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ESTABLISHING A PHARMA ENVIRONMENTAL MONITORING PROGRAM

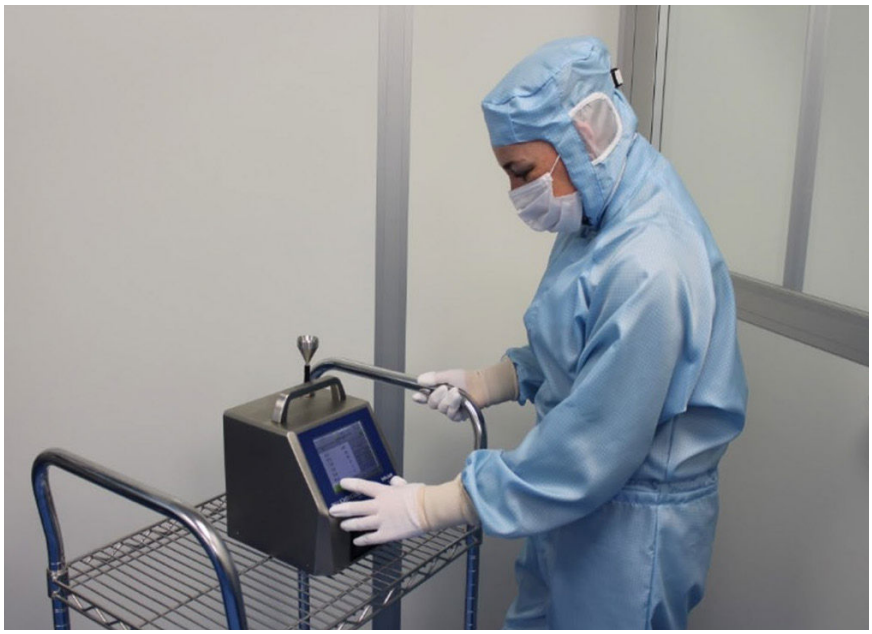
Lighthouse Worldwide Solutions

Overview

The United States Pharmacopeia (USP) Chapter 797 provides a comprehensive framework for compounding sterile preparations (CSPs) to ensure patient safety and product quality. This paper aims to provide an in-depth understanding of USP 797, focusing on its relevance and implementation in aseptic manufacturing environments. By incorporating real-world examples and textual references, the paper aims to elevate the reader's understanding to a high level, particularly in the context of cleanroom applications and the susceptibility of aseptic products to contamination.

The importance of an EM Program

"In aseptic processing, one of the most important laboratory controls is the environmental monitoring program. The EM program provides meaningful information on the quality of the aseptic processing environment (e.g., when a given batch is being manufactured) as well as environmental trends of ancillary clean areas. Environmental monitoring should promptly identify potential routes of contamination, allowing for implementation of corrective actions before product contamination occurs. The EM program should document the state of control for each environment being monitored. Data trending is a significant monitoring tool to verify the control levels are adhered to.



Identifying Sample Sites

According to the FDA the following applies; "It is important that locations posing the most microbiological risk to the product be a key part of the program. It is especially important to monitor the microbiological quality of the critical area to determine whether or not aseptic conditions are maintained during filling and closing activities. Air and surface samples should be taken at the locations where significant activity or product exposure occurs during production. Critical surfaces that come in contact with the sterile product should remain sterile throughout an operation. When identifying critical sites to be sampled, consideration should be given to the points of contamination risk in a process, including factors such as difficulty of setup, length of processing time, and impact of interventions... "All environmental monitoring locations should be described in SOPs with sufficient detail to allow for reproducible sampling of a given location surveyed. Written SOPs should also address elements such as:

1. Frequency of sampling,
2. When the samples are taken (i.e., during or at the conclusion of operations),
3. Duration of sampling,
4. Sample size (e.g., surface area, air volume),
5. Specific sampling equipment and techniques,
6. Alert and action levels, and
7. Appropriate response to deviations from alert or action levels."

"Microbiological monitoring levels should be established based on the relationship of the sampled location to the operation. The levels should be based on the need to maintain adequate microbiological control throughout the entire sterile manufacturing facility. .. Environmental monitoring data will provide information on the quality of the manufacturing environment."

Cleanroom Classification ; New ISO 14644-1:2015

- Routine cleanroom particle counting for classification,
- Risk based approach (once in every 6 to 12 months),
- Certain no# of sampling locations,
- Certain volume of air to be sampled at each location.

Should you follow ISO 14644-2 Guidelines?

ISO 14644-2 emphasizes the need to consider a monitoring strategy in addition to the initial or periodic execution of the classification of a cleanroom or clean zone in accordance with ISO 14644-1:2015.

ISO 14644-2:2015 stipulates that in order to gain assurance that a cleanroom/zone is performing, a monitoring plan shall be created, implemented and maintained.

The Development of a Monitoring Plan

- Perform a risk assessment to understand, evaluate and document the potential for adverse contamination events.
- Develop a written monitoring plan.
- Review and approve the plan.
- Implement the plan by performing the monitoring.
- Analyze, trend (where appropriate) and report performance.
- Document and implement actions or corrective actions required.
- Perform periodic reviews of the monitoring plan.

Factors to Consider in Selecting Sites for Routine Surveillance Are:

- At which sites would microbial contamination most likely have an adverse effect on product quality?
- What sites would most likely demonstrate heaviest microbial proliferation during actual production?
- What sites would represent the most inaccessible or difficult areas to clean, sanitize, or disinfect?
- What activities in the area contribute to the spread of contamination?
- Would the act of sampling at a given site disturb the environment sufficiently to cause erroneous data to be collected or contaminate product?

ISO 14644-2:2015 Reclassification Intervals

Manufacturers should ensure that:

- For ≤ISO 5 areas, the maximum time interval for requalification is 6 months. The 6 month time interval may be extended to 12 months when the area is equipped with a continuous monitoring device, and providing the results of continuous monitoring remain within specified limits.
- For >ISO 5 areas the maximum time interval for requalification is 12 months.

What Should Be Monitored?

Air Samples

- Total Particulates in the air sample
- Particle Counts (0.5µm in diameter or larger)
- Viable particles (typically bacterial and fungal spores)
- Settle Plates (Passive Air Sampling)
- Air Samplers (Active Air Sampling)

Surface Samples (Viables)

- Facilities (including walls, floors, etc.) and Instruments
- Contact Plates
- Swabs
- Personnel (Gloves, garment, etc.)

Frequency of Monitoring

- Methods: settle plates, volumetric air and surface sampling (e.g. swabs and contact plates).
- Surfaces and personnel should be monitored after critical operations.
- Include monitoring results in batch documentation for finished product release.
- Microbiological monitoring is also required outside production operations, e.g. after validation of systems, cleaning and sanitization.
- Appropriate alert and action limits should be set for the results of particulate and microbiological monitoring.