Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

INSPECTION REPORT

Aeropak (Chemical Products Limited)
Viking Road,
Gapton Hall Industrial Estate,
Great Yarmouth,
NR31 0NU
United Kingdom

Head Office:
Inspection, Enforcement & Standards Division, MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

Telephone: 020 3080 6000
Email: info@mhra.gov.uk

Section A Inspection Report Summary

Inspection requested by: MHRA

Scope of Inspection: Routine Re-Inspection

Licence or Reference Number: MIA 5170

Licence Holder/Applicant: Aeropak (Chemical Products) Limited

Details of Product(s)/ Clinical trials/Studies: Various Topical preparations.

Activities carried out by company:	Y/N
Manufacture of Active Ingredients	N
Manufacture of Finished Medicinal Products – Non sterile	Y
Manufacture of Finished Medicinal Products - Sterile	N
Manufacture of Finished Medicinal Products - Biologicals	Y
Manufacture of Intermediate or Bulk	N
Packaging – Primary	Y
Packaging - Secondary	Y
Importing	N
Laboratory Testing	Y
Batch Certification and Batch Release	Y
Sterilisation of excipient, active substance or medicinal product	N
Broker	N
Other:	N

Name and Address of site(s) inspected (if different to cover):

Site Contact: [redacted]

Date(s) of Inspection: 28-30 November 2023

Lead Inspector: [redacted]

Accompanying Inspector(s): N/A

Case Folder References: GMP 5170/16108-0016

The Quality Technical agreement with [redacted] and [redacted] dated 2 May 2023 was seen with no comments.

C14 Questions raised by the Assessors in relation to the assessment of a marketing authorisation

None

C15 Annexes attached

Annex 1 site risk rating

Section D List of Deficiencies

D1 Critical

D2 Major

2. MAJOR

2.1 Incident Management was deficient in that:
2.1.1 There was no documented assessment of the risk to product on the market following stability [redacted]
2.1.2 Complaint Management was deficient in that:
2.1.2.1 Complaint investigation did not always fully identify the risk to patient, document relevant CAPA and did not consider all investigation factors for example whether review of retained samples was required as exampled by complaint [redacted]
2.1.2.2 Entries on the complaint log were not attributable to the person making the entry.
2.1.2.3 There was no formal mechanism for Aeropak to communicate investigation findings to complaint management group.
2.1.3 The Batch Disposition decision had been made for Deviation [redacted] ahead of sign off and approval of all sections of the associated OOS [redacted]
2.1.4 There was no assessment of instances of previous occurrences of the same issue as required by deviation SOP [redacted] as evidenced by Deviation [redacted]
2.1.5 The rationale to discard one of the precision results in [redacted] was not adequately documented.

EU GMP C1.8(v), C6.17(iv), C6.35, C8.5, C8.9(ii), C8.9(vii), C8.9(ix), A16.1.7.1, A16.1.7.16

D3 Others

3.1 Controls to minimize the spread of cross contamination were deficient in that:
3.1.1 The extract equipment located in the Raw Materials sampling area was seen to be visibly contaminated with white powder.
3.1.2 The outer drum of production return [redacted] batch [redacted] was seen to be visibly contaminated with white residue and there was no instruction to ensure outer drums were cleaned prior to return to the warehouse.
3.1.3 [redacted] did not specify the frequency of garment change for manufacture and fill/pack areas.
3.1.4 It was not clear how it was established that the required double clean of manufacturing equipment following [redacted] had been completed.
3.1.5 Logbooks recording cleaning were not always correctly completed as exampled by logbook [redacted] where cleaning codes had not been completed and page 13 had not been reviewed.

3.1.6 The validation study for [redacted] had not assessed the recovery for all product contact materials.
3.1.7 There was no requirement for ongoing cleaning verification for the [redacted] product despite the cleaning process not being fully automated.

EU GMP C1.8(iv), C2.15, C2.18, C3.14, C4.8, C5.21 Organisational Measures, A15.10.12, A15.10.15

3.2 Outsourced activities were deficient in that:
3.2.1 The Quality Technical Agreement between [redacted] and Aeropak did not fully describe responsibilities and scope of required services as :
3.2.1.1 It did not describe QC activities undertaken by [redacted] such as routine checks of [redacted] for orphan data.
3.2.1.2 It did not state responsibilities for Supplier qualification.
3.2.1.3 It referenced [redacted] who were no longer used by the company.
3.2.1.4 It did not describe responsibility for pharmocovigilance activities.
3.2.1.5 It did not adequately describe responsibilities for stability management.
3.2.2 There was no Quality Technical Agreement which described responsibilities between [redacted] site and Aeropak.
3.2.3 The Quality Technical Agreement with the contract QP was not clear as to how the company would ensure the QP remained up to date with issues which may negate batch certification as the QP was contracted for one day a month.
3.2.4 The Quality Technical Agreement with the contract microbiological laboratory [redacted] and [redacted] did not specify services provided or products tested.

EU GMP Chapter 7 Principle, C7.4, C7.6, C7.15

3.3 QC operation were deficient in that:
3.3.1 The reason why samples were manually integrated was not sufficiently explained to ensure a clear audit trail as exampled by Sample [redacted] and furthermore Work Instruction [redacted] elating to Integration and Reporting of a Chromatographic Run did not require that the reason for integration was specified.
3.3.2 The freezer section of the QC fridge was not temperature mapped despite being in use.
3.3.3 The sampling regime for Purified Water set out in QC [redacted] did not provide adequate assurance that incidents or trends could be detected and investigated in a timely manner as consecutive alerts would take 24 weeks to action for some sampling locations.
3.3.4 It was not clear how environmental monitoring trend notifications which were required by the local SOP would be detected from the collated data.
3.3.5 The C of A result for pH for [redacted] batch [redacted] did not match the [redacted] value.

EU GMP C1.4(viii), C3.41, C4.2, A11.9, A15.3.1

3.4 Production operations were deficient in that:
3.4.1 Room [redacted] contained equipment which was not required for processing operations and furthermore equipment such as the [redacted] equipment table was rusted and in poor condition.
3.4.2 It was not clear how deliveries of incoming goods were protected from inclement weather conditions.
3.4.3 The reconciliation limit of applied to [redacted] was not appropriate to determine if there were issues during the serialization printing process.

EU GMP Chapter 3 Principle, C3.2, C3.20, C5.61

3.5 Status labelling and traceability was incomplete as:
3.5.1 The QC sampling area did not reflect the presence of [redacted] label batch [redacted] in the area.
3.5.2 There was no requirement to record the batch numbers of the bags used to hold product in the pallecons.

EU GMP C4.17(c), C5.12

D4 Comments

4.1 Licence update required for removal of tablets, herbals , removal of microbiology QC , removal of [redacted] as a contract laboratory and update to include primary packaging.

Section E Site Oversight Mechanism

Site referred or to be monitored by:	Tick (✓)	Referral date	Summary of basis for action
Risk Based Inspection Programme	✓	[redacted]	[redacted]
Compliance Management Team			
Inspection Action Group			

Section F Summary and Evaluation

F1 Closing Meeting

Deficiencies were verbally accepted.

F2 Assessment of response(s) to inspection report

The response to the post inspection letter was received 4 January 2024 and a request for further information sent on 8 January 2024, an acceptable response was sent on 9 January 2024.

F3 Documents or Samples taken

None

F4 Final Conclusion/Recommendation, Comments and Evaluation of Compliance with GMP and GDP

The site operates in general compliance with the requirements of:

Compliance statement	Tick all statements that apply
GMP as required by the Human Medicines Regulations 2012 (as amended) and the Human Medicines (Amendment) Regulations 2019	✓