Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

PHARMACOVIGILANCE INSPECTION REPORT

Pharmacovigilance System Name: Strides Shasun Limited

MHRA Inspection Number: GPvP 13606/4119-0017

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ABBREVIATIONS

ADR	Adverse Drug Reaction
AE	Adverse Event
CAPA	Corrective and Preventative Action
CHMP	Committee for Medicinal Products for Human Use
CRO	Contract Research Organisation
CSR	Clinical Study Report
EMA	European Medicines Agency
GVP	Good Vigilance Practice
ICH	International Conference on Harmonisation
ICSR	Individual Case Safety Report
MAH	Marketing Authorisation Holder
NCA	National Competent Authority
PASS	Post-authorisation Safety Study
PSMF	Pharmacovigilance System Master File
PSUR	Periodic Safety Updates Reports
QA	Quality Assurance
QPPV	Qualified Person responsible for Pharmacovigilance
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
SOP	Standard Operating Procedure
SUSAR	Suspected Unexpected Serious Adverse Reaction

SECTION A: INSPECTION REPORT SUMMARY

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Inspection type:	Re-inspection
Name and address(es) of site(s) inspected:	Strides Shasun Limited (formerly Strides Arcolab Limited) Inspection performed at the offices of PharSafer Associates: PharSafer House White Hart Meadows Ripley, Surrey, GU23 6ND
Main site contact:	[redacted] PharSafer House White Hart Meadow Ripley, Surrey, GU23 6ND Tel: [redacted] Email: [redacted]
Date(s) of inspection:	14 – 15 December 2015
Lead Inspector:	[redacted]
Accompanying Inspector(s):	
Previous inspection date(s):	27 – 28 November 2014 05 – 07 June 2013 28 – 29 April 2009 18 – 19 March 2008 31 October – 02 November 2006
Purpose of inspection:	Re-inspection to determine if appropriate action had been taken from the previous inspection and to review compliance with UK and EU requirements
Products selected to provide system examples:	As part of the re-inspection specific documents were examined for a number of products including fluoxetine, diclofenac, alfacalcidol and prednisolone.
Name and location of EU/EEA qualified person for pharmacovigilance:	[redacted] PharSafer House White Hart Meadow Ripley, Surrey, GU23 6ND Tel: +44 (0)1483 212155 Email: [redacted]
Global PV database (in use at the time of the inspection):	Oracle Argus Safety 7.0.4
Key service provider(s):	**Strides Arcolab** Pharmacovigilance services provided by PharSafer, Sciformix, VigiMedsafe and Techsol. Medical information services provided by Sciformix. PSURs submitted by European Localisation Centre. **Co-Pharma** Pharmacovigilance services provided by PharSafer, Sciformix, VigiMedsafe and Drug Safety Solutions. Medical Information services provided by Sound Opinion. PSURs submitted by Callisto.

Inspection finding summary:	0 Critical findings 2 Major findings 3 Minor findings
Date of first issue of report to MAH	15 January 2016
Deadline for submission of responses by MAH	Initial: 19 February 2016 Follow-up 1: 10 March 2016 Follow-up 2: 05 April 2016
Date(s) of receipt of responses from MAH	Initial: 18 February 2016 Follow-up 1: 09 March 2016 Follow-up 2: 05 April 2016
Date of final version of report	14 April 2016
Report author	[redacted]

SECTION B: BACKGROUND AND SCOPE

B.1 Background information

Strides Shasun Limited (hereafter Strides, formerly Strides Arcolab Limited) was selected for re-inspection as a result of a critical finding that was identified during the previous inspection of the MAH performed on 27 and 28 November 2014. The purpose of the re-inspection was to determine if appropriate action had been taken as a result of the previous inspection. In addition, the inspection provided an opportunity to re-examine the compliance of the pharmacovigilance system with currently applicable EU and UK pharmacovigilance regulations and guidelines. In particular, reference was made to 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 at Appendix I.

Strides is a global pharmaceutical company headquartered in Bangalore, India that develops and manufactures a wide range of generic pharmaceutical products. Strides received its first UK licence on 29 January 2011 and currently has 10 licensed products in the UK. Co-Pharma has been a subsidiary of Strides since 2009 and has approximately 56 licensed products in the UK.

The provision of EU QPPV services has been outsourced to PharSafer Associates since May 2010. ICSR processing for all products has been outsourced to VigiMedsafe, along with signal detection activities. Expedited reporting of ICSRs to EU competent authorities for Strides and Co-Pharma products is performed by Techsol and Drug Safety Solutions respectively. Compilation of PSURs is performed by Sciformix for all products, whilst submission to competent authorities is outsourced to European Localisation Centre (Strides products) and Callisto (Co-Pharma products). Medical information services for Strides products are outsourced to Sciformix, whilst the third-party, Sound Opinion, provides medical information services for Co-Pharma products.

B.2 Scope of the inspection

The inspection focussed on a review of the systems and processes which were associated with the critical and major findings identified during the previous inspection (namely, signal management [critical] and the PSMF [major]). In addition, the inspection covered safety data migration as there had been a change of global safety database since the previous inspection (see Section C.1).

The inspection was performed at PharSafer Associates' offices in Ripley, Surrey. Personnel from Strides in Bangalore, India and from Co-Pharma in Watford, UK attended the Ripley site in order to participate in the inspection.

The inspection was performed using interviews and document review. The systems reviewed during the inspection are highlighted in the Pharmacovigilance Inspection Plan (attached as Appendix II).

B.3 Documents submitted prior to the inspection

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The company submitted a PSMF [redacted] to assist with inspection planning and preparation. Specific documents relating to the validation of the Argus Safety database and the migration of safety data were also requested by the Lead Inspector and provided by the company prior to the inspection.

B.4 Conduct of the inspection

In general, the inspection was performed in accordance with the Inspection Plan (attached as Appendix II).

A closing meeting was held to present the inspection findings at Ripley, Surrey on 15 December 2015. 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 the company had made the following changes:

- As of 19 November 2015, Strides Arcolab Limited has merged with Shasun Pharmaceuticals Limited (a supplier and manufacturer of active pharmaceutical ingredients and formulations) to form a new entity called Strides Shasun Limited. There is no impact to the pharmacovigilance system as a result of the merger.

- The global safety database changed from Oracle AERS 4.6.2 to Argus Safety 7.0.4. Safety data was migrated from AERS to Argus in April 2015 and the go-live date of the new database was 05 May 2015.

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 at: https://www.gov.uk/good-pharmacovigilance-practice-gpvp#actions-after-the-inspection

C.4 Inspection findings

C.4.1 Critical findings

At the time of re-inspection, critical deficiencies identified during the previous inspection relating to signal management had been partially addressed; however a major finding remained in this area (see MA.1 below). No further critical deficiencies associated with the pharmacovigilance system were identified.

C.4.2 Major findings

MA.1 Signal Management

Requirements:

Directive 2001/83/EC as amended, Article 104 (2) (3(e)).

The Human Medicines Regulations 2012 (Statutory Instrument 2012 No. 1916), Part 11 Pharmacovigilance, Regulation 182 and 190.

Commission Implementing Regulation (EU) No. 520/2012, Article 21 (1).

GVP Module VI – Management and reporting of adverse reactions to medicinal products.

GVP Module IX – Signal management.

IX.B.3.2 "*Whichever methods are employed for the detection of signals, the same principles should apply, namely:*

- *any outputs from a review of cumulative data should be assessed by an appropriately qualified person in a timely manner;*"

IX.B.4.1 "*All validation, prioritisation, assessment, timelines, decisions, actions, plans, reporting as well as all other key steps should be recorded and tracked systematically.*"

IX.B.4.2 "*An essential feature of a signal management system is that it is clearly documented to ensure that the system functions properly and effectively…*"

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 the MHRA inspection performed in November 2014, a critical finding was reported due to a failure to perform signal detection activities for UK authorised products outside of the PSUR process. Since the 2014 inspection, a signal detection schedule had been put into place and at least one signal detection activity had been conducted for each active substance authorised in the UK. A number of safety variations had been filed for the products where an update to the Summary of Product Characteristics (SPC) was recommended by the signal detection team and where the signal report had been approved by the QPPV.

Despite significant improvement in this area, deficiencies with signal management activities were identified at the re-inspection and a major finding has been reported.

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Finding MA.1 a)

There were examples of delays in finalising signal detection reports. A signal detection report was considered finalised following review and approval by the EU QPPV.

i. The signal detection report for [redacted] was drafted by VigiMedsafe on 13-Jul-2015 but was not finalised at the time of the inspection. In the draft report, a recommendation to update sections 4.4 and 4.8 of the UK SPC with information on systemic lupus erythematosus was made; however a variation to update the UK SPC had not been submitted due to the draft status of the report. The specific proposed updates were as follows:

- Section 4.4 Warnings and precautions: possibility of exacerbation or activation of systemic lupus erythematosus.
- Section 4.8 Undesirable effects: Unknown frequency: exacerbation or activation of systemic lupus erythematosus.

ii. The signal detection report for [redacted] was drafted by VigiMedsafe on 21-Jul-2015 but was not finalised at the time of the inspection. The report concluded that "secondary angle closure glaucoma and any events concerning glaucoma will be assessed as a possible new signal and discussed at the next safety review or before if cases start to be reported", based on the findings from a literature article. However, due to the draft status of the report, this safety topic was not recorded on the signal tracker (or an alternative document for closely monitored events) and any associated decisions, actions and timelines were not documented for this event.

iii. The signal detection report for [redacted] was drafted by VigiMedsafe on 24-Nov-2015 but was not finalised at the time of the inspection. In the draft report, a recommendation to update section 4.4 of the UK SPC with information on seizures and irreversible non-selective monoamine inhibitors in line with the brand leader SPC was made, in addition to proposed updates of section 4.8 with new adverse event terms, such as Stevens - Johnson syndrome and Toxic Epidermal Necrolysis. However, due to the draft status of the report, this recommendation had not been approved and no further action had been taken at the time of the inspection.

iv. The signal detection report for [redacted] was drafted by VigiMedsafe on 30-Sep-2015 but was not finalised at the time of the inspection. No signals were identified during the review period.

It was noted that there were no documented timeframes for the preparation and finalisation of signal detection reports in Strides procedures.

Root Cause Analysis

[redacted]

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[redacted]

Further Assessment

[redacted]

Corrective Action(s)

[redacted]

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

Preventative Action(s)
[redacted]

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

Finding MA.1 b)

There were examples where signal detection activities had not been performed on all available safety data:

i. Invalid cases, i.e. those cases with a drug and event pair but missing reporter and/or patient identifiers, were recorded in a 'Master Intake Tracker'; however this was not reviewed at the time of preparing a signal detection report. Therefore, these cases were not considered as part of on-going safety evaluation activities.

   GVP Module VI.B.2 states "*Reports, for which the minimum information is incomplete, should nevertheless be recorded within the pharmacovigilance system for use in on-going safety evaluation activities.*"

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ii. The [redacted] signal report (dated 11-Feb-2015) stated that no cases had been reported. However, there were five cases in the Argus safety database where [redacted] was the co-suspect medication, which were received prior to the date that Strides obtained licensing approval for [redacted] on 05-Aug-2014. It is acknowledged that these reports relate to a non-company suspect drug; however the reports still represent relevant safety information for consideration as part of signal detection activities.

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]	

MA.2 Pharmacovigilance System Master File

Requirements:

Directive 2001/83/EC as amended, Article 104 (3(b)).

The Human Medicines Regulations 2012 (Statutory Instrument 2012 No. 1916), Part 11 Pharmacovigilance, Regulation 182.

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

GVP Module II – Pharmacovigilance system master file.

II.B.4.6 "*The pharmacovigilance system master file should include a description of the monitoring methods applied and contain as a minimum:*

- *A description of any metrics used to monitor the quality of submissions and performance of pharmacovigilance.*"

II.B.4.6 "*Targets for the performance of the pharmacovigilance system shall be described and explained.*"

II.B.4.8 "*An annex to the pharmacovigilance system master file shall contain the following documents:*

- *A list of medicinal products covered by the pharmacovigilance system master file including the name of the medicinal product, the name of the active substance(s), and the Member State(s) in which the authorisation is valid [IR Art 3];*

The list of medicinal products authorised in the EU should also include the authorisation number(s) including, per authorisation:

- *the presence on the market in the EU;*"

II.B.5 "*Changes to the pharmacovigilance system master file should be recorded, such that a history of changes is available (specifying the date and the nature of the change), changes to the PSMF must be recorded in the logbook described in Article 5(4) of the Commission Implementing Regulation No 520/2012.*"

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

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A major finding was reported at the previous inspection in relation to significant deficiencies with the information presented in the PSMF [redacted]. Improvements to the PSMF and associated SOP have been demonstrated since the previous inspection; however, deficiencies with the PSMF content still remain and constitute a breach of GVP. Therefore, a repeat major finding is reported in this area.

Finding MA.2 a)

i. There were deficiencies with regards to PSMF Annex 1 (List of medicinal products authorised in the EU):

   - Annex 1 (dated 23 November 2015) did not include the licence for

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[redacted]

- Annex 1 did not indicate the presence of products on the market in the EU.

ii. There were deficiencies with regards to the information on pharmacovigilance system performance in the PSMF:

a) Section 6.2 of the PSMF (Quality of submissions) did not describe the quality review activity conducted monthly by Strides, whereby a sample of ICSRs processed by VigiMedsafe underwent an independent check. Results of this quality review activity were presented in Annex 13.5.

b) There were no documented targets for the key performance indicators in PSMF Annex 13.1 to 13.5.

iii. The format of the logbook in the PSMF Annex 15 was deficient as it did not include the nature of the changes. It is acknowledged that a more detailed logbook was maintained separately; however this should be available in the PSMF Annex.

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.2 b)
SOP [redacted] (Preparation and Maintenance of the PSMF, [redacted] did not include a documented process for the inclusion of notes associated with any audit where significant pharmacovigilance findings are raised, and for documenting deviations from pharmacovigilance procedures, in the PSMF. It was described that the PSMF author received automated notifications from the TrackWise database regarding pharmacovigilance audit findings and deviations. However, this was not described in the SOP.

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Root Cause Analysis	
[redacted]	
Further Assessment	
[redacted]	
Corrective Action(s)	
[redacted]	
Deliverable(s)	**Due Date(s)**
[redacted]	
Preventative Action(s)	
[redacted]	
Deliverable(s)	**Due Date(s)**
[redacted]	

C.4.3 Minor findings

MI.1 Signal Management

The following minor findings were identified in relation to signal management:

Finding MI.1 a)

There were examples of signal detection reports prepared in 2015 that were not inclusive of cumulative adverse event data.

It is acknowledged that, following the critical finding raised at the previous MHRA inspection, signal detection on cumulative data was performed for all active substances authorised in the UK (performed between December 2014 and May 2015). However, signal detection activities performed subsequently had been limited to an analysis of interval data only, which was not reviewed in the context of cumulative adverse event data. For example:

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i. The first signal detection report for [redacted] was dated 28-Jan-2015 and covered all cumulative data up until the data lock point of 31-Dec-2014. A subsequent report dated 30-Oct-2015 covered the period 01-Jan-2015 to 30-Sep-2015 and contained an analysis of interval data only. (It was noted that the table contained in the Appendix that outlined the specific sources of data that had been reviewed, incorrectly indicated that a cumulative summary tabulation had been included in the signal report.)

ii. The first signal detection report for [redacted] was dated 18-Dec-2014 and covered all cumulative data up until the data lock point of 30-Nov-2014. A subsequent report dated 13-Apr-2015 covered the period 01-Dec-2014 to 15-Mar-2015 and contained an analysis of interval data only.

SOP [redacted] (Signal Detection and Benefit-Risk Assessments, [redacted] section 6.5.1.1 stated *"The periodic line listings will be compared with cumulative tabulations to assess changes in frequencies of events from the period compared to the cumulative period."* SOP [redacted] did not indicate that reviews of interval data only would be performed at specified timeframes in between cumulative data reviews. Therefore, there was no assurance that, going forward, signal reports would include cumulative adverse event data in the detection of a new potentially causal association or a new aspect of a known association.

This has been graded as a minor finding because cumulative safety reviews had been undertaken for all products in the past 12 months.

Root Cause Analysis

[redacted]

Further Assessment

[redacted]

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

Finding MI.1 b)

SOP [redacted] (Safety Review Meetings, [redacted] stated that Safety Review Meetings (SRM) should be conducted for all Strides products to discuss the conclusions from the signal reports prepared by VigiMedsafe and to agree any further actions that may be required. Attendees at the SRMs included the QPPV, Safety Physician and representatives from Strides Global Pharmacovigilance and Quality Assurance groups.

Signal reports were prepared by VigiMedsafe for the products scheduled for safety review in June 2015 [redacted] however these were not reviewed in a SRM. This resulted because the Quarter 2 SRM covered products that had signal reports prepared in March, April and May 2015 and the Quarter 3 SRM covered products that had signal reports prepared in July, August and September 2015.

It is acknowledged that in the signal reports prepared for these five products, no new signals were identified and no recommendations were made to update product labelling.

Root Cause Analysis	
[redacted]	
Further Assessment	
[redacted]	
Corrective Action(s)	
[redacted]	
Deliverable(s)	**Due Date(s)**
[redacted]	

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

Finding MI.1 c)
[redacted] was omitted from the 2015 safety review schedule in error. However, it is acknowledged that a signal report dated 21-Apr-2015 had been prepared for [redacted] and the product was on the 2016 safety review schedule.
Root Cause Analysis
[redacted]
Further Assessment
[redacted]
Corrective Action(s)
[redacted]

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

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

MI.2 Management of Adverse Drug Reactions

The following finding was noted in relation to the data migration from Oracle AERS to Argus that was performed in April 2015:

Finding MI.2 a)
i. The Data Migration Qualification Plan, dated 03-Mar-2015, stated that the outputs from the migration qualification should include a Migration Qualification Summary Report to summarise the outcome of the migration activity. However, this report was not produced until 02-Dec-2015, following a specific request by the MHRA Inspector. ii. It was also noted that, whilst User Acceptance Test scripts had been run, verified and approved by 24-Apr-2015 in order to verify the accuracy of the migrated data, there was no formal documentation to verify that all cases had in fact been successfully migrated from AERS to Argus. It is acknowledged that no discrepancies between the cumulative case data in the AERS and Argus line listings were identified by the Inspector.
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]	

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MI.3 Auditing of the Pharmacovigilance System

The following finding was noted in relation to quality assurance auditing of the pharmacovigilance system:

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Finding MI.3 a)
There was no documented audit strategy for conducting pharmacovigilance audits of third-parties. The audit schedule in the PSMF indicated that internal pharmacovigilance processes would be audited twice yearly, which was in accordance with SOP [redacted] (Conducting Internal Audit, [redacted]. However, there was no documented audit strategy (or risk assessment) for pharmacovigilance service providers or licensing partners, and these types of third-parties were not described in SOP [redacted] (Vendor Audit, [redacted]. It is acknowledged that audits of key service providers, such as Sciformix and VigiMedsafe, had been conducted in 2012 and 2014 respectively, and other service providers were included on the audit schedule in the PSMF. However, there was no documented frequency for audits of service providers or of commercial partners for EU authorised products listed in the PSMF at the time of the inspection; namely [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]	

C.4.4 Comments

Not applicable.

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.

The MAH is encouraged to share this inspection report with relevant service providers to whom it has sub-contracted pharmacovigilance activities. Service providers are reminded that deficiencies that are more broadly applicable to MAHs not subject to this inspection may need to be shared with those affected, such that appropriate CAPA can be derived. The service provider and MAH(s) affected should be able to demonstrate effective assessment and resolution of deficiencies that have been reported during any inspection.

APPENDIX I REFERENCE TEXTS

- Directive 2001/83/EC, as amended.
- Commission Implementing Regulation (EU) No 520/2012.
- Guideline on good pharmacovigilance practices (GVP) Modules.
- 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".
- CPMP/ICH/287/95: E2B (M) "Note for Guidance on Clinical Safety Data Management: Data Elements for Transmission of Individual Case Safety Reports" and ICH E2B(R2) "Maintenance of the Clinical Safety Data Management: Data Elements For Transmission Of Individual Case Safety Reports".
- EMA/CHMP/ICH/544553/1998: E2C (R2) "Periodic benefit-risk evaluation report (PBRER)".
- CPMP/ICH/3945/03: E2D "Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting".
- CPMP/ICH/5716/03: E2E "Pharmacovigilance Planning".
- CHMP/313666/05: "Guideline on the exposure to medicinal products during pregnancy: need for post-authorisation data".

APPENDIX II PHARMACOVIGILANCE INSPECTION PLAN

MHRA INSPECTION NUMBER	GPvP 13606/4119-0017	**DAY**	1
PHARMACOVIGILANCE INSPECTION OF	Strides Arcolab Ltd	**DATE**	14 December 2015
LOCATION	PharSafer House White Hart Meadow Ripley, Surrey, GU23 6ND	**START TIME**	09:30

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 and pharmacovigilance system, highlighting significant changes since the 2014 inspection.	[redacted]	All welcome
Document Review	-	Inspectors only
LUNCH	-	-

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Signal management • Signal detection, prioritisation and evaluation • Escalation of safety issues, governance and decision making	[redacted]	Interviewee(s): [redacted] (Available via telecom)
Computerised systems • Safety data migration from Oracle AERs to Argus	[redacted]	Interviewee(s): [redacted] (Available via telecom)

N.B.
Relevant SOPs, working practices, training records, CVs and job descriptions should be made available to the inspection team.
Other documents will be requested during the inspection.
The Inspection Plan may need to be amended during the inspection.

[redacted]

MHRA INSPECTION NUMBER	GPvP 13606/4119-0017	**DAY**	2
PHARMACOVIGILANCE INSPECTION OF	Strides Arcolab Ltd	**DATE**	15 December 2015
LOCATION	PharSafer House White Hart Meadow Ripley, Surrey, GU23 6ND	**START TIME**	09:00

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Purpose of Interview	**Session Lead**	**Staff to be interviewed**
Quality management system • Pharmacovigilance system performance and compliance • Management of the PSMF	[redacted]	[redacted]
Document Review	-	Inspectors only
LUNCH	-	-
Document Review	-	Inspectors only
Closing Meeting	[redacted]	All welcome