DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
Division of Pharmaceutical Manufacturing Assessment 10903 New Hampshire Avenue; White Oak Building 51, Room 2269, Silver Spring, MD 20993 Email: OPMABLAInspection483Responses@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	05/30/2024 - 06/07/2024 FEI NUMBER 3002617771

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Ms. Lisbet Jensen Young, Site Lead

FIRM NAME	STREET ADDRESS
AstraZeneca Pharmaceuticals LP Frederick Manufacturing Center	633 Research Court
CITY, STATE AND ZIP CODE Frederick, Maryland 21703 LA 06/07/24	TYPE OF ESTABLISHMENT INSPECTED Drug Substance Manufacturer

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DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

Observation 1: Drug substance upstream manufacturing systems have unmitigated risk in assurance of process performance, product quality. Specifically,

You provided evidence of eleven (11) contamination events in upstream manufacture, Building (b) (4) from 27 April 2022 to 29 February 2024. You also provided twelve (12) contamination events for Building (b) (4) from 27 January 2020 to 09 November 2023, with each manufacturing system used in the production of (b) (4) and other products. You failed to identify and address system deficiencies in a timely manner.

This is a repeat observation from the 03/02 - 19/2021 inspection.

Observation 2: Procedures in support of manufacture and the QC test laboratory are deficient. Specifically,

a. On 26 March 2022, a cleaning validation for (b) (4) line (b) (4) failed for (b) (4) Maintenance Run (b) (4) You failed to conduct a cleaning verification for equipment utilized for (b) (4) (b) (4) (Batch (b) (4) on 16 April 2022, pending the completion of a successful cleaning validation or deviation investigation for the validation failure. You fail to have a procedure for governance of an equipment cleaning validation failure and subsequent manufacture.

b. On 30 May 2024, we observed raw material dispense area (b) (4) labeled as clean, ready for use. Upon entry to the area, we observed residual material from the prior dispense activity on surfaces presenting a cross contamination risk. You identified SOP-0106577, "Operation and Maintenance of Floor Scales at the Frederick Manufacturing Center (FMC) Site - Building (b) (4)", v32.0, Effective date 18 March 2024 and SOP-0067369, "Operation, Use and Cleaning of the Weigh Booths at the Fredrick Manufacturing Center (FMC) Site, Building (b) (4)", v57.0, effective date 08 January 2024, as deficient in support of facility cleaning.

c. On 30 May 2024, we observed a ceiling HEPA screen dislodged in (b) (4) area (b) (4) with (b) (4)

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	Wayne Seifert Vidya Pai Liqun Zhao Kristen Nickens Christina Farris	Wayne Seifert, Senior Consumer Safety Officer Vidya Pai, Supervisory Chemist Liqun Zhao, Pharmaceutical Scientist Kristen Nickens, Lead Biologist & Christina Farris Interdisciplinary Scientist Chair 07Jun24	06/07/2024

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[redacted] (b) (4) with the wall return air grate frames with gaps, unsealed to the wall interface. We further observed deteriorated fixture sealant and deteriorated pipe penetrations throughout Building [redacted] (b) (4) GMP facility. You identified that the SAP program maintenance plans fail to include a requirement for sealant inspection in assurance the facility qualified state is maintained.

d. On 04 June 2024, we observed two cabinets within [redacted] (b) (4) Gown and [redacted] (b) (4) Media Preparation with the top external surface in an uncleaned state. You identified SOP-0106918, "Facility Cleaning and Disinfection Program at Frederick Manufacturing Center (FMC) Site, v37.0, effective date 22 May 2024, as deficient in support of cleaning external cabinet horizontal surfaces.

e. On 06 June 2024, we observed within the Quality Control Laboratory, numerous controlled temperature units (CTU) in varying alarm conditions. You fail to have a procedure for routine inspection of CTU units.

Observation 3: There is a failure to thoroughly document product quality impact of quality events. Specifically,

Deviation investigation reports QE-090861 and QE-084599 describe excursions of [redacted] (b) (4) drug substance manufacturing process controls, inclusive of both critical process parameters (CPPs) and non-key process parameters (NKPPs). The conclusion within the corresponding deviation reports indicated that there was no product impact as a result of the process deviation. However, the deviation investigation reports did not include a thorough and clear evaluation of product quality impact. You failed to provide clear and thorough documentation of the data and information used to support the determination of no impact to product quality as a result of the quality event.

Observation 4: Analytical instruments in support of manufacture are not adequately controlled in assurance of data integrity. Specifically,

You maintain manufacturing IPC test instrumentation, computerized systems that includes a [redacted] (b) (4) Integrity Tester, [redacted] (b) (4) and [redacted] (b) (4) with each instrument having an audit trail. You fail to conduct an instrument audit trial review at any frequency in support of data integrity.

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