



INSPECTION REPORT

VERTICAL PHARMA RESOURCES LIMITED

41 CENTRAL AVENUE

WEST MOLESEY

KT8 2QZ

UNITED KINGDOM

Head Office:

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Section A Inspection Report Summary

Inspection requested by: MHRA

Scope of Inspection: Routine Re-Inspection

Licence or Reference Number: MS 32879, MIA(IMP) 32879, WDA(H) 32879, API 32879

Licence Holder/Applicant: VERTICAL PHARMA RESOURCES LIMITED

Details of Product(s)/ Clinical trials/Studies:

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

* API – see section C1 of this report regarding potential future changes

Name and Address of site(s) inspected (if different to cover):
VERTICAL PHARMA RESOURCES LIMITED

41 CENTRAL AVENUE
WEST MOLESEY
KT8 2QZ
UNITED KINGDOM

Site Contact:

Date(s) of Inspection:

28 - 30 June 2022 (3 days GMP inspection)
Note: Fee for GDP aspect of this inspection was not included in this casefolder. Future inspections may need to consider if longer duration on site is required to include this.

Lead Inspector:

Accompanying Inspector(s):

Case Folder References:

(GDP - for first day of inspection)

Insp GMP/GDP/IMP 32879/93706-0022

Section B General Introduction

B1 Background information

Vertical Pharma Resources Ltd [REDACTED] is located on Central Avenue, West Molesey, Surrey in an area of businesses and light industry, for example several automotive services are located near to the site.

The site has a diverse range of operations and licensed functions with activities predominantly being importing and manufacture (compounding and packing) for supply of non-sterile unlicensed medicines with a large range of individual products manufactured to meet individual patient needs. Importation also includes a wide range of imported unlicensed products.

It was understood that the importation of herbal unlicensed products had significantly increased, and this may be of interest to review in greater depth at a future inspection.

This inspection included a variation to add QP oversight for IMPs. The site also performed infrequent small volume IMP packing activities that could include blinding and randomization.

The site had previously been inspected more frequently due to a referral to IAG (Inspection Action Group) in 2016 and subsequent transfer to CMT (Compliance Management Team). The previous inspection in April 2019 returned the site to the risk-based inspection programme and this inspection (June 2022) was performed as part of a routine re-inspection.

The inspection was physically on site and initially performed with GDP however the GDP aspects of the inspection were completed separately with an updated GDP certificate subsequently issued (certificate reference: UK WDA(H) 32879 Insp GDP 32879/93706-0024).

This report has been issued for completeness after it was identified that it was not issued at the time of the GMP certificate.

Previous Inspection Date(s): 2nd – 4th April 2019

Previous Inspectors: [REDACTED]

B2 Inspected Areas

Starting Materials: Approval, TSE compliance, API compliance, Goods receipt and storage.
Pharmaceutical Quality System: Deviations, CAPAs, Change Control, Management review.
Change to introduce Importation of QP certified IMPs from a country on the 'approved country for import list'.
Controls associated with manufacture of IMPs
Personnel: Training
Premises and Equipment:
Facility tour including goods receipt/material storage/manufacture including cross contamination controls/packing/batch release/dispatch/picking.
Routine maintenance / Calibration, BMS, Temperature mapping.
Documentation: Document control, Batch record review and release

Production: Production order, Label generation and controls
Quality Control: Sampling, Testing, Laboratory investigations, Stability
Outsourced activities
Complaints
Product Recall
Self-inspection

Limitations / exclusions to inspected areas

Distribution and shipment were inspected; however, this is not described in depth in this report as more detail was covered separately by the GDP inspector (see C13 of this report).
Stability data, validation master plan and HVAC controls were not inspected in depth and may be of interest at a future inspection.

Area for focus at next inspection

Due to the wide variety of starting materials - control of these and approval of suppliers will continue to be of interest.
Control/compliance for the supply of herbal API/products would be of interest.
GDP activities will continue to be of interest and the use of the Unit [REDACTED] area.
Reviewing incident investigation and deviation investigation records would continue to be of interest.

B3 Key Personnel met/contacted during the inspection

Name	Position
[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]

B4 Documents submitted prior to the inspection

Document	Version /Date of document	Reflected activities on site?
Site Master File	Rev [REDACTED] approved 07 Jun 2022	Y
Compliance Report	22 Jun 2022	Y
Comments: None.		

Section C Inspector's Findings

C1 Summary of significant changes

Detailed changes are recorded in the pre-inspection compliance report held in the case folder.

Changes since previous inspection which are of particular relevance to compliance / risk rating, or which relate to inspection deficiencies are listed below:

Variation casefolder MIA(IMP) 32879/M-0013 was triggered prior to this inspection to add 2.3.4 Importation of QP certified IMPs from a country on the 'approved country for import list. The changes associated with this variation was included in the scope of this inspection.

The site had also refurbished a separate unit that was close to the site (Unit [REDACTED] to enable more storage capacity. Refer to the compliance report for more details.

Future planned changes which are of particular relevance to compliance / risk rating, or which relate to inspection deficiencies are listed below:

Refer to the pre-inspection compliance report held in the case folder.

Following the inspection the site indicated that it may be involved in manufacture of API for an IMP (it was understood by the inspector that this specific activity, i.e. manufacture of API solely for use in an IMP does not solely require a GMP certificate, but in some cases a site may be inspected for this).

C2 Action taken since the last inspection

The site described that they were able to address all the deficiencies from the previous inspection. Detailed evidence of completion was not reviewed on this occasion.

C3 Starting Materials

General

The site manufactured a wide variety of unlicensed medicines with an associated range of APIs and excipients handled at the site.

A major deficiency was raised associated with storage that was in part relevant to starting materials, refer to Section D2.1 of this report.

Compliance with TSE Guidelines

The TSE policy was SOP [REDACTED] rev [REDACTED]. The BSE-TSE statement dated 05 Feb 2019 was provided for [REDACTED]. It was discussed that it was over 3 years old and that the TSE policy did not have a prompt to consider if the TSE statement/assessment was up to date. Refer to section D of this report.

API Compliance

Controls for [REDACTED] were reviewed that included the supply chain; it had been manufactured at [REDACTED] supplied to [REDACTED] and on to [REDACTED] where it was shipped to the site [REDACTED]

The request for approval to purchase a raw material [REDACTED] for [REDACTED] was reviewed. This identified that the material would be checked against the BP with ID testing on receipt. It required storage at 15 – 30°C with storage on site described as meeting this as 15–25°C. The associated ID testing (performed by a contract laboratory) for a batch received was reviewed.

It was understood that the API registration related to herbal products. Control/compliance of these activities for the supply of herbal products may be of interest at a future inspection.

C4 Pharmaceutical Quality System

The Pharmaceutical Quality System was inspected.

The procedures described below were reviewed. The site provided lists of records/investigations associated with each procedure and the inspector selected examples of these that were reviewed as part of the inspection.

Deviation investigations

SOP [REDACTED] rev [REDACTED] was the procedure for Handling Deviations.

The site also had a separate incident investigation process where incidents could be escalated as deviations.

Change control

The change control associated with the IMP licence variation for Importing into GB from approved countries was reviewed. Change Control [REDACTED] raised 26 Oct 2021. The format of the change control included before implementation actions & closeout.

IMPs

SOP [REDACTED] described [REDACTED] and had been updated to include the QP oversight process in line with MHRA guidance. It had been updated to revision [REDACTED] and subsequently further updates to revision [REDACTED] issued 10 May 22 at the time of inspection.

Deficiencies were raised, relating to investigations and how the controls required to maintain the blind of a clinical trial were described in procedures refer to Section D 3.3 and 3.4 of this report.

C5 Personnel

It was described that there were 85 people working at the site at the time of the inspection.

SOP [REDACTED] rev [REDACTED] was the Staff Training procedure, a spreadsheet was used as a matrix of job roles against SOPs. The training file for a QC officer was reviewed. The training file for an operator was also reviewed, who had joined the company in Sep 2019 and exited in August 2021.

No comments were raised.

C6 Premises and Equipment

The premises and equipment at the site were physically inspected and were as described in the site master file. Refer to Appendix [REDACTED] of the SMF for a floor plan that can assist with orientation of the manufacturing area. Unit [REDACTED] that was a separate building close to the site and was intended to be used for additional storage was also viewed (refer to interim compliance report in case folder for further information).

There was no water generation or distribution system on site other than for the supply of potable water. Any water required for manufacture (e.g. sterile water) was purchased in containers.

The manufacturing area had separate rooms from a common corridor to enable manufacture of different products to be performed separately.

There was a separate highly hazardous room with associated equipment wash area for handling more hazardous substances.

A major deficiency was raised associated with storage controls, refer to Section D2.1 of this report and a separate deficiency was raised associated with risk assessment and associated controls to avoid potential contamination and mix-ups, refer to Section D 3.1 of this report.

Examples of data from the [REDACTED] monitoring system for temperature data for the walk-in cold store and temperature/humidity data for raw material storage was reviewed. It was understood that the site intended to also use this system for monitoring in the new Unit [REDACTED] separate storage area.

Winter temperature mapping and summer temperature mapping had been performed in March and September 2018. It was described that mapping was planned to be repeated in 2023.

A deficiency was raised refer to Section D of this report.

C7 Documentation

The site provided a list of SOPs that were current at the time of inspection; a copy of this has been saved in the inspection casefolder with samples of procedures reviewed throughout the inspection. The site also had "Methods" that had a separate numbering system to SOPs. Documents were generally compliant although some deficiencies were identified as described in section D of this report.

Batch records were recorded on paper with [REDACTED] used to manage/control the batch status.

It was described that the separate IT group were the administrators of laboratory computerised systems and that analysts did not have access rights to delete data.

The [REDACTED] was SOP [REDACTED] rev [REDACTED]. It was discussed that this also included line clearance requirements such as when QC were verifying printed packaging materials such as labels and cartons i.e. to minimise risk of mix-ups.

C8 Production

There had been little IMP licensed activities at the site since the previous inspection. Records relating to operations to support one IMP trial that involved blinding and randomization performed at the site in 2022 was reviewed.

The site handled a relatively high demand of unlicensed patient specific medicines to pharmacies and hospitals with customers expecting products to be supplied relatively quickly from order placement. Operations were progressing throughout the inspection. It was understood that in some cases hospital orders had more notice whilst some pharmacy orders could require a quicker response.

Different activities at the site were observed during the inspection, including Goods In checks that were performed directly into [REDACTED] use of stickers for indicating QC status, material storage areas, packing and picking/dispatch area.

The manufacturing area was inspected including where Sampling was performed in the [REDACTED] room using disposable sampling tools. The site had a list of materials considered to be more hazardous and these were sampled in the separate "Cytotoxic" area. Raw material storage in the manufacturing area was inspected.

The temperature monitoring system was described as automatically triggering email and text alerts if limits were breached and magnehelic gauges monitored room pressures with checks performed 3 times a day.

A batch record for manufacture of [REDACTED] that was an unlicensed medicine was discussed.

Manufacturing of suspensions from tablets and capsules was described in [REDACTED] that had been issued 03 Sep 2021.

The inspector discussed concerns regarding the risk of potential contamination if a pH probe was placed directly into a product (rather than into a sample) and a deficiency was raised.

The following areas were also physically inspected: hazardous washroom, the associated 'cytotoxic' manufacturing room and the QC final release room (where [REDACTED] was observed being released).

Refer to Section D of this report for associated deficiencies raised.

C9 Quality Control

The QC analytical laboratory was used for some testing and was physically inspected. It was as described in the site master file. Laboratory controls inspected included testing of a sample of received starting material ([REDACTED] for FTIR, the associated procedure for [REDACTED] [REDACTED] SOP [REDACTED] rev [REDACTED] and refrigerated storage/traceability of the associated reference standard.

It was described that for excipients considered high risk, such as [REDACTED] that ID testing would include an appropriate method with gas chromatography described as an example. In this case it was performed by a third-party laboratory ([REDACTED]).

The tracking of samples using a spreadsheet was demonstrated.

There was an [REDACTED] (SOP [REDACTED] rev [REDACTED]). This was not inspected in detail and may be of interest at a future inspection.

A separate walk-in fridge was used for holding stability samples (as well as released refrigerated stock) with a deficiency raised associated with temperature logger location, refer to section D of this report.

C10 Outsourced Activities

The site provided a list of technical agreements, and the inspector selected examples of these that were reviewed as part of the inspection.

At the time of inspection, contract laboratories were being used with a laboratory chosen depending on the testing requirements and if for example a sample may be a controlled drug whether the laboratory was licensed to handle it.

The Technical Agreement was reviewed between [REDACTED] and Vertical Pharma, for [REDACTED], approved 28 Oct 2021, with product filled at [REDACTED]. This had not been updated to reflect that [REDACTED] did not actually do the blinding/randomisation. The associated QP (Qualified Person) 3-way agreement for [REDACTED] was also presented and included a signature from the Sponsor representative.

A deficiency was raised, refer to Section D 3.5 of this report.

C11 Complaints and Product Recall

The site provided lists of complaint investigations from the previous 2 years and the inspector selected examples of these that were reviewed as part of the inspection.

SOP [REDACTED] rev [REDACTED] was the procedure for Complaint Handling.

The most recent mock recall for an MS ([REDACTED]) was reviewed that was performed 27 Apr 2022. It did not review how quickly the mock recall was performed and did not discuss if there were any recommendations.

A deficiency was raised, refer to Section D 3.2 of this report.

C12 Self Inspection

The self inspection schedule for the current year and performance of audits against the previous year was reviewed.

No comments were raised.

C13 Distribution and shipment (including WDA activities if relevant)

The GDP aspects of the inspection were progressed independently of this report and included the assessment of adding Unit [REDACTED] (site number 29641350) to WDA(H) 32879.

An updated GDP certificate was subsequently issued (certificate reference: UK WDA(H) 32879 Insp GDP 32879/93706-0024).

A response to the separate GDP findings (2 Major and 5 Others) was provided by the site. A copy for reference and to assist in understanding the GDP findings has been included in this case folder for completeness and may be of interest at a future inspection.

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

None

D2 Major

- 2.1 Control and storage of materials was deficient in that:
- 2.1.1 Humidity was not being adequately monitored as alarms on sensors were not active in storage areas where these would be relevant, such as the raw materials store where capsules and some materials sensitive to humidity could be stored.
- 2.1.2 There was inadequate control to enable orderly storage of CDs as evidenced by a cabinet observed to be cluttered and storing a container of expired material with other different materials. In addition, [REDACTED] did not identify which CD store held received materials.
- 2.1.3 A logger was observed to have fallen off the wall of the walk-in fridge that was holding released refrigerated stock and stability samples and therefore was not monitoring the worst-case location identified.
- 2.1.4 There was no requirement to assess deliveries where the driver had 'run away', for example to consider the risk of them not being transported or stored correctly.
- 2.1.5 There was no record of contents of rooms when temperature mapping was performed (i.e. in order to enable assessment if the load had significantly changed since mapping).
- 2.1.6 The TSE policy did not consider assessing if a TSE statement/assessment was up to date.

EU GMP C3.18, C3.19, C4.5, C5.4, A15.2.1

D3 Others

- 3.1 Risk assessment and associated controls to avoid potential contamination and mix-ups was inadequate in that:
- 3.1.1 The risk of contamination from using a pH probe that was not easily cleanable to directly test liquid products had not been assessed.
- 3.1.2 [REDACTED] pro-filler product contact parts in the hazardous washroom were not etched to indicate that they were dedicated as described as required by procedures.

- 3.1.3 The risk of a disposable glove dispenser being located in the [REDACTED] sampling room that was difficult to clean between batches and could potentially be a cross contamination risk had not been adequately considered, such as potentially placing this in the cleaner corridor area.
- 3.1.4 Manufacturing instruction [REDACTED] did not specifically state to verify the integrity of primary packaging blisters after cutting.
- EU GMP C1.8(iv), C1.8(v), C5.10
- 3.2 Complaint handling and recall
- 3.2.1 The procedure for customer complaint handling (SOP [REDACTED] version [REDACTED] did not describe the timescales for the escalation process, for example if some actions may be required within 24 hours. In addition, the QA initial assessment for customer complaint [REDACTED] was documented one month after the complaint was received.
- 3.2.2 The mock recall of an unlicensed product from Apr 2022 did not review how quickly the mock recall was performed or discuss if there were any recommendations.
- 3.2.3 Investigation [REDACTED] described how an unlicensed product was being transported to a customer when it was identified as defective and required recall. This significant deviation was not reported to DMRC and the recall process was ambiguous as to at what point a released product would be classed as being recalled. It is acknowledged that none of this product was supplied to patients.
- EU GMP C8.9(v), C8.15, C8.30
- 3.3 Investigation processes were deficient as evidenced by:
- 3.3.1 Incident investigation [REDACTED] had not been completed in accordance with the procedure in that sections 3 & 4 required in cases where no deviation or vendor complaint was raised were incorrectly crossed through when these should have been completed.
- 3.3.2 SOP [REDACTED] did not describe the interpretation of incidents that was performed by QA as part of determining root cause of an incident.
- EU GMP C1.8(iv), C1.8(v), C4.3
- 3.4 It was ambiguous how the controls required to maintain the blind of a trial were described in procedures, such as but not limited to:
- 3.4.1 Controls when providing information to third parties.
- 3.4.2 Incident/deviation systems did not describe the risk if an event potentially unblinded a trial. It is acknowledged that training to staff was performed when the site had performed the first blinded packaging run performed at the site.
- EU GMP C4.3, A13.21
- 3.5 The Technical Agreement between [REDACTED] and Vertical Pharma, approved 28 Oct 2021 had not been updated to reflect that [REDACTED] were

no longer going to perform blinding/randomisation for this study. It is acknowledged that there was a QP agreement.

EU GMP C7.14, C7.15

D4 Comments

- 4.1 Due to inspector illness not all GDP aspects of the inspection were completed. The GDP inspector subsequently contacted the site to arrange completing these as a separate activity.
- 4.2 This inspection included a variation to add QP oversight for IMPs.

Section E Site Oversight Mechanism

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

Section F Summary and Evaluation

F1 Closing Meeting

A closing meeting was held on 30 Jun 2022 and the identified deficiencies were verbally accepted by the site.

F2 Assessment of response(s) to inspection report

A type 1 post inspection letter (PIL) was issued on 04 Nov 2022.

A response to the PIL was received on 09 Nov 2022 with the company having already addressed most of the findings and responding to each deficiency with CAPAs. No request for further information was requested and the responses accepted.

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	✓
The Medicines for Human Use (Clinical Trials) Regulations 2004	✓
Regulation 5 of the current Veterinary Medicines Regulations	
Regulation C17 of the Human Medicines Regulations 2012 (as amended) and the Human Medicines (Amendment) Regulations 2019	✓

and is acceptable for the products in question.

Name of Inspector (s):

Lead Inspector:

██████████

Date:

30 Jan 2025

Annex 1

GMP Site Risk Rating

(a). Inspection Findings

Critical deficiencies this inspection:	0	Last inspection:	0
Major deficiencies this inspection:	1	Last inspection:	0
Other deficiencies this inspection:	5	Last Inspection:	5

(b). Provisional Rating based on Inspection Output (✓ applicable box)

Risk rating level	Input from current Inspection Findings (last inspection findings applicable to rating V only)	Provisional rating – this assessment	Final rating last assessment
0	Serious triggers outside the inspection cycle		
I	Critical finding		
II	>= 6 Major findings		
III	<6 Major findings		
IV	No critical or Major findings		
V	No critical or Major findings from current or previous inspection and <6 other findings on each.		

(c). Risk Assessment Inputs – discriminatory factors (✓ applicable box)

	None relevant (default)
	Significant concern over robustness of quality system to retain adequate control
	Significant failures to complete actions to close previous deficiencies raised at the last inspection
	Complex site
	Significant changes reported in Compliance Report
	Significant mitigating factors applied by the site
	Higher risk rating identified by other GxP and considered relevant to the GMP site
	Relevant site cause recalls, notifications to DMRC or rapid alerts since last inspection
	Nature of batch specific variations submitted since the last inspection give concern over the level of control
	Regulatory action related to the site
	Failure to submit interim update and/or failure to notify MHRA of significant change or slippage in commitments from post inspection action plan
	First Inspection by MHRA (does not require counter-signature for RR II)
	Other discriminatory factor (record details and justify below)

(d)

[Redacted]

(e). Risk Rating Result Incorporating Discriminatory factors (✓ applicable box)

Risk rating level	Inspection Frequency	Inspector Proposed Risk Rating (✓)
0	Immediate (as soon as practicable)	[Redacted]
I	6 monthly	
II	12 months	
III	24 months	
IV	30 months	
V	30 months with 50% reduction in duration of the next inspection	

(f). Basis for risk-based acceptance of specific matters arising during the inspection

[Redacted]

(g). GMP or GDP certificate conditioning remarks required as a result of risk-based decisions noted in section (f) above

[Redacted]

(h)

[Redacted]

(i). Expert/ Operations Manager / Compliance Management Team (CMT) Comments
(Risk rating level 0, I, II):

[Redacted]

(j). Confirm Agreed Risk rating following this inspection:

[Redacted]	

Notes regarding re-inspection and GMP certificate validity

1. The inspection schedule is based upon risk and resource. This date may change at any time due to factors not pertaining to your site.
2. The GMP certificate does not 'expire' it is provisionally assigned 3 year validity date. For external questions regarding your validity thereafter; please advise that this can be confirmed by contacting the inspectorate at gmpinspectorate@mhra.gov.uk