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Board of Registration in Pharmacy

Policy 2019-08: Sterile Compounding Pharmacy Response to Above Action Level Environmental Monitoring Results

Purpose & Scope:

All sterile compounding pharmacies licensed by the Board of Registration in Pharmacy (Board) must report, respond to, and properly remediate above action level environmental monitoring (EM) results in ISO classified spaces in accordance with the terms of this policy.

This policy pertains to any Massachusetts licensed pharmacy that compounds sterile preparations to be dispensed into or from the Commonwealth.

Definition:

Above Action Level Environmental Monitoring Results are defined as EM results of non-viable air and viable air and surface meeting or exceeding the criteria as outlined below.

Non-Viable Air Sample Action Levels:

ISO Class 5	> 3520 particles 0.5 µm or larger per cubic meter of air
ISO Class 7	> 352,000 particles 0.5 µm or larger per cubic meter of air
ISO Class 8	> 3,520,000 particles 0.5 µm or larger per cubic meter of air

Viable Air Sample Action Levels (cumulative count):

ISO Class 5	> 1 CFU
ISO Class 7	> 10 CFU
ISO Class 8	> 100 CFU
Highly pathogenic microorganisms, including gram-negative rods, coagulase positive staphylococcus, and fungi	≥ 1 CFU

Surface Sample Action Levels (cumulative count):

ISO Class 5	> 3 CFU
ISO Class 7	> 5 CFU
ISO Class 8	> 50 CFU
Highly pathogenic microorganisms, including gram-negative rods, coagulase positive staphylococcus, and fungi	≥ 1 CFU

I. Required Board Notification

The pharmacist Manager of Record or his/her pharmacist designee is required to notify the Board of above action level EM results utilizing the Above Action Level EM reporting forms:
https://www.mass.gov/lists/reporting-forms-for-the-board-of-registration-in-pharmacy

II. Response to Above Action Level Environmental Monitoring Results

a. Upon notification of above action level EM results, a pharmacy must immediately assess and investigate above action level EM results and **must not prepare any compounded sterile products (CSPs) until a remediation plan of the affected area(s) is initiated**.
b. A pharmacy must properly remediate viable above action level EM results as outlined below (see Section III below, "Proper Remediation").
c. If there is a significant loss of control in an ISO-5 classified area, the pharmacy must recall any CSPs that are within their BUDs, perform adverse event surveillance, contact prescriber(s), and engage a microbiologist, industrial hygienist, or infection control professional. A

significant loss of control is defined as any excursion > 15 CFU recovered from any ISO-5 sample (adapted from USP <1160>).

d. A pharmacy must suspend compounding for above action level non-viable particle counts until remediated.
e. Pharmacies shall adhere to section IV below: “Requirements for Sterile Compounding During Remediation".
f. Pharmacies suspending sterile compounding activities must implement the pharmacy’s continuity of care plan to ensure patients’ needs are met during the remediation process.
g. A pharmacy with a repeat above action level EM result (consecutive or non-consecutive) for the same ISO-classified area occurring within 60 days must engage a microbiologist, industrial hygienist, or infection control professional.
h. The Board recommends that licensees review the “Remediation Considerations for Handling Above Action Level Environmental Monitoring (EM) Results” document for assistance with evaluation and remediation of above action level EM results including adverse event surveillance of dispensed CSPs.

III. Proper Remediation

Proper remediation is demonstrated through microbiology reports indicating that repeat EM results have been restored to within action levels as defined in this policy, and includes, at a minimum, the following elements:

a. Root Cause Analysis (RCA)

i. A pharmacy must conduct an investigation into the root cause of any above action level EM result or adverse trend in environmental monitoring.

b. Repeat Environmental Monitoring

i. A pharmacy must demonstrate successful remediation by performing repeat EM of air and surface. The pharmacy may limit the repeat EM to the affected ISO classified space based on the pharmacy’s EM sampling plan unless otherwise directed by the Board. All sample locations in the affected ISO classified space must be resampled.
ii. If the repeat EM falls within the action levels of this policy, the pharmacy may resume its standard BUDs or resume compounding, as applicable.

iii. If the repeat EM yields above action level results, the pharmacy shall follow section II above, “Response to Above Action Level Environmental Monitoring Results”.

c. **Corrective Action and Preventative Action (CAPA) Plan** must, at a minimum, include:
   i. Documentation of actions taken as result of the investigation into the RCA (e.g. triple clean, retraining, increased EM monitoring, etc.).
   ii. Repeat EM (resampling) and microbiology report review.

IV. Requirements for Sterile Compounding During Remediation

After initiation of remediation efforts, a pharmacy may consider resuming sterile compounding depending on the ISO-classified area (see below) and nature of the excursion, provided that:

a. The pharmacy has immediately assessed the above action level EM results, developed and implemented a remediation plan, and scheduled repeat monitoring.
b. The pharmacy has conducted a risk assessment which must include, but not be limited to:
   i. Type of compounding conducted (i.e. contamination risk level);
   ii. Frequency of EM and a thorough review of the EM excursion and trending history;
   iii. Personnel monitoring (i.e. operator failure of glove fingertip or media fill test); and
   iv. Product defect reports (i.e. failed sterility test).
c. The pharmacy has evaluated product risk and implemented an appropriate risk mitigation plan

ISO Class 5 Area(s):

a. A pharmacy shall not resume compounding in an ISO Class 5 primary engineering control (PEC) following an above action level EM result until remediation is completed and proven by microbiology reports of repeat EM demonstrating results within action levels.
b. If the pharmacy has multiple ISO Class 5 PECs within the compounding area, the pharmacy may continue to compound in the

unaffected ISO Class 5 PEC(s) if the results of the pharmacy's risk assessment deems appropriate.

c. If the pharmacy has only one ISO Class 5 PEC within the compounding area or has a clean room design consisting of custom built (non-commercially manufactured) "open" ISO Class 5 designs, including integrated vertical flow ISO Class 5 workbenches, any CSPs compounded in the ISO Class 5 environment **must follow the requirements for "Immediate Use CSPs"** as defined in the most current chapter of USP <797>.

ISO Class 7 Area(s):

Unless otherwise directed by the Board, a pharmacy choosing to resume compounding of CSPs during remediation of above action level results in an ISO Class 7 area **must limit the BUDs for CSPs to 24 hours room temperature or 3 days refrigerated** until the repeat EM reports demonstrate results within action levels.

ISO Class 8 Area(s):

Until the repeat EM reports demonstrate results within action levels or unless otherwise directed by the Board, a pharmacy choosing to resume compounding of CSPs during remediation of above action level results in an ISO Class 8 area **must limit the BUDs for CSPs to:**

a. **24 hours room temperature or 3 days refrigerated** if prepared from one or more **nonsterile** starting component(s); or
b. **30 hours room temperature or 9 days refrigerated** if prepared from **sterile** starting component(s).

V. Documentation

All reports and documentation related to above action level environmental monitoring results, including risk assessment and subsequent remediation activities, must be maintained in the pharmacy's records and available for Board inspection.

Please direct any questions to: **Pharmacy.Admin@MassMail.State.MA.US**