GDP INSPECTION REPORT

WDA(H) No: 17901

Astra Zeneca
Silk Road Business Park
Macclesfield
Cheshire
SK10 2NA

ISSUED BY:

[redacted]
GDP Senior Inspector/Operations Manager

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Medicines and Healthcare Products Regulatory Agency

File Ref: Insp GDP 17901/10117
Inspection Date: 17th August 2017
Company: AstraZeneca

GDP Inspection Report

1. Report Reference no.:	Insp GDP 17901/10117
2. Inspected site(s) and contact details:	
AstraZeneca Silk Road Business Park Macclesfield Cheshire SK10 2NA [redacted]	
3. Authorised operations:	
☒ Procurement ☒ Holding ☒ Supply ☐ Export ☐ Brokering ☒ Other activities: administration	
4. Inspection date(s):	17th August 2017
5. Inspector(s):	
[redacted] **MHRA**	
6. References:	Wholesale Distribution Authorisation Number:17901

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7. Introduction:

Business Background

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This is a large AstraZeneca manufacturing plant located on the outskirts of Macclesfield. In addition to manufacturing activities the site is also a location of holding and distribution. This inspection has focussed entirely on the relationship between AsteaZeneca and one of its distribution partners [redacted] and has not considered the physical operations at this site.

WDA(H) categories:

MEDICINAL PRODUCTS

☒ with a Marketing Authorisation in EEA country(s)

☒ without a Marketing Authorisation in the EEA and intended for EEA market*

☐ without a Marketing Authorisation in the EEA and intended for exportation

Medicinal products with additional requirements

☐ Products according to Art. 83 of 2001/83/EC

- ☐ Narcotic or psychotropic products
- ☒ Medicinal products derived from blood
- ☒ Immunological medicinal products
- ☐ Radiopharmaceuticals (including radionuclide kits)

☐ Medicinal gases

☒ Cold chain products (requiring low temperature handling)

☐ Other products: (please specify here or make a reference to Annex 5)

Date of previous inspection:

This site is inspected as part of a rolling GMP inspection programme, The last inspection was conducted in November 2015 and considered the API manufacturing activity. The previous inspection did not consider any of the aspects considered in this report

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

Not considered as part of this inspection

Major changes since the previous inspection:

This inspection has in part been triggered by the change in relationship and activity conducted between AstraZeneca and [redacted]

8. Scope of Inspection:

Targeted inspection assessing compliance with the Guidelines of 5 November 2013 on Good Distribution Practice of Medicinal Products for Human Use (2013/C 343/01) and the Human Medicines Regulations 2012 as amended.

9. Inspected activities:

Supply and export activities using third party contractor

10. Activities not inspected:
This inspection was limited to the management of the third-party distribution arrangements between AstraZeneca and Geodis.
11. Personnel met during the inspection:
[redacted]
12. Inspectors findings and observations relevant to the inspection and deficiencies:

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- **Quality Management**

The quality management system was considered in respect of the management of the deviation associated with the Geodis inspection on March 2017. A deviation report had been raised which addressed the [redacted] deviation in terms of the "holding" aspect of their operation but there was no formal report relative to the downstream packaging and transportation activities. Nevertheless, the deviations associated with the [redacted] inspection had been addressed within the QMS, with effective investigations and CAPA's as required. Processes involving the review and oversight of [redacted] operations had been put into place and delivery routes had been the subject of robust risk route assessments. It was noted that prior to the [redacted] nspection of March 2017 the outsourced activities had not been correctly identified and hence had not been effectively managed within the QMS.

- **Personnel**

AstraZeneca possess a strong, experienced quality team as would be expected of a site of this type and in that sense, there are no concerns about the capability to maintain the contract within GDP compliance moving forward. [redacted] (Quality Supply Manager) acts as the primary point of contact between the organisations and has responsibility to maintain effective liaison and address ongoing issues as they arise.

- **Premises and Equipment**

  Not considered at this inspection

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- **Documentation**

  Key documents reviewed as part of this inspection were the deviation report raised following the [redacted] inspection and the risk route assessment relative to each export route.

- **Operations**

  See "Transportation" section below.

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

  Not considered at this inspection.

- **Outsourced Activities**

  The export of medicines and some holding has been outsourced to [redacted] by means of a Quality Assurance Agreement which has been signed at a group level. There are no issues with the current agreement but the management of the agreement and particularly the failure to cascade its contents effectively to the transport or quality teams at either Astra Zeneca Macclesfield or [redacted] is a significant contributory factor to the deviations identified.

- **Self-Inspection**

  A well-managed self-inspection system is in place.

- **Transportation**

  Products destined for export are sent by temperature controlled trailers from AstraZeneca on the short road transit to [redacted] (approximately 15 minutes). Loads consists of volumes of individual pallets down to small boxes. All individual pallets or loads travel with a logger or temperature tag. These devices are downloaded at the point of arrival with the eventual customer and the information transmitted back to AstraZeneca. Any deviations are then assessed and a determination made as to any possible impacts on product quality. [redacted] pack the shipments for onward transportation in accordance with the route risk assessment provided by AstraZeneca. This may involve the use of one of two types of cold chain delivery system, packing a number of pallets onto an airfreight "build or wrapping in a particular way. Depending on the requirements within the route risk assessment ambient products are sent with a number of freezer packs attached to the exterior of the pallets. [redacted] dispatch to UK airports and manage the delivery to the point of arrival in the third country concerned where responsibility passes to the eventual customer.

- **Specific Provisions for Brokers**

  None

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

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

1. CRITICAL

None

2. MAJOR

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2.1 The arrangements relating to the outsourcing of transportation activity was deficient in that;

2.1.1 The distribution contract between Astra Zeneca and [redacted] had failed to consider the precise nature of the activities being undertaken. It had failed to identify the extent that active packaging solutions were being applied by [redacted] on behalf of Astra Zeneca.

2.1.2 There was evidence to suggest that local management responsible for using and overseeing the contract on a routine basis had not been involved in the development of the contract and had not been made fully aware at an early stage as to the implications of its contents.

2.1.3 Because of the failure to fully understand the activities being conducted by [redacted] the level of risk associated with the activities had not been correctly of fully assessed within the Quality Risk Management System. In consequence, the oversight provided by the company's Quality Management System had not been effectively deployed to encompass the range of activity being conducted by [redacted] and their compliance with the requirements of Good Distribution Practice.

2.1.4 The deviation report generated as a consequence of the MHRA inspection of [redacted] on 21st March 2017 had identified the deviation and hence had generated a CAPA entirely focused on the "Holding" aspects of the [redacted] operation and had not addressed deviations associated with the packaging and transportation activities conducted.
Reference: EU GDP 9.2, 7.2, 1.2, 1.5

3. OTHER

None

17. Inspectors' Comments:

The underpinning deviation here is associated with the content of the high level QA agreement not being cascaded effectively. This in turn has resulted in AstraZeneca failing to correctly assess the level of risk implicit in the activities conducted by [redacted] and hence effective management and controls have not been applied. These issues have now been identified and effective systems appear to now be in place.

18. Recommendations:

Site and authorisation pursuant to Regulation 18 of the Human Medicines Regulations 2012 [SI 2012/1916] (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 wholesale activities on this site will continue to be inspected as part of the ongoing GMP inspection programme.

19. Summary and conclusions:

Within the scope of the inspection, the company operates in accordance with the Guidelines of 5 November 2013 on Good Distribution Practice of Medicinal Products for Human Use (2013/C 343/01) and the Human Medicines Regulations 2012.

20. The inspection report should be signed and dated by the Lead Inspector:

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Name(s): [redacted]

Signatures(s): [redacted]

Organisation(s): MHRA

MHRA

Date: 15th September 2017

Distribution of Report: [redacted]