Medicines & Healthcare products
Regulatory Agency

PHARMACOVIGILANCE
INSPECTION REPORT

Pharmacovigilance System Name: Moderna

MHRA Inspection Number: Insp GPvP 53720/36115546-0001

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ABBREVIATIONS

ADR	Adverse Drug Reaction
AE	Adverse Event
CAP	Centrally Authorised Product
CAPA	Corrective and Preventative Action
CCDS	Company Core Data Sheet
DCP	Data Collection Programme
EMA	European Medicines Agency
EU	European Union
EVDAS	EudraVigilance Data Analysis System
FTE	Full Time Equivalent
GVP	Good Vigilance Practice
HCP	Healthcare Professional
HSA	Health Security Agency
ICSR	Individual Case Safety Report
KPI	Key Performance Indicator
MAA	Marketing Authorisation Application
MAH	Marketing Authorisation Holder
MedDRA	Medical Dictionary for Regulatory Activities
PASS	Post-Authorisation Safety Study
PEC	Product-Event Combination
PIL	Patient Information Leaflet
PRAC	Pharmacovigilance Risk Assessment Committee
PSMF	Pharmacovigilance System Master File
PSUR	Periodic Safety Update Report
PV	Pharmacovigilance
PVA	Pharmacovigilance Agreements
QA	Quality Assurance
QMS	Quality Management System
QPPV	Qualified Person responsible for Pharmacovigilance
RMP	Risk Management Plan
SDEA	Safety Data Exchange Agreement

[redacted]	[redacted]
SmPC	EU Summary of Product Characteristics
SOP	Standard Operating Procedure
UK	United Kingdom
VAERS	Vaccine Adverse Event Reporting System

SECTION A: INSPECTION REPORT SUMMARY

Inspection type:	Statutory National Inspection – MHRA and Health Canada Joint Inspection
System(s) inspected:	Moderna Biotech Spain S.L. [redacted]
Site(s) of inspection:	123 Victoria Street, SW1E 6DE, London
Main site contact:	[redacted]
Date(s) of inspection:	25 – 28 March 2025
Lead Inspector:	[redacted]
Accompanying Inspector(s):	[redacted]
Previous inspection date(s):	01 - 04 February 2021 (Insp GPvP 53720/19511623-0001)
Purpose of inspection:	Inspection of pharmacovigilance systems to review compliance with UK requirements.
Products selected to provide system examples:	As part of the general systems review, specific ADR reports were examined for [redacted]
Name and location of UK QPPV:	[redacted] Moderna France 19 rue Cognacq Jay 75007 Paris France [redacted]
Global PV database (in use at the time of the inspection):	[redacted] commercially available)
Key service provider(s):	Pharmacovigilance services provided by IQVIA and APCER. Medical information services provided by Propharma and Alphanumeric.
Inspection finding summary:	01 Major finding 05 Minor findings
Date of first issue of report to MAH:	09 May 2025
Deadline for submission of responses by MAH:	13 June 2025 25 July 2025
Date(s) of receipt of responses from MAH:	13 June 2025 25 July 2025 and 01 August 2025 (minor update)
Date of final version of report:	CAPA_1: 15 August 2025 CAPA_2: 15 September 2025 (MA.1 a) PA.1 and associated deliverable updated)
Report author:	[redacted]

SECTION B: BACKGROUND AND SCOPE

B.1 Background information

Moderna 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 Canadian pharmacovigilance regulations and guidelines. In particular, reference was made to The Human Medicines Regulations 2012 as amended, 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 which will be described in the Health Canada Inspection Report.

A list of reference texts is provided at Appendix I.

Moderna is an American biopharmaceutical company headquartered in Cambridge, Massachusetts, specialising in utilising [redacted] technology. At the time of the inspection Moderna had two UKMA(UK) Category 1 products authorised in the UK, [redacted]
A number of Moderna vaccines targeting different variants of [redacted] had been authorised by the MHRA since 2021. At the time of the inspection, the following [redacted] were authorised in UK (full marketing authorisation):

- [redacted] (no longer marketed in the UK)
- [redacted] were marketed at the time of the inspection and this was the updated vaccine approved by the MHRA on 02 September 2024 for the dominant subvariant.

The UK licences for previous [redacted] had been cancelled at the time of the inspection.

The role of MAH in Europe was assumed by Moderna Biotech Spain S.L. located in Madrid, Spain.

Moderna outsourced pharmacovigilance activities to IQVIA, which acted as the global case processing vendor, and case intake and triage to APCER Life Sciences.
In addition, global contact centre activities were outsourced to Alphanumeric Systems Inc. and ProPharma Group.
Moderna employees were responsible for oversight of these vendors as well as other pharmacovigilance activities, medical information and regulatory affairs activities conducted in the United States and in several affiliates worldwide.

B.2 Scope of the inspection

The inspection included a review of the global pharmacovigilance systems and was performed at Moderna's offices in London. Personnel from Moderna were available on site or via teleconference in order to participate in the inspection.

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).

Non-interventional post-authorisation safety studies (NI-PASS) and quality management system processes 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 on 12 November 2024 (version 14, effective date 12 November 2024) to assist with inspection planning and preparation. Specific additional documents including an updated version of the PSMF were also requested by the inspection team and provided by the company prior to the inspection. The detail of these requests is contained within the inspection document request Excel spreadsheet.

B.4 Conduct of the inspection

In general, the inspection was performed in accordance with the Inspection Plan.

A closing meeting was held to review the inspection findings at Moderna's offices in London, on 28 March 2025.

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

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

- Significant expansion of internal PV system resources from 10 Full Time Equivalents (FTEs) in 2021 to 180 FTEs in 2025
- Internalisation of critical PV processes in 2022
- Implementation of new computerised systems and digital tools, for example, [redacted] for PV Signal and PV Reports
- Outsourcing of case intake and triage to APCER Life Sciences from 26 June 2023
- Outsourcing of Global contact centre activities to Alphanumeric Systems Inc. and ProPharma Group since 30 January 2024.

At the time of the inspection, Moderna were continuing the internalisation and optimisation of pharmacovigilance processes.

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 Drug Reactions

Requirements:

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 licensing authority to make sure that the minimum criteria are included in the reports. Four minimum criteria are required for ICSRs validation:
[…]
b. one single identifiable patient [..]
An ICSR should not be considered valid for submission unless information is available for at least one of the patient qualifying descriptors.'

VI.B.6.4. Lack of therapeutic efficacy
'In certain circumstances, reports of lack of therapeutic efficacy with no suspected adverse reactions may require to be submitted within a 15-day time frame […] vaccines are examples of such cases.'

VI.C.2.2.7. Period between the submission of the marketing authorisation application and the granting of the marketing authorisation
'*In the situation where a medicinal product application is under evaluation in the UK while it has already been authorised in a third country, valid ICSRs from outside the UK, originating from unsolicited reports (see VI.B.1.1. for definition) or solicited reports (see VI.B.1.2. for definition), should be submitted in accordance with the time frames and modalities provided in VI.C.3., VI.C.4. and VI.C.6.'*

The following findings were noted in relation to management and reporting of adverse reactions:

Finding MA.1 a)

The delayed and/or incorrect activation date in the [redacted] product dictionary of [redacted] products resulted in ICSRs not being reported to the MHRA in the time between submission of marketing authorisation application (MAA) and granting of the licence.

It was confirmed during the interview session that Moderna had made the [redacted] products active in the [redacted] product dictionary, and therefore triggering expedited reporting of ICSRs

to the MHRA, following approval of the marketing authorisation and not from the submission of the MAA as required by GVP VI.C.2.2.7. This meant that reportable ICSRs received in the time period between MAA submission and configuration in the [redacted] product dictionary were not reported to the MHRA. In addition, further delays were observed where the products were configured in the dictionary after MAA approval.

For example, MAAs for [redacted] were submitted to the MHRA on 22 November 2022 and MAA was granted on 21 February 2023. However, in the [redacted] product dictionary, the product was made active on 28 February 2023, over three months after MAA submission and seven days after approval of the relevant products in the UK.
As a result, examples were identified of ICSRs received by Moderna in the time period between MAA submission and MA grant that had not been reported to the MHRA:

a) Reports of lack of efficacy (reportable ICSRs within 15 days for vaccines), [redacted] initially received on 04 January 2023 and on 31 January 2023, respectively.

b) Serious reports of [redacted] accident initially received by Moderna between 09 December 2022 and 16 February 2023: [redacted]

Similarly, the following additional [redacted] licences were incorrectly activated in the [redacted] product dictionary after the MAA submission date, with delays of up to five months from MAA submission date, and up to two months from the MAA approval date. Therefore, there is the potential that a high number of ICSRs had not been reported to the MHRA, particularly considering the high volume of ICSRs received for [redacted]

[redacted]	**Days MAA submission to Argus configuration**	**Days MAA Approval to Argus configuration**
[redacted]	155	8
[redacted]	126	7

[redacted]	126	7
	125	61
	91	7
	58	6

Furthermore, the MAH confirmed that the error in the [redacted] configuration was replicated with the most recently approved vaccine [redacted]

Post-inspection action:

The MAH is required to conduct an impact assessment to determine the extent of missed ICSR reporting to the MHRA for both [redacted] (all licences) and [redacted]

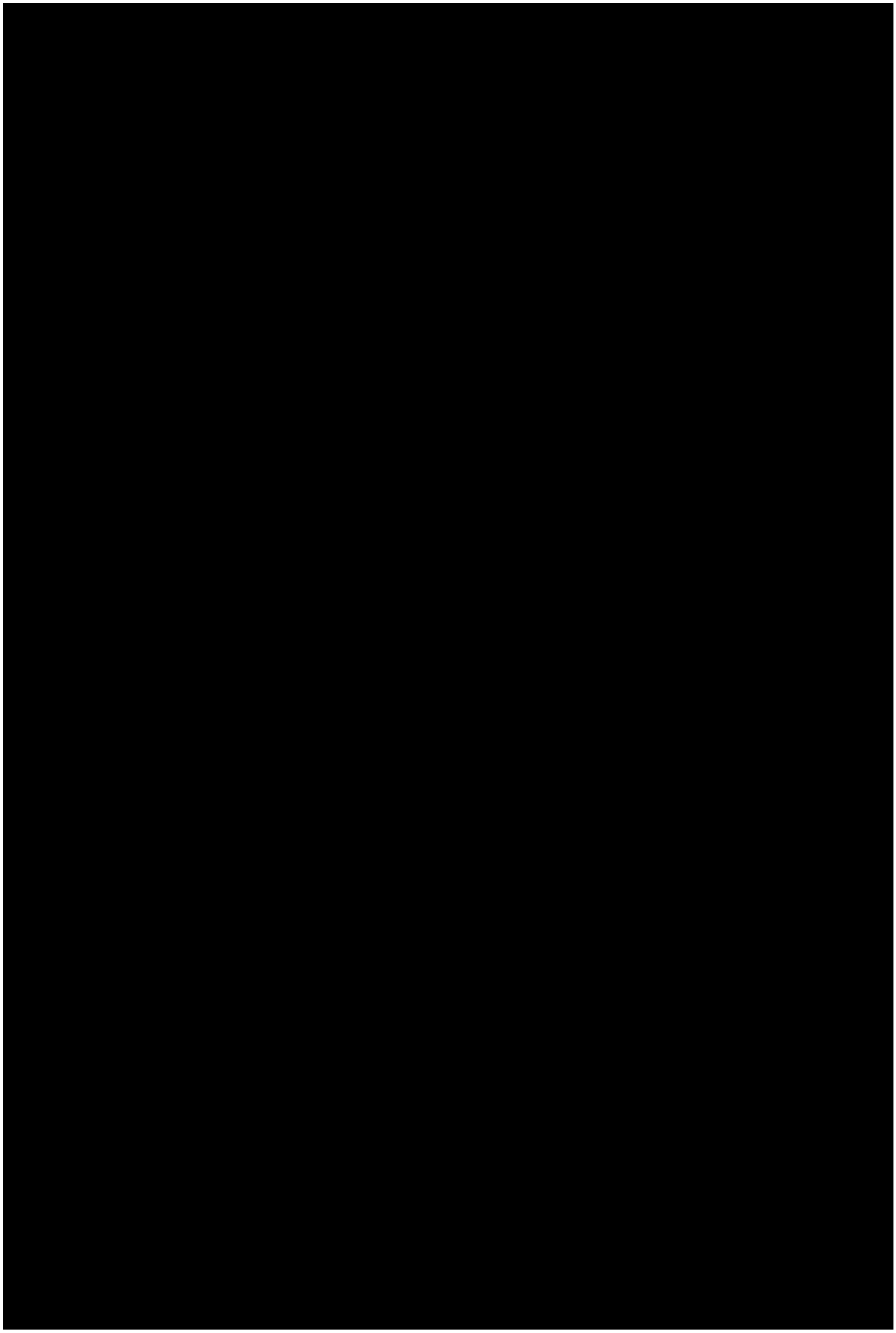
Root Cause Analysis

[redacted]

[redacted]

Further Assessment

[redacted]



Corrective Action(s)
[redacted]

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

Preventative Action(s)
[redacted]

[redacted]

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

Finding MA.1 b)

The following cases had been reported to the MHRA despite not meeting the four minimum criteria for ICSR validation, as required by GVP VI.B.2

- [redacted] eported to the MHRA on 06 May 2021
- [redacted] reported to the MHRA on 23 October 2023
- [redacted] reported to the MHRA on 10 April 2024
- [redacted] 5 reported to the MHRA on 18 June 2024

These cases were invalid since there was no identifiable patient in the source documentation. Reporting rules were configured in [redacted] to prevent expedited reporting to the MHRA when the "No Patient Identifiers" case classification was selected in a case.
These four cases were reported to the MHRA due to a data entry error whereby the case classification as "No Patient Identifiers" was erroneously omitted in [redacted] at the time of initial processing.

It is acknowledged that the MAH submitted an amendment report to downgrade two of the four reports identified [redacted] in the lead up to the inspection on 10 March 2025, however, the other two were not downgraded.

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]	

C.4.3 Minor findings

MI.1 Maintenance of Reference Safety Information

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, PILs and IBs, so that healthcare professionals, patients or trial subjects are able to use the medicinal product correctly on the basis of full and comprehensive information.

Moderna was responsible for the submission and implementation of safety variations.
For [redacted] multi-vial packs, Moderna was responsible for providing updated PILs and ordering print runs of the PILs via a service provider, Harlow Printing Limited (hereafter Harlow Printing). Paper PILs were then delivered to the UK Health Security Agency (HSA) directly by Harlow Printing. UK HSA was responsible for receiving the paper PILs from the printers and onward distribution to the vaccination centres in accordance with their procedure.

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

Finding MI.1 a)

The UK QPPV and MAH had insufficient oversight mechanisms to monitor the timeliness of safety variation submissions and implementation via the distribution of updated PILs to the UK HSA and via the electronic medicines compendium (emc). As a critical process, the UK QPPV and MAH should have oversight and authority of the fulfilment of pharmacovigilance in relation to maintaining and making available up-to-date product information in a timely manner.

Firstly, there was no adequate system for tracking safety variation submissions. This was evidenced by the fact that Moderna was unable to provide accurate information on safety variations submission when requested for inspection purposes. For example,

I. The safety variation tracker was missing information relating to the submission of a Type 1A safety variation to implement a PRAC recommendation adopted at the [redacted] PRAC meeting. The variation was to add information for [redacted] The MAH stated that "*It was overlooked to include the safety variation information for* [redacted] *in the safety variation tracker Request 24*." The variation had been submitted on time on 07 April 2022, in line with timelines outlined in PRAC recommendations.

Secondly, the tracking of safety variation implementation was also inadequate:

II. The MAH had no mechanism in place to track the implementation of safety variations into paper PILs and ensure that safety variations had been implemented on time. This was evidenced by the fact that the safety variation tracker provided for inspection did not include any details of the implementation of safety variations into paper PILs. It is recognised that [redacted] was a seasonal vaccine with batches released twice a year, and therefore it was unlikely that a new safety variation would be required to be implemented before a new vaccine variant was released. However, there was an example of a change to the safety information in the [redacted] SmPC and PIL of [redacted] and multiple batches had been released in the months following the safety variation approval. The safety variation related to the inclusion of [redacted] to PIL section 2 and 4, approved by the MHRA on 16 August 2021 [redacted]
Although Moderna was able to evidence the dates this safety variation was

implemented (i.e. implemented via distribution of updated PILs to [redacted]) and shipped to the UK HSA for provision to patients, this information was not systematically tracked to ensure appropriate oversight of the timeliness of safety variation implementation. In addition, there was no monitoring of the compliance of implementation of safety variations by the QPPV to ensure that the updated PIL had been implemented on time.

III. There was no tracking of the electronic implementation of updated SmPCs and PILs on the Moderna website or onto the emc website to ensure that these were being uploaded in a timely manner. The MAH is reminded that the MHRA expectation for the submission/upload of updated product information to the emc or company sponsored website is:

- within 10 business days of the Type IAIN variation submission for purely national procedures.
- within 10 business days of variation approval for Type IB and II variations.

As part of the impact assessment and CAPA, the MAH should assess historic electronic uploads and confirm their compliance with these timelines.

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.1 b)

The following deficiencies were identified in the procedural documents describing the process for the implementation of safety variations:

I. There was no procedural document outlining the maximum timelines for the implementation of safety variations via the introduction of updated PILs into product packs. MHRA expects safety variations to be implemented into printed product information (PILs and SmPCs):
   - within 3-6 months of the Type IAIN variation submission for purely national procedures
   - within 3-6 months of variation approval for Type IB and II variations.

II. Although the MHRA requirement to implement SmPC and PIL updates onto the emc website within 10 days from variation approval was documented in the guidance 'Instruction for upload of SmPCs and PILs through new emc publishing tool (UK)', this was not a formal version controlled or dated procedural document within the quality management system. It is acknowledged that the MAH indicated that it was their intention to turn this document into a formal work instruction.

III. The document "Instruction for upload of SmPCs and PILs through new emc publishing tool (UK)' stated a requirement to implement SmPC and PIL updates onto the emc website within 10 days from variation approval, however, it did not clarify that for Type IA(IN) safety variations, the electronic update of SmPC and PIL should be within 10 days of the submission of the variation (for purely national safety variations).

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 Pharmacovigilance System Master File

Information provided by MAHs to the licensing authority in the Pharmacovigilance System Master File (PSMF) should be complete and accurate in order to facilitate the supervisory duty of the licensing authority.

The following findings were noted in relation to the PSMF:

Finding MI.2 a)

The following deficiencies were identified in the content of the UK PSMF version 16.0 dated 11 March 2025:

I. UK PSMF Annex [redacted] dated 11 March 2025) did not include signal management performance indicators although these were used by Moderna as per [redacted] dated 10 March 2025). According to GVP Module IX.B.5 (as modified by the MHRA exception and modification document), signal management performance indicators should be presented in the annex to the PSMF, when used.

II. It was not clear from UK PSMF Annex [redacted] dated 11 March 2025) that the following partners were MAHs of [redacted] in various regions:

- [redacted] was described as a distributor in the Latin American (LATAM) region for [redacted] despite also being an MAH in Brazil.
- [redacted] was described as a distributor despite being the MAH in Saudia Arabia
- [redacted] was described as a logistics and distribution partner despite being the MAH in the Philippines.

These were also not included within PSMF Annex [redacted] dated 11 March 2025) or mentioned in PSMF Annex [redacted] dated 11 March 2025). Moderna is reminded that information on marketing arrangements should be included in the PSMF sections describing contracts and arrangements to ensure that the licensing authority has visibility in the

PSMF of all contractual arrangements for UK authorised products.

III. Harlow Printing was not listed as a vendor in the UK PSMF version 16.0 dated 11 March 2025. Harlow Printing was responsible for supplying printed patient information leaflets for [redacted] to the UK HSA and to inform Moderna of safety reports in the event such information was received by the service provider, in accordance with the Master Service Agreement amendment 01 dated June 2023. As this relates to services subcontracted by the MAH for the fulfilment of pharmacovigilance obligations, Harlow Printing should have been listed as vendor in the PSMF.

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]	

MI.3 Management of Adverse Drug Reactions

Finding MI.3 a)
There were issues identified with case coding: I. There were a number of cases where reporter type had not been entered into the [redacted] safety database structured data field due to a data entry error. Hence, the 'All report sources' data field was blank in the line listing provided in a pre-inspection document request. Examples included the following foreign, non-serious cases, received from a consumer: [redacted]

[redacted]

III. Case [redacted] was a serious literature case of portal vein thrombosis identified in a literature search conducted on 27 April 2021; however, the initial received date by the company was erroneously entered as 28 April 2021. This case was not valid for reporting to the MHRA due to no patient identifiers (see also MA1.b)).

IV. Case [redacted] was included in [redacted] as an invalid fatal case reporting multiple events (e.g. paralysis, anaphylactic reaction, cerebrovascular accident, acute cardiac event). Upon review of the source documentation, this case had been inappropriately coded in the safety database since there was no evidence in the source documents that a single individual patient had been reported to experience all the events.

Lead Inspector note (15 August 2025): following the receipt of further rationale and evidence that was no impact on expedited and aggregate reporting as part of the responses to the inspection report, finding MI.3 a) II was removed.

Root Cause Analysis

[redacted]

[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 Collection and Collation of Safety Information

~~Finding~~ ~~MI.4 a)~~
[redacted]

[redacted]

Lead Inspector note (15 August 2025): finding MI.I a) was removed since the MAH provided evidence as part of the responses to the inspection report that the AE had been entered into the global safety database.

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 MAH had failed to appropriately follow-up a medical information query to confirm whether there was an associated adverse event or special situation which was required to be reported to the global safety database. A medical information enquiry [redacted] was received by the contact centre on 16 January 2025 via email. The enquirer stated that he had a patient who had been vaccinated with [redacted] and another [redacted] roughly four weeks apart. He asked for clinical advice and guidance. This was initially identified as a potential special situation and sent to the AE portal by the contact centre; however, it was rejected as the MAH stated that they interpreted the chronology of product administration based on the order in which the information was reported and as [redacted] was mentioned first, they did not evaluate it as being off label for [redacted] However, this was an assumption, and no follow-up was conducted to confirm this or indeed verify whether the patient had suffered an adverse event due to the potential off-label use.
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 c)
A deviation regarding the incorrect management of a UK Data Collection Programme (DCP) was handled inadequately. Deviation [redacted] was raised on 29 January 2025 when it was identified that a UK programme conducted by the Market Access and Health Economics teams between 25

October 2024 and 21 November 2024 had not been handled as per [redacted] dated 15 June 2022), despite meeting the criteria of a DCP.

Although it is acknowledged that training was given to commercial and medical teams, and a review was conducted to ensure no AE reports had been missed, no further impact assessment was performed to ensure that no further programmes meeting the definition of a DCP had been missed by the team.

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 d)

No evidence was provided during the inspection that reconciliation of medical information enquiries had been conducted as per the pharmacovigilance agreement (PVA) in place with [redacted]

[redacted] was the MAH in Brazil and distributor in the LATAM region for [redacted] The PVA (version 1 dated 23 February 2023), stated that medical information enquires should be reconciled monthly. It is acknowledged that the PVA stated that this was the responsibility of the partner to initiate this reconciliation, however, Moderna should have oversight that the terms of the PVA are being adhered to. In addition, an audit conducted in September 2024 [redacted] of the partner did not identify or report this deficiency.

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 Contracts and Agreements

Finding MI.5 a)
The Quality Agreement (date of last signature 27 August 2024) and Master Service Agreement between Moderna Biotech Distributor UK Ltd and the UK HSA lacked information on the provision of PILs to patients. According to the Quality Agreement, Moderna UK was responsible for selling and supplying [redacted] to the UK HSA and the UK HSA was responsible for storing and distributing the product to vaccination centres. Although the agreement described the roles and responsibilities with respect of the handling of the products, there was no clause that Moderna would ensure that sufficient printed PILs would be provided to enable the UK HSA to distribute one PIL to each patient, or any other measures associated with the provision of up to date and accurate PILs.
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.5 b)

The master services agreement (MSA) between Moderna Switzerland and Harlow Printing Limited (effective date 12 August 2021) Clause 5.4 Record Retention stated that records should be retained for a minimum of five years following the completion of the statement of work, or longer if required by applicable law or regulation. However, in line with HMR Schedule 12A paragraph 16(3), records relating to pharmacovigilance should be retained for at least 10 years after the marketing authorisation has expired.

Root Cause Analysis

[redacted]

Further Assessment

[redacted]

Corrective Action(s)

Deliverable(s)	**Due Date(s)**
Preventative Action(s)	
Deliverable(s)	**Due Date(s)**

C.4.4 Comments

- **Management of Adverse Drug Reactions**

  Two examples were identified where the MAH had not conducted any follow-up for events of [redacted] associated with [redacted]:
  - [redacted]
  - [redacted]

  Although it is acknowledged that these were received via other MAHs this does not negate the fact that the other MAH could be requested to conduct courtesy follow-up on behalf of Moderna, and to provide further information, if available.

- **Signal Management**

  The following procedural documents describing signal detection methodologies could be more detailed to facilitate the identification of potential signals, and therefore to limit the chance of missing a potential signal.
  - [redacted] dated 10 March 2025)
  - [redacted] dated 16 January 2023)
  - [redacted] dated 16 January 2023)

  The global safety database, EVDAS and VAERS were reviewed within the Moderna electronic Signal Detection and Management System (eSDMS) based on the generation of alerts flagging Product-Event Combinations (PEC) reaching predefined disproportionality thresholds, as well as alerts for Adverse Events of Special Interest (AESI), Safety Concerns, and standard topics (e.g. off-label use, overdose, medication errors, lack of efficacy). As described in [redacted] the signal management scientist and/or Clinical Safety Physician would review the alerts to determine whether these would meet the definition of a potential signal. It was confirmed during the interview session that 'scientific judgment' was applied; however, the procedural documents could be more detailed to provide guidance on qualitative criteria to aid the selection of PEC for further medical review or to be classified as potential signals requiring

signal validation (for example, qualitative review of ICSRs, confounding factors, temporal association, reference safety information).

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) as amended.
- 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.

APPENDIX II PHARMACOVIGILANCE INSPECTION PLAN

INSPECTION NUMBER	TBC (MHRA) 85869 (HEALTH CANADA)	**DAY**	1
PHARMACOVIGILANCE INSPECTION OF	Moderna	**DATE**	Tuesday, 25 March 2025
LOCATION	123 Victoria Street, SW1E 6DE	**START TIME**	09:00
INSPECTION TEAM	[redacted]		

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

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

- Collection and collation of safety information
- ICSRs management
- Signal management
- Risk management
- Periodic reporting
- Training, CV, Job Description
- Computer System Validation
- Maintenance of Records

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.

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.

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.

Session	Time	Attendees/interviewees
Opening Meeting Review of scope of inspection and inspection plan **Company Presentation** Overview of the company, the pharmacovigilance system and the quality system. The presentation may also include information on any relevant ongoing remediation work in the pharmacovigilance system. *(approx. 20 minutes)*	09:00 -09:45	All welcome **Opening meeting attendees:** [redacted]
Document review and ad hoc sessions as required	-	Inspectors only
LUNCH		

Collection and collation of safety information (spontaneous and solicited): • Medical information and product quality complaints and other spontaneous sources • Partners incl. SDEAs/PVAs • Solicited sources • Literature • Health Canada and UK specific regulatory requirements	13:00 – 15:00	Interviewee(s): [redacted] <u>Additional interviewees may be called in as needed for:</u> • Medical information • Product Quality Complaints • Partners incl. SDEAs/PVA • Solicited Sources • Literature
Document Review and ad hoc sessions as required	-	Inspectors only

MHRA INSPECTION NUMBER	TBC(MHRA) 85869 (HEALTH CANADA)	**DAY**	2
PHARMACOVIGILANCE INSPECTION OF	Moderna	**DATE**	Wednesday, 26 March 2025
LOCATION	123 Victoria Street, SW1E 6DE	**START TIME**	09:00

Session	**Time**	**Attendees/interviewees**
ICSR management: • Case processing, coding and expediting reporting • Follow-up activities • Health Canada and UK specific regulatory requirements	10:30 – 12:30	Interviewee(s): [redacted]
Document review and ad hoc sessions as required	-	Inspectors only
LUNCH		
Signal management: • Detection, validation, evaluation and tracking of signals • Notifying Health Canada of foreign actions	13:30 – 15:00	Interviewee(s): [redacted]
Document review and ad hoc sessions as required	-	Inspectors only

MHRA INSPECTION NUMBER	TBC(MHRA) 85869 (HEALTH CANADA)Insert inspection number	**DAY**	3
PHARMACOVIGILANCE INSPECTION OF	Moderna	**DATE**	Thursday, 27 March 2025
LOCATION	123 Victoria Street, SW1E 6DE	**START TIME**	09:00

Session	**Time**	**Attendees/interviewees**
Risk Management: • Identification, submission, implementation and tracking of safety variations • Terms & Conditions that apply to MA, Label and product monographs update	11:00 – 13:00	Interviewee(s): [redacted]
Document review and ad hoc sessions as required	-	Inspectors only
LUNCH		
Periodic reporting • Submission, authoring and QC of periodic reports (including Annual summary reports, Issue-related summary reports)	14:30 – 15:30	Interviewee(s): [redacted]
Document review and ad hoc sessions as required	-	Inspectors only

MHRA INSPECTION NUMBER	TBC(MHRA) 85869 (HEALTH CANADA)	**DAY**	4
PHARMACOVIGILANCE INSPECTION OF	Moderna	**DATE**	Friday, 28 March 2025
LOCATION	**Error! Reference source not found.**	**START TIME**	09:00

Session	**Time**	**Attendees/interviewees**
Document review and ad hoc sessions as required	-	Inspectors only
LUNCH		
Document review and ad hoc sessions as required	-	Inspectors only
Closing meeting	TBC	All welcome

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:

[redacted]