Medicines & Healthcare products Regulatory Agency

MHRA

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RESTRICTED – COMMERCIAL
[redacted]
STRIDES PHARMA UK LIMITED
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THE METRO CENTRE
DWIGHT ROAD
WATFORD
WD18 9SS
UNITED KINGDOM

Date 08/12/2022

Case No: Insp GMP/GDP 13606/4119-0023

SUBJECT: THE HUMAN MEDICINES REGULATIONS 2012 (as amended) (SI 2012/1916)

AUTHORISATION / REGISTRATION NO. MIA 13606, WDA(H) 13606

Dear [redacted]

Thank you for the courtesy and co-operation shown during the inspection of your premises at the above address on 06/12/2022.

During the inspection a number of failures to comply with the principles and guidelines of Good Manufacturing Practice and / or Good Distribution Practice were observed and these are listed in the Appendix to this letter.

Please reply within 28 days, giving your proposals for dealing with these matters, together with a timetable for their implementation. Please send your response electronically by e-mail to me at the email address below.

It would be appreciated if your response was in the following format:

1. Restate the deficiency number and the deficiency as written below.
2. State the proposed corrective action and the target date for completion of these action(s)
3. Include any comment that the company considers appropriate.
4. Please provide the response as a word document.

Further guidance on responding to inspection deficiencies can be found at the following web link https://www.gov.uk/guidance/guidance-on-responding-to-a-gmpgdp-post-inspection-letter

Yours sincerely

[redacted]
GMP/GDP Inspector

E-mail [redacted]

FAILURES TO COMPLY WITH THE GUIDE TO GOOD MANUFACTURING / DISTRIBUTION PRACTICE

1. CRITICAL

None

2. MAJOR

2.1 The deviation process was deficient, as evidenced by;

2.1.1 The appropriate level of root cause analysis was not applied during the investigation of deviations. This was evident in both [redacted] and [redacted] for example;

2.1.1.1 The investigation of root cause had not been documented or categorised using documented tools within the deviation such as 5 whys or a fishbone diagram, as required by the procedure.

2.1.1.2 Probable root causes were identified before the formal investigation had started, and not all causal factors were identified.

2.1.1.3 A root cause of human error had not been justified or documented in the deviations to ensure that process, procedural or system-based errors had not been overlooked.

2.1.1.4 Appropriate corrective actions or preventative actions (CAPAs) were not identified and taken, as not all root causes had been identified. Both deviations identified issues where change control had not been raised appropriately but the investigations did not identify why this had occurred on more than one occasion or the underlying reasons why change control had not been raised other than human error.

2.1.1.5 The effectiveness of actions (CAPA) identified in the deviations was not documented, monitored or assessed.

2.1.1.6 Evidence of completion of actions had not been documented, for example there was no evidence that release and distribution of [redacted] batch [redacted] had been suspended as required by [redacted] There was no evidence or documented consideration when it was acceptable to recommence batch certification and release.

2.1.2 Quality risk management principles were not used during the investigation of deviations, for example;

2.1.2.1 The potential impact of the deviations had not been assessed or documented.

2.1.2.2 There was no reference to validation documentation to support the justification of accepting batches manufactured at an unregistered blending speed [redacted]

2.1.2.3 The justification to use an unregistered contract laboratory in [redacted] did not assess whether a contract laboratory had been appropriately approved within the Pharmaceutical Quality System (PQS).

2.1.3 [redacted] relating to [redacted] being released not in accordance with the MA was deficient in that;

2.1.3.1	There was no consideration to notify MHRA (DMRC) where there was a potential for the quality defect to result in recall of the product.
2.1.4	Deviation forms did not contain sufficient space for entries, as such deviation investigations were recorded on uncontrolled Word documents.
EU GMP	C1.4(xiv), C1.8(vii), C4.1, C4.6, C8.15

3. OTHER

3.1	The management of outsourced activities / supplier approval was deficient as evidenced by;
3.1.1	Audit durations were not always of an appropriate duration and scope to ensure that a full and clear assessment of GMP was made, as evidenced by a one-day virtual audit of API manufacturer [redacted]
3.1.2	The audit report of the contract manufacturing organisation (CMO) [redacted] did not include [redacted] Capsule products within the scope.
3.1.3	There was no notarised translation of the auditor's CV [redacted] who conducted the audit of [redacted] in 2021. The auditor did not appear to have sufficient GMP manufacturing experience.
EU GMP	C2.23, C5.29, A16.1.7.3 A21.5.4
3.2	Completed Product Quality Reviews (PQR) were deficient, as evidenced by:
3.2.1	The content of [redacted] 2021 PQR was not always accurate, as evidenced by:
3.2.1.1	The SPUK PQR stability summary stated that the results were satisfactory, however, a number of failures were identified and the PQR did not explain or justify the issues encountered. The issues identified did not appear to reflect the content of the CMO PQR.
3.2.1.2	The SPUK PQR stated that there were no OOT or OOS, despite there being one OOT being raised [redacted]
3.2.1.3	Section 14.2 contained contradictory information on whether any complaints had been received.
3.2.2	Despite the deliverable volume importation test results, for batch [redacted] being significantly different from the CMO results (120mL versus 125.8mL against a specification of NLT 120mL), there was no recognition of the difference in the PQR, and no OOT had been raised.
3.2.3	The [redacted] 2021 PQR conclusion could not be supported by the data presented e.g. that there were no Out of Trends, or Out of Specifications observed.
3.2.4	Insufficient information was provided to confirm the supply chain traceability of APIs.

EU GMP	C1.10(i-xii), C4.2
3.3	The OOS/OOT procedure and process was deficient, as evidenced by:
3.3.1	The definition of OOT in the SOP was not sufficiently clear to ensure a consistent determination of what was an OOT.
3.3.2	OOTs that would be required to be raised by SPUK were not proceduralised, for example if results between the manufacturing site and the importation lab were significantly different.
3.3.3	There was no explanation of how to handle OOS/OOTs for microbiological tests.
3.3.4	The procedure did not define the number of retests required by SPUK to invalidate an initial test result, where no root cause could be identified.
3.3.5	The procedure did not define that all retest results were required to pass the specification to invalidate the initial result.
EU GMP	C4.3, C6.7(iv), C6.16, C6.35
3.4	The procedure for Handling Export of Medicinal Products was deficient for example;
3.4.1	There was no explicit instruction in the Export procedure to ensure that all exported products were delivered to customer qualified addresses.
3.4.2	The requirement for checks of the applicable legal and administrative provisions of the country concerned was limited to Scheduled Controlled Drugs only.
3.4.3	The export checklist did not confirm checks to ensure that countries receiving products were entitled to receive them in accordance with the applicable legal and administrative provisions of the country concerned.
EU GMP EU GDP	C4.3 5.9
3.5	The training process was deficient as evidenced by:
3.5.1	The training provided to the [redacted] at site was insufficient to ensure a full understanding of the system.
3.5.2	The questions used to evaluate the effectiveness of the annual GMP training were inadequate to confirm comprehension.
EU GMP	C2.3, C2.11
3.6	The Change Control process and procedure was deficient, as evidenced by there being no change control raised for the introduction of the proposed electronic Batch Release Management

(BRM) system, despite a draft URS already having been generated.

EU GMP C1.4(xii)

4. COMMENT

4.1 SPUK confirmed that they would provide the MHRA with the updated communication with a customer regarding the most recent bona fide checks.