MAH is required to submit ICSRs in an expedited manner, or at a minimum, contact the MHRA to agree on a submission strategy.

ii. There was a delay of three months in opening Quality Issue (QI) [redacted] to document the failure to submit ICSRs to the MHRA. While the impact on UK reporting was identified on 04 August 2025, the QI was only opened on 11 November 2025, immediately prior to the inspection. Bayer stated in a document request that the analysis was conducted between 04 August 2025 to 11 November 2025 to determine the number of cases that had not been reported to the MHRA. While it is acknowledged that the full assessment of self-identified deficiencies may span a longer time period, the documentation of the deficiency in the quality management system should not be delayed ensuring that relevant open deviations and CAPA are transparently included in the UK PSMF.

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)
Ineffective CAPA were implemented by Bayer after identifying an issue on 17 December 2024 with the failure to report non-serious ICSRs to the MHRA since June 2021 (quality issue [redacted]). While CAPA [redacted] was put in place and the reporting rules were checked, this CAPA was ineffective since it had failed to identify the deficiency relating to the submission of MLM cases to the MHRA (refer to finding MA.1 a)).
Root Cause Analysis
Not applicable
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 Collection and Collation of Adverse Drug Reactions

Finding MI.1 a)
The process for monitoring the Source Document Repository and Archiving (SDRA) system to ensure that all appropriate actions had been completed including successful transmission of source documents from local PV affiliates to the central case processing team was not adequate and resulted in at least five cases that had not been created and processed in [redacted]. At the time of the inspection, an SDRA output showed that 30 source documents created between 17 January 2019 and 13 November 2025 were still present with an incomplete status in the system: i. Three documents [redacted] created on 17 January 2019, 22 January 2019 and 18 August 2020, respectively) within SDRA were identified during the inspection that could not be found within [redacted] Bayer confirmed in a document request that, if these cases were missing in [redacted], this would result in three late cases. ii. Four source documents from France that were missed to be created due to human error [redacted] created on 13,14, 21,22 October 2025, respectively), which will result in two late cases. iii. Seven documents [redacted] created on 22 February 2023, 10 and 11 September 2025, 12 November 2025 and 13 November 2025, respectively) were processed in [redacted] but not marked as completed in SDRA. iv. Eleven documents [redacted] created between 19 September and 13 November 2025) that were rejected in [redacted]s and therefore the status needed to be updated in SDRA. v. Five source documents [redacted] created between 22 August 2025, and 22 October 2025) had no 'Sent to Intake' date included in the SDRA output provided by Bayer during the inspection. The SDRA system was a repository used by local PV to store and transmit source documents received locally to the Central Receipt and Triage (CR&T) team. Source documents uploaded on the SDRA by local PV were transmitted to the [redacted] intake worklist via a Bayer custom component. The file would then be reviewed by the CR&T team and subsequently accepted for processing and inclusion in the [redacted] global safety database or rejected, as applicable. The monitoring of SDRA Source documents that were transferred to [redacted] was performed by the TCS SDRA Support team daily following their own internal SDRA Monitoring Sheet (no version or date provided). They were responsible for checking the SDRA Dimension "Send to Next Step - More than 48 hours" and contacting the [redacted] Support Team for every source document that was on that list for more than seven business days. [redacted] Support Team would then check the status of the file in the [redacted] Intake worklist. If the file had been already accepted or rejected, [redacted] Support Team gave this information back to the Support team to include this information manually in SDRA and to change the status to "completed", so that the document disappears from the Dimension list.
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 MI.1 b)
Two medical information enquiries from Canada were incorrectly rejected by PV despite reporting a safety-related special situation: i. Enquiry [redacted] included information implying a medication error had occurred [redacted] Therefore this report should have been recorded in the safety database.

ii. [redacted]

Lead inspector note (17 March 2026): Subfinding MI.1 b) ii. was removed following receipt of additional information and evidence from Bayer.

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 Management and Reporting of Adverse Reactions

Finding MI.2 a)
Serious, spontaneous US case [redacted] reporting the event of [redacted] (received on 01 July 2021) was not submitted to the MHRA in error since the report was incorrectly marked for non-submission with the following reason: 'No studies currently running in UK with this IMP'. This was the only example of missed ICSR reporting out of a sample of 199,089 cases reviewed during the inspection, therefore this finding was graded as minor.
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.2 b)

For four Bayer products sampled during the inspection, the EudraVigilance ICSR reporting rules in [redacted] were set up with a delay of up to 7.5 months after the marketing authorisation application (MAA) submission date to the EMA.

[redacted]	Delay
	7.5 months
	2.5 months
	1 month
	6 days

It is acknowledged that the delay did not result in ICSRs being underreported to the EMA as none of the four active substances had been authorised in any ex-EU territories at the time of MAA submission to EMA.

Post inspection request: As the sample reviewed on inspection was limited to the products mentioned above, the MAH is required to conduct an impact assessment to determine whether there were any other Bayer products for which the reporting rules were set up after the MAA submission date to the EMA or MHRA and whether this practice resulted in ICSRs not being reported to the EMA and/or MHRA in the period between the MAA submission date and the ICSR reporting rule set up.

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 MI.2 c)

Deficiencies were identified with regards to the conduct of follow up to obtain additional information on pregnancy outcomes and to obtain patient identifiers:

i. [redacted] (received on 05 May 2021) for [redacted] had not been followed up to request the pregnancy outcome after the expected delivery date (EDD). Although a pregnancy form was sent on 09 June 2021, which included a request for the pregnancy outcome, this was not followed up after the EDD in January 2022 due to human oversight.

ii. No follow-up was conducted to obtain individual patient identifiers due to human error for the following cases:

- Case [redacted] received on 09 August 2024 via Bayer field staff from Canada, reported a recent increase in [redacted] reactions for multiple patients. While the report was added to the safety database, no follow-up was conducted to obtain individual patient identifiers due to human error.

- Case [redacted], received on 04 February 2025 from a market research programme in Canada, reported off-label use for [redacted] for multiple patients. No follow-up attempt was performed to identify individual patients due to human error.

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 MI.2 d)

The following deficiencies were identified with regards to the quality of data entered into the [redacted] safety database:

i. 35 cases were identified whereby the "'Initial Receipt at HQ" field (i.e. receipt date by central case processing team) was erroneously populated with dates earlier than the actual date of first awareness at Bayer (captured in [redacted] as "Initial Receipt Date"). This error was a result of human oversight while performing data entry. This type of error was noticed internally at Bayer earlier in 2025 and was addressed by the technical team via implementation of an automatic check to prevent re-occurrence on 24 June 2025. However, at the time of the inspection, these 35 cases, all received prior to June 2025, had not been corrected.

ii. For case [redacted] the "reporter country" field was left empty. The MAH stated during the inspection that the value "0" was entered in the safety database which resulted in a blank field in the adverse event line listing provided for the purposes of the inspection. During the inspection, the MAH found 26 other cases where the "reporter country" had been left empty.

iii. The country of origin was incorrectly recorded as "Canada" for case [redacted] which was received on 19 May 2021 from the United States.

iv. Incorrectly coded adverse drug reactions were present in several cases:
- Case [redacted] the reaction of 'Congestion' was incorrectly coded to the PT 'Congenital anomaly' due to human error. The verbatim events as reported for this case were 'chills, feeling hot and then cold, dry cough and congestion'.
- Case [redacted] involved a [redacted]-year-old consumer who reported using [redacted] for contraception and management of heavy menstrual bleeding but experienced daily heavy bleeding for the past two months. According to the MAH, changes in bleeding patterns, including prolonged or heavy bleeding, are recognised and listed adverse effects of Mirena, particularly during the initial months of use. The adverse event should therefore have been coded to "abnormal uterine bleeding" rather than "drug ineffective".

v. Two non-UK cases [redacted] were coded in the safety database as invalid due to missing patient identifiers; however, in both instances the case narrative referred to a "female patient". While case [redacted] was non-serious and therefore did not qualify for submission to the UK, case [redacted] reported drug hypersensitivity with [redacted] therefore Bayer should comment as part of the Further Assessment whether the classification as invalid impacted on the submission of the case to the MHRA.

Root Cause Analysis

[redacted]

[redacted]

Further Assessment

[redacted]

[redacted]

Corrective Action(s)
[redacted]

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

Preventative Action(s)
[redacted]

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

MI.3 Signal Management

Finding MI.3 a)

The following deficiencies were identified with Bayer's signal detection methodology:

i. Bayer conducted quantitative (statistical) signal detection at product level only for products that shared the same active substances, either as a mono or combination ingredient. Bayer used this stratified approach to quantitative signal detection for products with the same active substance where products differed in indications or delivery routes to facilitate the identification of potential signals in a product-specific context.

While this approach was appropriate to detect potential signals which may be due to differences in product indication, administration route or formulation, the stratification of ADRs according to product association would reduce the statistical power of quantitative signal detection as the same ADR reported for individual products with the same active substance may not meet the threshold to be flagged as a potential signal.

For example, quantitative signal detection for levonorgestrel was stratified into eight Bayer-defined product groups:

[redacted]

Other affected active substances in mono and combination products included:

[redacted]

It is also noted that Bayer had limited documentation of the rationale supporting their approach to quantitative signal detection.

This finding was graded as minor as Bayer also employed qualitative signal detection methodologies and some of the impacted active substances were also part of the 'Signal detection in EudraVigilance' pilot, which applied statistical signal detection at active substance level. In addition, potential signals were evaluated and assessed in the context of ADRs at active substance level.

ii. Bayer's current quantitative and qualitative signal detection methodology did not facilitate the detection of changed frequencies of known ADRs for a subset of products.

For products for which high volumes of ADRs were received and which had a core

datasheet configured in [redacted], the statistical signal detection method applied a filter to exclude all ADRs listed in the core datasheet that were otherwise meeting the threshold for a potential signal. While Bayer also conducted routine qualitative signal detection in [redacted] on spontaneous, literature as well as interventional and non-interventional study cases, the qualitative reports produced by the system were configured to only display cases that fulfilled any of the Bayer Ongoing Monitoring criteria:

- Fatal cases
- All events that are serious, unlisted and related
- Case of special interest (anaphylactic/anaphylactoid shock conditions. haematopoietic cytopenia affecting more than one type of blood cell, Torsade de point/QT prolongation, drug-related hepatic disorders (severe events only), acute pancreatitis, severe cutaneous adverse reactions)
- Cases with events from the Designated Medical Event list

As a result any listed reactions not meeting the above criteria would not be visible to Bayer safety leads during qualitative signal detection and changes to their frequency would not be identified through this route either. It is also noted that no written instructions were available to safety leads conducting the individual case review on how they should monitor changes in frequency and that this depended on their personal experience and knowledge of the product.

There were 36 UK authorised active substances that had a core datasheet configured in [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]	

MI.4 Reference Safety Information

Finding MI.4 a)

Procedural documentation describing the processes regarding the update of product information by the marketing authorisation holder in the light of scientific knowledge was deficient with regards to the following aspects:

i. Bayer had not formally documented in any quality documents the timelines within which safety variations under the International Recognition Procedure should be submitted to the MHRA following approval from the reference regulator. For example, Bayer had received approval from the EU reference regulator on 12 November 2025 regarding an updated safety warning regarding [redacted] in the product information for [redacted] but at the time of the inspection Bayer had not yet decided on a timeline by which they would submit the UK-specific variation under the International Recognition Procedure.

ii. Procedural documentation governing the update of product information with new safety information following signal confirmation would allow potential non-compliance against the requirements outlined in GVP Module IX (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).

If a signal was confirmed with a recommended action to update the product information, Bayer allowed a timeline of 90 days to present the signal to the Global Safety and Labeling Committee (GSLC)/ Global Labeling Commitee (GLC) for a decision on whether the product information should be updated [redacted] date effective 09 December 2024). Following GSLC/GLC decision, a priority-driven timeline of 3-6 months was applied for submission of the corresponding safety variation to the health authorities ([redacted] dated effective 29 April 2024). In the case of a 'minor priority' safety update, this approach would mean that safety variations may only be submitted nine months after signal confirmation, which is longer than the timelines defined in GVP IX.C.4.1., which states "*A marketing authorisation holder may conclude, based on their assessment of a signal detected, that the product information and/or the RMP should be updated through a variation. In such cases, the marketing authorisation holder should submit the variation application to the licensing authority as soon as possible and no later than 3 months after completing the assessment of the signal if it corresponds to an important risk (see GVP Annex I), or within 6 months for adverse reactions or risks not considered important.*" GVP IX.C.4. further clarifies that "*the conclusion that a signal represents a new or changed risk and […] is the starting point ('Day 0') of the timelines indicated herein*".

During the inspection no examples were identified where this procedural misalignment had led to the actual late submission of a safety variation triggered by the signal management process.

Root Cause Analysis

[redacted]

[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 MI.4 b)

Out-of-date labelling and product information was released in [redacted] product packs following an update of the outer carton and product information in accordance with the latest QRD template. The Article 61(3) notification [redacted] was approved by the MHRA on 23 August 2022; however, batch [redacted] containing the superseded outer labelling and leaflet version was QP-certified on 07 March 2023, 12 days after the cut-off date of 23 February 2023.

While Bayer followed their own process and raised an internal implementation waiver request on 23 November 2022 to extend the implementation date to 09 March 2023, no approval was

requested from the MHRA to delay the use of the updated materials.

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 MI.4 c)

Bayer inappropriately delayed the submission data and information to the MHRA following a request from the MHRA Safety and Surveillance division with regards to [redacted] of [redacted]

MHRA sent a letter to Bayer on 06 October 2025 requesting among other items, [redacted] In subsequent email exchanges, Bayer informed the MHRA that a Type II variation was submitted to the EU to include immediate postpartum insertion in the product information and that the same change was planned for the UK, to be submitted via IRP. Bayer indicated complete information on this topic would be included in Bayer's full response to the MHRA request. At the same time Bayer requested an extension to provide the requested information. The extension was agreed to by the MHRA with the caveat that any completed sections should be submitted before the deadline to facilitate the timely review of data by the MHRA.

The EU submission package contained the Module 2.5 *Addendum to the Clinical Overview*, which presented the supporting rationale and data amend the indication for immediate post-partum use.

As this information was readily available at the time of the MHRA request, Bayer should have submitted this to the benefit-risk assessor when requested, rather than delaying the submission until the final deadline.

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.5 Pharmacovigilance System Master File

Finding MI.5 a)
Bayer did not provide a current and up-to-date UK PSMF to MHRA following a request made on 18 September 2025 to support the inspection planning. For example: • Outdated Annex [redacted] dated 25 June 2025) was provided, which did not yet include [redacted] authorised on 14 July 2025. • Annex [redacted] dated 07 July 2025) listed a number of planned audits to take place in Q3 2025; however, corresponding Annex [redacted] dated 07 July 2025) only listed completed audits until 23 June 2025, so it was not clear which of the planned audits for Q3 had already been completed.
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.5 b)
Minor discrepancies were identified with regards to the UK PSMF: i. Annex [redacted] dated 03 July 2025)

and PSMF section 7.1 stated that Accenture was carrying out case processing activities in Japan; however, since March 2025, they were only active in China on behalf of Bayer.

ii. UK PSMF Annex [redacted] dated 18 November 2025) did not include whether UK authorised products were classified as Category 1 or Category 2 under the Windsor Framework arrangements.

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. The process for ensuring that all AEs recorded within the medical information (MI) system [redacted] included an email sent by the [redacted] support team to TCS (MI support) in case of transmission failures and monitoring of AEs pending transmission to [redacted] after three days and contact the relevant users to resolve the issue. It was described during the inspection that AEs should not be pending for more than ten working days and if after this period the case was still pending, the AE would be manually submitted to PV. This could potentially lead to delays in reporting to the MHRA if a serious case is received that required a 15-calendar day timeline for submission.

2. [redacted] was opened to capture a self-identified issue with the transfer of [redacted] action items, which was identified on 10 October 2025. The action items were used to trigger requests for follow-up information. 7,029 action items relating to 4,158 cases had not been transferred to the safety database. At the time of the inspection, investigations and CAPA were either initiated or in progress, including:
   - [redacted] to implement the necessary system changes to resolve the issue by 30 November 2025.
   - [redacted] to determine which of the 7,029 non-transferred action items required follow-up attempts and to initiate these (due date 31 January 2026).
   - [redacted] to re-train staff for adhering to the coding best practices and code review guidelines (due date 28 February 2026).

   Post-inspection request: due to the impact of this quality issue on Bayer's ability to conduct follow-up activities, the MAH is requested to provide the following information post-inspection to the lead inspector:
   a) Confirmation of CAPA completion at the time of the determined due date:
      - [redacted] (28 February 2026)
      - [redacted] (28 February 2026)
      - [redacted] (28 February 2026)
   b) Once available, please provide a summary of the planned effectiveness check and its planned completion date. Once the effectiveness check has been conducted, a summary of the results should also be submitted to the lead inspector.

      Lead inspector note (dated 23 February 2026): Bayer submitted the updated quality event overview report for [redacted] to inspectors on 16 December 2025, which contained additional information regarding planned effectiveness check [redacted] "*Review the retrievals of [redacted] action items that are not displayed in [redacted] for the period from March 2026 to May 2026. The check will be considered effective if no action items were missed in displaying in [redacted] due to the mitigated coding errors.*" with a due date of 30 June 2026.

      Lead inspector note (dated 16 March 2026): Bayer provided updated CAPA and effectiveness check due dates
      - [redacted] 30 April 2026
      - [redacted] 30 April 2026
      - [redacted] 30 April 2026
      - [redacted] 31 August 2026

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.

As indicated in comment 2, Bayer is requested to provide the following information post-inspection to the lead inspector:

a) Confirmation of CAPA completion
   - [redacted] 30 April 2026
   - [redacted] 30 April 2026
   - [redacted]: 30 April 2026

b) Summary of the Effectiveness Check results, planned to be completed by 31 August 2026.

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).
- Regulation (EC) No. 726/2004 (Title II, Chapter 3), as amended.
- 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.
- EMEA/CHMP/313666/2005: “Guideline on the exposure to medicinal products during pregnancy: need for post-authorisation data”.

APPENDIX II PHARMACOVIGILANCE INSPECTION PLAN

Good Pharmacovigilance Practices (GVP) Inspection Plan

Market authorization holder (MAH) Profile	
Name of MAH: Bayer group of companies	
UKPSMF number: [redacted]	
Address:	
Bayer Inc 2920 Matheson Blvd E Mississauga, ON. Canada L4W 5R6	Bayer plc 400 South Oak Way Reading RG2 6AD United Kingdom

Inspection information
Main contacts
[redacted]

[redacted]

Inspection location
Name of the building: Bayer Canada
Building address: 2920 Matheson Blvd E, Mississauga, ON., Canada L4W 5R6
Inspection method: ☒ On-site ☐ Remotely ☐ Hybrid
Inspection details
Inspection type: Good Pharmacovigilance Practices (GVP)
Inspection sub-type: Inspection
Standards used: Health Canada: To verify compliance with the *Food and Drug Regulations*, Part C, Division(s) 1 and 8 (C.01.016 to C.01.020, C.01.050, C.08.007(1)(h), C.08.007(1.1) and C.08.008(c)). MHRA: To verify compliance with the Human Medicines Regulation 2012, Commission Implementing Regulation (EU) No 520/2012 and the published EU Good Vigilance Practice (GVP) Modules, as modified by the guidance note 'Exceptions and modifications to the EU GVP that apply to UK MAHs and the licensing authority'.
Inspection date(s): **17-21 November 2025** *Please note that if considered required, the inspection may last longer than indicated.

Inspectors
[redacted]

Inspection information		
Agenda Items (*if applicable):		
Day 1 – 17 November 2025		
The first day will be conducted as a remote inspection day conducted at the Health Canada offices. No interviews are planned during this day; however, inspectors may submit document requests during this day.		
Day 2 – 18 November 2025 (09:00 arrival for a 09:30 start)		
Purpose of Interview	*Session lead*	*Bayers staff to be interviewed*** [redacted]
09:30 – 10:30 Opening Meeting	[redacted]	Opening meeting attendees: [redacted]

Review of inspection scope, plan and logistics **Company Presentation** (max. 30 minutes) Overview of the company, the pharmacovigilance system and the quality system, including an overview of shared as well as separate PV and quality functions of Bayer Pharmaceuticals and Bayer Consumer Health. The presentation should also include information on: • Significant changes since the last GVP inspection (Health Canada and MHRA) • All relevant ongoing remediation work in the pharmacovigilance system		[redacted]
Session 1 **11:00 – 12:00 Contractual agreements** ***(global and Canada local processes)*** • Contractual agreements with third-party/other companies that conduct pharmacovigilance activities (e.g. corporate partners, third-party private labels, consultants)	[redacted]	**Interviewee(s):** [redacted]
12:00 – 13:00 Lunch		
Session 2 **13:30 – 15:15 Sources of ADRs**	[redacted]	**Interviewee(s):** [redacted]

(global and Canada local processes) • Processes and procedures for the receipt and handling, of ADRs and unusual failures in efficacy of new drugs • Quality complaints, medical information requests and other spontaneous sources involving ADRs. • Phase IV clinical trials & Patient support programs / Patient reimbursement / Patient assistance programs (if applicable)		[redacted]
Session 3 15:15 – 16:45 ICSR management *(global process)* • End-to-end ICSR process and data flow from intake tool/[redacted] interfaces to regulatory reporting to MHRA and Health Canada, incl. the reporting of unusual failures in efficacy of new drugs • Case management • Follow-up activities • Database configuration *Please provide an overview presentation (maximum 20 minutes). Please provide the presentation slides in advance of the session by COB 11 November 2025. Please be prepared to demonstrate any relevant systems and show principal documents.*	[redacted]	Interviewee(s): [redacted]
Summary of deficiencies noted at the end of each day		

Day 3 – 19 November 2025 (9:00 start)		
Purpose of Interview	*Session lead*	*Bayers staff to be interviewed*
Session 4 09:30 – 11:00 Signal management *(global process)* • Signal detection and management activities • Safety data flow between [redacted] and [redacted] • Safety data retrieval for signal management purposes *Please provide an overview presentation (maximum 20 minutes). Please provide the presentation slides in advance of the session by COB 11 November 2025. Please be prepared to demonstrate any relevant systems and show principal documents.*	[redacted]	Interviewee(s): [redacted]
Extra session: [redacted] *Interfaces*	[redacted]	*Interviewee(s):* [redacted]
12:00 – 13:00 Lunch		
Session 5 13:30 – 15:00 Aggregate reports	[redacted]	Interviewee(s): [redacted]

(global and Canada local processes) • Annual summary reports • Issue-related summary reports • Safety data retrieval for aggregate reports		[redacted]
Summary of deficiencies noted at the end of each day		
Day 4 – 20 November 2025 (9:00 start)		
Purpose of Interview	*Session lead*	*Bayers staff to be interviewed*
Session 6 09:30 – 11:00 Product information maintenance and updates *(global and UK/Canada local processes)* • Maintenance of Reference Safety Information (RSI) including submission of safety variations, implementation of updated product information and communication of safety information updates • Responding to competent authority requests • Notification of foreign actions to Health Canada	[redacted]	Interviewee(s): [redacted]
Extra session: [redacted] *reporting rules GB*	[redacted]	*Interviewee(s):* [redacted]
12:30 – 13:30 Lunch		

Extra session: [redacted]	[redacted]	*Interviewee(s):* [redacted]
Session 7 14:00 – 15:00 Computer systems validation *(global and Canada local processes)*	[redacted]	Interviewee(s): [redacted]
Extra session: Signals with GSLs	[redacted]	*Interviewee(s):* [redacted]
Summary of deficiencies noted at the end of each day		
Day 5 – 21 November 2025 (9:00 start)		
Purpose of Interview	*Session lead*	*Bayers staff to be interviewed*
~~*Session 9*~~ ~~*09:30 – 10:30 Quality systems*~~ ~~*(Canada local process)*~~	[redacted]	~~*Interviewee(s):*~~ [redacted]

• ~~*Quality systems surrounding pharmacovigilance activities including deviations, change controls, simulation exercises, self-inspection program*~~		~~***Additional experts may be added based on questions***~~
Extra session SDRA and [redacted] live demo of cases [redacted]	[redacted]	*Interviewee(s):* [redacted]
Session 8 *11:00 Training and record management* *(Canada local process)* • *Qualifications of personnel and job descriptions* • *Training program and records* • *Maintenance of records*	[redacted]	*Interviewee(s):* [redacted]
12:30 – 13:30 Lunch		
Extra session: Case review	[redacted]	*Interviewee(s):* [redacted]

Extra session: UK + Signal	[redacted]	*Interviewee(s):* [redacted]
Closing meeting	[redacted]	All welcome [redacted]
27 November 2025, 09:30		
Extra Session: Signal Detection (remote)	[redacted]	*Interviewee(s):* [redacted]

*Please note that this inspection plan is subject to changes before or during the inspection. Additional documentation may be requested earlier in the inspection for review. If additional days are required, this inspection may extend beyond 21 November 2025.

**Bayer: Please note that depending on the nature of your questions, additional interviewees can be involved during the inspection.