

**DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER 10903 New Hampshire Ave, Bldg 51, Rm 4225 Silver Springs, MD 20993 (301) 796-3334 Fax: (301) 847-8738	DATE(S) OF INSPECTION 2/12/2018-2/20/2018*
	FEI NUMBER 3008461619

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED  
Rajesh Shashikant Kulkarni, Associate Vice President -QA/QC

FIRM NAME Aurobindo Pharma Limited - Unit IV	STREET ADDRESS Unit IV, Plot No. 4, 34-48 EPIP, APIIC, IDA-Pashamylaram, Pantancheru Mandal
CITY, STATE, ZIP CODE, COUNTRY Medak District, Hyderabad, Telangana, 502307 India	TYPE ESTABLISHMENT INSPECTED Manufacturer of sterile drug products

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 I OBSERVED:  
OBSERVATION 1**

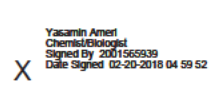
Aseptic processing areas are deficient regarding systems for maintaining any equipment used to control the aseptic conditions.

Specifically, on February 13, 2018 during the machine set-up and filling preparation for (b) (4) injection lot # (b) (4), I observed dirty (b) (4) with black stains on the filling machine (b) (4) and mentioned it to the management. No action was taken by the management on that day.

On Feb. 14, 2018, I observed that the filling is in process and the dirty (b) (4) is in use. Despite of informing the management of the dirty (b) (4) by me, the management failed to take action to investigate the dirt on the (b) (4) and to remove the (b) (4) with potential quality impact on the drug product. The filling of the lot was completed in the (b) (4).

**OBSERVATION 2**

Equipment and utensils are not cleaned, maintained and sanitized at appropriate intervals to prevent contamination that would alter the safety, identity, strength, quality or purity of the drug product.

<b>SEE REVERSE OF THIS PAGE</b>	EMPLOYEE(S) SIGNATURE Yasamin Ameri, Chemist/Biologist	 <p>Yasamin Ameri Chemist/Biologist Signed By: 2001565939 Date Signed: 02-20-2018 04:59:52</p>	DATE ISSUED 2/20/2018

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Specifically, (b) (4) on the filling machine in suite (b) (4) which are used for aseptic interventions during the filling operation inside the aseptic fill zone (grade A) had obvious built-up dirt and stains. These (b) (4) are used for production of (b) (4) injection since June 2017.

**OBSERVATION 3**

Equipment used in the manufacture, processing, packing or holding of drug products is not of appropriate design to facilitate operations for its intended use.

Specifically, the qualification of the vial washer and (b) (4) in (b) (4) -block suite (b) (4), that are used for washing and sterilizing of (b) (4) mL vials are not adequate. For example, qualification studies:

- a) for vial washer failed to demonstrate if vial washer (Eq. Id. # L-PR-QASHM-001) is able to remove bioburden from (b) (4) mL glass vials that are used for filling and (b) (4) of (b) (4) injection.
- b) failed to use statistically sound number of vials to demonstrate the effectiveness of the wash cycle and (b) (4) processes.
  - 1. During the qualification study of the vial washer, you conducted one run cycle using (b) (4) vials of (b) (4) mL glass vials as the representative of the lot and spiked those with (b) (4) to demonstrate the cleaning of the vials after wash. You placed these vials in the (b) (4) of the wash cycle. The batch of the vials used for this study included (b) (4) vials. You used less than 1% of the lot to demonstrate the cleaning. A commercial lot size for (b) (4) injection contains (b) (4) vials.

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2. During the qualification study of the (b) (4), you spiked (b) (4) mL glass vials with endotoxin and performed one (b) (4) run to demonstrate the effectiveness of the (b) (4) in reduction of endotoxin level in those vials. You placed (b) (4) vials in (b) (4) different rows; (b) (4) row before vials entering the (b) (4). These (b) (4) vials represented a batch of (b) (4) vials and were less than 1% of total vials. Currently you use this (b) (4) to (b) (4) about (b) (4) vials for a production of a commercial lot of (b) (4) injection.

**OBSERVATION 4**

Buildings used in the manufacture, processing, packing or holding of drug products are not free of infestation by rodents, birds insects, and other vermin.

Specifically, during the walkthrough of the facility on February 12, 2018, a large mosquito which appeared to be a female, was observed inside room (b) (4), Semi-finished product storage area holding. This room is located inside the unclassified but controlled environment corridor (corridor-1) and is connected to room (b) (4), collection vials for visual inspection. To reach this room personnel should pass (b) (4) sets of doors (b) (4) (b) (4)]. This room is two sets of doors away from the grade "B" and grade "A" areas where the filling and (b) (4) activities for (b) (4) injection takes place.

**OBSERVATION 5**

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Procedures for the cleaning and maintenance of equipment are deficient regarding sufficient detail of the methods, equipment, and materials used in the cleaning and maintenance operation, and the methods of disassembly and reassembling equipment as necessary to assure proper cleaning and maintenance.

Specifically, your firm failed to demonstrate the efficacy of the (b) (4) process, which is part of your cleaning activities, to eliminate contaminants in the hard to reach areas in the aseptic fill and (b) (4) areas (grade A & B).

**OBSERVATION 6**

Employees engaged in the manufacture, processing, packing and holding of a drug product lack the training required to perform their assigned functions.

Specifically, during the machine set-up and filling preparation for (b) (4) injection lot # (b) (4) on February 13, 2018, I observed that two operators inside the cleanroom cleaned the (b) (4) that were already installed on the filling machine's (b) (4); (b) (4) times with (b) (4) and cloth without paying attention to the black stains and obvious black marks on the (b) (4). These (b) (4) were in use from June 2017 and had been sterilized 5 times.

**OBSERVATION 7**

The statistical quality control criteria fail to include appropriate acceptance levels and rejection levels.

Specifically, your procedure for receiving and inspection of the components and packaging materials (procedure # FU4-QC-GEN-026, Sampling of packing materials) follows an unspecified level of AQL of ANSI Z1.4-2008 with no clear criteria for acceptance and rejection level. This procedure is deficient to provide clear reject and acceptance levels based on ANSI Z1.4-2008.

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**OBSERVATION 8**

Established laboratory control mechanisms are not followed and documented at the time of performance.

Specifically, laboratory control is deficient in that (b) (4) USP reference standards, code #USP-(b) (4) with lot # (b) (4), used to determine the identity, strength, quality and purity of (b) (4) (b) (4) injection which were received in laboratory on January 11, 2018:

- a) were not received in laboratory inventory management system (LIMS) as required by your procedure, however they were stored in the same container as other standards which were previously received and were in use.
- b) were not placed in desiccator as it is recommended on the COA.

**OBSERVATION 9**

Appropriate controls are not exercised over computers or related systems to assure that changes in master production and control records or other records are instituted only by authorized personnel.

Specifically, master batch records that are submitted in (b) (4) for (b) (4) (b) (4) injection, have different batch codes (document number) than the batch records that are currently in use for commercial production. There are no traceability for the changes made to the batches used for commercial production and master batch records that are submitted in the (b) (4) (b) (4).

**\*DATES OF INSPECTION**

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2/12/2018(Mon), 2/13/2018(Tue), 2/14/2018(Wed), 2/15/2018(Thu), 2/16/2018(Fri), 2/19/2018(Mon), 2/20/2018(Tue)

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