DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
CDER/OPQ/OPMA/Division of Biotechnology Manufacturing 10903 New Hampshire Avenue; White Oak Building 51, Room 2269 Silver Spring, MD 20993 Email: OPMABLAInspection483Responses@fda.hhs.gov	04/24/2023-05/09/2023
	FEI NUMBER 3010606982
NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED Mr. Inghou Loh, Vice President, QA Head	
FIRM NAME WuXi Biologics Co. Ltd.	STREET ADDRESS 108 Meiliang Road
CITY, STATE, ZIP CODE, COUNTRY Wuxi, Jiangsu, China	TYPE ESTABLISHMENT INSPECTED Drug Substance and Sterile Drug Product Manufacturer

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

1. The Quality Unit oversight is deficient. Specifically,
   a. Not all (b) (4) drug substance (DS) batches are withheld from use until the lots have been fully released by the Quality Unit. Specifically, multiple (b) (4) DS batches have been partially released and manufactured into drug product (DP) batches prior to obtaining unprocessed bulk (UPB) sample results and all DS release testing results, and completing all document and data reviews by the Quality Unit.
   b. The Quality Unit oversight over retesting after obtaining positive sterility test results is inadequate. Specifically, product (b) (4) DP PPQ Batches (b) (4) failed sterility test in September 2022. The initial sterility test results were invalidated without an unequivocal root cause and the test was repeated. Investigation attributed the most likely root cause to deficient sterilization of the sterility test media containers by the vendor.
   c. Batch disposition of contaminated production culture is not addressed in written procedures. Specifically, the (b) (4) cell culture is continuously harvested using (b) (4) (b) (4) The (b) (4) culture (b) (4) before (b) (4) is not monitored for bioburden prior to harvest of (b) (4) For the situation that the production culture is confirmed contaminated based on bioburden data of (b) (4) the disposition of the process intermediates manufactured from the (b) (4) is not addressed in written procedures.

2. The visual inspection program for (b) (4) DP vials is deficient. Specifically,
   a. The current acceptance criteria and procedure (WX-SOP-00318-29 and WX-SRD-00694-08) for acceptance quality limit (AQL) testing do not ensure (b) (4) DP batches are essentially free from visible particles. Specifically, the AQL acceptance criteria allow up to (b) (4) vials with light particles, black particles, or fibers to be found during the AQL process, potentially allow (b) (4) DP batches still containing visible particles to be released.

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	Bo Chi -S Digitally signed by Bo Chi -S Date: 2023.05.09 01:25:35 -04'00' Jun Liu -S Digitally signed by Jun Liu -S Date: 2023.05.09 01:39:05 -04'00'	Bo Chi, Ph.D., Microbiologist Jun Liu, Ph.D., Senior Biologist	5/9/2023

b. SOP WX-AMP-00206-09, "Appearance assessment and (b) (4) time determination for (b) (4) drug product" specifies that (b) (4) vials of a (b) (4) DP batch are (b) (4) and inspected for visible particles in addition to the 100% inspection of the (b) (4) for visible particles. There is no justification for the small sample size of (b) (4) vials.

c. According to document WX-OJT-00038-03, "OJT of visible particles test", no deviation is required to be initiated to evaluate the impact on the previously inspected batches when personnel who conduct visual inspection of (b) (4) drug product vials fail a visual inspection requalification.

3. The cleaning and disinfecting of the aseptic processing areas are deficient to ensure aseptic conditions are produced. Specifically, the non-product contact surfaces within the RABS are not always disinfected with a sporicidal agent before each DP batch. The surfaces are disinfected by (b) (4) a sporicidal agent (b) (4) disinfectants (b) (4) WX-SRD-01859-04).

4. The in-process parameter setup is inadequate to ensure product quality and process consistency. Specifically,

   a. The process intermediate physicochemical stability validation studies for (b) (4) DS (b) (4) are deficient. Specifically, for the hold time studies of steps (b) (4) at manufacturing scale, instead of comparing physicochemical test results obtained at the start of storage with results obtained at the end of storage of the same step, the hold time studies were conducted comparing physicochemical test results obtained at the start of storage of a step with results obtained at the start of storage of the subsequent purification or chromatography step. Due to the purification step in between of the two data points for each (b) (4) the impact of the proposed hold time on the physicochemical stability of (b) (4) DS cannot be assessed.

   b. The pH value of the (b) (4) of (b) (4) DS manufacturing process is not measured at the end of (b) (4) step before (b) (4) to ensure the pH of the (b) (4) is still within the target pH value and completeness of (b) (4)

5. (b) (4) hold time validation is inadequate. Specifically, the validation study (Report VD4322-PVR) for the (b) (4) hold time in (b) (4) tanks of the in-process (b) (4) used for (b) (4)

DS manufacturing was conducted using (b) (4) There are no data to support that these (b) (4) are worst-case from microbial growth promoting perspective to represent the other (b) (4) In addition, the study was only conducted in (b) (4) tanks and not in the (b) (4) anks, which are also used to hold (b) (4) in-process (b) (4)

6. Established procedures for DP equipment cleaning and facility surface cleaning are not adequately documented at the time of performance. Specifically,
   a. The manual cleaning process and testing results for the (b) (4) DP (b) (4) prior to use are not individually documented. Specifically, the (b) (4) are manually cleaned using (b) (4) and pH tested to ensure (b) (4) removal. However, the cleaning and rinse steps and pH testing of the (b) (4) are not individually documented for each (b) (4) to ensure (b) (4) cleaning and (b) (4) removal.
   b. SOP WX-SOP-00202-15, "Operation of (b) (4) in (b) (4) manufacturing facility" specifies that when (b) (4) materials from area of higher grade to area of lower grade (b) (4) the (b) (4) should be cleaned after taking out materials from the (b) (4) at the area of lower grade. However, the cleaning of the (b) (4) ID 10108416 location (b) (4) located in Building (b) (4) between the Grade B (b) (4) and the Grade D (b) (4) after each material (b) (4) is not documented.

7. The labelled maximum reuse times for (b) (4) for (b) (4) DS manufacturing process are not supported by the actual (b) (4) lifetime study results. Specially,

   a. During the production suite tour of building (b) (4) on April 24, 2023, it was noted that the labels for (b) (4) (ID: MFG-DCA-3002), (b) (4) ID: MFG-DCA-3004), (b) (4) ID: MFG-DCA-3003), and (b) (4) (ID: MFG-DCA-3005) located at 2-8°C in room (b) (4) showed that the maximum reuse times of the (b) (4) are (b) (4) use cycles; the labels for (b) (4) (ID: MFG-DCA-4009) and (b) (4) (ID: MFG-DCA-4014) located at room temperature in room (b) (4) showed that the maximum reuse times of the (b) (4) (b) (4) are (b) (4) use cycles. However, the (b) (4) Lifetime and Carryover Study Report (Document No: VD4474-PVR-03) concluded the maximum reuse cycle numbers for (b) (4) are (b) (4) and (b) (4) use cycles, respectively.

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b. Two incomplete loading cycles were counted in the validated use cycles during the concurrent (b) (4) lifetime study for the (b) (4) Specifically, the (b) (4) loading capacities for batch (b) (4) (b) (4) and batch (b) (4) were (b) (4) respectively; both were not within the (b) (4) - (b) (4) normal operating range (NOR) and (b) (4) - (b) (4) proven acceptable range (PAR). Both cycles are partial cycles and should not be counted as validated use cycles.

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	Bo Chi -S Digitally signed by Bo Chi -S Date: 2023.05.09 01:27:46 -04'00' Jun Liu -S Digitally signed by Jun Liu -S Date: 2023.05.09 01:41:08 -04'00'	Bo Chi, Ph.D., Microbiologist Jun Liu, Ph.D., Senior Biologist	5/9/2023