DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

OBSERVATION 1

There is a failure to thoroughly review any unexplained discrepancy whether or not the batch has been already distributed.

Specifically, batch records reviewed and approved by quality department included Environmental Monitoring (EM) Interventions into the grade A unit which recorded unexplained durations for those interventions. Unexplained discrepancies in the batch records were not investigated to determine whether (QCM) employees followed written procedures during interventions into the Grade A space during filling. For Example:

- Filling batch record shows on 10 January 2020 from Environmental Monitoring was performed in Grade A interventions to collect/dispense 7 EM plates and subsequent personnel monitoring was recorded as completed at after initiation of the intervention.
- Undocumented interventions into the Grade A unit, related to collection and distribution of EM plates was observed in the batch records and Personnel Monitoring Details as far back as February 2019.
- Filling batch records from 2018 and 2019 documented Environmental interventions as short as respectively.

No investigation was initiated during quality review to determine if these interventions negatively impacted product quality. Filling room Environmental Monitoring locations include 7 inside of the grade A unit and 14 outside of the grade A unit in the immediate vicinity. For comparison on 17 February 2020, EM sampling was observed to require of grade A and of
intervention time was required to complete the immediate vicinity EM monitoring before the grade A unit was fully closed.

**OBSERVATION 2**

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

Specifically, Performance requalification approved by quality on 10 February 2020, for the airflow visualization of the grade A filling unit does not appropriately correspond to filling processes or document all critical aspects of unidirectional airflow. For Example:

- Protocol, BM/PDP/RQ/P/067-01, lists acceptance criteria in sections 10.3 and 10.4 to exclude lower quality air from outside or after contacting the operator. Interventions for periodic component replenishment were marked as “Satisfactory”, however, the video files for visualizations under dynamic conditions did not demonstrate the acceptance criteria were met during periodic component replenishment of stoppers.
- Air flow visualization videos provided did not correspond with periodic component replenishment intervention times observed in batch records.

**OBSERVATION 3**

The responsibilities and procedures applicable to the quality control unit are not in writing and fully followed.

Specifically,

- Equipment Qualification SOP BM/QA/SOP/057, states that operational qualification includes “…verification that all aspects of an equipment which can affect product quality, operate as intended...”
throughout all anticipated ranges...". Your firm’s quality department was unable to provide an operational qualification for the integrity tester used for intervention [b][4] which are part of your firm’s grade A filling unit.

- Your firm opened CAPA - BM / CAPA / QA – 19 – 088 to investigate out of trend results from a product quality review conducted for the period of April 2018 to March 2019. Your firm’s quality department closed this CAPA in November 2019 without completing the derivative investigations, corrective actions and effectiveness checks.