Medicines & Healthcare products Regulatory Agency

MHRA

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United Kingdom

gov.uk/mhra

RESTRICTED – COMMERCIAL
[redacted]
GLAXOSMITHKLINE RESEARCH & DEVELOPMENT LIMITED
CGT QC CENTRAL TESTING LABORATORY (CGT QC CTL)
CELL AND GENE THERAPY (BUILDING 5)
GLAXOSMITHKLINE MEDICINES RESEARCH CENTRE
GUNNELS WOOD ROAD
STEVENAGE
SG1 2NY
UNITED KINGDOM

Date 07/06/2021

Case No: Insp GMP 5866/19598555-0001

SUBJECT: CONTRACT TESTING LABORATORY:
THE HUMAN MEDICINES REGULATIONS 2012 (as amended) (SI 2012/1916)
THE MEDICINES FOR HUMAN USE (CLINICAL TRIALS) REGULATIONS 2004 (SI 2004/1031)
THE VETERINARY MEDICINES REGULATIONS 2013 (SI 2013/2033)

Dear [redacted]

Thank you for the courtesy and co-operation shown during the inspection of your premises at the above address on 24/05/2021.

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. The response should be sent electronically 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

In view of the serious inspection findings, urgent improvement is required. MHRA may consider that a special inspection is necessary after a shorter interval than normal, to determine whether alterations or improvements have been satisfactorily carried out. Failure to demonstrate the required improvements during a subsequent inspection may result in consideration of regulatory action against the company.

Yours sincerely

[redacted]
GMP Inspector

E-mail: [redacted]

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

1. CRITICAL

None

2. MAJOR

2.1 Data Integrity and Management was deficient in that:

2.1.1 Overall, the management of data and documentation; and connections between different policies and procedures was not clearly defined; across global, R&D and CGT QC records; with a lack of local controls in place.

2.1.2 The [redacted] was a high-level SOP that described requirements; but did not detail actual processes undertaken. This included Backup and Restore Testing expectations; however, this was only required as annual restore testing regulated [redacted] servers rather than GxP data. There was no evidence that this was completed at a level to confirm any accuracy of site data retention.

2.1.3 The Archiving SOPs [redacted] and [redacted] did not describe management of records from a local perspective. It was not clear what the retention timelines for CGT data were.

2.1.4 [redacted] using form [redacted] for the ddPCR and [redacted] only addressed a review of the audit trail information on [redacted] and did not include any reference or referral back to the original source data on the individual instruments. There was no evidence that CAPAs had been raised to resolve the issues identified from the review, such as inconsistent use of [redacted] forms and user names; lack of deactivation for leavers and lack of controls over validated spreadsheets for management of passwords.

2.1.5 There was no risk assessment or justification in place for not updating the older system software for the application software [redacted]

2.1.6 The global QTA with [redacted] did not include any focus on DI, and only required records to be retained for 3 years; after which physical documentation were returned to GSK or formal approval for destruction was required. There was no consideration for raw or original electronic data and no formal process in place to manage bringing materials back from third parties.

2.1.7 The site could not provide evidence of the back-up process for the [redacted] system and all stored QC data, nor any restore challenge process.

2.1.8 Risk assessment [redacted] assessing the impact of the ability to delete data through windows explorer, did not include an assessment

of current control measures to ensure the integrity of data while longer term controls were implemented.

2.1.9 QC PC equipment included both [redacted] and [redacted] software packages, which would not prevent potential adaption of reports.

EU GMP Chapter 4 Principle, C1.3, C4.1, C4.10, C4.11, C4.12, C6.8, A11.1, A11.5, A11.7.1, A11.7.2, A11.11, A11.12.3, A11.17

3. OTHER

3.1 Change Control (CC) processes were deficient in that:

3.1.1 CC Details were routinely contained within attached [redacted] presentations that were not controlled, with no author or dating detail, nor with any revision history. Actions listed in the presentation were not cross-referenced to any action numbers within the quality system.

3.1.2 CC [redacted] related to an upgrade in firmware to version [redacted] for [redacted] series dataloggers was lacking in that:

3.1.2.1 Updates to the recorded [redacted] were not dated to show when additional or updated entries were made to allow contemporaneous recording evidence.

3.1.2.2 Multiple actions such as [redacted] and [redacted] were not completed by the 2019 due dates.

3.1.3 No Change Control or Risk Assessment was raised related to the site transition or application for EU GMP certification for QC testing.

3.1.4 No Change Control or Risk Assessment was raised related to ensuring that the site formally managed a transition from [redacted] to [redacted] across the site for all GxP systems as required, where [redacted] is no longer supported

EU GMP C1.4(xii), C1.12, C4.8, C4.9, A11.1

3.2 Quality Control processes and equipment were deficient in that:

3.2.1 The approved methods for [redacted] did not indicate the correct filename for the sample acquisition template file.

3.2.2 Fortnightly fluidic flushing was not consistently completed according to the fortnightly cycle procedurally required; as evidenced by the log records for [redacted]

3.2.3 The [redacted] system 6 Monthly and 12 Monthly servicing did not address laser intensity and there were no maximum life / operating hours for the laser; only a usage (by hours) number was recorded.

3.2.4 The Testing proforma [redacted] was not designed to allow appropriate or sufficient space for entries, such as hand-written information for reagent batch numbers and total cell numbers; nor attaching control labels.

EU GMP	C3.41, C4.6, C6.5, C6.7(ii)
3.3	Validation processes were deficient in that:
3.3.1	The ddPCR validation report [redacted] stated that the version of [redacted] software validated was [redacted] but the version installed in the laboratory was version [redacted]
3.3.2	Validation of ddPCR instrument [redacted] contained two exception conditions, which were typed documents. Consequently, it was not possible to determine who had recorded the exception.
3.3.3	Validation records for the [redacted] system equipment [redacted] did not include any applicable evidence to confirm that the second [redacted] process was carried out to assess the update to the [redacted]
EU GMP	Chapter 4 Principle, C4.8, A11.4.2, A11.4.3, A15.2.1
3.4	Facilities management was deficient in that:
3.4.1	There were no facility procedures to periodically test the dial out function of the [redacted] Environmental System.
3.4.2	The location of the storage stability cabinets was in the basement and there had been no risk assessment against water ingress from pipes within the building or from nearby ponds.
EU GMP	Chapter 3 Principle, C3.19, C3.41

4. COMMENT

4.1	Please provide the following information for assessment by the inspectors; prior to issuance of GMP cert.
4.1.1	Evidence of the active back up process or mirror server system etc of the [redacted] and QC data
4.1.2	Access roles and permissions for [redacted] and [redacted] for PCR testing (Note: both requested during inspection but not provided)
4.1.3	An electronic copy of the method validation report for the PCR test (Note: provided during inspection but review not completed)
4.2	Please ensure that the responses focus on site / CGT QC actions, reducing reliance on global or R&D policies. I.e. provide clear information on control of local data, systems and processes to the inspectors; to give confidence on the implementation and management of site controls.