FDA Compounding Quality Center of Excellence Working Together for Patient Safety

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Why are we here?

Insider's look into how best to respond to

FDA 483 observations

Why is This Important?

- Protect Public/Patient Health
- Ensure Availability of Quality Pharmaceuticals
- Ensure Building Quality into System
- Achieve Better Understanding of Your Operations
- Meet Regulations and Requirements

Scenario

- FDA Investigators conducted an inspection of your 503B facility and operations
- Your firm was issued a FORM FDA 483 and additional deficiencies were discussed but not documented on the FDA 483
- How should you respond to the inspection and findings?

How to Respond to the Agency?

- Follow Guidance Provided by the FDA Investigators
- Provide Adequate Corrective Actions that Address Deficiencies
- Comprehensive and Well Organized
- Timely: Respond within 15 Business Days

LET’S DISCUSS A FEW EXAMPLES…

Your firm failed to establish an adequate quality control unit with the responsibility and authority to approve or reject all components, drug product containers, closures, in-process materials, packaging materials, labeling, and drug products. (21 CFR 211.22(a)).

- Quality Control Unit (QCU) failed to investigate to prevent the distribution to patients of the following drug product lots which did not pass sterility testing.
- QCU did not review and approve production records such as: sterility test results, analytical method validation, aseptic processing simulation, and cleaning logs.

Your firm failed to have buildings used in the manufacture, processing, packing, or holding of drug products with adequate space for the orderly placement of equipment and materials to prevent mix-ups and contamination (21 CFR 211.42(b)).

- The facility design allowed the influx of poor-quality air into a higher classified area.
- The facility was designed in a way that permits poor flow of personnel or materials.

No evaluation has been performed to show the adequacy and efficacy of the cleaning and disinfection process used to produce aseptic conditions (21 CFR 211.42(c)(10)(v)).

- A sporicidal agent is applied to surfaces with a 15-minute contact time. Manufacturer's labeling requires a 30-minute contact time.

Failure to exercise appropriate controls over computer or related systems to assure that only authorized personnel institute changes in master production and control records, or other records (21 CFR 211.68(b))

- Insufficient control over data and software used during production
- Data, which per SOP are required to be protected and verified, were not protected from manipulation; SOP did not contain audit trail provisions
- Document control not maintained as multiple versions of spreadsheets were found on computers used by the quality staff
- Software used to run equipment not qualified at the time of installation
- Software not password protected
- Technicians stated that they are able to override the software to make setting adjustments during production and changes are not documented or saved

Your firm failed to establish and follow appropriate written procedures that are designed to prevent microbiological contamination of drug products purporting to be sterile, and that include validation of all aseptic and sterilization processes (21 CFR 211.113(b)).

- Inadequate Smoke Study
- Not conducted under dynamic conditions
- Smoke not sufficient enough to visualize airflow pattern
- Study did not demonstrate unidirectional air flow
- Study did not cover the entire length and height of the HEPA filters in the ISO 5 work area

Summary:
What Should Your Response Include?

- Documentation/Evidence
- Immediate Action: Correction and Resolution
- Actions Completed
- Actions Planned

Ultimately, our shared goal …

WORKING TOGETHER FOR PATIENT SAFETY


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