DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
FDA,12420 Parklawn Drive, Room 2032 Rockville, MD 20857 ORAPHARMInternational483responses@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	10/21-28/2019
	FEI NUMBER 3004051616

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Bhagwat Patil, Senior General Manager-Operations

FIRM NAME	STREET ADDRESS
Aurobindo Pharma Ltd., Unit V	Plot 68-70,73-91,95,96,260 & 261, I.D.A. Chemical Zone
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Pashamylaram,Patancheru,Sanga Reddy,Telangana India 502307	Sterile & Non-Sterile Bulk Drug Manufacturer

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

Observation 1

Laboratory controls do not always include the establishment of scientifically sound and appropriate procedures designed to assure that drug substances conform to appropriate standards of identity, strength, quality and purity.

Specifically, when there is no scientific basis found for invalidating initial out-of-specification (OOS) API test results and no assignable cause for the OOS is determined, procedures (SOP ZQA005) allow re-testing (following Phase I and II investigations), which permits reporting the average of (b) (4) additional analyses performed by (b) (4) separate analysts that meet specifications as the final data, overcoming original OOS data (No retests to overcome original OOS data have been reported).

Observation 2

Equipment for adequate control over micro-organisms is not always provided when appropriate for the manufacture, processing, and packing of drug substances.

a) Filling equipment (b) (4) Block Module (b) (4) grade A) is located in a position where aseptic procedures for operators during filling include bending down and squatting, which may result in bellowing of viable and non-viable particulate from personnel gowning during these activities having a potential affect on the sterile drug substance (e.g., (b) (4) Injection-bulk).

b) Goggles used by operators to protect against exposed skin in the Grade A/B areas during aseptic operations have built-in unprotected openings (holes) in the top, creating a lack of protection against a source of particles generated by, and microorganisms shed from, the body, having a potential affect on the sterile drug substance.

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Observation 3

The aseptic processing area is deficient regarding the system for monitoring environmental conditions.

During aseptic operations (b) (4) Block Module (b) (4) in grade A where sterilized stoppers are unsealed and transferred to the filling area (along with depyrogenated (b) (4) canisters), there is an absence of continuous monitoring of viables in the immediate proximity of exposed stopper packaging materials within the airflow of intervention activities and in a quantity and location intended to optimize detection of potential viable environmental contaminants during aseptic operations.

Observation 4

Process validation does not always include inclusion and establishment of all process parameters that should be controlled for reproducible operations.
For example:

a) Validation of (b) (4) and (b) (4) bag sealing processes (used in package sealing of non-sterile bulk drugs) and validation of (b) (4) bag sealing of packaged and sterilized gowning (used in aseptic operations) and sterilized stoppers (used in package sealing of sterile bulk drugs) are not complete in establishing optimum ranges for sealing parameters such as the temperature, pressure and time required to achieve consistent reproducible sealing results. Also, temperature, pressure and time used for sealing during packaging processes are not recorded/ documented, nor are the sealing machines used calibrated for temperature, pressure and time.

b) Concerning (b) (4) manufacturing (used in API manufacturing and the source (b) (4) for (b) (4) production, (b) (4) and used in cleaning), operating ranges for process parameters are not fully established, such as determining and monitoring acceptable levels/ranges of pressures and flow for routine production, in order to sufficiently validate and control this manufacturing process. For example, appropriate ranges (upper and lower limits) for the monitoring of flow/pressure for retention time and proper filtering and manufacturing have not been fully established for processing (b) (4) through (b) (4) and

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(b) (4) Also, (b) (4) do not have sanitization procedures and schedules in order to control microbial proliferation (biofilm growth) and govern a potential source of endotoxins.

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