



Medicines & Healthcare products
Regulatory Agency

PHARMACOVIGILANCE INSPECTION REPORT

Pharmacovigilance System Name: Aspen Pharma Trading Limited

MHRA Inspection Number: Insp GPvP 39699/3147196-0002

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ABBREVIATIONS

ADR	Adverse Drug Reaction
AE	Adverse Event
CAPA	Corrective and Preventative Action
CCDS	Company Core Data Sheet
CHMP	Committee for Medicinal Products for Human Use
EMA	European Medicines Agency
EU	European Union
GVP	Good Vigilance Practice
HCP	Healthcare Professional
ICH	International Conference on Harmonisation
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
PIL	Patient Information Leaflet
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
SDEA	Safety Data Exchange Agreement
SmPC	EU Summary of Product Characteristics
SOP	Standard Operating Procedure
UK	United Kingdom

SECTION A: INSPECTION REPORT SUMMARY

Inspection type:	Statutory National Inspection
System(s) inspected:	Aspen Pharma Trading Limited UKPSMF01535 / MFL3687
Site(s) of inspection:	Remote
Main site contact:	[REDACTED] PV QMC Manager, Deputy EU QPPV [REDACTED] [REDACTED]
Date(s) of inspection:	25 – 28 June 2024
Lead Inspector:	[REDACTED]
Accompanying Inspector(s):	[REDACTED]
Previous inspection date(s):	09 and 10 September 2014 05 to 07 February 2013
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 review of signal management and maintenance of reference safety information, information was examined for products [REDACTED] and [REDACTED]
Name and location of UK QPPV:	[REDACTED] Aspen Pharma Trading Ltd, 3016 Lake Drive, Citywest Business Campus, Dublin 24 Switchboard: [REDACTED] [REDACTED]
Global PV database (in use at the time of the inspection):	[REDACTED] (commercially available)
Key service provider(s):	Pharmacovigilance services provided by Alphamed. Medical information services provided by ProPharma group. Global and local medical literature monitoring services provided by MS Pharm. PV auditing services as required provided by ZigZag Associates Ltd
Inspection finding summary:	03 Major findings 05 Minor findings
Date of first issue of report to MAH:	14 October 2024
Deadline for submission of responses by MAH:	22 November 2024 10 January 2025 10 April 2025
Date(s) of receipt of responses from MAH:	22 November 2024 10 January 2025 10 April 2025
Date of final version of report:	14 April 2025
Report author:	[REDACTED]

	Pharmacovigilance Inspector
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SECTION B: BACKGROUND AND SCOPE

B.1 Background information

Aspen Pharma Trading Limited (APTL) was selected for routine inspection as part of the MHRA's statutory, national pharmacovigilance inspection programme. The purpose of the inspection was to review compliance with currently applicable UK and 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'.

A list of reference texts is provided at Appendix I.

Aspen Holdings, referred to hereafter as Aspen, a company with its strategic head office in South Africa, was a supplier of branded and generic pharmaceuticals in over 100 countries globally and was comprised of several legal entities. Under the umbrella of Aspen Holdings, Aspen Pharmacare and Aspen Global Incorporated (AGI) were separate companies that were holders of Intellectual Property for products marketed in Europe and worldwide. APTL was the marketing authorisation holder (MAH) in the UK and EU and other selected regions on behalf of Aspen Pharmacare and AGI. APTL headquarters were based in Dublin, Ireland.

Aspen Pharmacare UK Limited (APUK) was a subsidiary of Aspen Pharma Ireland Limited, which was a subsidiary of AGI. These subsidiaries were non-market authorisation (MA) holding entities which provided support to the MA holding entities.

Aspen companies also had commercial partners in all markets and some affiliate offices of the partners acted, for Aspen medicinal products, as Aspen subsidiaries, receiving ICSRs and other safety information and forwarding this to Aspen Group PV.

All pharmacovigilance functions for the entire Aspen Group of Companies globally was outsourced to Alphamed Formulations Private Ltd., a wholly owned subsidiary of Aspen Pharmacare, based in Hyderabad, India. Alphamed, was referred to as 'Group PV'. In the EU, Group PV were overseen by the PV department at APTL in Dublin. The Europe Quality department was responsible for the Quality Management System (QMS) and was also based in Dublin.

Additional PV activities were outsourced as follows:

- Medical information first-line enquiries from the UK were handled by ProPharma group under the supervision of the Aspen Medical Governance department; while second-line enquiries were handled by the Group Medical Information (GMI) department, at Alphamed.
- Global and local medical literature monitoring outsourced to MS Pharm
- PV auditing service outsourced to ZigZag Associates Ltd (based in UK) as required

B.2 Scope of the inspection

The inspection included a review of the local (UK) and global pharmacovigilance systems and was performed remotely. Personnel from APTL, Group PV and the local UK affiliate, participated in the inspection via videoconference

The inspection was performed using interviews and document review (including outputs from the global safety database and listings of medical information enquiries and product complaints). The systems reviewed during the inspection are highlighted in the Pharmacovigilance Inspection Plan (attached as Appendix II).

Management of reference safety information was not reviewed in detail and it is recommended that this area is subject to closer review during a subsequent pharmacovigilance inspection.

B.3 Documents submitted prior to the inspection

The company submitted a PSMF (version [REDACTED] effective 30 April 2024) and annexes (version [REDACTED] effective 21 May 2024) to assist with inspection planning and preparation.

Specific additional documents were also requested by the inspection team and provided by the company prior to the inspection. The detail of those requests is contained within document request sheet A and B.

B.4 Conduct of the inspection

In general, the inspection was performed in accordance with the Inspection Plan. An additional half day of document review post-inspection was required.

A closing meeting was held remotely via videoconference on 28 June 2024.

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 inspection in 2014 the company had made the following changes to the pharmacovigilance system:

- Change in EU QPPV to [REDACTED] from November 2015.
- Transfer of global safety database provider from [REDACTED] to [REDACTED] in 2017.
- Aspen changed the signal management process from a manual method to an automated one using the [REDACTED] application. In February 2022, use of [REDACTED] went live, but Aspen continued to perform the manual signal detection process alongside [REDACTED] until August 2022 to validate the different methodology and ensure no safety signal was missed during the implementation stage.

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 <u>outputs</u> 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 Provision of information to enable supervision by the licensing authority

Requirements:

The Human Medicines Regulations 2012 (Statutory Instrument 2012 No. 1916), Part 11 Pharmacovigilance

Regulation 182

- (2) *“The holder must (as part of its pharmacovigilance system) — [...] (b) maintain and make available on the request of the licensing authority a pharmacovigilance system master file”*
- (5) *“Where the licensing authority requests that the pharmacovigilance system master file is made available under paragraph (2)(b), the holder must submit a copy of the pharmacovigilance system master file to the licensing authority before the end of the period of 7 days beginning on the day after the day when the request was made.”*

Commission Implementing Regulation (EU) No. 520/2012, Chapter I, Article 3,

“The pharmacovigilance system master file shall have an Annex containing the following documents: [...]

- (3) *the list of subcontracts referred to in Article 6(2); [...]*
- (5) *a list of all scheduled and completed audits;”*

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

II.B.4.2. PSMF section on the organisational structure of the marketing authorisation holder Delegated activities

“The PSMF, where applicable, shall contain a description of the activities and/or services subcontracted by the marketing authorisation holder [IR Art 2 (6)] relating to the fulfillment of pharmacovigilance obligations. This includes arrangements with other parties in any country, worldwide, if applicable to the pharmacovigilance system applied to products authorised in the UK.”

II.B.4.3. PSMF section on the sources of safety data

“The description of the main units for safety data collection should include all parties responsible, on a global basis, for solicited and spontaneous case collection for products authorised in the UK. (...)

Information about third parties (licence partners or local distribution/marketing arrangements) should also be included in the section describing contracts and agreements (see II.B.4.2. and II.B.4.8.). (...)

For the purposes of inspection and audit of the pharmacovigilance system, sources include data arising from study sources, including any studies, registries, surveillance or support programmes sponsored by the marketing authorisation holder through which ICSRs could be reported. MAHs should be able to produce and make available a list of such sources to support inspection, audit and QPPV oversight.”

II.B.4.6. PSMF section on pharmacovigilance system performance

“Targets for the performance of the pharmacovigilance system shall be described and explained.”

II.B.4.8. Annex to the PSMF

“An annex to the PSMF shall contain the following documents: [...]

- A list of contractual agreements covering delegated activities including the medicinal products and territory(ies) concerned in accordance with Article 6(2) of Commission Implementing Regulation (EU) No 520/2012 (see II.B.4.3.) [IR Art 3(3)]; [...]
- A list of all completed audits, for a period of five years, and a list of audit schedules [IR Art 3(5);”

The licensing authority has an obligation to supervise MAHs to ensure that legal requirements governing medicinal products are complied with. The Human Medicines Regulations 2012 (as amended) regulation 327 empowers the licensing authority to inspect the premises, records, documents and PSMF of the MAH or any firms employed by the MAH to perform the activities described in Part 11. Information provided by MAHs to the licensing authority should be complete and accurate in order to facilitate the supervisory duty of the licensing authority. This could include information provided in response to requests made in the context of an inspection or a post-authorisation measure, information submitted to the licensing authority in relation to the pharmacovigilance system or information included in the PSMF.

The following findings were noted in relation to provision of information to the licensing authority:

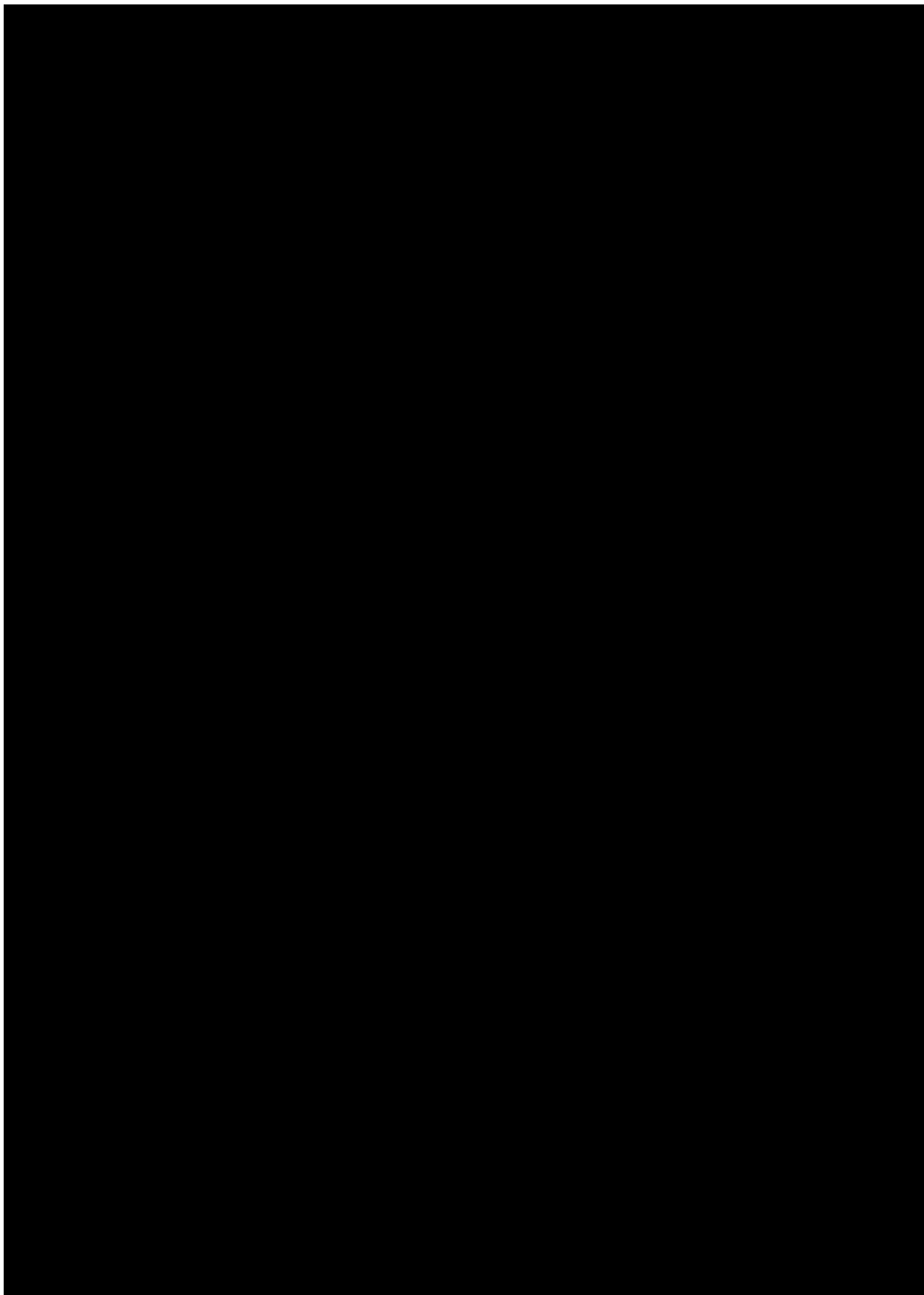
Finding MA.1 a)

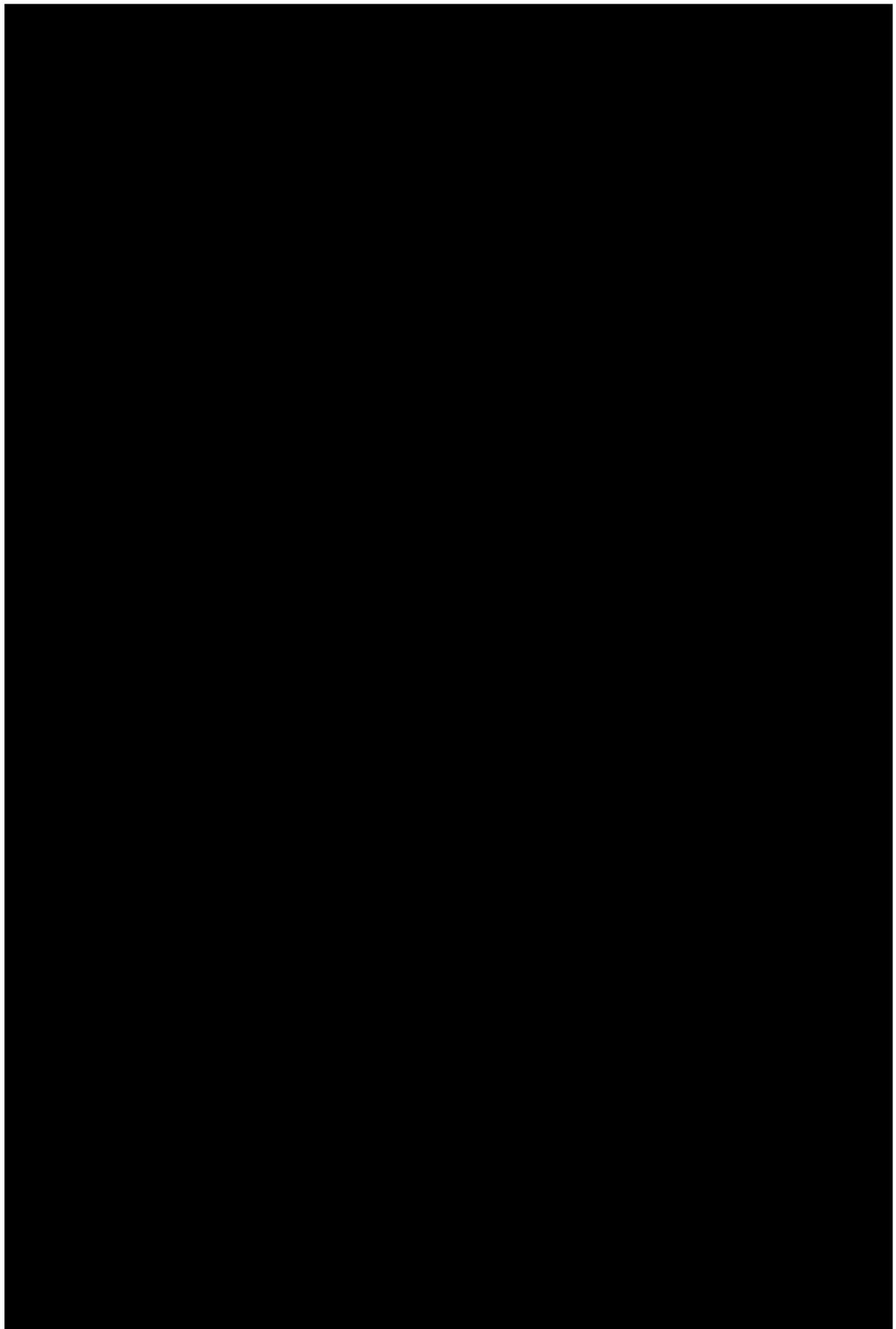
Incomplete and inaccurate information was provided in the PSMF (version [REDACTED] effective 30 April 2024). Specifically:

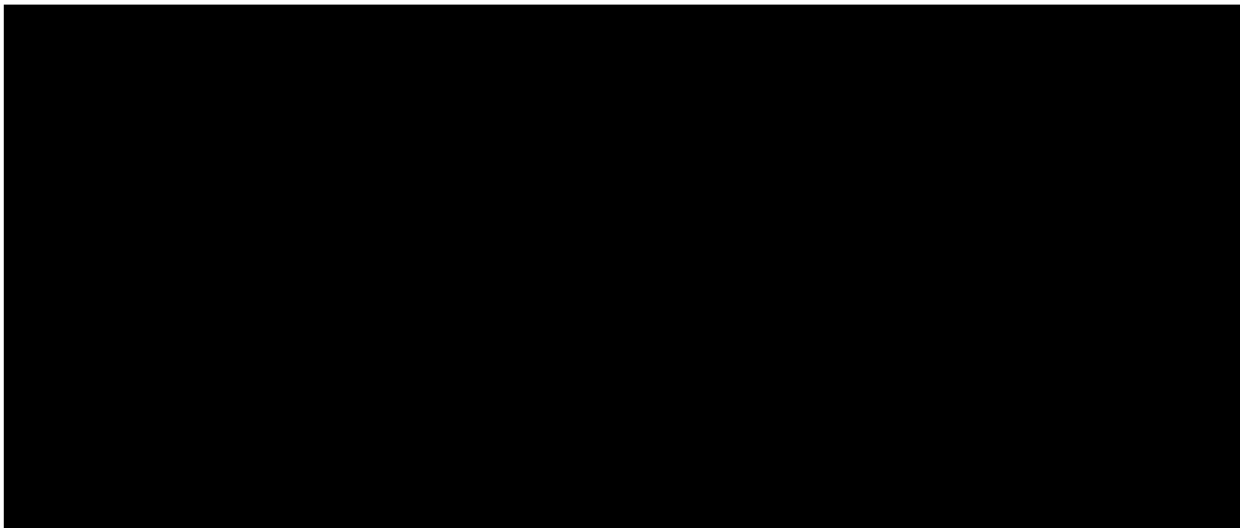
- i. A number of commercial partners, including distributors, were not listed within PSMF Annex B or C.
The missing license partners included:
 - a. [REDACTED]
 - b. [REDACTED]
The missing distributors included:
 - c. [REDACTED]
 - d. [REDACTED]
 - e. [REDACTED]
- ii. Two service providers were not included in Annex B, these included:
 - a. Twist of Lime: managed [REDACTED] social media accounts and website which involved posting and management, as well as managing complaints and questions.
 - b. [REDACTED] provided promotional services including a sales team for [REDACTED]
- iii. The [REDACTED] website and 29 social media pages were not listed in the PSMF main body or Annex C as sources of safety information. These social media pages spanned the media channels of [REDACTED] and had the ability for consumers to leave comments. For the UK this involved the [REDACTED] and [REDACTED]. A complete list of the social media pages is provided in appendix III.
- iv. Annex C listed a market research study for [REDACTED] with a progress status of ‘planned’ and a recruitment status of ‘Not started’. However, the programme had been completed and the final report was issued on 11 June 2021.

- v. Annex F did not transparently communicate that the compliance target for expedited reporting of ICSRs to the MHRA was 100%, instead the graph indicated it was 90%.
- vi. Annex G did not include the audit conducted of distributor [REDACTED] on 25 October 2023. Furthermore, according to the [REDACTED] (version [REDACTED] effective 08 June 2023)' the previous audit of [REDACTED] was conducted on 19 August 2021 but this also was not presented in Annex G.
- vii. UK PSMF number [REDACTED] was not present in the body of the PSMF. This number was provided with the response note to the pre-inspection document request sheet A.
- viii. Cross-referencing of annexes in the PSMF main body was not always accurate with regards to the actual location of the annex. For example:
 - a. PSMF section 2.6 stated that local contact persons were located in Annex A.VIII, when they actually appeared in Annex A.IX.
 - b. PSMF section 2.1 stated that proof of QPPVs EV registration was located in Annex A.VII, when it appeared in Annex A.VIII

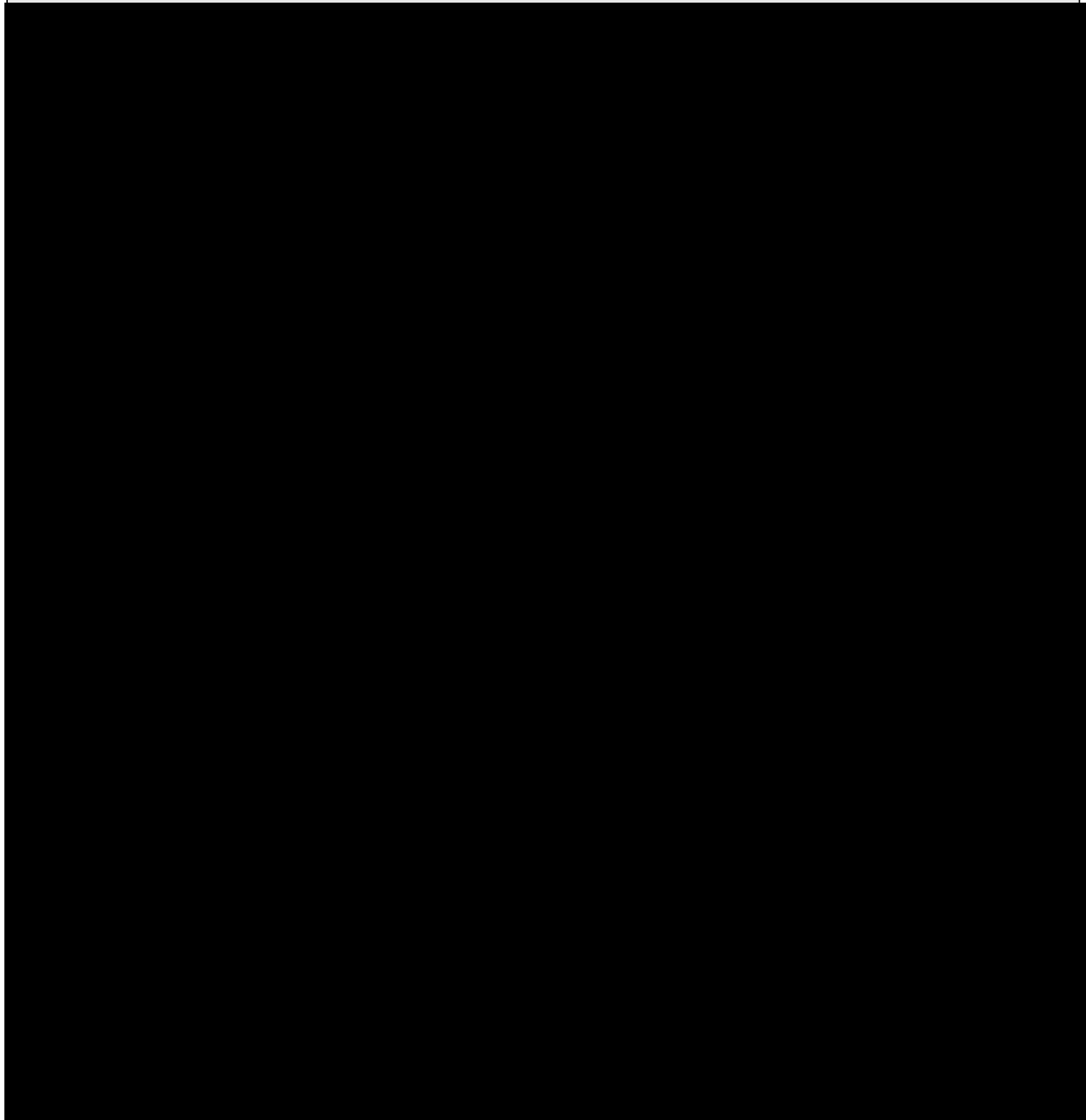
Root Cause Analysis

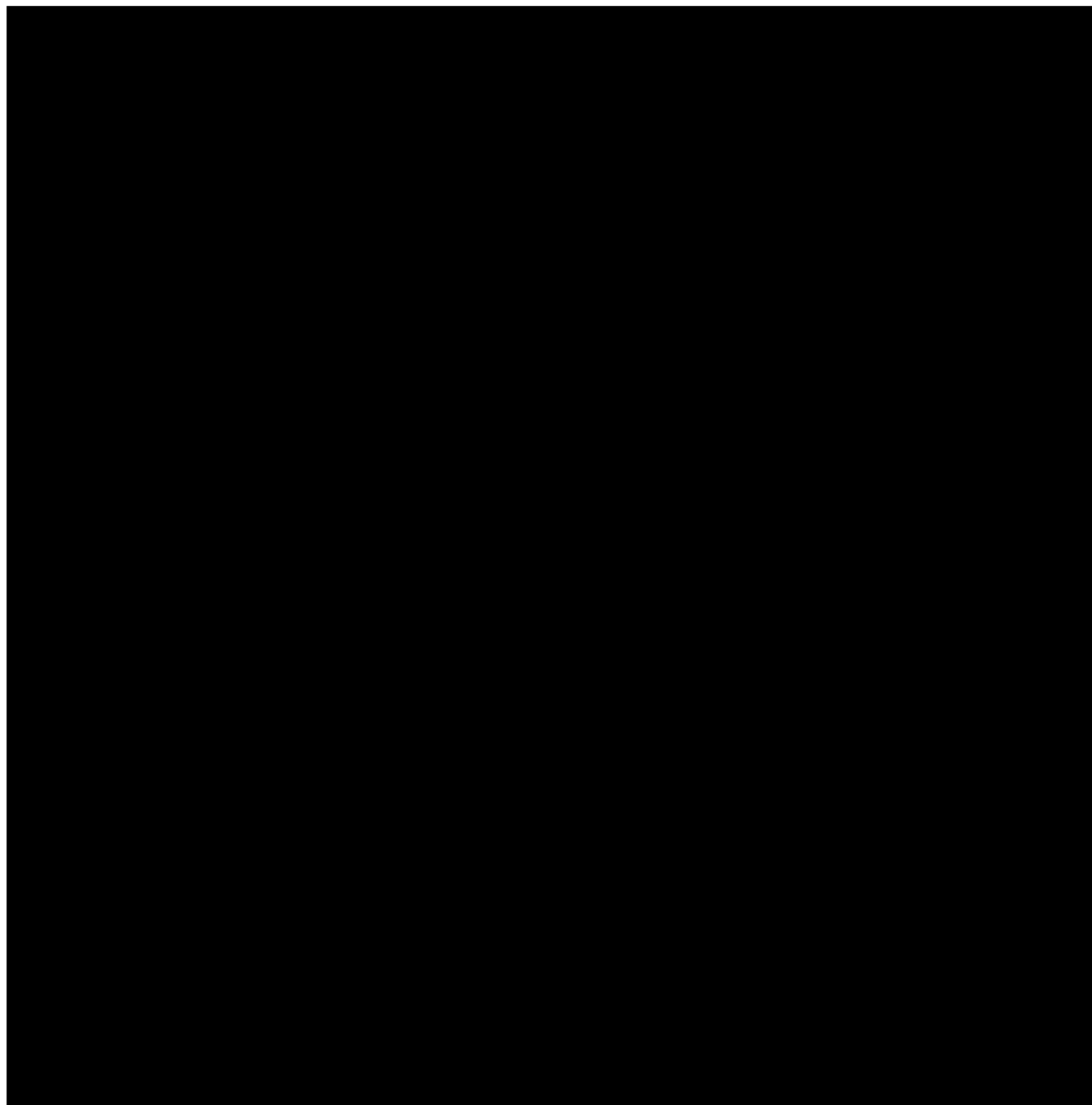




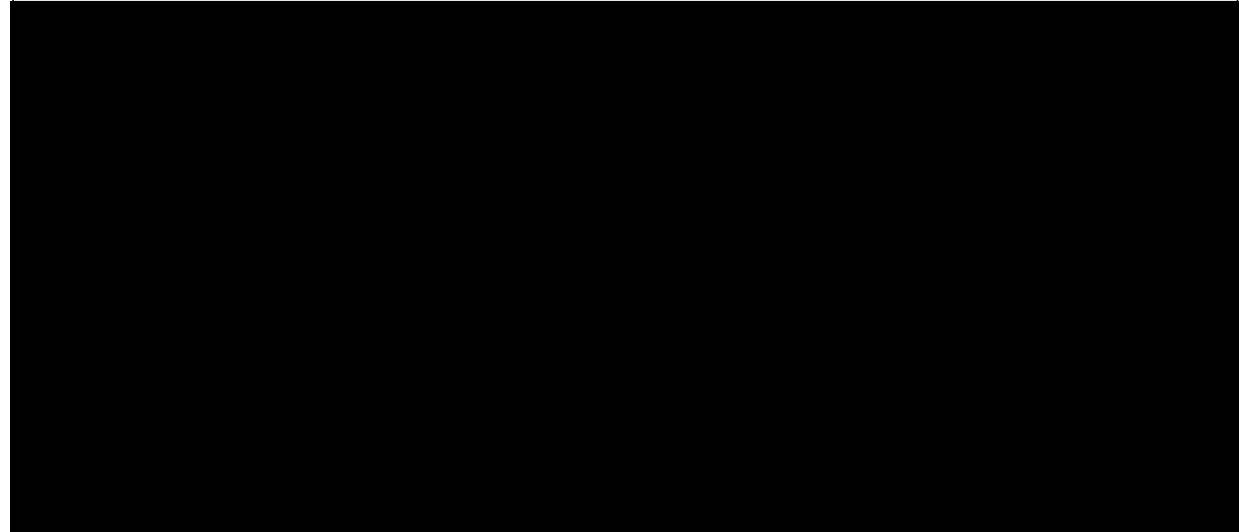


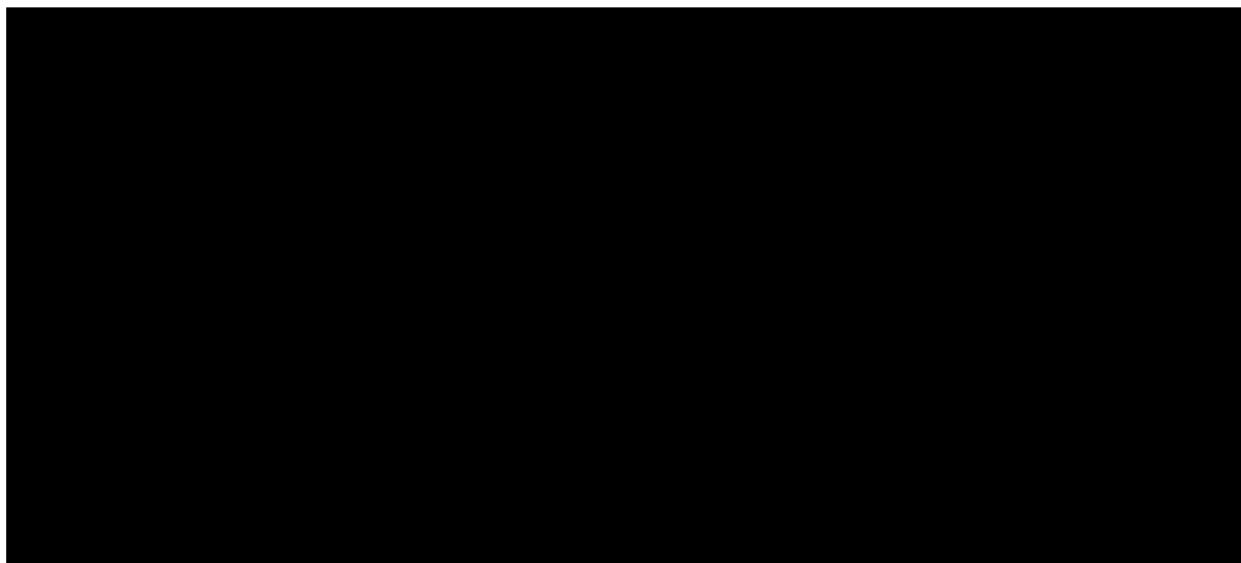
Further Assessment



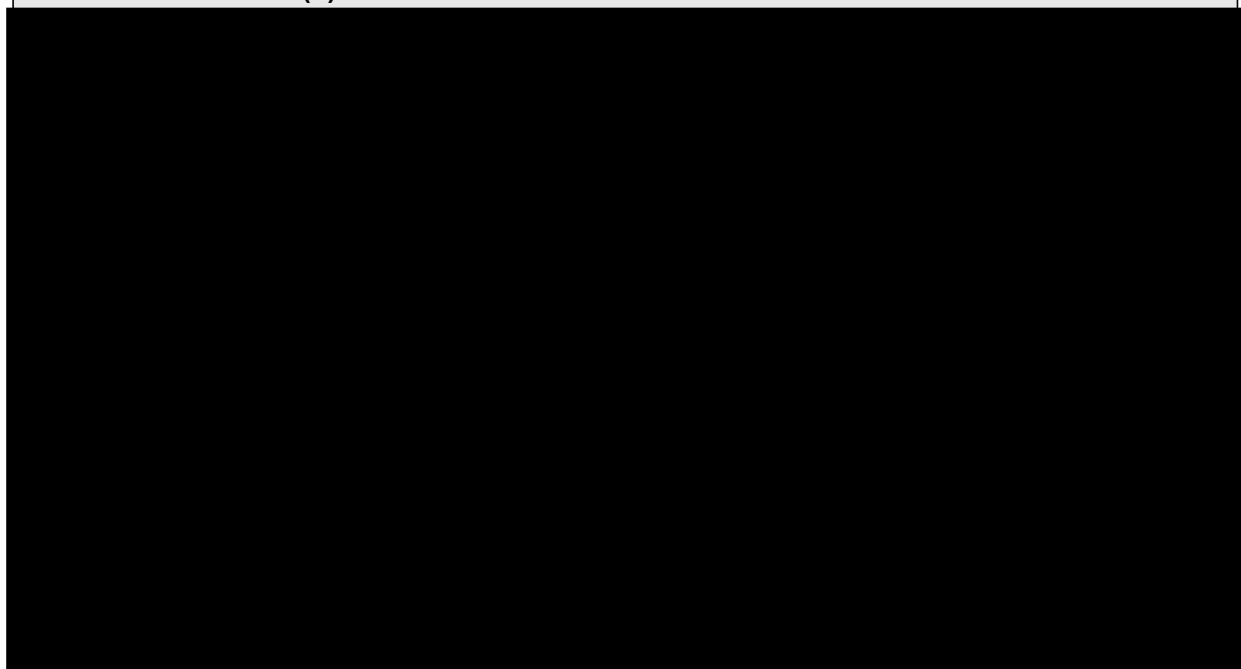


Corrective Action(s)

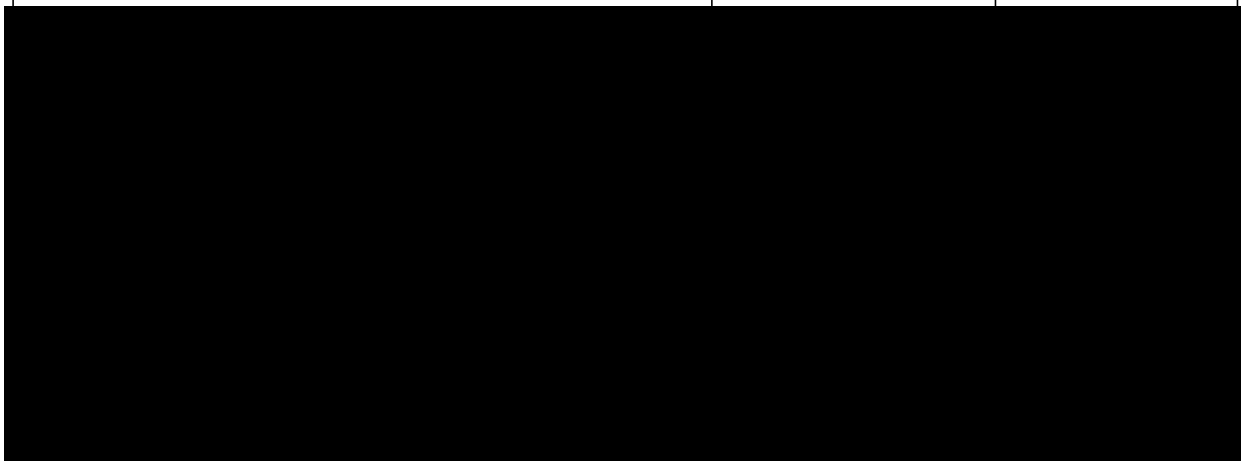


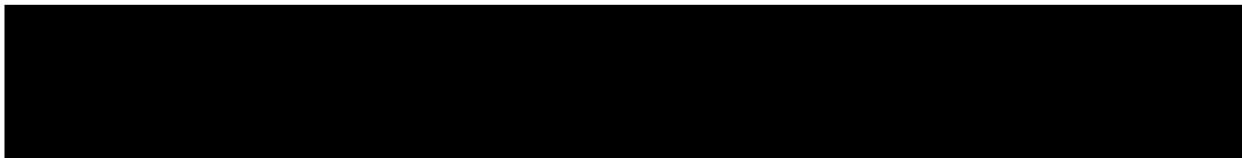


Preventative Action(s)



Deliverable(s)	Due Date(s)	CAPA Due
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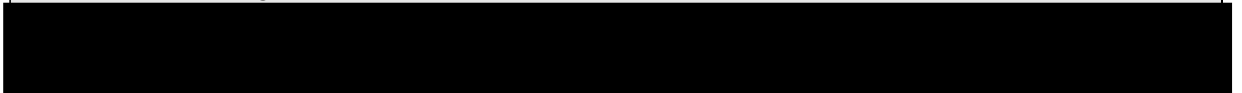


Finding MA.1 b)

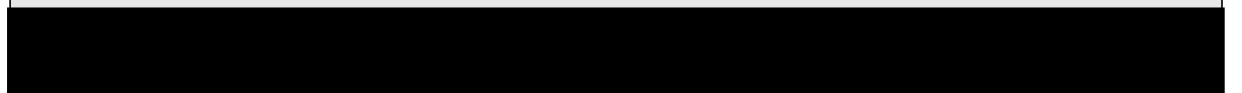
In advance of the inspection on 09 May 2024, notification of the intent to inspect Aspen alongside a request for the UK PSMF and pre-inspection document requests (sheet A) was sent by email to the MAH via the UK national contact person. However, this communication was not acknowledged or responded to within the timeframes stipulated.

A subsequent request from the inspector was sent to the UK QPPV on 20 May 2024 which resulted in confirmation of receipt of the communication. The PSMF and sheet A documents were submitted on 24 May 2024.

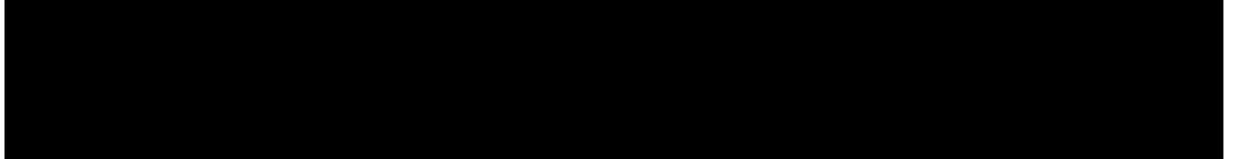
Root Cause Analysis



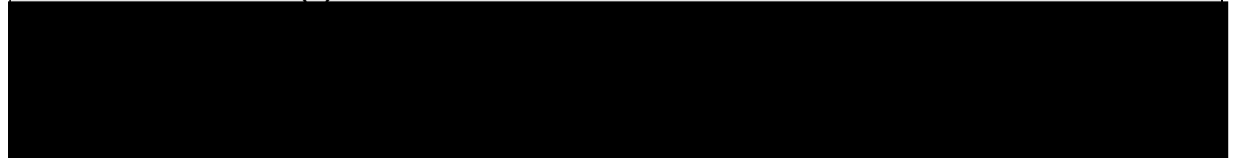
Further Assessment



Corrective Action(s)



Preventative Action(s)



MA.2 Management and Reporting of Adverse Reactions

Requirements:

The Human Medicines Regulations 2012 (Statutory Instrument 2012 No. 1916), Part 11 Pharmacovigilance

Regulation 187

(1) "Subject to paragraph (2), the holder must record all suspected adverse reactions to the product occurring in the United Kingdom or another country [...]"

(4) The holder must ensure that reports recorded under paragraph (1) are accessible (electronically or physically) at a single point within the United Kingdom."

Regulation 188

(1) "The holder of a UK marketing authorisation [...] must in relation to the product —

(a) submit electronically to the licensing authority a report on all serious suspected adverse reactions that occur in the United Kingdom and countries other than the United

Kingdom before the end of the period of 15 days beginning on the day following the day on which the holder gained knowledge of the reaction;

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.A.1.6. Seriousness

“Medical judgement should be exercised in deciding whether other situations should be considered serious. Some medical events may jeopardise the patient or may require an intervention to prevent one of the above characteristics/consequences. Such important medical events should be considered serious. The EudraVigilance Expert Working Group has co-ordinated the development of an important medical event (IME) terms list based on the Medical Dictionary for Regulatory Activities (MedDRA) (see GVP Annex IV). This IME list aims to facilitate the classification of suspected adverse reactions”

Finding MA.2 a)

A total of 50 reports from affiliates containing safety data had not been transferred from [REDACTED] to [REDACTED] and as a result two serious cases were not submitted to the MHRA.

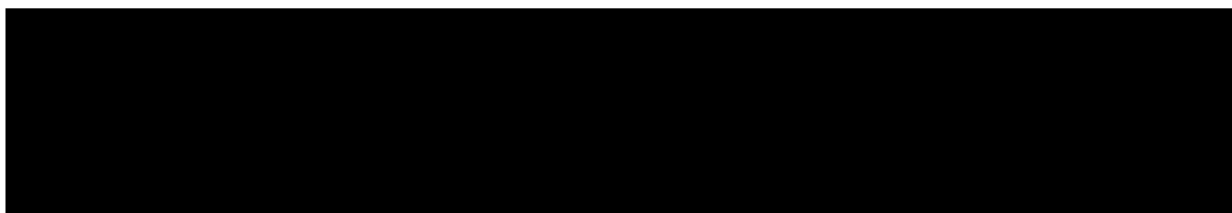
[REDACTED] was the safety system that allowed local entry of case information by affiliates, local assessment of case reportability and onward reporting of case information to [REDACTED] database if required. It was the responsibility of the Pharmacovigilance Co-ordinator or designee to route all required cases from [REDACTED] to [REDACTED]. The reason given for the reports not being transferred to [REDACTED] was that routing of the cases was inadvertently missed.

Prior to finalisation of this inspection report, the MAH was requested to provide information on the impact to ICSR reporting. Of the 50 LAM reports, 5 reports were rejected as per the exclusion criteria which confirmed the reports did not relate to an Aspen product. Out of the 45 accepted cases, 45 unique cases were created accordingly in [REDACTED]. Of these accepted cases, two spontaneous, serious cases were reportable to the MHRA [REDACTED]

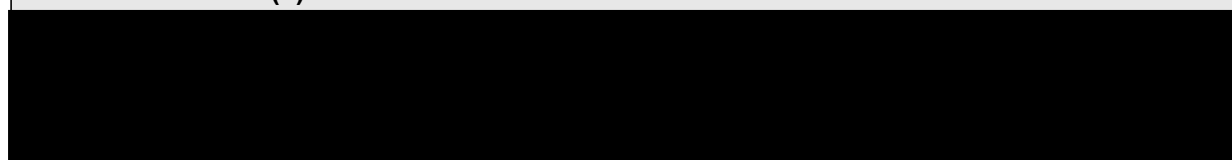
The MAH should provide details of the cases as part of response to this finding.

Root Cause Analysis

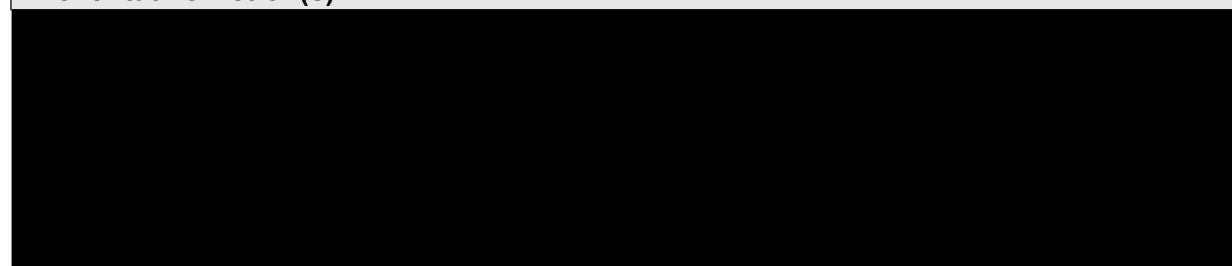
Further Assessment



Corrective Action(s)



Preventative Action(s)



Finding MA.2 b)

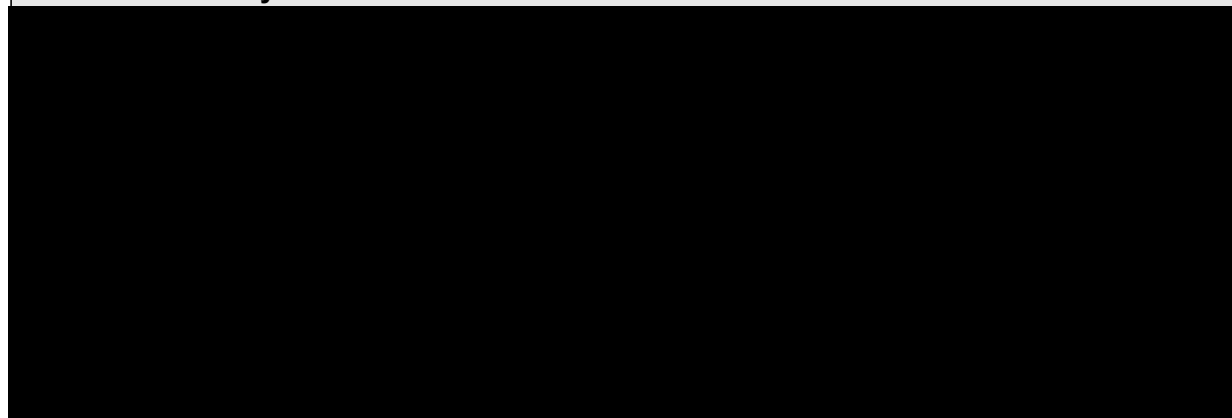
For the two most recent versions of the IME list, which was used to conduct seriousness assessment of ICSRs, there were significant delays in the updates being configured into the [REDACTED] database. Furthermore, the procedural documents which governed how updates to the IME list were handled with respect to the configuration of [REDACTED] did not specify the timelines for implementing updated IME lists.

IME version [REDACTED] was published on 25 September 2023 and was implemented on 29 February 2024.

IME version [REDACTED] was first published on 18 March 2024 and was implemented on 29 May 2024.

This deficiency is not constrained to recent updates only, as the inspector identified one case impacted by the untimely implementation of IME updates for version [REDACTED] dated September 2022. Literature case [REDACTED] was initially received on 21 November 2022 and reported PT [REDACTED] with [REDACTED]. The event should have been graded as serious but was not due to the delay in implementation. The case overall however was still considered as serious.

Root Cause Analysis



Further Assessment

Corrective Action(s)

Preventative Action(s)

Finding MA.2 c)

A serious case originating from outside the UK was not reported to the MHRA.

Case [REDACTED] was a valid serious case originating from [REDACTED] reporting PTs: [REDACTED] with [REDACTED]

The report originated from a study and was received on 15 March 2022. The MAH explained that the case was not submitted as the case designee inadvertently missed scheduling the report to the MHRA.

Root Cause Analysis

[REDACTED]

Further Assessment

[REDACTED]

Corrective Action(s)

[REDACTED]

Preventative Action(s)

[REDACTED]

MA.3 Signal Management

Requirements:

The Human Medicines Regulations 2012 (Statutory Instrument 2012 No. 1916), Part 11 Pharmacovigilance

Regulation 182

(2) *“The holder must (as part of its pharmacovigilance system)— [..]*

(e) *[..] monitor pharmacovigilance data to determine whether in relation to the product—*

(i) there are new risks,

(ii) risks have changed, or

(iii) there are changes to the risk-benefit balance.”

GVP Module IX – Signal management (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)

IX.C.1.1. Responsibilities of the marketing authorisation holder in the UK

“The marketing authorisation holder in the UK should continuously monitor the safety of their medicinal products.”

MAHs are obliged to ensure that information on the benefits and risks of their products is evaluated on an ongoing basis and appropriate action is taken in response to new information that impacts on the benefit-risk balance.

At Aspen, signal detection to identify potential safety concerns included the review of statistical scores for drug-event combinations (DECs) generated by ██████████ to identify any ADRs with disproportionate reporting (SDR) or increased frequency of reporting. The SDR alert was configured in ██████████ to flag when the following assigned threshold was passed: at least one new report of the DEC was received during the period, and the EB05 score is at least 2, and the event is not a listed event, and current comment on the event is not one of ('Labeled', 'Indication Related', 'Uninformative', 'Prior Review').

Signal detection activities were conducted at a frequency designated by the Signal management (SM) schedule. For ██████████ this was a six-monthly frequency due to the product being well established, few cases received a month on average (17) and no ongoing safety concerns or commitments. The most recent review of ██████████ was conducted in March 2024 for the review period of September 2023 to February 2024.

The following findings were noted in relation to signal management:

Finding MA.3 a)

██████████ was inappropriately configured to repress disproportionate reporting alerts for DECs that had the comments 'Labeled', 'Indication Related', 'Uninformative' and 'Prior Review' added to ██████████. As such, from August 2022 onwards, when signal detection activities were solely conducted via ██████████ for DECs that had these comments added there was no continuous monitoring of PV data to determine if there were new risks or changed risks. As a

result, four DEC's were observed on inspection for [REDACTED] for which new cases had been received in the period that had significantly raised EB05 scores which had not been reviewed as potential signals.

The DEC's were as follows:

- [REDACTED] (non-serious PT term): 6 new cases received between August 2022 to February 2024, EB05 was 5.30.
- [REDACTED] (non-serious PT term): 10 new cases received between August 2022 to February 2024, EB05 was 2.67.
- [REDACTED] (non-serious PT term): 4 new cases received between August 2022 to February 2024, EB05 was 8.75.
- [REDACTED] (non-serious PT term): 19 new cases received between August 2022 to February 2024, EB05 is 21.6.

These PT's were not listed in the product information for the [REDACTED] products.

The SDR alert was not flagged for the four DEC's with [REDACTED] as the comment 'Closed prior review' was added in April 2022 which repressed the alert being triggered. Documentation of the assessment conducted for this prior review could also not be provided, and so there was no evidence that these DEC's had ever been reviewed, with the exception of [REDACTED] DEC's: [REDACTED], which were reviewed in September 2018 when the process of signal detection was still conducted manually.

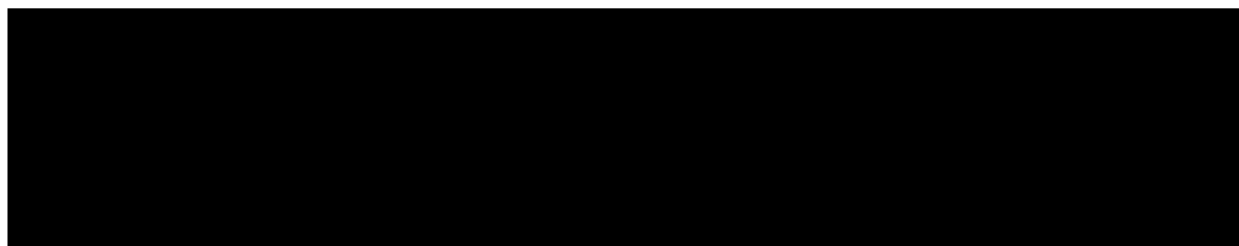
As per [REDACTED] version [REDACTED] effective 22 April 2024) and [REDACTED] (version [REDACTED] effective 15 December 2022), a single report of a serious or severe adverse reaction may be sufficient to raise a signal and to take further action, however in practice the MAH was heavily reliant on disproportionality signalling. The MAH would only evaluate a DEC for a potential signal once the disproportionality threshold was crossed. Furthermore, non-serious cases would not undergo medical review, and so safety issues could only be picked up via disproportionality signalling.

The Signal Management Actions Tracker, which recorded all potential signals (validated or not) and safety topics, gave an indication of the scale of the output of potential signals from [REDACTED] Since August 2022, for all UK authorised products ([REDACTED] of which were currently marketed), for which approximately 7958 cases had been received since August 2022, five DEC's overall had been identified from [REDACTED] and evaluated as potential signals. Four of these were identified in August 2022 and the final and most recently identified potential signal from [REDACTED] was identified on 24 September 2022.

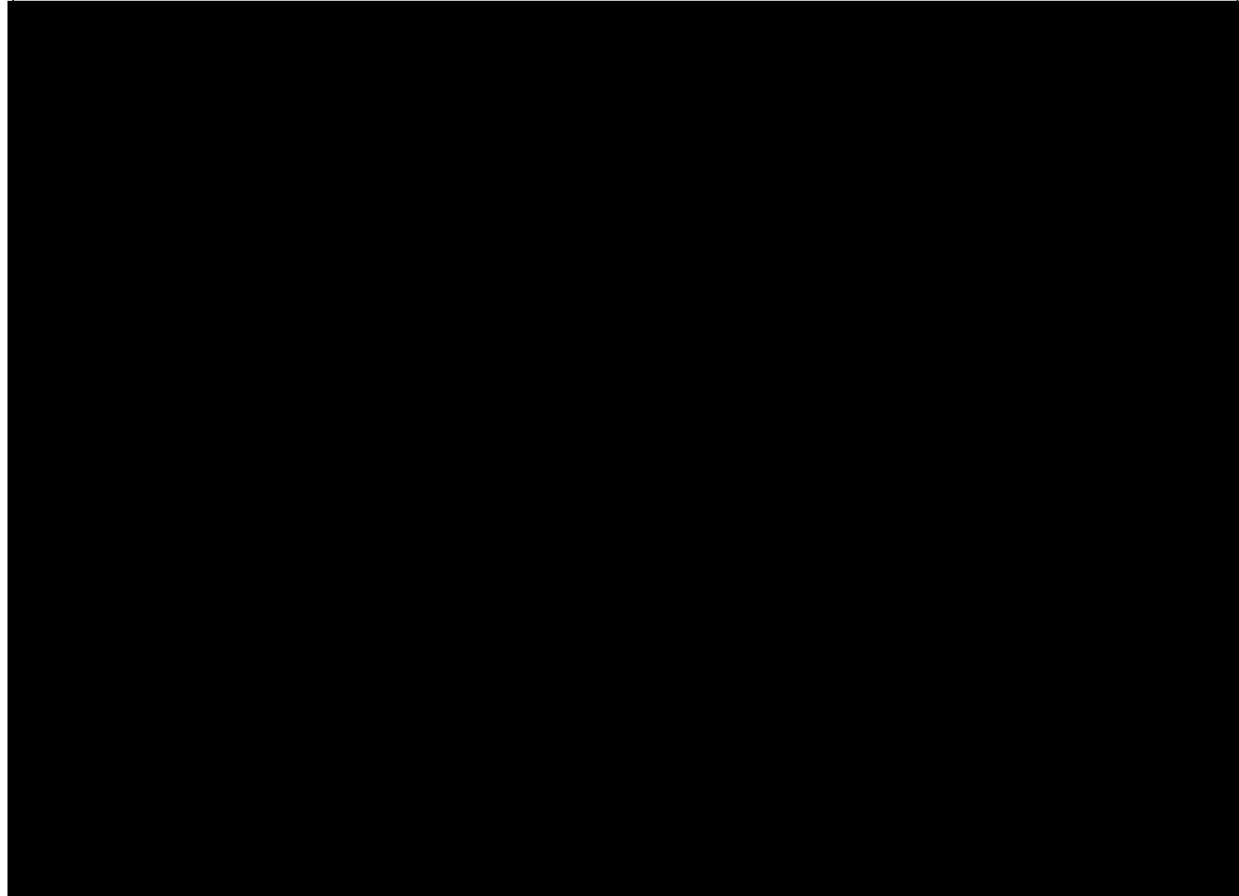
MAH request: as part of the response to this report, Aspen is requested to conduct the following:

- a signal assessment for the DEC's listed in the finding and confirm whether a signal exists.
- The MAH stated in response to a document request that they planned to remove the "Prior Review" clause from the SDR alert. However, the suitability of the other comments 'Labeled', 'Indication Related' and 'Uninformative' should be assessed for their potential to wrongly repress future cases for which the comments do not apply.

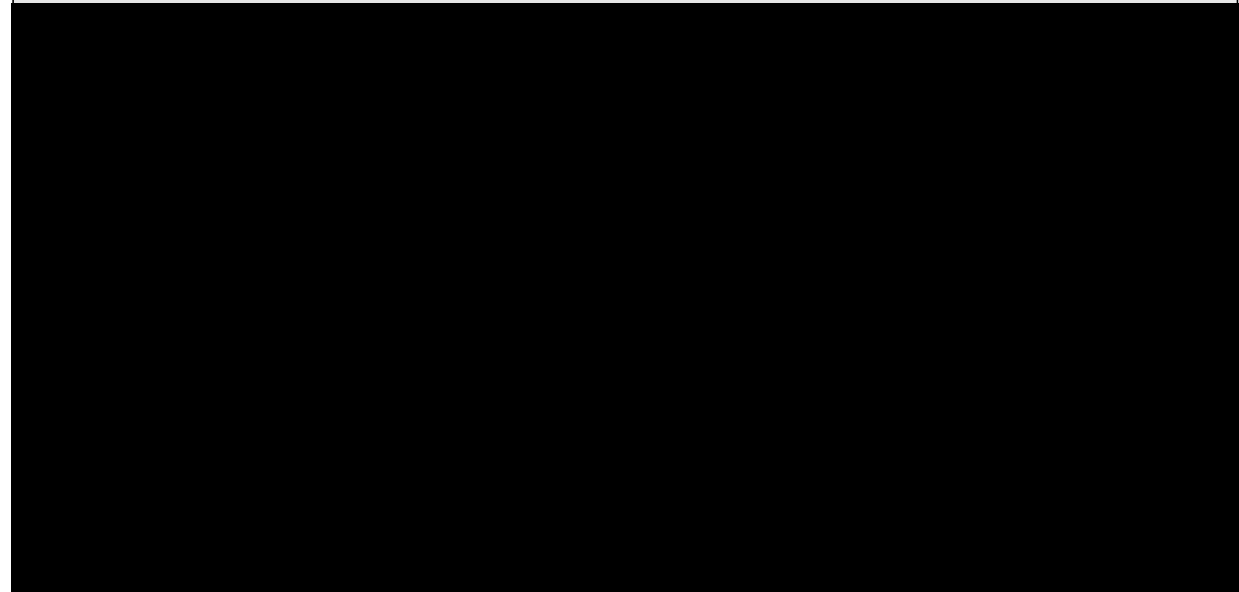
Root Cause Analysis



Further Assessment



Corrective Action(s)



Preventative Action(s)

MA.4 Auditing of the Pharmacovigilance System

Requirements:

~~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.A. Introduction~~

~~“Section IV.B. outlines the general structures and processes that should be followed to identify the most appropriate pharmacovigilance audit engagements and describes the steps which can be undertaken by marketing authorisation holders, [...], to plan, conduct and report upon an individual pharmacovigilance audit engagements. This Section also provides an~~

~~outline of the general quality system and record management practices for pharmacovigilance audit processes.”~~

~~IV.B.2.1. Strategic level audit planning~~

~~“The audit strategy should cover the governance, risk management and internal controls of all parts of the pharmacovigilance system including: [...]~~

- ~~• all pharmacovigilance processes and tasks;~~
- ~~• the quality system for pharmacovigilance activities;~~
- ~~• pharmacovigilance activities conducted by affiliated organisations or activities delegated to another organisation (e.g. regional reporting centres, MAH affiliates or third parties, such as contract organisations and other vendors).”~~

Internal audits (termed self-inspections) and PV vendor audits were managed by the Quality department at APTL. Commercial partners and distribution service providers however were out of scope of vendor audits and were audited by Aspen Group rather than APTL.

Finding MA.4 a)

For vendor audits and audits of the internal pharmacovigilance system carried out by Aspen in Europe there was no strategic level audit plan or strategy.

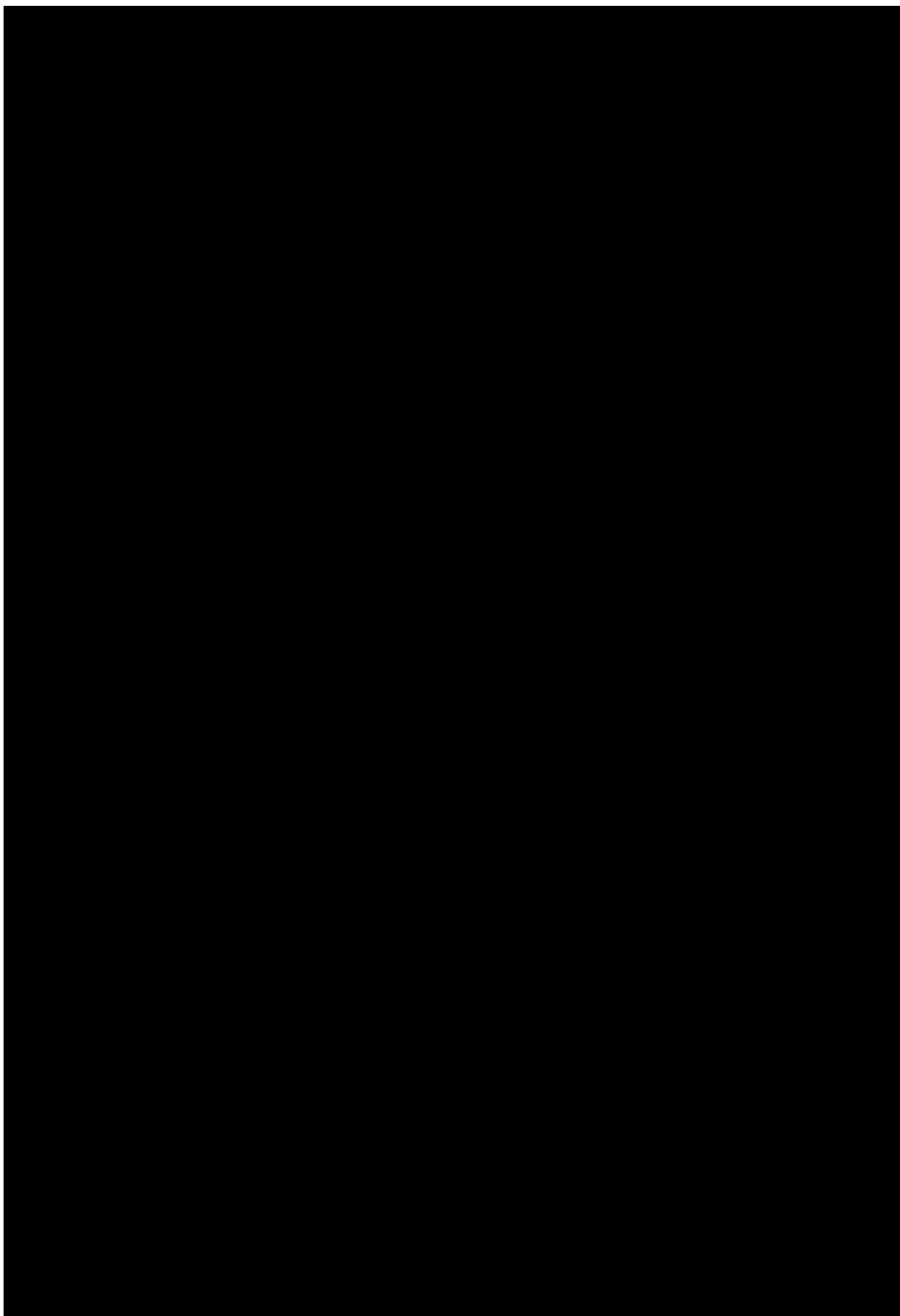
There were also no pharmacovigilance strategic audit plans produced by any other part of the quality function within the Aspen group that covered this GVP requirement. As such there is the potential that the delivery of audits for vendors which includes commercial partners and distributors has not been considered over a longer time period which may have had an impact on the MAHs ability to conduct regular risk-based audits of these entities. Aspen is required to review this as part of the impact assessment.

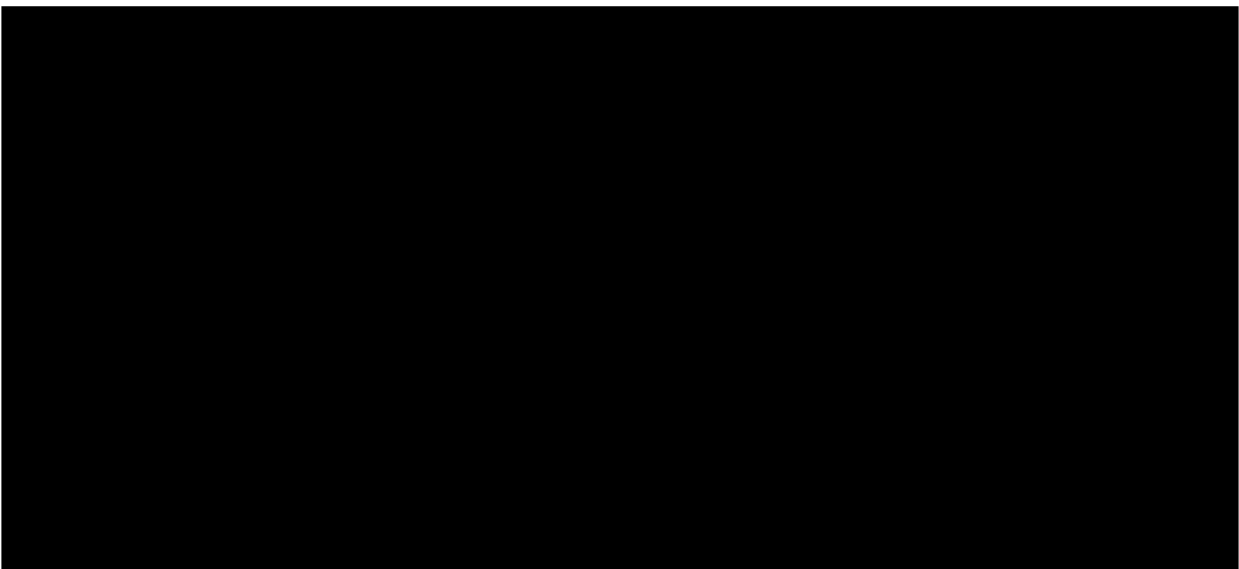
MAH request: as part of the response to this report, Aspen is requested to conduct the following:

- Assessment of the impact on audits scheduled and conducted in the past five years to determine whether all internal and external entities (especially audits of third parties that were not covered by ‘PV vendor audits’) have been considered for audit, assessed for risk, and whether the outputs of these were documented effectively. The workings of this assessment should also be provided separate to the inspection report and should clearly list all entities considered (with a clear description of the type of entity they are e.g. internal or commercial license partner etc), the dates they were considered in a risk assessment, dates they were scheduled for audit and audited. Please also provide the dates the PV agreements or commercial relationships started and ended (if applicable). Please provide these in Excel format, with filtering enabled.

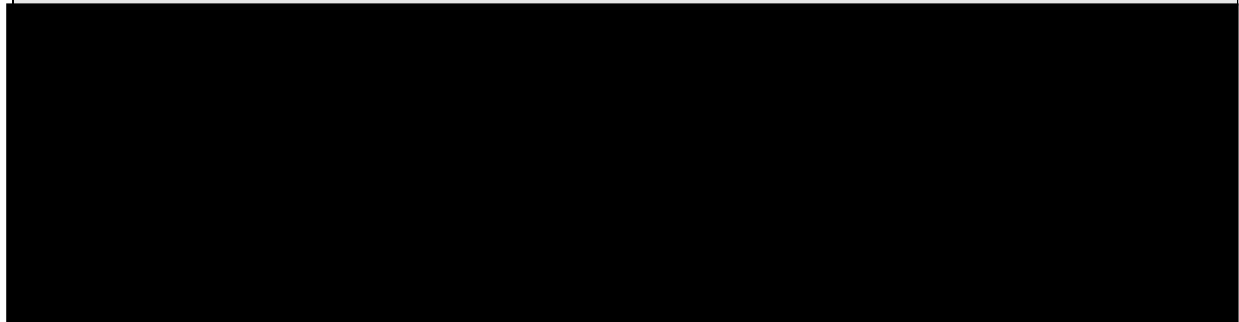
Post-inspection note: The finding has been removed following further clarification from the MAH and review of documentary evidence. It should be noted that the clarifying information was not communicated to inspectors on the inspection, nor was the procedural documentation reviewed on inspection explicitly clear in demonstrating the MAHs compliance with GVP IV.B.2.1. Therefore, Aspen is strongly encouraged to update the SOP, as originally indicated in the CAPA response, to avoid any future confusion.

Root Cause Analysis

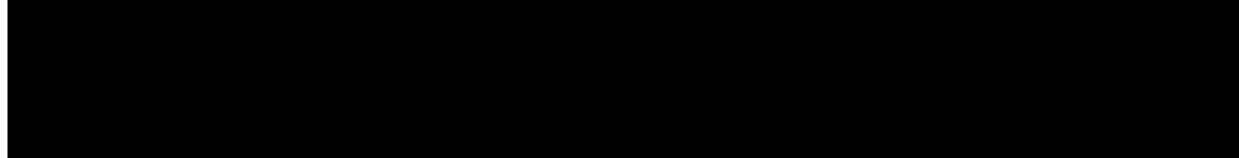




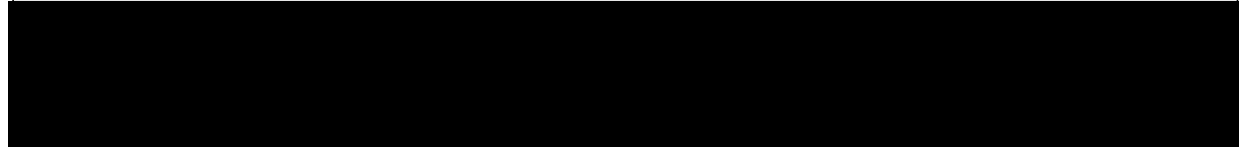
Further Assessment



Corrective Action(s)



Preventative Action(s)



C.4.3 Minor findings

MI.1 Maintenance of Reference Safety Information

Finding MI.1 a)

There were deviations in the information presented between the UK SmPC and the CCDS for [REDACTED] and [REDACTED]. This was contrary to procedural documentation which stipulated that the CCDS should contain the core safety information to be listed in all countries where the company markets the product.

Examples where the UK SPC was missing information considered as the core minimum labelling information in the CCDS

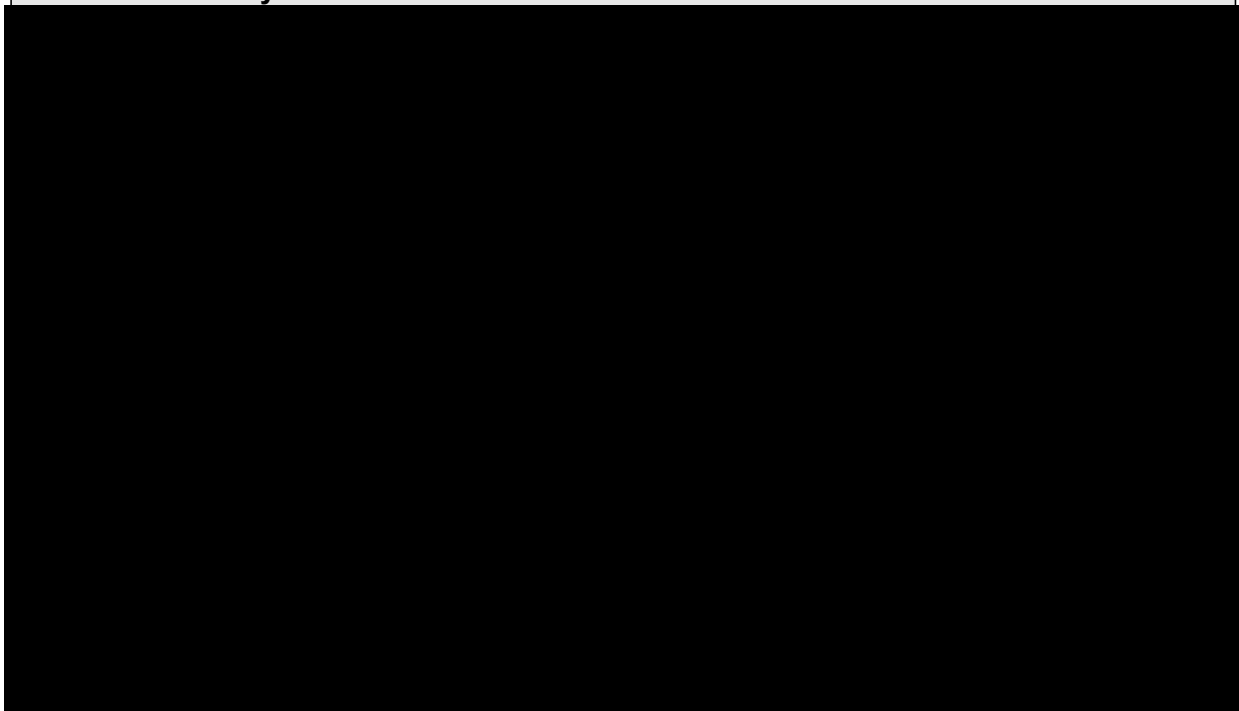
- i. The CCDS for [REDACTED] included a warning in section 4.8 for [REDACTED], which was not reflected in the UK SPC. The warning of [REDACTED] was present however in the PIL and therefore the impact of the deficiency is minor.
- ii. The CCDS for [REDACTED] listed in section 4.8 [REDACTED] as an ADR, which was not reflected in the UK SPC. However, the topic of [REDACTED] is covered in 'Section 4.4 Special warnings and precautions for use' in relation to [REDACTED]

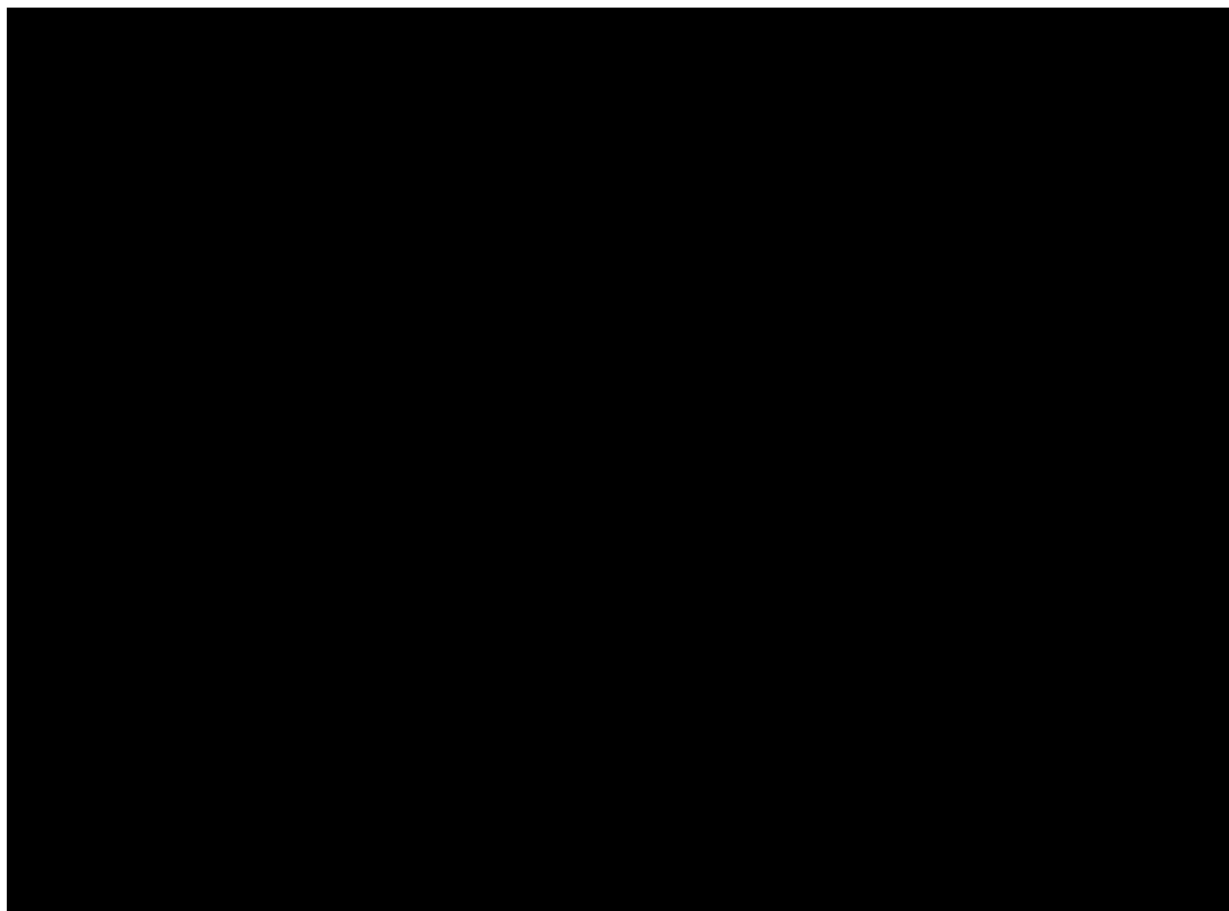
Additionally, a number of ADRs were listed in section 4.8 of the UK SmPC for [REDACTED] product, but were not present in the CCDS and there was no documentation to demonstrate that the MAH was aware of the divergence and the origination for the divergence:

- [REDACTED]
- [REDACTED]
- [REDACTED]

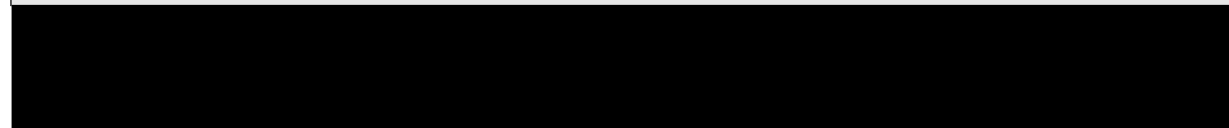
As per [REDACTED] (version [REDACTED] effective 02 November 2023) the core safety information refers to all relevant safety information contained in the company core data sheet prepared by the MAH and which the MAH requires to be listed in all countries where the company markets the product, except when the local regulatory authority specifically requires a modification.

Root Cause Analysis

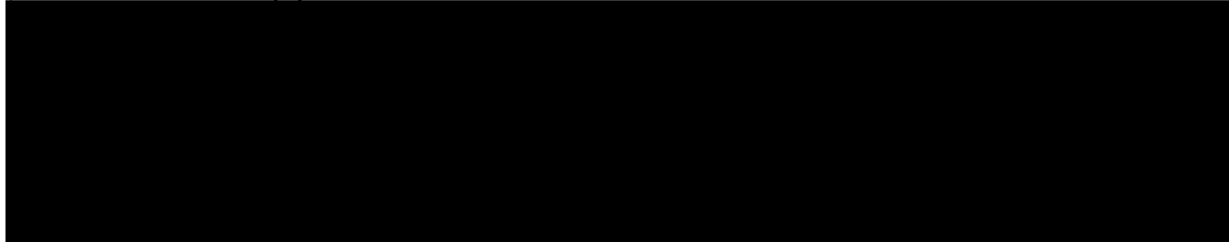




Further Assessment



Corrective Action(s)

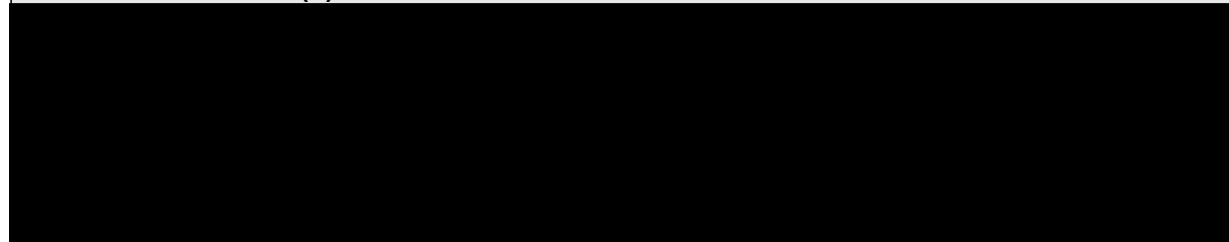


Deliverable(s)

Due Date(s)



Preventative Action(s)



Deliverable(s)

Due Date(s)

MI.2 Collection and collation of safety information

Finding MI.2 a)

One lack of efficacy case was identified which was not shared with Apsen QA as per documented procedures.

Medical information enquiry [REDACTED] was received on 02 November 2023 from a consumer who stated:

[REDACTED]
This enquiry was sent to the PV safety team on 02 November 2023 [REDACTED] but was not sent to the QA department as required per the core working practice [REDACTED] (version [REDACTED] effective 25 August 2023) which stated that lack of efficacy should be reported as an AE and a PQC.

Root Cause Analysis

Further Assessment

Corrective Action(s)

Preventative Action(s)

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

Finding MI.2 b)
<p>The Aspen Holding website (www.aspenpharma.com) did not contain European hub contact details for the reporting of adverse events in the event that a UK or EU patient would use this global website instead of the dedicated UK/EU website.</p> <p>The Aspen Holding website contained a contact us page, for which a drop down option was listed for AE reporting. The page listed numbers and emails to report AEs for each region, however there was no contact details for Europe or the UK.</p> <p>It is acknowledged that there was a separate Aspen Europe website which did include UK/EU details, however for those patients and HCPs who visited the Aspen Holding website these details would not be available.</p>
Root Cause Analysis
[Redacted]
Further Assessment
[Redacted]
Corrective Action(s)
[Redacted]
Preventative Action(s)
[Redacted]

MI.3 Contracts and agreements:

Finding MI.3 a)
<p>The following deficiencies were observed with contracts and agreements between Aspen and a number of service providers and distributors.</p> <p>i. In the SDEA ([Redacted]) between Aspen and [Redacted] effective from 30 April 2024, the section on reconciliation was omitted. As a result, the commercial partner which acted as MAH in the EU for a number of products, was not added to the reconciliation tracker which was used to track all reconciliation conducted with partners. However, evidence was obtained that</p>

reconciliation for the period of 30 April 2024 to 31 May 2024 was initiated by [REDACTED] on 12 June 2024 and completed on 14 June 2024.

- ii. For a number of SDEAs, a deficiency in the wording regarding the transfer of adverse reactions as opposed to adverse events was identified.

For example, in the SDEA (version [REDACTED] effective 14 March 2024) with [REDACTED] a contract sales team responsible for the promotion of [REDACTED], the wording in section 8, 'Exchange of adverse events and special situation events' stated:

"Applicable individual case safety reports (ICSRs) include but are not limited to the following: Adverse Reactions from any source [...]"

Where the definition of 'Adverse Reactions' given was:

"Means all noxious and unintended responses to a medicinal product related to any dose. The "responses to a medicinal product" means that a causal relationship between a medicinal product and an Adverse Event is at least a reasonable possibility"

However, the expectation would be that all adverse events are transferred to the MAH irrespective of whether they are causal in nature.

This deficiency in terminology was also observed for the following contracts:

- [REDACTED] (version [REDACTED] effective 31 October 2019) between [REDACTED] and distributor [REDACTED]
- [REDACTED] (version [REDACTED] effective September 2022) between [REDACTED] and [REDACTED] who are responsible for the oversight of [REDACTED] page.
- [REDACTED] (version [REDACTED] effective 10 October 2023) between APTL and Brood (A Twist of Lime) responsible for monitoring the [REDACTED] page.

- iii. Regarding the Quality technical and PV Agreement (version [REDACTED] effective 13 January 2023, amended 16 March 2023 and 23 October 2023) between [REDACTED] and distributor [REDACTED] there was no specific provision for the exchange of information on special situations from [REDACTED] to Aspen. There was also no specified timeframe within the agreement regarding reconciliation.

Section 4.1.1, 'Exchange of adverse events', stated:

"To provide Aspen Group PV representative (Appendix 1) with all relevant safety information received in relation to any APUK product (see Appendix 2), from any source within 1 working day of becoming aware of the information (incl. Adverse Events, Product Complaints associated with Adverse Drug Reactions and Medical Information enquiries)"

It was noted that a list of special situation events is described within the definitions section under ICSRs, however the provision to exchange this information is not specifically set out in section 4.

- iv. The hospital distribution agreement between [REDACTED] and [REDACTED] (dated 02 March 2022) specified the exchange of unexpected AEs only, and did not specify the exchange of information regarding special situations, or the timeframes for which the events should be reported.

Section 7, 'Complaints and safety reports' stated:

[REDACTED] shall notify the Manufacturer promptly of any customer complaints, medical queries and any information relating to the Products which come to its attention concerning any unexpected adverse events and/or any unexpected incidence or severity of any adverse events whether or not determined to be attributable to the

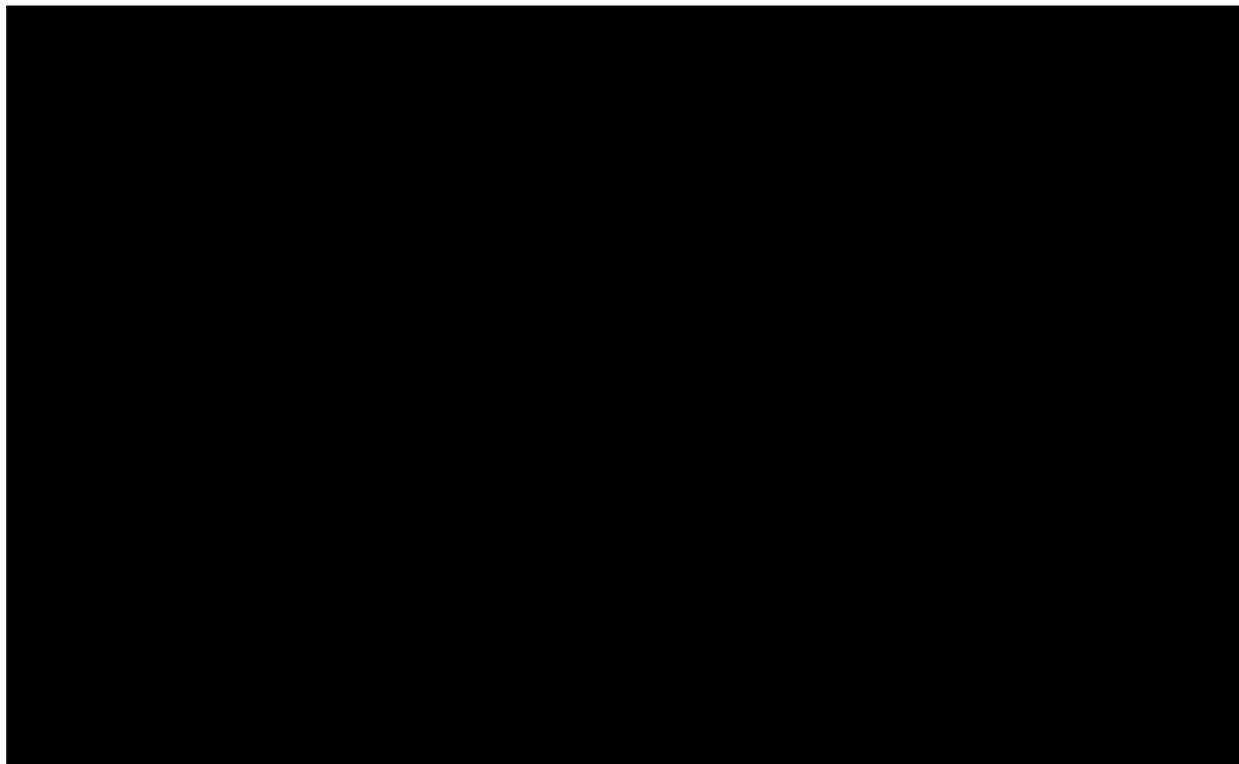
Products.”

However, it is expected that all AEs are reported, not just those which may be unexpected in nature.

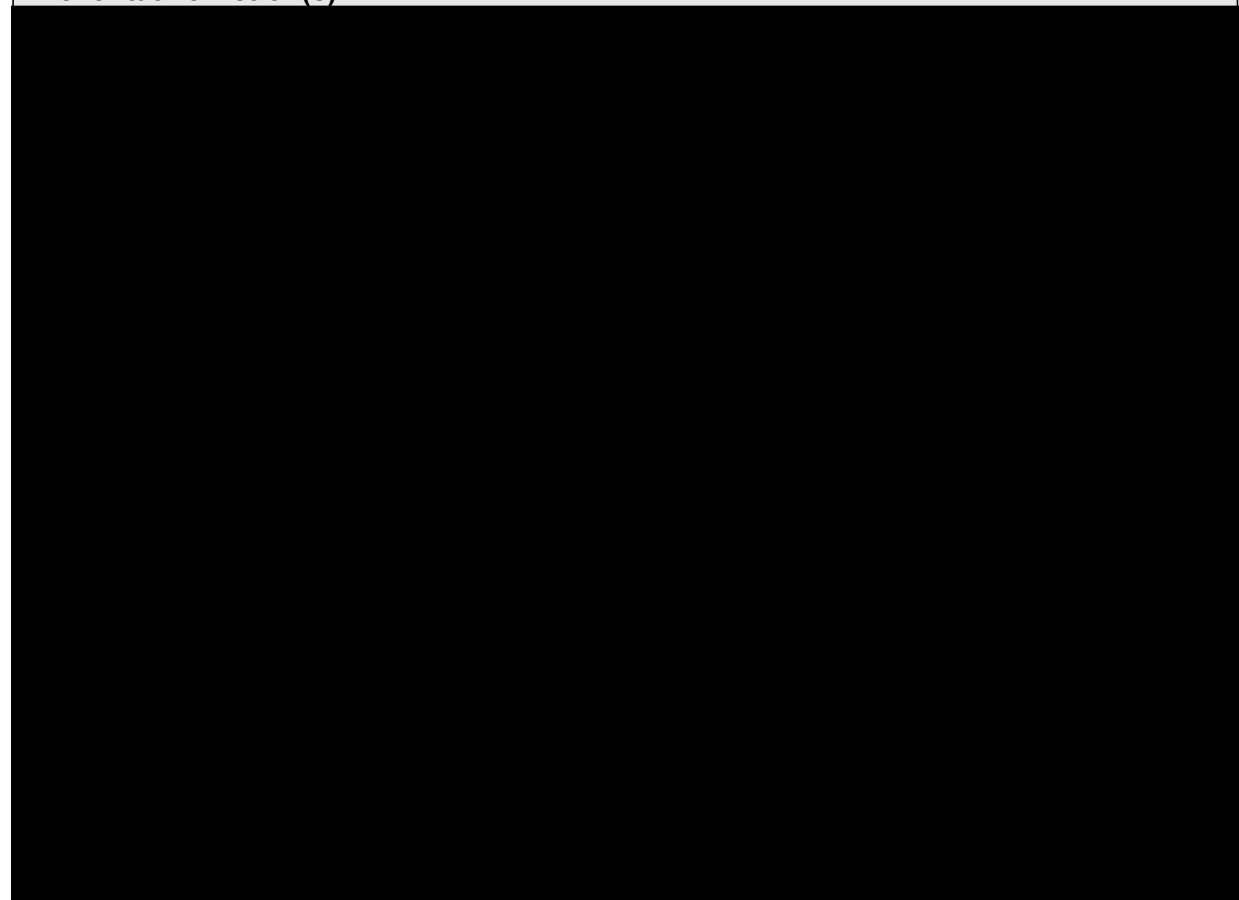
Root Cause Analysis

Further Assessment

Corrective Action(s)



Preventative Action(s)



Finding MI.3 b)

The PV SDEA tracker used to track all SDEAs, Quality Technical Agreements (QTA) and

Memorandum of Understandings within the organisation contained incorrect information.

The QTA with distributor [REDACTED] (version [REDACTED] effective 14 January 2021), was incorrectly noted as effective on the tracker despite having been terminated on 08 June 2023. The company stated that the decision to terminate the agreement was not relayed to the relevant parties.

Root Cause Analysis

[REDACTED]

Further Assessment

[REDACTED]

Corrective Action(s)

[REDACTED]

Preventative Action(s)

[REDACTED]

MI.4 Training

Finding MI.4 a)

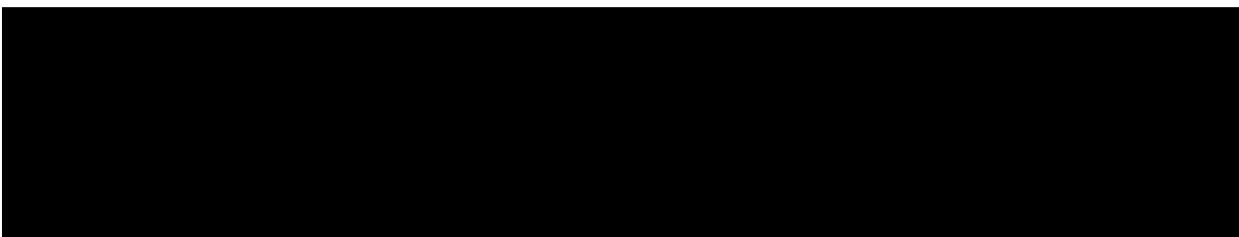
Training on the reporting of AEs had not been conducted for personnel of the service provider Brood/Twist of Lime, which had been subcontracted to oversee and review AEs posted in the social media accounts and website for [REDACTED] since 10 October 2023.

No AEs were identified as being missed during the inspection, however as part of the further assessment the MAH are asked to review the impact further to confirm whether the failure to train personnel had caused a failure to identify and report safety information.

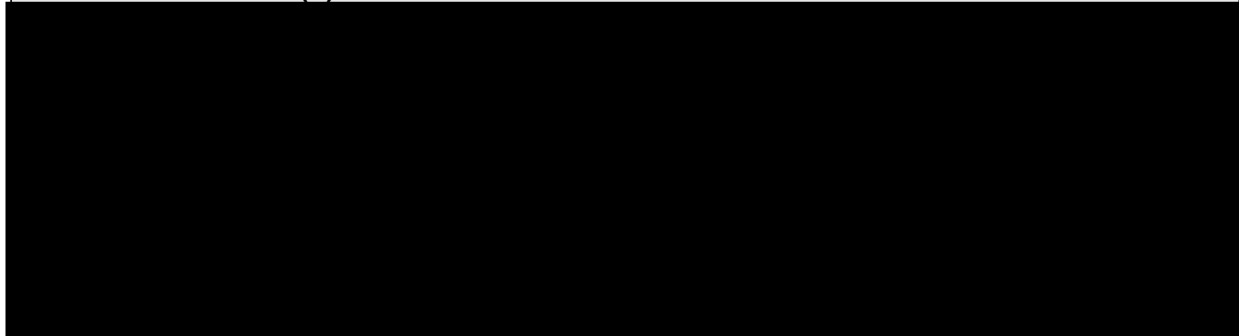
Root Cause Analysis

Further Assessment

Corrective Action(s)



Preventative Action(s)



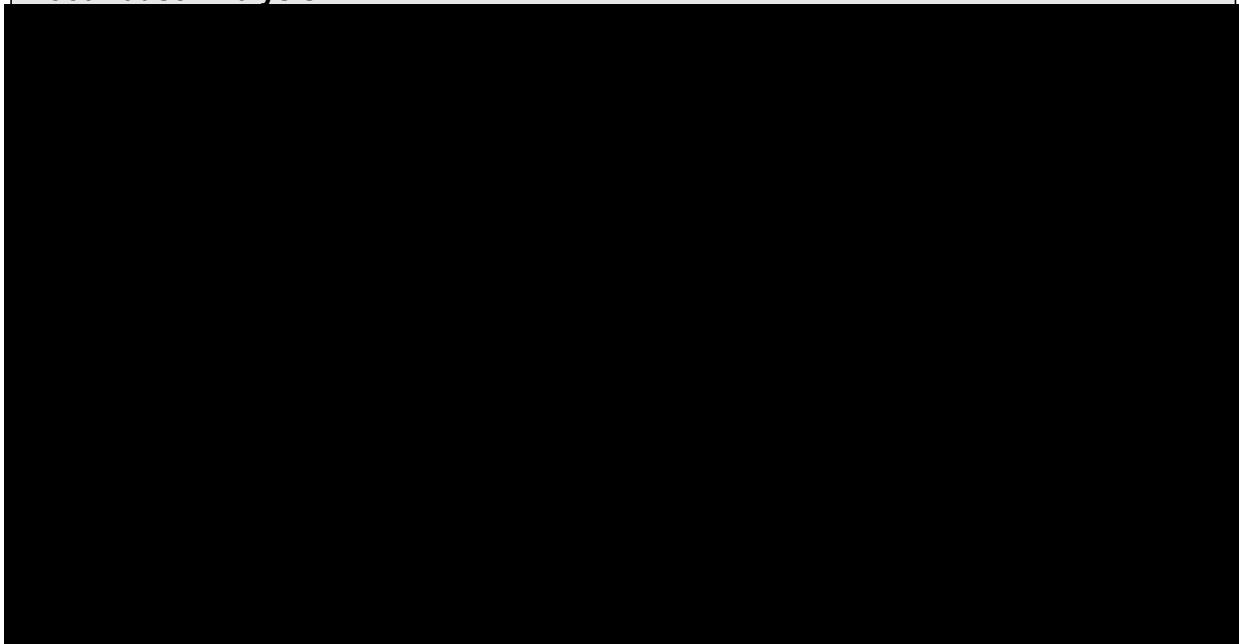
MI.5 Management of Adverse Reactions

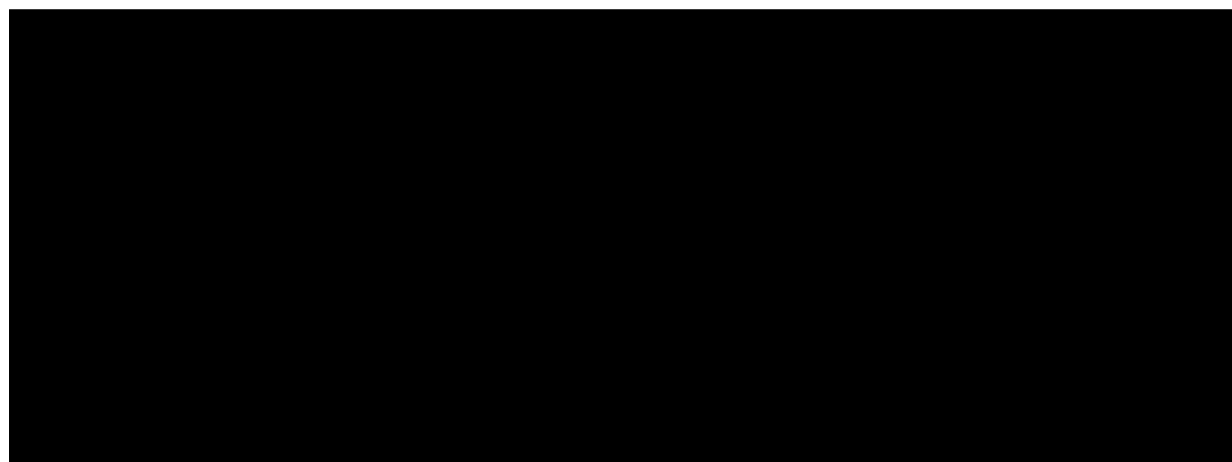
Finding MI.5 a)

Case processing errors for two related cases were identified.

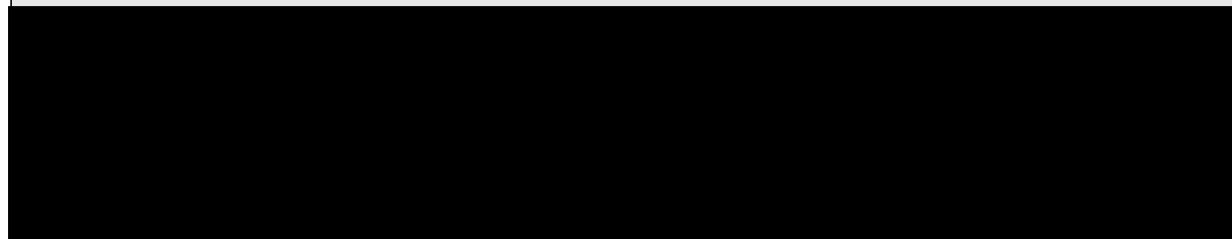
For cases [REDACTED] (master case) and [REDACTED] the incorrect initial case receipt date was coded. For both cases, which originated from the same source, the initial communication from the patient was sent to Aspen on 5 March 2024, however the initial case receipt date was coded as 23 April 2024. Case [REDACTED] was a valid non-serious case reporting PTs Product use complaint, Product adherence issue, Wrong technique in product usage process, and [REDACTED] with [REDACTED]. The case was initially reported to the MHRA on 20 May 2024, and hence there was no impact to the timeliness of reporting. Case [REDACTED] was invalid as the reporter mentioned the same reactions were experienced in many other patients but no patient identifiers were included.

Root Cause Analysis

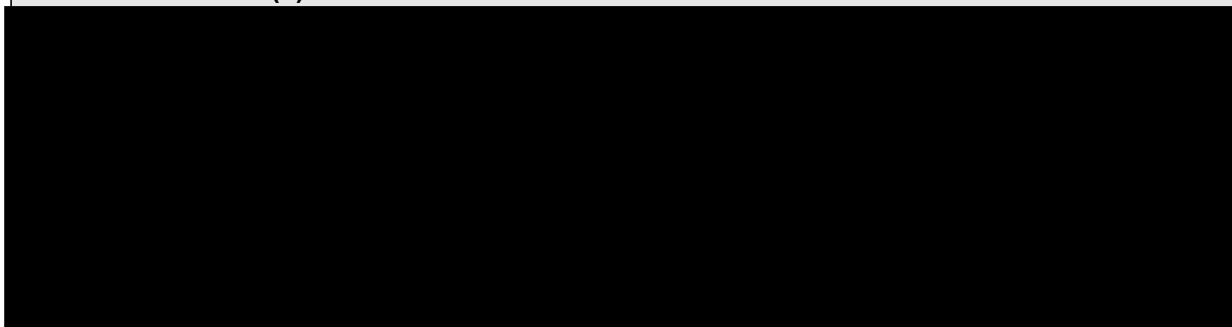




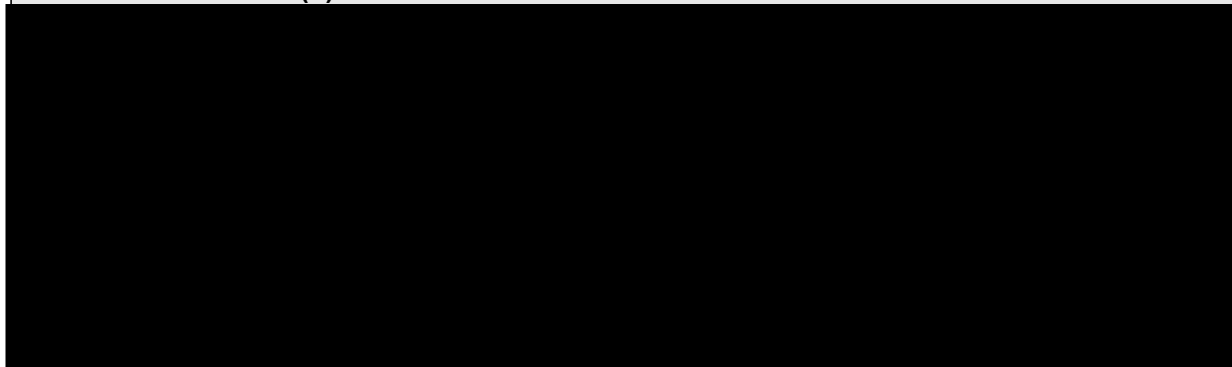
Further Assessment



Corrective Action(s)



Preventative Action(s)



C.4.4 Comments

No comments.

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

APPENDIX II PHARMACOVIGILANCE INSPECTION PLAN

MHRA INSPECTION NUMBER	TBD	DATES	25 – 28 June 2024
PHARMACOVIGILANCE INSPECTION OF	Aspen Pharma Trading Limited (APTL)	START TIME	09:00 BST
LOCATION	Remote	INSPECTION TEAM	[REDACTED]
<p>This inspection will primarily focus on a review of the following topics:</p> <ul style="list-style-type: none"> • Collection and collation of pharmacovigilance data • Management and reporting of ADRs • Signal detection and signal management, including outcomes of signal detection such as the update of reference safety information • Quality management system <p>The inspection plan below outlines the topics for which specific sessions are requested to orientate inspectors around the systems and processes in place. Additional ad hoc discussions with company personnel may also be required. Demonstration of live systems such as the safety database or systems used in the activities under review may also be requested. Please ensure that subject matters experts are available and indicate any times personnel may be unavailable in the below. The inspectors will liaise with the designated inspection host to arrange ad hoc discussions as required.</p> <p>The remainder of the inspection will consist of document review and document requests will be submitted throughout the course of the inspection.</p>			
Tuesday 25 June 2024 (Day 1)			

Opening Meeting

09:30 – 10:30 BST, led by [REDACTED]

Agenda:

- Introductions
- Review of inspection logistics and plan
- **Company Presentation.** The MAH is requested to provide an overview of the company's PV system with a focus on the topics above and the quality systems supporting these topics (to last no longer than 20 minutes). Please highlight any relevant ongoing remediation work on the PV system and any significant recent or upcoming changes to the pharmacovigilance system.

Company attendee(s):

[REDACTED] EME Head of Pharma Affairs, EU QPPV

[REDACTED] PV QMC Manager, Deputy EU QPPV

[REDACTED] Head of PV, Deputy EU QPPV

[REDACTED] Head of Regulatory Affairs + Quality UK, Responsible Person (RP + RPi), UK Devices Responsible Person, National PV contact

[REDACTED] Deputy Head of Quality MAH

[REDACTED] Deputy Quality Manager

[REDACTED] Quality Systems Manager Europe CIS

[REDACTED] Quality Officer

[REDACTED] PV QMC Specialist

Session 1 – Signal detection and signal management, including outcomes of signal detection such as the update of reference safety information

11:00 – 12:00 BST, led by [REDACTED]

Including but not limited to:

- Detection, validation, evaluation and tracking of signals
- The outcomes of signal detection, including updates to RSI
- Pre-submission processes of safety variations

Interviewee(s):

[REDACTED] EME Head of Pharma Affairs, EU QPPV

[REDACTED] PV QMC Manager, Deputy EU QPPV

[REDACTED] Interim Head of PV, Deputy EU QPPV

[REDACTED] Head of Regulatory Affairs + Quality UK, Responsible Person (RP + RPi), UK Devices Responsible Person, National PV contact

[REDACTED] Head of Regulatory Affairs Europe CIS

[REDACTED] Deputy Head of Quality MAH

[REDACTED] Deputy Quality Manager

[REDACTED] Quality Systems Manager Europe CIS

[REDACTED] PV QMC Specialist

Session 2 - Quality management system

14:00 – 15:30 BST, led by [REDACTED]

Including but not limited to:

- Pharmacovigilance system oversight
- Vendor oversight
- Deviation and CAPA management
- Pharmacovigilance audits

The MAH is requested to deliver a presentation (no longer than 10 minutes) to provide an overview and orientation of the processes listed above.

The MAH is also requested to be ready to demonstrate any IT systems that are used in relation to QMS activities.

Interviewee(s):

- [REDACTED] EME Head of Pharma Affairs, EU QPPV
- [REDACTED] PV QMC Manager, Deputy EU QPPV
- [REDACTED] Interim Head of PV, Deputy EU QPPV
- [REDACTED] Head of Regulatory Affairs + Quality UK, Responsible Person (RP + RPi), UK Devices Responsible Person, National PV contact
- [REDACTED] Deputy Head of Quality MAH
- [REDACTED] Deputy Quality Manager
- [REDACTED] Quality Systems Manager Europe CIS
- [REDACTED] Quality Officer
- [REDACTED] PV QMC Specialist

Wednesday 26 June 2024 (Day 2)

Session 3 - Management and reporting of ADRs

09:30 – 10:30 BST, led by [REDACTED]

Including but not limited to:

- Data entry, case processing and assessments
- Case quality in the safety database
- Expedited reporting of ICSRs
- Follow-up activities

MAH should be ready to show the live database to demonstrate core steps of the process as requested and directed by the inspector.

Interviewee(s):

[REDACTED] **EME Head of Pharma Affairs, EU QPPV**

[REDACTED] **PV QMC Manager, Deputy EU QPPV**

[REDACTED] **Interim Head of PV, Deputy EU QPPV**

[REDACTED] **Head of Regulatory Affairs + Quality UK, Responsible Person (RP + RPi), UK Devices Responsible Person, National PV contact**

[REDACTED] **Project Manager Medical Writing and ICSR**

[REDACTED] **Deputy Head of Quality MAH**

[REDACTED] **Deputy Quality Manager**

[REDACTED] **Quality Systems Manager Europe CIS**

[REDACTED] **PV QMC Specialist**

<p>Session 4 - Collection and collation of pharmacovigilance data 11:30 – 12:30 BST, led by [REDACTED]</p> <p>Including but not limited to:</p> <ul style="list-style-type: none"> • Spontaneous sources • Reconciliation • Management of contracts and agreements (PVAs/SDEAs) 	<p>Interviewee(s):</p> <p>[REDACTED] EME Head of Pharma Affairs, EU QPPV</p> <p>[REDACTED] PV QMC Manager, Deputy EU QPPV</p> <p>[REDACTED] Interim Head of PV, Deputy EU QPPV</p> <p>[REDACTED] Head of Regulatory Affairs + Quality UK, Responsible Person (RP + RPi), UK Devices Responsible Person, National PV contact</p> <p>[REDACTED] Project Manager Medical Writing and ICSR</p> <p>[REDACTED] PV QMC Specialist</p> <p>[REDACTED] PV Project Manager</p> <p>[REDACTED] Deputy Head of Quality MAH</p> <p>[REDACTED] Deputy Quality Manager</p> <p>[REDACTED] Quality Systems Manager Europe CIS</p> <p>[REDACTED] PV QMC Specialist</p>
<p>Thursday 27 June 2024 (Day 3)</p>	
<p>Document Review 09:00 – 17:00 BST</p>	<p>Inspectors only</p>
<p>Friday 28 June 2024 (Day 4)</p>	

A closing meeting will be held via videoconference on Friday 28 June 2024 (timing to be confirmed) during which feedback on the inspection will be provided to the company. All relevant personnel are welcome to attend the closing meeting.

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

Designated contact point/inspection host and contact details:

Name: [REDACTED]

Job title: **PV QMC Manager, Deputy EU QPPV**

Email: [REDACTED]

Phone: [REDACTED]

APPENDIX III LIST OF SOCIAL MEDIA PAGES FOR FINDING MA.1 a) iii.

Asset/Project Name:	Asset/Project Description:	Type Of Asset/Project:	Country/Affiliate:
[REDACTED]	The [REDACTED] Page will enable us to post consumer communication, brand promotion, competitions and other consumer-targeted marketing on the Aspen [REDACTED]. The brands involved are [REDACTED].	Social Media Account	[REDACTED]
[REDACTED]	[REDACTED] for business, specifically for [REDACTED] commercial content.	Social Media Account	[REDACTED]
[REDACTED]	[REDACTED] for business for [REDACTED] commercial content.	Social Media Account	[REDACTED]
[REDACTED]	As part of the process of [REDACTED] Commercial building an online presence, we have created the [REDACTED] page for the business [REDACTED] page which will fall under [REDACTED].	Social Media Account	[REDACTED]
[REDACTED]	Online presence for business	Social Media Account	[REDACTED]
[REDACTED]	[REDACTED]	Social Media Account	[REDACTED]
[REDACTED]	[REDACTED] Page	Social Media Account	[REDACTED]
[REDACTED]	[REDACTED] Page	Social Media Account	[REDACTED]

[REDACTED]	This will be a [REDACTED] channel will help promote and advertise the brand	Social Media Account	[REDACTED]
[REDACTED] Page	[REDACTED] page for the promotion of [REDACTED]	Social Media Account	[REDACTED]
[REDACTED] Page	This is the [REDACTED] page used for [REDACTED] and links to the website. The [REDACTED] page provides information about [REDACTED] and links to the website.	Social Media Account	[REDACTED]
[REDACTED]	The [REDACTED] account used to promote [REDACTED] The account provides informative pictures and videos about [REDACTED] as well as a direct link to the website.	Social Media Account	[REDACTED]
[REDACTED]	The [REDACTED] page for [REDACTED] provides informative videos about the product, and links to purchase the item.	Social Media Account	[REDACTED]
[REDACTED] Page	[REDACTED] page to drive disease awareness	Social Media Account	[REDACTED]
[REDACTED] Page	[REDACTED] page to drive disease awareness	Social Media Account	[REDACTED]
[REDACTED] Page	[REDACTED] page to drive disease awareness	Social Media Account	[REDACTED]
[REDACTED] channel	This is the dedicated [REDACTED] channel.	Social Media Account	[REDACTED]
[REDACTED] page	[REDACTED] campaign driven by [REDACTED] [REDACTED] is gearing up for big things with the launch of the brand's first ever, direct-to-consumer campaign, made possible by [REDACTED]	Social Media Account	[REDACTED]

<p>[REDACTED]</p>	<p>[REDACTED] Adding even more impact to our first direct consumer contact, is that [REDACTED] can now proudly claim to [REDACTED] [REDACTED] [REDACTED] [REDACTED] [REDACTED] [REDACTED]</p> <p>Driven by [REDACTED] will be the face of an ongoing consumer campaign which will catapult the brand onto [REDACTED] with a high impact social media campaign coupled with an interactive [REDACTED] aimed at bringing our number 1 status to the attention of our consumer, driving top of mind brand name recall, as well as education on product indications. The brand has also launched a convenient [REDACTED] [REDACTED] which is also highlighted in the campaign.</p> <p>In these difficult economic times that [REDACTED] currently finds itself, the campaign offers consumers a chance to win cash cards, as well conveying a friendly, reassuring and interactive brand tonality during these months.</p> <p>With the demise of many print titles [REDACTED] during the COVID pandemic, bringing the brand, its claims and its consumer promise to life using digital platforms, is more relevant than ever. Look out for [REDACTED] or the website.</p> <p>This is a [REDACTED] created for the purpose of [REDACTED] branded [REDACTED] ads. These ads are in line with the Strategy for the Brand as it is</p>		
<p>[REDACTED]</p>		Social Media Account	<p>[REDACTED]</p>

	Schedule [redacted] and Direct to consumer marketing is permitted.		
[redacted] Page	[redacted] page aimed at driving disease area awareness on [redacted] so as to reach untreated patients. Products involved are as follows: [redacted] [redacted] [redacted]	Social Media Account	[redacted]
[redacted] Page	[redacted] Page	Social Media Account	[redacted]
[redacted] account	Get visibility on social media by publishing posts regarding different topics (interesting news, corporate information, Aspen events/activities) and sharing and reposting content published by other [redacted] accounts.	Social Media Account	[redacted]
[redacted] Page	An [redacted] page for the purpose of promoting the [redacted] brand	Social Media Account	[redacted]
[redacted] Page	[redacted] page to drive disease awareness	Social Media Account	[redacted]
[redacted] Page	[redacted] Page for Consumer	Social Media Account	[redacted]
[redacted] Page	[redacted] page to drive disease awareness	Social Media Account	[redacted]
[redacted] Page	[redacted] page for consumer campaigns.	Social Media Account	[redacted]
[redacted] Page	[redacted] page to drive disease awareness	Social Media Account	[redacted]

[REDACTED] page	[REDACTED] page will be used to increase brand awareness and engagement with consumers on social platform.	Social Media Account	[REDACTED]
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