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Abstract

In the biopharmaceutical manufacturing environment, Environmental Monitoring (EM) provides continuous trending, while the Disinfectant Efficacy Study (DES) provides validation data to assist with process evaluation and improvement. The EM processes need to be designed to identify excursions (biological and numerical), recurrent and objectionable organisms and trends. The process should assess cleaning protocols based on data collected. The information acquired through EM and DES helps to determine if processes are effective. When issues with contamination are encountered, Root Cause Analysis and Corrective Action must be implemented. The EM and DES processes, when performed and evaluated consistently, and together will help ensure that manufacturing environments are in a state of control and that the sterile and aseptic environments where the products are manufactured do not cause the product to be harmful or adulterated.

Introduction

Environmental monitoring- The process of collecting meaningful data from environmental samples (i.e. air, surface, water, gas) collected from within the manufacturing space is a vital part of demonstrating a facility and equipment are adequately cleaned and maintained.

Disinfectant Efficacy Study- A test that is designed to mimic the scope of the cleaning that will provide further assurance (or reveal areas of concern), through data, to assess if the cleaning is effective.

The term “process” is intentional as it denotes a progressive, ongoing, endless evaluation. The process will likely be modified for improvement as data is collected and evaluated over time. Both the EM and DES could be subject to modification via the continuing evaluation, through process improvement.

Components of the DES Matrix- Representative surfaces, disinfectants, organisms, and contact time

Common Surfaces:
Stainless Steel (304, 316), Glass, Lexan/Acrylic, uPVC, FRP, Epoxy Paint, Epoxy Floor, Vinyl, Latex

Uncommon Surfaces: High Modulus Rubber, Anodized Aluminum, Ceramic, Polystyrene, Chrome, Neoprene, Hypalon, Silicone

Disinfectants: Sodium hypochlorite, Alcohol, Phenols, Peracetic acid, Hydrogen peroxide, Quaternary ammonium

Organisms: Bacteria- Gram positive rod spore, Gram positive cocci, Gram negative rod; Fungi- Yeast, Mold spore

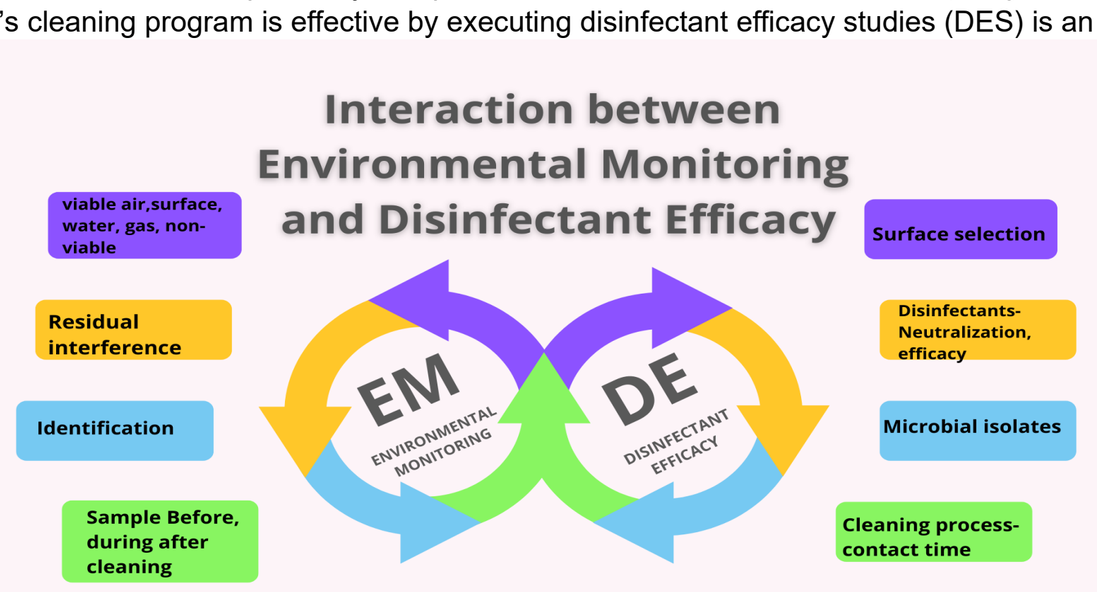
Contact time: Per manufacturer’s recommendation or internal procedures. Wet contact times are recommended for the sake of consistency and control in the laboratory environment. Mechanical action (i.e. wiping) will improve the effect of the cleaning and is not utilized when an evaluation of the disinfectant effectiveness only is being evaluated.

Does Disinfection Influence Your Environmental Monitoring (EM) Data?
or
Does Your EM Data Influence Your Disinfection Protocols?

The answer to these questions are yes, and yes. The two subjects co-exist within pharmaceutical aseptic and sterile manufacturing environments. Just like cogs of a set of gears that are joined together, changes to one part of the system will cause changes to another part. It's important to understand how they impact each other and how that can be utilized to enhance your entire facility validation and manufacturing processes.

Bio/Pharmaceutical companies, and companies planning to build new facilities, require a comprehensive cleaning program that includes **disinfection and environmental monitoring (EM)**. To comply with FDA 21CFR Part 210 & 211 or other regulations, these processes must be in a state of control.

When an EM sample shows growth, it's critical to understand the impact on your operation. Once excursions are identified, they must then be investigated and appropriate actions taken to mitigate the issue. Demonstrating your facility's cleaning program is effective by executing disinfectant efficacy studies (DES) is an essential part of the on-going plan.



Environmental Monitoring

When objectionable organisms are isolated- Compare with finished product testing results, identify root cause.

Isolates are NOT common- Is it a seasonal occurrence or a unique organism? Determine the likely source (human, environment, other)

Isolates are common or frequent – Determine the likely source (human, environment, ingredient or raw materials, other). Continue routine monitoring.

Further EM Evaluation needed:

When facility changes are made- Add relevant new sites to the EM program

The action limit was exceeded- Perform investigation to determine root cause and an effective Corrective Action

Check cleaning logs, activity in area, confirm valid result, check bracketing data for trends

Evaluate DE matrix- perform additional testing as needed.

Disinfectant Efficacy

Challenge disinfectants - With new, frequent isolates, and objectionable organisms
Include product contact surfaces, hard to clean surfaces, and significant adjacent surfaces

Further DES Evaluation needed when:

- Regulatory inspection results in a finding or a significant breach is found
- Formulation/dilution/expiration changes are made to a disinfectant preparation
- Cleaning process changes (dwell time, application method)
- Supply issues resulting in substitutions (different water type, mop/wipe material, or a disinfectant is on backorder)- It's prudent to anticipate these changes and incorporate worst case scenarios upon initiating a DES to avoid additional testing later. Perform Risk Assessment

When facility changes occur - new construction, renovation, new equipment add new surface to DES matrix, Add to EM scope

Author:

Diane Lockard, Group Leader III,
Eurofins Lancaster Labs LLC

Presenter:

Nyssa-Marie Finegan, Sr. Scientist
Eurofins Lancaster Labs LLC

Components of the EM Program- Viable air and surface samples, non-viable particle counts, water, gas (i.e. compressed air, nitrogen) samples

Viable Samples: **Agar plates/strips or flocked swabs used to assess the microbial load in a specified area (i.e. 25cm^2). Air/Gas samples are collected by passing a specified volume of air over an agar plate using a machine (active sampling) or allowing the air to settle for a period onto the plate (passive sampling).**

Non-viable samples:
Measures the particles present in a quantified volume of air that are of a specific size.

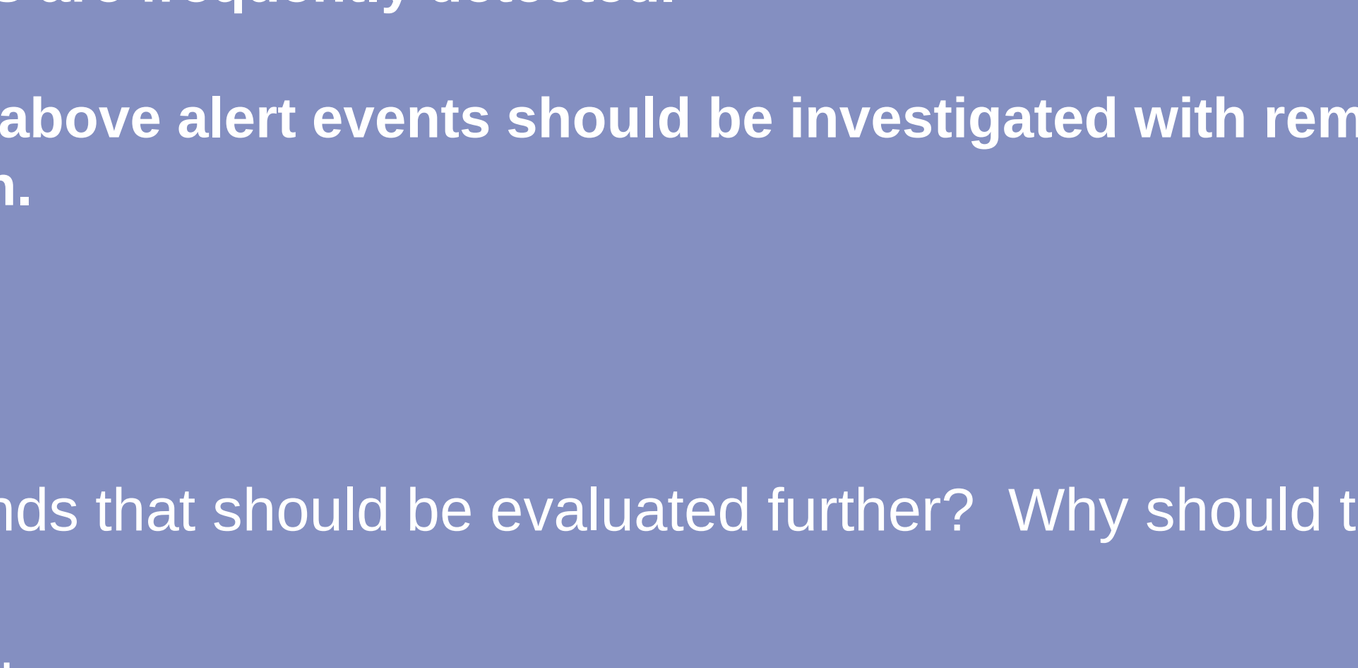
Water samples:
Incoming water, Purified water, Highly purified water, Water for injection- Each type has attributes that need to be evaluated. Consult the applicable regulatory Compendia for details.

Alert and Action Limits:
Limits should be based on achievable data and desired classification. Trend analysis may necessitate adjusting the limits lower if data demonstrates that an area consistently achieves results well below the limit. On the other hand, the analysis may show that the process needs adjusting if deviations are frequently detected.

Multiple consecutive above alert events should be investigated with remediation to prevent an action level excursion.

Trend Analysis:

Can you spot any trends that should be evaluated further? Why should they be evaluated?*
Alert limit = 35 CFU
Action Limit = 50 CFU
*The yellow line has multiple data points in consecutive order that are increasing (although below the alert limit). This trend should be evaluated before an excursion occurs.



Conclusions/Observations

A comprehensive contamination control strategy is crucial for regulatory compliance and operational excellence in facility cleaning and environmental monitoring. Facilities need to follow a structured approach involving ongoing monitoring and show adaptability to changes based on data acquired from the EM and DES evaluations. The involvement of stakeholders and adherence to protocols ensure a clean and safe environment, meeting regulatory scrutiny and supporting optimal operations.