DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

OBSERVATION 1

Procedures describing the handling of all written and oral complaints regarding a drug product are not followed.

Specifically,

On 11/24/14, your firm was notified of an adverse event associated with a dose of hydromorphone administered to a patient and produced by your firm. Your firm failed to notify the Corporate Clinical Services Department of the incident as delineated in procedures CLIN-PH107: Drug and Product Defect Reporting, effective 03/01/07, and ADMOPS15: Adverse Event Reporting, effective 03/01/07. The issue was noted in an electronic chart and a replacement was sent to the patient.

OBSERVATION 2

Clothing of personnel engaged in the processing of drug products is not appropriate for the duties they perform.

Specifically,

a) Sterile drugs are aseptically manipulated by the cleanroom operators who were observed wearing non-sterile gowns, caps, and face masks. Non-sterile eye protection may be used in the event of splashes.

b) The operator's area around the eyes is not fully covered allowing exposed facial skin over the critical ISO 5 laminar flow areas where sterile injectable drug products are processed.

OBSERVATION 3

Aseptic processing areas are deficient regarding the system for monitoring environmental conditions.

Specifically,

a) Environmental monitoring for viable and non-viable air counts in the ISO 5 zones is not performed at least daily during periods of production. The firm only monitors viable and non-viable air counts during the cleanroom certification by an outside vendor; lastly on 03/18/15.
**OBSERVATION 4**

Aseptic processing areas are deficient regarding the system for cleaning and disinfecting the room and equipment to produce aseptic conditions.

Specifically,

a) Non-sterile wipes are used to disinfect the ISO 5 hoods' sterile processing surfaces and they are composed of particle shedding material.

b) The firm does not use sporicidal agents to disinfect the ISO 5 surfaces.

c) A non-sterile liquid is used in disinfecting the ISO 5 surfaces.

d) No disinfectant efficacy studies have been performed to determine the disinfection procedures and disinfectants that are used can maintain an aseptic environment in the hoods.

e) On 05/12/15, operators were observed to wipe ISO 5 hood surfaces against the direction of the air flow.

**OBSERVATION 5**

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not established, written, and followed.

Specifically,

a) No media fills/process simulations have been performed under the most stressful or challenging conditions. Instead, the firm uses an [redacted] which doesn't utilize equipment and containers used in normal processing.
b) Operators were observed touching non-sterile items in the clean room such as the lining of the trash can (where disinfectants are maintained hanging) and a telephone. Gloves were not replaced after touching non-sterile surfaces.

c) On 05/12/15, operators were observed obstructing ISO 5 air flow patterns by placing vials in a random order on the surface and handling infusion bags one in front of another.

OBSERVATION 6

Each batch of drug product purporting to be sterile and pyrogen-free is not laboratory tested to determine conformance to such requirements.

Specifically,

Your firm has not conducted any sterility testing for any products.

OBSERVATION 7

The separate or defined areas necessary to prevent contamination or mix-ups are deficient.

Specifically,

a) Your firm is processing Penicillin-type injectable drugs, such as Ampicillin, Penicillin and Nafcillin, in the same ISO 5 hood as for non-penicillin products. The absence of a structurally isolated area creates the potential that accidental breakage of vials of penicillin powders could contaminate your other sterile drug products.

b) There is no separate air handling unit for penicillin drugs.

c) Your firm is processing Beta-lactam non-penicillin injectable drugs, such as Cefazolin, Cefazidime and Aztreonam, in the same ISO 5 hood as for non-beta-lactam products. The absence of a structurally isolated area creates the potential that accidental breakage of vials of beta-lactam powders could contaminate your other sterile drug products.

OBSERVATION 8

Testing and release of drug product for distribution do not include appropriate laboratory determination of satisfactory conformance to the final specifications prior to release.

Specifically,

Your firm does not perform visual checks of sterile injectable drugs for clarity/discoloration and/or particulates/contaminants.
OBSERVATION 9

There is no written testing program designed to assess the stability characteristics of drug products.

Specifically,

Your firm has not tested for sterility or potency over the assigned Beyond Use Dates (BUD) for any sterile injectable, all of which are preservative free. For example, your firm has not conducted any testing to support the BUDs such as 14 days refrigerated for Vancomycin or 14 days room temperature for Fluoracil. You have no data available to show that the sterility and potency will be maintained over the time period of the BUD.

OBSERVATION 10

Buildings used in the holding of a drug product are not maintained in a good state of repair.

Specifically,

Dust and debris were observed in the big warehouse which holds packaged materials and in a refrigerator utilized for holding packaged orders ready to be distributed. In addition, there was an approximate half an inch opening around the perimeter of the docking door in the big warehouse.