Medicines & Healthcare products Regulatory Agency

MHRA

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RESTRICTED – COMMERCIAL
[redacted]
GLAXO OPERATIONS UK LIMITED
HARMIRE ROAD
BARNARD CASTLE
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UNITED KINGDOM

Date 13/02/2023

Case No: Insp GMP/IMP 4/3848-0042

SUBJECT: THE HUMAN MEDICINES REGULATIONS 2012 (as amended) (SI 2012/1916)
THE MEDICINES FOR HUMAN USE (CLINICAL TRIALS) REGULATIONS 2004 (SI 2004/1031)

AUTHORISATION / REGISTRATION NO. MIA 4, MIA(IMP) 4

Dear [redacted]

Thank you for the courtesy and co-operation shown during the inspection of your premises at the above address on 06/02/2023.

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/IMP Inspector

E-mail: [redacted]

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

1. CRITICAL

None

2. MAJOR

None

3. OTHER

3.1	Precautions to minimize the risk of contamination at all processing stages were deficient as evidenced by:
3.1.1	Non-production staff could wear outdoor shoes in the grade C rooms in some areas, e.g. C Block.
3.1.2	[redacted] labelling on equipment inside the [redacted] filling line appeared worn. It was discussed that the site may consider reviewing these types of labels in case they pose a potential source of contamination to the process, for example as a potential source of particles.
3.1.3	A 600 mL beaker in the [redacted] dispensary that was described as clean had visible tape residue on it.
3.1.4	A shelf in [redacted] dispensary for equipment dedicated to [redacted] included a container that was described as not used for this product. In addition, it was observed that the storage cupboard in this area appeared full.
3.1.5	An external gasket on a rapid transfer port (RTP) in the Grade C area of the [redacted] had evidence of wear with cracks that were not easily cleanable.
3.1.6	A blue pipe support in the [redacted] CIP/SIP station appeared damaged that could potentially be a source of contamination to the area.
3.1.7	The airflow visualization for [redacted] did not adequately demonstrate that at the point that the [redacted] equipment autoclave door was opened that there were appropriate airflow patterns, for example to assure that airflows did not distribute particles from a particle-generating person, operation or machine, such as from the Grade B environment to the area where sterile equipment was handled during unloading of the autoclave. Note: This is an example, and the company should consider if this observation may apply to other activities.
EU GMP	C5.10, A1.44, A1.47, A1.54, A1.64
3.2	Some documents were ambiguous in how processes or systems were used as evidenced by:

3.2.1 The procedure for critical alarms generated by the [redacted] building management system [redacted] was ambiguous on timescales for investigations in that it was unclear what "completed in 5 days" meant and if there was an extension process (there were a number of investigations that exceeded 5 days). In addition, it was also ambiguous how these investigations were trended to consider if events were repetitive.

3.2.2 For technical studies used to support processes, e.g. [redacted] it was unclear how test methods were assessed to determine that they were appropriate for their intended use, for example, but not limited to considering if the method had appropriate sensitivity for the intent of the study.

3.2.3 The manual inspection procedure [redacted] for [redacted] vials pre-irradiation did not describe what would be done if an increasing trend of rejects was observed, for example to maintain traceability of which vials had been rejected from which tray from the filling machine that could potentially support an investigation.

3.2.4 It was ambiguous in the [redacted] who was responsible for understanding the timelines for a recall and that this information was clearly shared in a recall scenario. It is acknowledged that the site described that the recall requirements for different markets could vary.

3.2.5 SOP-[redacted] did not consider irradiation.

3.2.6 It was ambiguous what action or investigation was expected if a "target" date for annual water reviews was not completed on time.

3.2.7 There was inadequate risk assessment to consider data integrity controls where the site was relying solely on a printed test result in the batch record and had not considered if there were potential relevant electronic records from the equipment, e.g. for filter integrity testing.

EU GMP C1.9(iii), C4.1, C4.3, A11.1, A15.5.9

3.3 Complaint investigations were deficient as evidenced by:

3.3.1 Complaint investigation [redacted] did not follow the complaint procedure in that it was understood that an assessment to notify/escalate would be done in 1 day, however this had not been documented until over 3 months later.

3.3.2 It was ambiguous when it was appropriate to refer to a previous complaint investigation or what would trigger a review when new data was received as evidenced by complaint [redacted] from Dec 2022 relating to auto injector misfire that referred to an evaluation performed the previous May but had not considered if the increase in complaints received since then affected the validity of the evaluation in the investigation.

EU GMP C1.8(v), C8.16, C8.19

4. COMMENT

4.1 It was discussed that the scope of the inspection included the new Q Block.

4.2 The site will continue to be inspected as part of a rolling inspection cycle.