OBSERVATION 1

There are no written procedures for production and process controls designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess.

Specifically,

Your firm failed to implement written procedures to adequately manage glass vial breakage that may occur during drug product filling operations after the vial washing step. For example, two vials were broken as documented on batch [redacted] at 14:24 on April 5, 2018. The batch record states, “The debris and vials around the affected areas were removed in filling room [redacted].” The record does not state how many vials were removed or any additional details. Your firm has no written procedure to ensure the vials that have the potential to be compromised with glass particles are removed from the filling line.

In addition, the batch record for [redacted] states on March 25, 2018, at [redacted] “broken vials were found at the outlet of the [redacted] zone” during the filling process. However, the filling operations continued until [redacted]. The outlet of the [redacted] zone leads to the [redacted] that feeds empty glass vials to the filling line. Your firm lacks adequate documentation to ensure vials that may have been compromised with glass particles did not proceed to the filling step.
OBSERVATION 2

Employees engaged in the processing of a drug product lack the training required to perform their assigned functions.

Specifically, your firm performs 100% visual inspection on finished drug product. Your qualification for the operators is inadequate in that the qualification vials with glass particles are on the neck of the vial, not at the cap of the vial. Your firm only utilizes photographs for training on this defect, however these photographs are unclear and inadequate to identify glass particles in vials. Without an adequate qualification vial, your firm cannot ensure your operators can observe this defect during 100% visual inspection.

Furthermore, the review of the visual inspection qualification records revealed your firm does not have a procedure to address an employee who repeatedly failed to identify a specific defects during all qualification runs as observed during the most recent qualification for Operator performed in January 2018.

OBSERVATION 3

Routine checking of automatic equipment is not performed according to a written procedure designed to assure proper performance.

Specifically, your firm utilizes a sensor to reject drug product vials that have not been prior to the capping process. However, your firm does not perform challenge testing of the sensor prior to running batch of drug product. In addition, your firm does not document the the sensor is set to in the batch record.
OBSERVATION 4

Procedures describing the calibration of instruments, apparatus, gauges, and recording devices are deficiently written or followed.

Specifically,

Your firm does not adequately monitor the incubator rooms used to incubate environmental, media fill, and sterility samples. Your most recent temperature mapping study determined hot and cold spots for the incubators however your routine temperature monitoring gauge is not located in these areas.

OBSERVATION 5

Your firm confirmed the presence of contamination on the surface of the culture fluid in the 100 L bioreactor as stated in deviation report DE-P2-17-170. The contamination were first documented in 2017, during post PPC 100 L bioreactor runs. Your firm has not identified the composition of these contamination.

OBSERVATION 6

On July 11, 2018, during the walkthrough of the harvest unit operation, we observed the transfer of harvest tank contents to the load tank. The distance the harvest must travel from the harvest tank to the load tank is > and requires connecting transfer hoses between the tanks. All connections are performed in an open ISO 8 environment without environmental monitoring during unit operation. The connection requires more than 15 min of open exposure because of the transfer line, prior to making the open hose connection to the load tank. In addition, your firm identified the open hose connections as the root cause for the out-of-specification bioburden result for load, lot# documented in Deviation DE-P2-17-167.
On July 9, 2018, during the walkthrough of the unit operation in Suite C2 372, we observed product, formulation, and excipients on the floor and basin. While walking through the room, our shoe covers were sticky to the floor which was attributed to the excipient in the purification steps as this is the final unit operation prior to transfer into a holding bag and drug substance filling.

During the review of QC equipment logsheets, we observed your firm failed to document the time and temperature of release, stability, and reference standard samples during transfer between freezers. For example:

- Samples from freezer LEQ-94297 located in Suite C2 372 were transferred to LEQ-94201 for Maintenance of Validation (MOV) on June 6, 2018.
- Stability samples from freezer LEQ-94255 located in Suite W2 307, were transferred to FC103 for MOV execution on September 19, 2017.
- Samples from freezer LEQ-93097 located in Suite W2 302 transferred to LEQ-93098 on August 31, 2017.

In addition, your firm had not established sampling handling procedures to ensure the frozen samples are not exposed to room temperature for extended periods of time during transport from one storage location to another.

*DATES OF INSPECTION*

7/09/2018(Mon), 7/10/2018(Tue), 7/11/2018(Wed), 7/12/2018(Thu), 7/13/2018(Fri), 7/16/2018(Mon), 7/17/2018(Tue)