Medicines & Healthcare products Regulatory Agency

MHRA

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RESTRICTED – COMMERCIAL
[redacted]
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UNITED KINGDOM

Date 25/11/2022

Case No: Insp GMP/IMP 20075/16488800-0006

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 20075, MIA(IMP) 20075, API 20075

Dear [redacted]

Thank you for the courtesy and co-operation shown during the inspection of your premises at the above address on 22/11/2022.

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/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	Documentation and records were deficient, as evidenced by:
3.1.1	The level of detail captured in deviations and OOS reports was not always sufficient to fully describe the outcome of the investigation and/or the decisions taken. For example:
3.1.1.1	Deviation [redacted] failed to explain which potential failure modes had been considered and discounted, and did not clearly describe how the assigned root cause had been determined.
3.1.1.2	Deviation [redacted] (checkweigher not added to PM schedule) did not consider a review of other equipment to determine whether there were any other missing maintenance plans.
3.1.1.3	The CAPA associated with deviation [redacted] had been extended from Oct 2022 to Feb 2023, however no interim control measures had been considered.
3.1.1.4	[redacted] did not explain that the batch of [redacted] was part of a product transfer process, and therefore there was limited trend data available on site
3.1.1.5	[redacted] did not explain that the product was uncommercialised, and therefore the confirmed OOS result did not require notification to DMRC.
3.1.2	The raw data from the set-up of checkweighers was not retained or recorded.
EU GMP	C1.4(xiv), C1.8(vi), C1.8(vii), C1.9(iv), C4.8, C4.10
3.2	Control of starting materials was deficient, in that:
3.2.1	In regard to the sampling of incoming materials:
3.2.1.1	There was no documented justification for the practice of taking 20 samples of printed packaging components (e.g. cartons) which was not statistically based.
3.2.1.2	There was no formal consideration of the number of print stations for components as applicable (for example cartons), as two samples were reviewed in all cases.
3.2.1.3	There was no limit to the number of samples that could be blended to

	form a composite sample taking into account the nature of the material, knowledge of the supplier and the homogeneity of the composite sample.
3.2.2	There was no formal process to check for withdrawn GMP certificates or API WCs.
3.2.3	There was no TSE statement available for food-grade lubricants, such as [redacted] used on punches and dies.
EU GMP	C4.25, C5.27, A8.4, A8.5 Note for guidance on minimising the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products (EMA/410/01 rev.3)
3.3	Control of storage areas was deficient in that:
3.3.1	Regarding routine temperature mapping:
3.3.1.1	There was no routine mapping of storage areas formally within the Planned Maintenance Instruction system at the time of inspection (November 2022), despite the associated SOP being updated to include the frequencies in April 2022.
3.3.1.2	There was no documented risk assessment available to support the mapping frequencies defined in SOP [redacted]
3.3.1.3	The mapping procedure was silent with respect to the controlled drug store.
3.3.1.4	The most recent temperature mapping of the ambient warehouse, conducted in July 2022 remained open at the time of inspection, despite there being OOS results observed. [A deviation was raised for this during the inspection following the inspector's request to review the report].
3.3.2	The 'Materials Received' area at goods-in was not monitored for temperature despite materials being procedurally permitted to remain in this area for up to 24 hours.
EU GMP EU GDP	C1.8(ix), C3.3, C3.19 3.2.1
3.4	With respect to IMP activities:
3.4.1	The QP batch certificate template for IMPs was not in line with the requirements of the template associated with GMP Annex 13. For example:
3.4.1.1	The MIA(IMP) number was not included.
3.4.1.2	There was no regulatory statement referring to the relevant legislation under which the certification was made.
3.4.1.3	The certificate reviewed stated that the IMP was in compliance with the Marketing Authorisation
3.4.2	There was no procedure in place to support the process for preparation and issuance of a QP Declaration for import of IMPs, despite the site being authorised for this activity.
EU GMP	C1.8(iii), C4.1

	EU GMP Annex 13: Explanatory Note re Harmonised format of the Certification
3.5	Management of dissolution baths in the QC lab was deficient, in that:
3.5.1	The routine qualification and maintenance of dissolution baths did not include any periodic chemical testing, such as the pharmacopoeial [redacted] test. There was no justification to support the absence of this test.
3.5.2	The calibration records for bath [redacted] indicated a failed speed test at 100rpm, which required a replacement motor. The failure was not captured in the quality system, and there was no assessment of the potential impact on previous analyses.
EU GMP	C1.4(xiv), C1.8(vii), C3.41 BP Appendix XII B Annex, Ph Eur 5.17.1
3.6	The recall procedure [redacted] did not require the company to contact the MA holder, in cases where a potential recall situation arose on a product where Accord were not the MAH.
EU GMP	C8.15

4. COMMENT

4.1	It was discussed that as the site did not perform any complex, blinded / randomised packaging activities, a clarifying remark would be included on the associated GMP certificate.