

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER ORA OPQO HQ, 12420 Parklawn Drive, Room #2032 Rockville, MD 20857 ORAPHARMInternational483responses@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	DATE(S) OF INSPECTION 03/22/2021 - 04/02/2021
	FEI NUMBER 3010606982

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Xuejian Xu, Chief Quality Officer

FIRM NAME WuXi Biologics Co. Ltd.	STREET ADDRESS 108 Meiliang Road
CITY, STATE AND ZIP CODE Mashan, Wuxi, Jiangsu, 214092, China	TYPE OF ESTABLISHMENT INSPECTED Drug Substance & Drug Product Manufacturer

THIS DOCUMENT LISTS OBSERVATIONS MADE BY THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OF YOUR FACILITY. THEY ARE INSPECTORAL 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 (I) (WE) OBSERVED:

OBSERVATION 1

Appropriate controls are not exercised over computer systems or related systems to prevent changes to data.

Specifically, per procedure WX-SOP-00154, entitled PAS (b) Batch Operation and Maintenance Procedure, Form WX-FORM-001141-03 is required to modify certain parameters in the Process Automation System (b) (4) Batch (b) (4) system. While this document requires that QA approve the change, it does not require QA to verify the change(s) for accuracy once complete. In addition, although a second person verification of the change is required, this is not always performed. For example, on 02/08/2021 a request to change an alarm limit (e.g., Parameter 1970PIC101) in (b) (4) was submitted, approved by QA on 02/09/2021, and then implemented in (b) (4). However, a review of the modification application form revealed the signatures for the person who performed the alarm modification and the second verification were missing. On 03/22/2021, Deviation DV39507 for (b) (4) Lot (b) (4) was initiated after an issue occurred with alarm 1970PIC101 during the (b) (4) step. The investigation is on-going. This deviation required (b) (4) Lot (b) (4) to be reprocessed.

OBSERVATION 2

The Quality Unit oversight over the issuance of controlled documents is deficient.

Specifically, your Quality Assurance department does not have adequate controls established for the distribution and/or reconciliation of all quality forms issued to other departments. For example:

a) On 03/22/2021, Form WX-FORM-000970-09, Registration Form of Samples for Analyses, was observed in the Quality Control laboratory. A review of your documentation controls revealed this controlled record is issued to Quality Control by your Quality Assurance department, however, there is not an adequate reconciliation plan in

SEE REVERSE OF THIS PAGE <i>[Signature]</i>	EMPLOYEE(S) SIGNATURE <i>[Signature]</i>	EMPLOYEE(S) NAME AND TITLE (Print or Type) Jonathan W. Chapman, Investigator	DATE ISSUED 04/02/2021
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place.

b) On 03/22/2021, Form WX-FORM-002218-02, Incoming Material Checklist, was observed in the Warehouse Management Office. A review of your documentation controls revealed this form is issued by the Warehouse Documentation group with no oversight from the Quality Assurance documentation group. As such, Quality Assurance has no control over the distribution and/or reconciliation of this form.

OBSERVATION 3:

Adequate schedules have not been established for the preventative maintenance of equipment.

Specifically, your firm failed to establish adequate preventative maintenance schedules for the following equipment: (b) (4) (MFG-UOE-3290), (b) (4) (MFG-DFC-3016), and (b) (4) (MFG-DFC-3017). For example, WX-SOP-00171, entitled Operation and Cleaning of Biologic (b) (4) Pump, states the (b) (4) of biologic (b) (4) pumps will be replaced (b) (4). In January 2021, a review of the preventative maintenance for the three (b) (4) mentioned was performed and identified to not be in agreement with the maintenance requirements specified in WX-SOP-00171. As such, the preventative maintenance schedules for the three (b) (4) were updated. However, a review of the preventative maintenance schedules identified the following issues:

a) Although the preventative maintenance schedule for (b) (4) (MFG-UOE-3290) was updated in 01/2021 to require the (b) (4) replacement of the (b) (4) of the (b) (4) pump, in accordance with WX-SOP-00171. The PM due date was set for 07/06/2021. This PM schedule is inadequate as this (b) (4) has been in use since 03/30/2018 and the (b) (4) of the (b) (4) pump has never been replaced.

b) Although the preventative maintenance schedule for the (b) (4) (MFG-DFC-3017) was updated in 01/2021 to require the (b) (4) replacement of the (b) (4) of the (b) (4) pump, in accordance with WX-SOP-00171. The PM due date was set for 07/31/2021. This PM schedule is inadequate as the last time the (b) (4) of the (b) (4) pump was replaced on this (b) (4) was 09/24/2019.

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c) Although the preventative maintenance schedule for the (b) (4) (MFG-DFC-3016) was updated in 01/2021 to require the (b) (4) replacement of the (b) (4) of the (b) (4) pump, in accordance with WX-SOP-00171. However, this PM update was incorrect as this (b) (4) does not contain (b) (4) pumps.

OBSERVATION 4

The specifications established for components used in the production of drug substance are deficient in that they do not include a description of the sampling plan.

Specifically, raw material specifications do not provide sufficient instructions to ensure samples collected are representative and reproducible. For example, the raw material specifications for (b) (4) chromatography media (Document WX-SPEC-000233), (b) (4) (Document WX-SPEC-000234), and (b) (4) (b) (4) media (Document WX-SPEC-000236), do not contain instructions requiring sampling operators to perform a (b) (4) of the material prior to collecting a sample. These materials are known to separate. These chromatography (b) (4) are used in the (b) (4) purification of (b) (4) drug substance.

OBSERVATION 5:

Effectiveness Checks for corrective and preventative actions implemented in response to a deviation investigations are not always initiated.

Specifically, SOP WX-SOP-00422, Corrective Action and Preventative Action (CAPA) procedures states Effectiveness checks are required for action items involved in the non-conformance caused (e.g., deviations) unless a detailed and reasonable justification is provided. Deviations PR17464 was initiated to investigate events which resulted in the termination of (b) (4) batches, Lots (b) (4). The investigation resulted in several CAPAs including CAPA PR 19821. This CAPA was identified to be a risk mitigating, however, no effectiveness check was initiated to evaluate the effectiveness of the CAPA.

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OBSERVATION 6:

There is a failure to thoroughly review any unexplained discrepancy and the failure of a batch or any of its components to meet any of its specifications whether or not the batch has been already distributed.

Specifically, Complaint Investigation CI-19-001 was initiated on 03/15/2019, after a product complaint was submitted for a potential low fill vial of (b) (4) Lot (b) (4). The complaint investigation performed included an evaluation of the retention samples. However, no scientific rationale was provided to justify the visual inspection of only 11 of the (b) retention sample vials. In addition, SOP WX-SOP-00425, entitled Product Complaints, section 4.4.1.3, states to review retention samples and does not provide instructions for reviewing reduced amounts.

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The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or
2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration.

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgement, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."