Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

PHARMACOVIGILANCE INSPECTION REPORT

Pharmacovigilance System Name: UCB Pharma Ltd.

MHRA Inspection Number: Insp GPvP 39/15119-0006

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ABBREVIATIONS

ADR	Adverse Drug Reaction
BADBIR	British Association of Dermatologists Biologic Intervention Register
BSRBR-RA	British Society for Rheumatology Biologics Register for Rheumatoid Arthritis
CAPA	Corrective and Preventative Action
CCDS	Company Core Data Sheet
CHMP	Committee for Medicinal Products for Human Use
DCP	Decentralised Procedure
DHPC	Direct Healthcare Professional Communication
DSUR	Development Safety Update Report
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
MAH	Marketing Authorisation Holder
mos.	months
MRP	Mutual Recognition Procedure
PIL	Patient Information Leaflet
PSMF	Pharmacovigilance System Master File
PSUR	Periodic Safety Update Report
PV	Pharmacovigilance
QA	Quality Assurance
QPPV	Qualified Person responsible for Pharmacovigilance
aRMM	Additional Risk Minimisation Measures
RMP	Risk Management Plan
SDEA	Safety Data Exchange Agreement
SmPC	EU Summary of Product Characteristics
SOP	Standard Operating Procedure
yrs.	years

SECTION A: INSPECTION REPORT SUMMARY

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Inspection type:	Statutory National Inspection
System(s) inspected:	UCB Pharma Ltd., [redacted]
Site(s) of inspection:	208 Bath Road, Slough, SL1 3WE, UK
Main site contact:	[redacted]
Date(s) of inspection:	Onsite inspection from 13 – 16 August 2019. Document review continued office-based and was concluded on 30 August 2019.
Lead Inspector:	[redacted]
Accompanying Inspector(s):	
Previous inspection date(s):	21 – 22 February 2011, 06 – 09 September 2010, 24 – 27 February 2009, 16 – 18 October 2007, 26 – 29 January 2004
Purpose of inspection:	Inspection of pharmacovigilance systems to review compliance with UK and EU requirements.
Products selected to provide system examples:	As part of the general systems review, specific ADR reports were examined for a number of centrally and nationally authorised products.
Name and location of EU QPPV:	[redacted] Address and contact details as above.
Global PV database (in use at the time of the inspection):	[redacted] (based on Argus [redacted] commercially available))
Key service provider(s):	Global ICSR management and global literature search provided by Accenture. Aggregate report writing and signal management provided by Sciformix. Local case processing provided by Bioclinica. Regulatory affairs services provided by Parexel and ProductLife Group.
Inspection finding summary:	0 Critical finding(s) 5 Major finding(s) 2 Minor finding(s)
Date of first issue of report to MAH:	05 November 2019
Deadline for submission of responses by MAH:	10 December 2019; 10 January 2020
Date(s) of receipt of responses from MAH:	10 December 2019; 09 January 2020
Date of final version of report:	20 January 2020 CAPA update #1 received 31 January 2020
Report author:	[redacted]

SECTION B: BACKGROUND AND SCOPE

B.1 Background information

UCB Pharma Ltd. 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 EU and UK pharmacovigilance regulations and guidelines. In particular, reference was made to Regulation (EC) No 726/2004 as amended, Directive 2001/83/EC as amended, Commission Implementing Regulation (EU) No 520/2012 and the adopted good pharmacovigilance practices (GVP) Modules.

A list of reference texts is provided in Appendix I.

UCB are a global pharmaceutical company with headquarters in Braine-l'Alleud, Belgium. Global pharmacovigilance activities are performed by the Patient Safety department at several locations (Braine-l'Alleud, Belgium; Slough, UK; Raleigh, USA and Atlanta, USA) with support from local safety offices. The following key service providers have been contracted for local and global pharmacovigilance activities:

1. Accenture: Global ICSR management and global literature search.
2. Bioclinica: Affiliate ICSR management activities comprising of data entry into the local affiliate module of the safety database including source data verification, follow up activities, local literature search and reconciliation with internal and external partners such as medical information or vendors.
3. Sciformix: Authoring of aggregate reports and other clinical, safety or medical communications, signal management activities.

UCB's product portfolio includes the following centrally authorised products which are predominantly indicated for use in the areas of immunology and neurology:

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[redacted]

The product portfolio also includes a number of established products authorised via national or MR/DC procedures. Marketed products in the UK at the time of the inspection included [redacted]

At the time of the inspection, the PSMF was located at UCB's headquarter in Belgium, therefore the Federal Agency for Medicines and Health Products was the Supervisory Authority responsible for conducting pharmacovigilance inspections on behalf of the EU.

B.2 Scope of the inspection

The inspection included a review of the local (UK) pharmacovigilance systems and was performed at UCB's offices in Slough, Berkshire. Personnel from Belgium and the US attended the Slough site 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).

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

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B.3 Documents submitted prior to the inspection

The company submitted a PSMF ([redacted] approved date 05 June 2019) 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 these requests is contained in document request sheets A and B.

B.4 Conduct of the inspection

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

The inspection was not completed during the onsite days (13 – 16 August 2019) and an interim closing meeting was held at the UCB offices, Slough on 16 August 2019 to summarise the inspection status and to provide preliminary feedback regarding the inspection findings. The inspection was concluded via office-based document review and interviews were held via teleconference. A formal closing meeting was conducted via teleconference on 04 September 2019.

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 2011, the company had made the following changes to the pharmacovigilance system:

- The safety database changed from EmpiricaTrace 4.2. to Argus in June 2014.
- Local ICSR management, follow-up and reconciliation activities have been subcontracted to the service provider Bioclinica since September 2018.
- Pharmacovigilance activities such as aggregate report writing and signal management were previously subcontracted to UBC and were transferred to the service provider Sciformix in September 2018.

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 which are graded as critical or major will be shared with the EMA, other EU competent authorities and the European Commission.

C.3 Guidance for responding to inspection findings

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

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

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

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

C.4 Inspection findings

C.4.1 Critical findings

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

C.4.2 Major findings

MA.1 Management and Reporting of Adverse Reactions

Requirements:

Directive 2001/20/EC as amended, Article 2(p)

Directive 2001/873/EC as amended, Article 107(3)

Commission Implementing Regulation (EU) No 520/2012, Article 11(1)(c)

GVP Module VI – Collection, management and submission of reports of suspected adverse reactions to medicinal products (Rev 2)
VI.B.2. Validation of reports
"*Four minimum criteria are required for ICSRs validation: […]*
d. one or more suspected adverse reaction
(see VI.A.1.1. for definition). If the primary source has made an explicit statement that a causal relationship between the medicinal product and the reported adverse event has been excluded and the notified competent authority or marketing authorisation holder agrees with this assessment, the report does not qualify as a valid ICSR since the minimum information for validation is incomplete (there is no suspected adverse reaction). […]

Similarly, the report is not valid if only an outcome (or consequence) is notified and (i) no further information about the clinical circumstances is provided to consider it as a suspected adverse reaction, or (ii) the primary source has not indicated a possible causal relationship with the suspected medicinal product. For instance a marketing authorisation holder is made aware that a patient was hospitalised or died, without any further information. In this particular situation, medical judgement should always be applied in deciding whether the notified information is an adverse reaction or an event."

VI.B.6.1. Use of a medicinal product during pregnancy or breastfeeding
"*Other cases, such as reports of induced termination of pregnancy without information on congenital malformation, reports of pregnancy exposure without outcome data, or reports which have a normal outcome should not be submitted as ICSRs since there is no suspected adverse reaction*".

VI.B.6.4. Lack of therapeutic efficacy
"*Reports of lack of therapeutic efficacy should be collected and recorded when notified and followed-up if incomplete. They should normally not be submitted as ICSRs if there is no associated suspected adverse reaction, but they should be discussed in periodic safety update reports as applicable […].*"

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During the inspection approximately 50 post-marketing and clinical trial cases received for [redacted] and [redacted] were reviewed.

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

Finding MA.1 a)
Ten cases were identified that had been incorrectly submitted to EudraVigilance despite not meeting the minimum reporting criteria.

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i. Reports of death only

- [redacted] was a solicited UK case received from the BSRBR-RA registry on 22 January 2018 reporting that a 95-year-old patient who had taken [redacted] from 10 August 2011 to 15 November 2013 for the indication of rheumatoid arthritis had died on 23 December 2016. No further details were provided; however, the case was reported to EudraVigilance on 24 January 2018.

- [redacted] was a spontaneous UK case received from a neurologist on 06 November 2018 reporting the death of a patient who had taken [redacted] No further details were provided; however, the case was reported to EudraVigilance on 15 November 2018.

- [redacted] was a solicited UK case received from Healthcare at Home on 11 April 2019 reporting that a patient who had taken [redacted] for the indication of rheumatoid arthritis had deceased. No further details were provided; however, the case was reported to EudraVigilance on 16 April 2019.

- Other examples identified included cases [redacted]

ii. Report of hospitalisation only

- [redacted] was a spontaneous, serious case from the US reporting the hospitalisation of a patient taking [redacted] for the indication of Crohn's disease. No further information was available; however, the case was reported to EudraVigilance on 10 June 2019.

iii. Pregnancy with therapeutic abortion

- [redacted] was a solicited UK case received from study [redacted] on 17 December 2018 reporting the pregnancy of a patient taking [redacted] for the indication of epilepsy that resulted in therapeutic abortion. The therapeutic abortion was deemed as not related to the drug and no adverse reaction or adverse pregnancy outcome were reported, however, the initial case was reported to EudraVigilance on 28 December 2018 and follow-up information was submitted on 05 February 2019.

iv. Report of lack of efficacy

- [redacted] was a spontaneous UK case received from a nurse on 03 January 2018 via another pharmaceutical company reporting that a patient had stopped using [redacted] as it was ineffective. No further information was available, but the case was reported to EudraVigilance on 29 January 2018.

Root Cause Analysis

[redacted]

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[redacted]

Further Assessment

[redacted]

Corrective Action(s)

[redacted]

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

Preventative Action(s)

[redacted]

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

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[redacted]

Finding MA.1 b)

There were examples of cases for which information was incorrectly recorded in the company's safety database. In some examples this also impacted the submission to EudraVigilance.

i. [redacted] was a spontaneous, serious case received on 06 March 2019 as part of a presentation slide deck reporting the results of a study where [redacted] was given to adult patients following [redacted] exposure. The source documentation stated that 20% of patients deteriorated with regards to seizure control; however, the information was incorrectly recorded in the safety database and in the submission to EudraVigilance as "patient presented 20 percent deterioration in seizure control". The case was reported to EudraVigilance on 04 April 2019 with a delay of 14 days past the 15-day ICSR reporting timeline.

ii. [redacted] was a serious solicited case from the interventional trial [redacted] *A* [redacted] reporting the adverse event "seizure" for [redacted] It was entered in the safety database with a company listedness as listed even though the event was not included in the RSI effective at the time of case receipt (IB section 7, dated 26 October 2018).

There was no impact of the incorrect listedness assessment on expedited reporting as the event was considered to be not related by the investigator and the MAH.

Root Cause Analysis

[redacted]

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[redacted]

Further Assessment

[redacted]

Corrective Action(s)

[redacted]

Preventative Action(s)

[redacted]

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[redacted]

[redacted]	

Finding MA.1 c)

There were examples of ICSRs that had been received from a competent authority but that were incorrectly re-submitted to EudraVigilance by the MAH.

i. [redacted] was an Anonymised Single Patient Report (ASPR) received from MHRA on 02 November 2017. The serious case reported that a patient had experienced Stevens-Johnson Syndrome with [redacted]. The case was submitted to EudraVigilance on 22 November 2017.

ii. [redacted] was an ASPR received from MHRA on 06 November 2017 reporting the serious event of pancreatitis. The case was incorrectly reported to EudraVigilance on 22 November 2017.

iii. [redacted] related to a competent authority report downloaded from EudraVigilance on 29 May 2019 (worldwide unique case identification number [redacted] reporting the event of pancreatitis that had occurred for the product [redacted] The medical history included the event of pancreatitis under [redacted] (brand unspecified) and UCB incorrectly reported this event of pancreatitis back to EudraVigilance on 29 July 2019 (worldwide unique case identification number [redacted].

iv. [redacted] related to a case initially downloaded from EudraVigilance on 16 May 2019 reporting the death of a patient who had taken [redacted] Follow-up information was downloaded from EudraVigilance on 03 June and 07 June 2019. The case was incorrectly re-submitted to EudraVigilance on 24 May 2019 and 12 June 2019.

Guidance published in the EMA Note for clarification *Recording by marketing authorisation holders of information on suspected adverse reactions held in EudraVigilance* (EMA/396720/2018, dated 12 July 2018) states in section *3. Recording and reporting principles* that "As regards EudraVigilance, the database is to be considered as the 'target' for such reporting, where ICSRs should be stored, and not as the source of new case reports to be (again) recorded and reported." (emphasis added)

Root Cause Analysis

[redacted]

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[redacted]

Further Assessment
[redacted]

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

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

MA.2 Additional Risk Minimisation Measures

Requirements:
GVP Module XVI – Risk minimisation measures: selection of tools and effectiveness indicators (Rev 2)

XVI.B.6. Quality systems of risk minimisation measures
"*The marketing authorisation holder should ensure appropriate version control of the risk minimisation tools in order to ensure that all healthcare professionals and patients receive up-to-date risk minimisation tools in a timely manner and that the tools in circulation are consistent with the approved product information. For this purpose the market authorisation holders are encouraged to keep track of the receipt of any risk minimisation tools by target audience. These records may be subject to audit and inspection.*"

GVP Module XVI Addendum I – Educational materials
XVI. Add I.2. Principles for educational materials
"The national versions of the educational material should only be submitted, by the marketing authorisation holder, to the respective competent authorities of Member States, following the conclusion of the regulatory procedure in which the aRMM was agreed."

XVI. Add I.3. Submission of educational materials
"If no other national requirements apply, the draft educational material should be submitted to the competent authorities of Member States as follows:

- *with a cover letter and/or request form including the following information:*
  - *a detailed implementation plan for the educational material with the following information:*
  - *target population(s);*
  - *dissemination method (e.g. paper, e-mail, via social media, learned societies and/or patient associations, publication on websites);*
  - *time point when dissemination is anticipated to start and frequency of further disseminations;*
  - *estimated date of launch or date of start of the marketing of the product (in the case of a new marketing authorisation); […]"*

Risk minimisation measures are interventions intended to prevent or reduce the occurrence of adverse reactions associated with the exposure to a medicine, or to reduce their severity or impact on the patient should adverse reactions occur.

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At the time of inspection, UCB had two products [redacted] for which educational materials were required in the EU RMP. The [redacted] educational materials consisted of a physician information pack which included the SmPC and a patient alert card (PAC). The [redacted] educational programme aimed to increase awareness on the product's posology and important risks, and included an HCP checklist, FAQ patient information sheet, patient brochure and patient alert card.

For both products, the distribution method in the UK was hard-copy distribution to prescribers and patients were receiving alert cards via the prescribers. In addition, for [redacted] the materials were provided via the home care programmes. At the time of the inspection, the current materials for both products were also available on eMC.

The following findings were noted in relation to risk management systems:

Finding MA.2 a)

There was an example where the records provided during the inspection regarding hard-copy dissemination of educational materials required as per approved EU RMP did not adequately demonstrate fulfilment of the MAH's regulatory commitments:

i. The [redacted] UK educational materials were updated to version 5.0 following an update

to the EU RMP v11.0 in December 2016 and were approved on 02 November 2017. The implementation plan agreed with the MHRA stated *"The materials will be posted to all potential prescribers, as this is an established product, the list is derived from sales data. This distribution will be actively tracked and confirmation of receipt requested from the target prescribers."*

Evidence of the hard-copy distribution was provided for the initial mailing to healthcare professionals that took place in February and March 2018. Subsequently, UCB contacted the MHRA on 11 March 2019 to inform the assessor that the physician educational materials would be discontinued following a decision at EU level but confirmed that the PAC [redacted] would continue to be disseminated to patients. The MHRA assessor emphasised that this dissemination should be via the patients' healthcare professionals so that the risks outlined on the PAC could be explained to them and that five copies of the PAC should be provided to each HCP.

It was verbally stated during the inspection that this hard-copy distribution to relevant HCPs in the areas of dermatology and rheumatology took place in July 2019; however, the records provided during the inspection did not provide adequate evidence of this as there was no link between the Royal Mail proof of postage and the [redacted]

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ii. Both the [redacted] educational packs included a "Confirmation of Receipt Form". Confirmation of receipt of the educational materials from the target prescribers was not being actively requested by UCB, despite the implementation plans outlined in emails to the MHRA dated 02 August 2017 (for [redacted] of the [redacted] materials) and 21 December 2017 (for v2.2 of the Xyrem materials) which stated "*This distribution will be actively tracked and confirmation of receipt requested from the target prescribers.*"

Root Cause Analysis

[redacted]

Further Assessment

[redacted]

Corrective Action(s)

[redacted]

Deliverable(s)	Due Date(s)

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[redacted]

Preventative Action(s)
[redacted]

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

Finding MA.2 b)

There were examples where updated versions of educational materials for [redacted] and [redacted] had been submitted to MHRA without an adequate implementation plan.

i. [redacted] The email to the MHRA (dated 09 November 2015) included a proposed distribution list but did not clearly outline the dissemination method (e.g. paper, email, etc.) or the timepoint when dissemination was anticipated to start.

ii. [redacted] The email to the MHRA (dated 21 December 2017) included a proposed implementation plan but did not include a timepoint when dissemination was anticipated to start.

During the inspection it was seen that there was a delay of six months in the distribution of the [redacted] educational materials following MHRA approval. The approval was received on 13 February 2018; however, the first distribution only took place on 10 August 2018.

The changes to v2.2 of the materials included the addition of "psychotic events" to the PAC and updates to the Treatment Initiation and Follow-Up Visit Form to prompt the prescriber to counsel the patient on dosing intervals and the potential emergence of thought disorders, including thoughts of committing violent acts.

Root Cause Analysis

[redacted]

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[redacted]

Further Assessment

[redacted]

Corrective Action(s)

[redacted]

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

Preventative Action(s)

[redacted]

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

Finding MA.2 c)

There was a delay of nine months in the submission of the [redacted] educational materials [redacted] to the MHRA for approval following the update and approval of the [redacted] EU RMP [redacted] in May 2014. A communication from Global Medical Affairs to the affiliates concerning local implementation of the educational materials was sent on 23 May 2014; however, the updated UK materials were not submitted to the MHRA for approval until 20 February 2015.

Root Cause Analysis

[redacted]

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[redacted]

Further Assessment

[redacted]

Corrective Action(s)

[redacted]

[redacted]	

Preventative Action(s)

[redacted]

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

Finding MA.2 d)

There was no proactive communication to the [redacted] home care providers in the UK to request the withdrawal of the superseded educational materials following approval of v5.0 of the [redacted] materials by the MHRA in November 2017.

The [redacted] home care providers in the UK were [redacted] and [redacted]. Healthcare at Home was informed on 19 February 2018 that the materials had been updated and that existing stock should be destroyed; however, this information was only communicated in response to a purchase order request for additional materials sent on 06 February 2018.

The procedure that was effective at the time ([redacted] *Pharmacovigilance Interfaces in BII Affiliate*, superseded by version 2 [redacted] on 22 July 2019) stated in Appendix 7.2 *"Notify Home care providers of the new approved version of educ. materials. Request home care providers to withdraw any previous versions within 7 working days and send a confirmation email of the destruction of the older versions."*

Root Cause Analysis

[redacted]

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[redacted]

Further Assessment

[redacted]

Corrective Action(s)

[redacted]

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

Preventative Action(s)

[redacted]

MA.3 Quality Management System

Requirements:

Commission Implementing Regulation (EU) No 520/2012, Article 13(2)

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

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

I.C.1.3. Role of the qualified person responsible for pharmacovigilance in the EU
"*Specifically for the adverse reaction database, if applicable, the QPPV should be aware of the validation status of the database, including any failures that occurred during validation and the corrective actions that have been taken to address the failures. The QPPV should also be informed of significant changes that are made to the database (e.g. changes that could have an impact on pharmacovigilance activities).*"

GVP Module IV – Pharmacovigilance audits (Rev 1)
IV.B.2.4. Actions based on audit outcomes and follow-up of audits
"*The management of the organisation is responsible for ensuring that the organisation has a mechanism in place to adequately address the issues arising from pharmacovigilance audits. Actions should include root cause analysis and impact analysis of identified audit findings and preparation of a corrective and preventive action plan, where appropriate.*"
[emphasis added]

The following findings were noted in relation to the quality management system:

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Finding MA.3 a)

An incomplete impact assessment was conducted after pharmacovigilance deviation PR ID [redacted] occurred, which resulted in the underreporting of serious spontaneous ICSRs to EudraVigilance.

The automated reporting rules governing the expedited reporting of serious cases from the safety database to EudraVigilance were updated on 04 June 2019 to exclude hospitalisation only cases from being reported. However, it was discovered on 14 June 2019 that the rule was only triggered for spontaneous cases reporting hospitalisation only but not for any other serious cases. The reporting rule was corrected on 25 June 2019.

At that time no full assessment was conducted to investigate the impact of the incorrect reporting rule on the expedited reporting of serious ICSRs. It was only discovered a month later during inspection preparation that all serious, valid ICSRs which had been entered in the safety database between 04 June and 25 June 2019 had not been reported to EudraVigilance. This affected 149 serious spontaneous cases that were subsequently submitted late to EudraVigilance between 22 July to 30 July 2019. The QPPV was only informed of the non-compliance on 26 July 2019.

Furthermore, as a result of the incorrect reporting rule, two non-valid cases [redacted]

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and [redacted] see finding MA.1 a) and c)) were submitted to EudraVigilance in the aforementioned period but this was not identified by the MAH in their impact assessment of PR ID [redacted]
Root Cause Analysis
[redacted]
Further Assessment
[redacted]
Corrective Action(s)
[redacted]

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

Preventative Action(s)
[redacted]

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

Finding MA.3 b)
There were delays of up to 18 months in the development of CAPA plans in response to identified pharmacovigilance deviations and following pharmacovigilance audits.

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i. At the time of inspection, the PSMF (v85.0, approved date 31 July 2019), section 7.4.3.1 *List of Open Major & Critical DS and DS IT Deviations with CAPAs ongoing Deviation states: Unagreed* included the following major deviations for which no CAPA plan had been agreed yet:

PR ID	Deviation issued on	Deviation workflow status	CAPA plan overdue by
[redacted]			

Global [redacted] *Pharmacovigilance Deviation Management* [redacted] date effective 18 September 2017), section 5.2.1, stated that the maximum timeframe for developing a CAPA plan to the point of internal approval was 60 days following initiation of the deviation.

ii. At the time of inspection, there were nine audits with critical or major findings which were reported in 2018 and early 2019 but for which the CAPA plans had not yet been approved within procedural timeframes. The following audits listed in PSMF Annex G *Quality System* ([redacted] approved date 31 July 2019) were examples of such audits:

Audit number	Audit type	Date of audit report	CAPA plan overdue by
[redacted]			

Global [redacted] Pharmacovigilance Audit Process [redacted] date effective 17 November 2017) section [redacted] *Development and Agreement of CAPA Plans* stated that "A final agreed CAPA Plan should be approved by the auditee and the Lead Auditor or designee, as soon as possible but no later than 45 calendar days after distribution of the audit report. Failure to provide an acceptable and timely response is escalated to relevant line management and the Head of PVQA."

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Root Cause Analysis

[redacted]

Further Assessment

[redacted]

Corrective Action(s)

[redacted]

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[redacted]

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

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[redacted]

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

Finding MA.3 c)

Delays were seen in the implementation of CAPA proposed to address major and critical pharmacovigilance deviations and findings from audits. These CAPA had not been completed in line with the planned due date and were still open as of 26 June 2019.

i. The CAPA associated with the critical and major observations from the audit of the home care provider Healthcare at Home in the UK were completed with a delay of 12 months. The MAH had audited Healthcare at Home UK (audit reference [redacted] in October 2016 and the audit report was subsequently issued on 15 December 2016. The CAPA associated with the critical and major observations [redacted] and [redacted] had a due date of 02 July 2018; however, they were not completed until July 2019.

   Critical observation [redacted] referred to several deficiencies in the content of the SDEA (dated 04 February 2013) between UCB and Healthcare at Home which were considered to impact the identification, collection, verification and onward reporting of safety information from Healthcare at Home to UCB.

   Major observation [redacted] related to the inadequate oversight of the activities

undertaken by Healthcare at Home on behalf of UCB and associated deficiencies in the SDEA.

It is acknowledged that the PVQA function had escalated the CAPA delay to the UCB PV Quality Council on 24 September 2018 and it was agreed on 16 October 2018 to set up a Safety Agreement outside of the Business Agreement. The Safety Agreement was negotiated and concluded in the following seven months; however, no impact analysis of the overdue CAPA was carried out in the meantime to ensure that all relevant safety information was collected by Healthcare at Home and reported to UCB during the delayed resolution period.

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ii. PSMF section [redacted] *List of Open Major & Critical DS and DS IT Deviations with CAPAs ongoing* and section [redacted] *Overview of Open Critical and Major Findings and CAPA from PV System Audit* [redacted] approved date 31 July 2019) included further examples of CAPA proposed to address major and critical pharmacovigilance deviations and findings from audits that had not been completed in line with the planned due dates. The following lists are non-exhaustive and highlight the CAPA that are the most overdue.

Examples from PSMF section [redacted] *List of Open Major & Critical DS and DS IT Deviations with CAPAs ongoing:*

PR ID	Severity	Deviation issued	CAPA due date	Overdue by
[redacted]				

Examples from PSMF section [redacted] *Overview of Open Critical and Major Findings and CAPA from PV System Audit:*

Audit & observation number	Grading	Audit completed	CAPA due date	Overdue by
[redacted]				

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[redacted]

Post-inspection request: As part the responses to the inspection report, UCB should provide information on how overdue CAPAs will be prioritised for remediation and on the steps that were taken to mitigate the impact of the deviations and findings in the interim.

Root Cause Analysis

[redacted]

Further Assessment

[redacted]

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[redacted]

Corrective Action(s)

[redacted]

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[redacted]

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

Preventative Action(s)

[redacted]

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

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[redacted]

Finding MA.3 d)
The UCB Monthly Compliance and Performance Reports included KPIs for monitoring the performance of the pharmacovigilance system. The reports produced between November 2018 and February 2019 included data on inbound reporting of ICSRs from business partners according to SDEA timelines. However, there was no target associated with this KPI. As an example, the data in November 2018 showed that Jazz Pharmaceuticals reported 62 serious ICSRs late to UCB, which resulted in 91% compliance with the SDEA timelines. However, it was not clear what threshold of non-compliance would trigger specific actions by UCB. This finding is graded as minor but has been grouped within the major Quality Management System finding.
Root Cause Analysis
[redacted]
Further Assessment
[redacted]
Corrective Action(s)
[redacted]
Deliverable(s) / **Due Date(s)**
[redacted]
Preventative Action(s)
[redacted]

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

MA.4 Auditing of the Pharmacovigilance System

Requirements:

GVP Module IV – Pharmacovigilance audits (Rev 1)
IV.B.2. The risk-based approach to pharmacovigilance audits
"Risk assessment should be documented appropriately for the strategic, tactical and operational planning of pharmacovigilance audit activity in the organisation […]".

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: […]*

- *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).*"

IV.B.3.1.2. Qualifications, skills and experience of auditors and continuing professional development
"*Auditors should demonstrate and maintain proficiency in terms of the knowledge, skills and abilities required to effectively conduct and/or participate in pharmacovigilance audit activities. The proficiency of audit team members will have been gained through a combination of education, work experience and training and, as a team, should cover knowledge, skills and abilities in: […]*

- *applicable laws, regulations and other requirements relevant to pharmacovigilance;*
- *pharmacovigilance activities, processes and system(s); […].*"

The following findings were noted in relation to quality assurance auditing of the pharmacovigilance system:

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Finding MA.4 a)

The risk assessment carried out for the purposes of audit planning did not include all contractors and vendors carrying out pharmacovigilance activities in the UK. The risk assessment was recorded in document [redacted] *PV Risk Assessment Audits 2019* [redacted] approved date 20 December 2018). The following contractors and vendors were missing:

- [redacted]: Provider of patient support and home care for [redacted]
- Daws & Associates Ltd.: Printing of [redacted] educational materials.

Furthermore, there was one vendor (National Ankylosing Spondylitis Society) listed as providing patient support programme service in PSMF Annex B [redacted] *List of Contracts and Agreements* ([redacted] approved date 31 July 2019) which had not been included in the risk-assessment. The MAH acknowledged during the inspection that the categorisation of the vendor needed to be reviewed and would be re-considered for inclusion in a future risk-assessment.

Root Cause Analysis

[redacted]

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[redacted]

Further Assessment
[redacted]

Corrective Action(s)
[redacted]

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

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Preventative Action(s)

[redacted]

Finding MA.4 b)

There was no procedural guidance on how the various audit tiers utilised in the annual audit risk assessment mapped to the scheduling of individual audits in the annual audit plan.

An audit tier of 1 to 4 was attributed to each entity in the risk assessment following evaluation of the individual risk factors. However, there was no written procedure that documented how the classification of an entity in a tier linked to its inclusion and prioritisation in the audit plan.

The MAH stated during the inspection that auditable units with Tier 1 scores were considered to have the highest risk and were therefore included in the PVQA Annual Audit Program.

Root Cause Analysis

[redacted]

Further Assessment

[redacted]

Corrective Action(s)

[redacted]

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[redacted]

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

Preventative Action(s)

[redacted]

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

Finding MA.4 c)

In relation to the pharmacovigilance audit of the UCB British and Irish Isles (BII) affiliate that was conducted on 08 November 2018, there was no evidence that the auditor had sufficient training and experience of the applicable laws, regulations and other requirements relevant to pharmacovigilance and pharmacovigilance activities, processes and systems.

The auditor's background was in GMP and while there was evidence of training on some of the BII pharmacovigilance procedural documents, this was not considered sufficient to ensure adequate knowledge of the regulations and requirements relevant to pharmacovigilance. In addition, the auditor's training record indicated that internal training on "Module V – Fundamentals of PV Auditing" was only completed on 21 May 2019, six months after the pharmacovigilance audit was conducted.

Root Cause Analysis

[redacted]

Further Assessment

[redacted]

Corrective Action(s)

[redacted]

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

Preventative Action(s)

[redacted]

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

MA.5 Maintenance of Authorised Product Information

Requirements:

Directive 2001/20/EC as amended, Article 23(3), which states that the MAH "*shall ensure that the product information is kept up to date with the current scientific knowledge*".

Commission Implementing Regulation (EU) No 520/2012, Article 11(1)(f), which states that procedures and processes shall be in place to ensure "*the update of product information by the marketing authorisation holder in the light of scientific knowledge*".

Finding MA.5

UCB Pharma's process for the handling of safety variations for active substances where it held MRP and national licences was not considered appropriate by the MHRA as it resulted in delays to updating the product information of the national licence. The company's approach was to submit variations for the MRP licences first and wait for the approval for these procedures, before then making submissions to update the national licences.

As an example, the company identified the safety signals of "arthralgia" in March-April 2015, "nightmare" in July 2015 and "acute generalised exanthematous pustulosis" in July 2016, respectively, for [redacted], licensed both nationally and via the mutual recognition route.

The safety variation for the MRP licence was submitted on 07 October 2016 to add all three ADRs to the SmPC. The RMS approved the variation on 19 June 2017. In contrast, for the licences approved via the national procedure in the UK, submission to MHRA was only made on 17 November 2017, over a year after the variation submission for the MRP licences (but within 5 months following MRP approval on 19 June 2017).

Global [redacted] *Preparation, Review, Approval and Implementation of Company Core Data Sheet (CCDS)* [redacted] date effective 14 December 2018) Appendix 2 stated that a variation for "wave 2 countries", i.e. those countries where national licences for the same active substance were held, would be submitted within 3 months from RMS approval for category 2 changes (major safety changes) and within 5 months from reference country approval for category 3 changes (other change (including safety)).

For Type [redacted] and [redacted] variations, submission of safety updates to national licences should not be delayed until MRP variation approval is received.

Root Cause Analysis

[redacted]

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Further Assessment
[redacted]
Corrective Action(s)
[redacted]

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

C.4.3 Minor findings

MI.1 Pharmacovigilance System Master File

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Finding MI.1

The following deficiencies were noted in relation to the PSMF and its annexes [redacted] approved date 31 July 2019):

i. There was a discrepancy between PSMF Table 7.4.4.2 *Overview of Open Critical and Major Findings without Agreed CAPA from PV System Audit* and Annex G Table 8.7.1.1 *Audit List extracted from QAAD and Trackwise*. For audit [redacted] (Partner audit of Jazz Pharmaceuticals), Table 7.4.4.2 listed this audit as being without an agreed CAPA plan and showed that three major findings had been reported. However, Annex G showed that there were no critical or major findings with uncompleted CAPA.

ii. PSMF Annex B, section 8.2.3.2 *List of Pharmacovigilance Master Service Agreements* included the vendor Daws & Associates Ltd. who printed and distributed educational materials for [redacted]. However, during the inspection UCB confirmed that Daws & Associates Ltd. were only contracted until May 2017 for [redacted] educational materials but have since been contracted to provide the same services for the [redacted] educational materials.

iii. PSMF Annex C *Sources Of Safety Data* did not include the retrospective multicentre study *The efficacy, tolerability & quality of life impact of* [redacted] *A UK wide service evaluation* that was conducted in collaboration with the University of Sheffield. The study started in March 2017 and ended in January 2019.

iv. PSMF Annex C, section [redacted] *Non UCB studies* incorrectly stated that the investigator-initiated study [redacted] *The Human Epilepsy Project* included study sites in the UK; however, no UK study sites were set up and the UK sites had been removed in the first protocol amendment.

v. PSMF Annex F, section [redacted] *List of the Performance Indicators* (v85.0, approved date 31 July 2019) did not include a specific key performance indicator to monitor the timeliness of implementation of CCDS updates into local product information despite the fact that UCB did have a KPI, which was presented to the PV Quality Council. A table of safety variations submitted within the last two years or those due for submission was presented in section 8.6.3 *Overview on safety variations* of the Annex.

vi. PSMF Annex G, section [redacted] *Quality Assurance Auditing of the Pharmacovigilance System: rolling 5-year history of UCB audits and UCB audits scheduled for Next Quarter* did not include the audit of the [redacted] affiliate that took place on 08 November 2018. The audit was conducted under UCB's self-inspection programme as described in [redacted] *Affiliate Quality Self-Inspection and Local Vendor Auditing (Regional Quality)* [redacted] date effective 21 November 2018) and its scope was "Pharmacovigilance processes and procedures at UCB [redacted]

It was noted that [redacted] was predominantly focused on self-inspection of GMP/GDP activities. However, section [redacted] (Self-inspection Program) stated "Any finding impacting the PV System will be noted as such in the audit management tool to ensure inclusion of the audit information in the Pharmacovigilance System Master File."

This finding has been graded as minor as the noted deficiencies appear to be isolated

examples and do not indicate systematic omission or incorrect presentation of data in the PSMF and did not impact on the planning or conduct of the inspection.

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Root Cause Analysis

[redacted]

Further Assessment

[redacted]

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[redacted]

Corrective Action(s)
[redacted]

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

Preventative Action(s)
[redacted]

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[redacted]

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

MI.2 Collection and collation of safety information

Section 43

Finding MI.2 a)

The following deficiencies were noted in relation to the contracts and contractual obligations between UCB and the vendor JJ Marketing who was responsible for supporting promotional activities in the UK and the Republic of Ireland including the management of the [redacted] social media accounts.

i. There was a delay of two months in implementing the SDEA with JJ Marketing.

The Services Agreement became effective on 07 March 2017; however, the SDEA was not in place until 15 May 2017. It is acknowledged that the Services Agreement included a general statement on adverse event reporting in section 5.3 *Pharmacovigilance*; however, this did not include any provisions on the reporting timelines to UCB, recipients at UCB or definitions of reports that need to be send to UCB.

ii. No monthly reconciliation was undertaken between JJ Marketing and UCB between May 2017 and January 2019. The SDEA (SDEA No. [redacted] v1.0, dated 15 May 2017), section I.5 stated "For the purpose of ensuring Safety Information had been successfully transmitted between the Parties (when applicable), Contract Partner shall send to UCB on a monthly basis an electronic mail to the relevant contact designated in "Contact Information", either to:

- confirm that no Safety Information relating to the Product was received or identified by Contract Partner during the period;
- confirm that it did send all required Safety Information that it received or identified during the previous period, including an inventory list of all Safety Information transmitted during the period."

It is acknowledged that a retrospection reconciliation had been conducted in January 2019 and there had been no cases or safety information which had not been sent to UCB.

Root Cause Analysis

[redacted]

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[redacted]

Further Assessment
[redacted]

Corrective Action(s)
[redacted]

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

Preventative Action(s)
[redacted]

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

Finding MI.2 b)
No 6-monthly company report was received from the BADBIR registry in July 2019 which covered the period from 01 December 2018 to 31 May 2019 and UCB had not followed this up with BADBIR until the report was requested during the inspection. The agreement between both parties (dated 05 September 2018) stated in section 3.3 that

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"BAD shall, provide UCB with copies of all Observations, together with all Results. The Results shall be […] provided […] on at least a six (6) monthly basis […]." In addition, the BADBIR SOP *Pharmacovigilance and Reporting* [redacted] date effective 01 August 2018) stated in section [redacted] *BADBIR 6 monthly company reports* that "BADBIR produces 6-monthly reports for each company which are circulated during January and July. The reports provide data on the company's drug and the comparison cohort." This finding has been graded as minor as no adverse event reports had been received by BADBIR in the specified period that required sending to UCB.
Root Cause Analysis
[redacted]
Further Assessment
[redacted]
Corrective Action(s)
[redacted]

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

Preventative Action(s)
[redacted]

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

C.4.4 Comments

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i. During the inspection, some historical delays were noted in submitting variations to update the safety section of EU SmPCs and PILs for [redacted] product following identification of the following safety signals:

Arthralgia

- Safety Signal Assessment Report (SSAR) approved in March-April 2015
- CCDS update approved by the Global Labelling Committee on 15 March 2016
- Submission for MRP licence made on 07 October 2016
- Approval from MRP RMS received on 19 June 2017
- Submission for national UK licence made on 17 November 2017

Nightmare

- SSAR approved in July 2015
- CCDS update approved by the Global Labelling Committee on 15 March 2016
- Submission for MRP licence made on 07 October 2016
- Approval from MRP RMS received on 19 June 2017
- Submission for national UK licence made on 17 November 2017

Hepatitis

- SSAR approved in December 2015
- CCDS update approved by the Global Labelling Committee on 15 November 2016
- Submission for MRP licence made on 14 September 2017
- Approval from MRP RMS received on 14 May 2018
- Submission for national UK licence made on 31 August 2018

These examples have been reported as a comment because UCB had taken action to mitigate these types of delays by updating [redacted] (Benefit Risk Team Labeling Interface) [redacted] date effective 22 March 2017) to introduce a 5-week timeline to be followed from trigger of Benefit Risk Team (BRT) recommendation for label updates to Global Labelling Committee review. UCB further tightened these timelines in the update of [redacted] to version 3.0 (date effective 14 December 2018) to introduce a 4-week timeline to be followed from trigger of BRT recommendation for label update to GLC review. In addition, no further delays in the submission of safety updates were noted in the more recent examples reviewed during the inspection.

ii. [redacted] (Management of local labelling) (v1.0, date effective 14 December 2018) stated that "the LRA is responsible for monitoring on a regular basis (at least yearly), according to a risk-based approach and according to local requirements, the labeling of the innovator and informing the relevant BRT." However, the procedure did not describe how the review of innovator/ reference medicinal product labelling should be documented. Evidence was requested of the most recent reviews of the reference medicinal product information for [redacted] An Excel spreadsheet was provided which included the name of the brand leader product, the date the labelling was checked and whether there were any changes. It is recommended that the SOP is updated to describe how this activity should be documented. [redacted]

SECTION D: CONCLUSIONS AND RECOMMENDATIONS

D.1 Conclusions

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

<This section of the report will be completed when the final version containing the MAH's responses is issued by the Inspector.>

D.2 Recommendations

<This section of the report will be completed when the final version containing the MAH's responses is issued by the Inspector.>

APPENDIX I REFERENCE TEXTS

- Directive 2001/83/EC, as amended.
- Commission Implementing Regulation (EU) No 520/2012.
- Guideline on good pharmacovigilance practices (GVP).
- Directives 2001/20/EC and 2005/28/EC in relation to Clinical Trials.
- The Human Medicines Regulations 2012 (Statutory Instrument 2012 No. 1916).
- CPMP/ICH/377/95: E2A "Clinical Safety Data Management: Definitions and Standards for Expedited Reporting".
- 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: E2D "Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting".

APPENDIX II PHARMACOVIGILANCE INSPECTION PLAN

MHRA INSPECTION NUMBER	Insp GPvP 39/15119-0006	**DAY**	1
PHARMACOVIGILANCE INSPECTION OF	UCB Pharma Ltd	**DATE**	13 August 2019
LOCATION	208 Bath Road, Slough, SL1 3WE	**START TIME**	09:00 arrival for a 09:30 start

Purpose of Interview	**Session Lead**	**Staff to be interviewed**
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)*	[redacted]	[redacted]
Document collation and review		
LUNCH		
Spontaneous sources of safety information in the UK, including but not limited to • Medical enquiries • Product quality complaints	[redacted]	[redacted]

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Solicited sources of safety information in the UK, including but not limited to • Compassionate use programmes • Patient support programmes • Market research programmes	[redacted]	[redacted]
[redacted]		

MHRA INSPECTION NUMBER	Insp GPvP 39/15119-0006	**DAY**	2
PHARMACOVIGILANCE INSPECTION OF	UCB Pharma Ltd	**DATE**	14 August 2019
LOCATION	208 Bath Road, Slough, SL1 3WE	**START TIME**	09:00

Purpose of Interview	**Session Lead**	**Staff to be interviewed**
Local management of ICSRs, including but not limited to • Case receipt and transfer of ICSRs into the global safety database • Follow-up activities • Submission of ICSRs to MHRA (CT cases) and EV	[redacted]	[redacted]
Additional risk minimisation measures in the UK, including but not limited to • Implementation and maintenance of UK educational materials • DHPCs	[redacted]	[redacted]
LUNCH		

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Sources of safety information in the UK from investigational studies, including but not limited to • Interventional trials • Non-interventional studies • Investigator-initiated studies	[redacted]	[redacted]

MHRA INSPECTION NUMBER	Insp GPvP 39/15119-0006	**DAY**	3
PHARMACOVIGILANCE INSPECTION OF	UCB Pharma Ltd	**DATE**	15 August 2019
LOCATION	208 Bath Road, Slough, SL1 3WE	**START TIME**	09:00

Purpose of Interview	**Session Lead**	**Staff to be interviewed**
Maintenance of local product information, including but not limited to • Communication and implementation of CCDS updates • Submission of safety variations • Post-approval implementation	[redacted]	[redacted]
LUNCH		
UK Quality management system, including but not limited to • Management of procedural documents relevant to UK Pharmacovigilance • Training of UK staff • Mechanisms to monitor pharmacovigilance processes and identify non-compliance, including audit and key performance indicators • Management of deviations, non-compliances and CAPA	[redacted]	[redacted]

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MHRA INSPECTION NUMBER	tbc	**DAY**	4
PHARMACOVIGILANCE INSPECTION OF	UCB Pharma Ltd	**DATE**	16 August 2019
LOCATION	208 Bath Road, Slough, SL1 3WE	**START TIME**	09:00

Purpose of Interview	**Session Lead**	**Staff to be interviewed**
Document review and ad-hoc questions	-	As required
Closing meeting	[redacted]	All welcome