Medicines & Healthcare products Regulatory Agency

MHRA

GDP INSPECTION REPORT

WDA(H) 19569/9024085

OTSUKA PHARMACEUTICALS (UK) LIMITED

ISSUED BY:

[redacted]

GDP Inspector

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Medicines & Healthcare products Regulatory Agency

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File Ref: **Insp GDP 19569/9024085-0008**
Inspection Date: **22/11/2021**
Company: **OTSUKA PHARMACEUTICALS (UK) LIMITED**

GDP Inspection Report

1. Report Reference no.:	Insp GDP 19569/9024085-0008
2. Inspected site(s) and contact details:	
OTSUKA PHARMACEUTICALS (UK) LIMITED GALLIONS WEXHAM SPRINGS FRAMEWOOD ROAD WEXHAM SLOUGH SL3 6PJ UNITED KINGDOM	
3. Authorised operations:	
☒ Procurement ☐ Holding ☒ Supply ☐ Export ☐ Products imported from countries on a list ☐ Products certified under Article 51 of Directive 2001/83/EC ☐ Products not certified under Article 51 of Directive 2001/83/EC ☐ Other activities: (please specify)	
4. Inspection date(s):	22/11/2021
5. Inspector(s):	
Name(s) of the Inspector(s). [redacted] **MHRA**	
6. References:	Wholesale Distribution Authorisation Number or Registration Number of Broker: WDA(H) 19569

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7. Introduction:

Business Background

Otsuka Pharmaceuticals Europe Ltd (OPEL) is a global pharmaceutical company which is Part of the Otsuka Pharmaceutical Co, Ltd group of companies headquartered in Tokyo, Japan. OPEL manage the supply chain for Otsuka Pharmaceutical Netherlands (OPNL) who are the EU marketing authorisation holder for 5 products. OPEL distribute these products internationally to a range of affiliate sites using contracted service providers for storage and transport.

Otsuka Pharmaceuticals (UK) Limited (OPUK) is the UK affiliate of OPEL and is involved in the distribution of Otsuka products throughout GB.

Review of WDA(H)

MEDICINAL PRODUCTS

☒ With "an authorisation" (a UK, Great Britain or Northern Ireland Marketing Authorisation, an Article 126a authorisation, a certificate of registration or traditional herbal registration)

☐ Without "an authorisation" (a UK, Great Britain or Northern Ireland Marketing Authorisation, an Article 126a authorisation, a certificate of registration or traditional herbal registration) in GB or EEA and intended for the UK market

☐ Without "an authorisation" (a UK, Great Britain or Northern Ireland Marketing Authorisation, an Article 126a authorisation, a certificate of registration or traditional herbal registration) in the UK and not intended for the UK market

☐ With a Marketing Authorisation in EEA member state(s) and intended for the GB parallel import market

Medicinal products with additional requirements

☐ Narcotic or psychotropic products

☐ Medicinal products derived from blood

☐ Immunological medicinal products

☐ Radiopharmaceuticals (including radionuclide kits)

☐ Products authorised under regulation 174 (supply in response to spread of pathogenic agents etc)

☐ Medicinal gases

☐ Cold chain products (requiring low temperature handling)

☐ Other products

Date of previous inspection:

Name(s) of Inspector(s) involved in previous inspection: [redacted]

Date of last inspection: 02/05/2019

Overview of inspection findings from last inspection and the corrective action taken:

One major and two other findings resolved as part of the inspection response to the 2019 inspection.

Major changes since the previous inspection:

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Nomination of [redacted] as the Responsible Person for Otsuka Pharmaceuticals (UK) Limited.

8. Scope of Inspection:
For cause inspection assessing compliance with the Guidelines of 5 November 2013 on Good Distribution Practice of Medicinal Products for Human Use and the Human Medicines Regulations 2012.
9. Inspected activities:
GDP Inspection of all GDP activities, operations, records and documentation under the licence pertaining to this site; Procurement and Supply.
10. Activities not inspected:
N/A
11. Personnel met during the inspection:
[redacted]
12. Inspectors findings and observations relevant to the inspection and deficiencies:

- **Quality Management**

  Both OPEL and OPUK operated individual quality systems which were managed by the respective entities individual quality teams. OPEL primarily operated a global quality system with localised elements that were relevant for GDP operations whilst OPUK operated a highly localised, UK specific set of processes that were relevant to the UK business model.

  In both instances, there was a level of separation between the operations carried out by each entity and this was reflected within the processes reviewed. Individual processes for risk management, CAPA and deviation management were in place as were procedures for the management and control of changes.

- **Personnel**

  Job Descriptions for key staff were available. Separate organisational charts for OPUK and OPEL were presented during the inspection. Personnel involved in GDP activity were required to conduct an initial training exercise which included SOP training relevant to the individual's role and responsibilities. Effectiveness and

competency was assessed using an online training test tool. Similar methods for training were used across both OPEL and OPUK. Training records were reviewed for a range of staff members and found to be complete and up to date.

It should be noted however that for the OPUK operation, the RP had failed to document a list of all delegated duties.

- **Premises and Equipment**

  Procurement only sites all storage and distribution activities are handled by [redacted]. Distribution activities from packaging contractors were managed by OPEL through [redacted]. An inter-company agreement between OPEL and OPUK was in place to enable OPEL contractors to manage OPUK products.

- **Documentation**

  Processes were in place for version control and both OPEL and OPUK maintained records for the minimum periods as defined within regulations. Both OPEL and OPUK operated an electronic QMS via the [redacted] system.

- **Operations**

  OPEL and OPUK managed their stock inventory level at the [redacted] through a live interface and daily reports from [redacted] These are then used to forecast the sales and demand and orders are placed with the packaging contractors to maintain stock levels. [redacted] provides a full contract service which includes a customer service dedicated team, customer invoicing.

  Concerns were raised during the inspection in relation to the customer qualification process maintained by OPEL for its international Otsuka affiliates. During the inspection it became evident that OPEL had only qualified third party storage sites where Otsuka products had been exported and had failed to appropriately qualify international customers who were other Otsuka affiliates (see section 16 for further information).

- **Complaints, Returns, Suspected Falsified Medicinal Products and Recalls**

  Processes were in place for the management of returns, complaints and falsified medicines. Complaints could either be reported to OPEL or OPUK directly or via the [redacted] service provider. Service complaints were typically reported to and managed by [redacted]. Written agreements between OPEL and [redacted] were in place which detailed the responsibilities for the management of complaints, returns and falsified medicines. However, it should be noted that the contract presented failed to provide any clarity in relation to how returns for Otsuka UK products would be handled (see section 16).

- **Outsourced Activities**

  Holding was outsourced to [redacted] with transport managed by [redacted] These were managed by way of formal contracts between OPEL and relevant service providers. OPEL maintained oversight of these service providers via regular audits which were made available during the inspection.

  An agreement was also in place between OPEL and [redacted] for contracted [redacted] provided by [redacted]

- **Self-Inspection**

  A self-inspection programme was in place for both OPEL and OPUK. Self-inspections were overseen by the relevant [redacted] for OPEL and OPUK respectively. Several OPEL self-inspection activities were delegated to members of the quality team. Self-inspections involved assessment of compliance of the relevant operations to live processes and the guidelines of GDP. Separate self-inspections were conducted for OPEL and OPUK.

- **Transportation**

Transport for both OPEL and OPUK products was primarily managed by [redacted] would typically maintain oversight of subcontracted transport activities and this was captured within the agreements presented during the inspection.

- **Specific Provisions for Brokers**

  Not applicable

13. Other specific issues identified:
None
14. Miscellaneous:
N/A
15. Annexes attached:
N/A

16. List of Deficiencies classified into critical, major and others:

1 CRITICAL

None

2 MAJOR

2.1 Supplier and Customer qualifications were deficient in that:

2.1.1 There was a lack of clarity in relation to the approved export customers that Otsuka Europe Ltd had qualified. It was confirmed during the inspection that export customers were Otsuka entities in overseas territories, but the customer qualification presented only involved qualification of third party storage sites where products were delivered. There was no evidence to demonstrate qualification of the international Otsuka entities.

2.1.2 There was no evidence that additional bona fides checks to qualify export customers were being carried out with the qualification of export customers being limited to license checks with the relevant national competent authority.

2.1.3 There was no evidence to demonstrate periodic requalification of the export customers including third party storage sites.

GDP Guidelines Chapters 5.2, 5.3 and 5.9

3 OTHER

3.1 The Responsible Person for Otsuka UK had not documented tasks or arrangements for deputising.

GDP Guidelines Chapter 2.2

3.2 There was a lack of clarity in regard to how product returns to the [redacted] for Otsuka UK customers would be handled. The written agreement with [redacted] did not contain any stipulations for the handling of returned Otsuka UK products.

GDP Guidelines Chapters 6.3 and 7.1

4 COMMENT

17. Inspectors' Comments:
No additional comments
18. Recommendations:
Your application for variation to a wholesale dealer's authorisation [WDA(H) 19569] granted pursuant to Regulation 18 of the Human Medicines Regulations 2012 (a "wholesale dealer's licence") will be recommended to the licensing authority. *Site and authorisation pursuant to Regulation 18 of the Human Medicines Regulations 2012 (a "wholesale dealer's licence") will next be inspected as part of the MHRA's risk-based inspection programme, the frequency of inspection being determined by the nature of the activities the licence holder undertakes and previous compliance history. The risk profile of a company may change over time and consequently provisional re-inspection dates given in this report may change".* *The provisional date for the next inspection of this site is 22/11/2024*
19. Summary and conclusions:
Within the scope of the inspection, the company operates in accordance with the principles of good distribution practice referred to in regulation C17 of the Human Medicines Regulations 2012. The GDP certificate reflects the status of the inspected site at the time of the inspection noted above. Inspections of other sites that are named on the licence may cause this certificate to be withdrawn if Regulatory action against the licence is taken by the Licensing Authority.

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20. The inspection report should be signed and dated by the Lead Inspector:
Name: [redacted]
Signature: [redacted]
Organisation: MHRA
Date: 28/03/2022
Distribution of Report: [redacted]