GMP Trends

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NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

To: Responsible Person, Director of Quality Assurance

FIRM NAME	STREET ADDRESS
Pharmaceutical and Related Industries	5600 Regulation Lane
CITY, STATE AND COUNTRY	TYPE OF ESTABLISHMENT INSPECTED
United States of America and Worldwide	Pharmaceutical and Medical Device

DURING A REVIEW OF INSPECTION REPORTS OF U.S. FIRMS (I) (WE) OBSERVED:

MANUFACTURING-STERILE PRODUCT CONTROLS

1. …..The number of containers to be sampled is not based upon appropriate criteria.

   Specifically, your firm fails to execute an adequate incoming glass vial sampling scheme based on the evaluation of deviation investigations, customer complaints and on-site audit findings at the supplier site.

   a. Field Alert Reports ….. were submitted to the FDA due to glass vial defects found in finished products confirmed by your customer complainant sample investigation. Your firm failed to evaluate your existing incoming glass vial sampling scheme based on product market experience and investigation findings.

   b. A "for-cause" on-site audit of your glass vial vendor performed by your regional office found ….. deficiencies. Your firm failed to evaluate your existing incoming glass vial sampling scheme based on these audit findings.

2. …..The quality control unit lacks responsibility to approve and reject all procedures or specifications impacting on the identity, strength, quality, and purity of drug products.

   Specifically, the ….. shut down for maintenance and repairs was not performed under formal change control procedures. The firm performed numerous activities including ….. There is no QA assessment of the activities to be performed to determine if they impact validated systems. Furthermore, there is no formal release of the facility back into production by QA based on review of required cleaning, environmental monitoring, and media fills.

3. …..Investigations into out of specifications of water test results and environmental monitoring excursions of the aseptic core area and personnel do not thoroughly assess product impact or root causes.

   Specifically, Environmental Impact Report (EIR) ….. was issued for an environmental monitoring action limit excursion for a filling operator involved in the filling of lot ….. The sample collected from the filling operator's chest exceeded the action limit of ….. cfu/plate. The investigation did not extend to the activities of the filling operator prior to the environmental monitoring excursion. There is no documentation within the batch record to identify the filling operator's activity such as involvement in interventions during the fill.

4. …..Procedures to prevent microbiological contamination of drug products are not established and followed.

   SOP ….., Aseptic Processing Events (Interventions and Activities), establishes that both planned and unplanned process interventions may occur as part of the manufacturing process. Despite the establishment of the aforementioned procedure, the Validation Engineer confirmed that the airflow pattern evaluations did not include an assessment of major and minor manual interventions that are commonly performed during aseptic filling operations and media fills.

5. …..Aseptic process areas are deficient regarding the system for monitoring environmental conditions.

   Specifically, current procedures and practices for the monitoring of surfaces in aseptic filling room ….. do not assure that the tools most frequently used in the execution of interventions during the aseptic filling are surface-sampled at the conclusion of filling operation.

6. …..Your firm has not established scientifically sound specifications for in-process and finished drug products.

   Specifically, SOP ….., Environmental Monitoring, states the action limits for viable particles which would result in an investigation. The action limit for the mold action limit is ….. However, the mold action limit is based on statistical analysis of historical data and not on a scientific rationale that explains the desired characteristics of the clean environment.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE	DATE ISSUED
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