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Board of Registration in Pharmacy

Policy 2023-09: Action Level Environmental Monitoring Results

Purpose & Scope:

All sterile compounding pharmacies, including institutional sterile compounding pharmacies licensed by the Board of Registration in Pharmacy ("Board") must report, respond to, and properly remediate action level environmental monitoring ("EM") results in ISO Classified areas in accordance with the terms of this policy. This policy pertains to any Board licensed pharmacy that compounds sterile preparations to be dispensed into, within, or from Massachusetts.

Action Level Environmental Monitoring Results are defined as EM results of non-viable air as well as viable air and surface meeting or exceeding the criteria as outlined below. Action levels are based on the cumulative counts of all CFUs and non-viable particles recovered from all sampling locations within a specific ISO Classified area.

A microbiologist, or similarly qualified professional, must be engaged to identify (to the **species** level) any microbial growth resulting from EM in an ISO Class 5 area, ISO Class 7 **buffer room**, or **any action level growth** in any other ISO Classified areas. The microbiologist/qualified professional must also be engaged to guide remediation activities, particularly for organisms they find to be of concern.

****Action levels for any pass-throughs would be in accordance with the ISO classification of the cleaner space.

Non-Viable Air Sample Action Levels (cumulative count):

ISO Class 5	> 3520 particles 0.5 µm or larger
ISO Class 7	> 352,000 particles 0.5 µm or larger
ISO Class 8	> 3,520,000 particles 0.5 µm or larger

Viable Air Sample Action Levels (cumulative count):

ISO Class 5	> 1 CFU
ISO Class 7	> 10 CFU
ISO Class 8	> 100 CFU

Surface Sample Action Levels (cumulative count):

ISO Class 5	> 3 CFU
ISO Class 7	> 5 CFU
ISO Class 8	> 50 CFU

I. Required Board Notification

The Manager of Record, Designated Pharmacist-in-Charge, or their pharmacist designee is required to notify the Board of action level EM results utilizing the Action Level Environmental Monitoring Results reporting form.

II. Response to Action Level Environmental Monitoring Results

A. Upon notification, a pharmacy must immediately assess and investigate action level EM results and **must not prepare any compounded sterile products ("CSPs") until a remediation plan of the affected area(s) has been initiated or completed as required below**.
B. A pharmacy must properly remediate action level EM results as outlined in Section III below, "Proper Remediation".
C. If there is a significant loss of control in an ISO Class 5 area, the pharmacy must recall any CSPs that are within their BUDs, perform adverse event surveillance, contact prescriber(s), and engage a qualified microbiology professional. A significant loss of control is defined as any excursion **>15 CFU recovered from any ISO Class 5 area** (adapted from USP <1160>).
D. Unless otherwise directed by the Board, a pharmacy must suspend compounding for action level non-viable particle counts until fully remediated and all ISO Classified areas are recertified.
E. Except for action level non-viable particle counts, pharmacies shall adhere to section IV below: "Requirements for Sterile Compounding During Remediation of Viable Action Levels" if they choose to compound 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 action level EM result (consecutive or non-consecutive) in the same ISO Classified area occurring within 60 days must engage a qualified microbiology professional.
H. The Board recommends that licensees review the "Action Level Environmental Monitoring Remediation Considerations" document for assistance with evaluation and remediation of action level EM results including adverse event surveillance of dispensed CSPs.

III. Proper Remediation

Proper remediation is demonstrated when the results of repeat EM sampling indicate restoration to below action levels as defined in this policy, and includes, at a minimum, the following elements:

A. **Root Cause Analysis ("RCA")**
A pharmacy must investigate the root cause of any 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 area based on the pharmacy's EM sampling plan unless otherwise directed by the Board. All sample locations in the affected ISO Classified area must be resampled at the same time.
ii. If the repeat EM falls below the action levels of this policy, the pharmacy may resume its standard BUDs or resume compounding, as applicable.
iii. If the repeat EM yields action level results, the pharmacy shall follow section II above, "Response to Action Level Environmental Monitoring Results".
C. **Corrective Action and Preventative Action ("CAPA") Plan** must, at a minimum, include:
i. Documentation of remedial actions taken (e.g., triple clean, retraining, increased EM monitoring, replaced HEPA filter, etc.).
ii. Repeat EM (resampling) and microbiology report review.

IV. Requirements for Sterile Compounding During Remediation of Viable Action Levels

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

A. The pharmacy has immediately assessed the action level EM results, developed, and implemented a remediation plan, and scheduled repeat sampling.
B. The pharmacy has conducted a risk assessment which must include, but not be limited to:
    i. Type of compounding conducted (e.g., contamination risk level, complexity of compounding, etc.);
    ii. Frequency of EM and a thorough review of the EM excursion and trending history;
    iii. Personnel monitoring (i.e., failure of glove fingertip or media fill test);
    iv. Product defect reports (i.e., failed sterility test);
C. The pharmacy has evaluated product risk and implemented an appropriate risk mitigation plan; and
D. BUDs may not exceed those listed below for each ISO Classified area.

ISO Class 5 Area(s):

A. Except as indicated below, a pharmacy shall not resume compounding in a specific ISO Class 5 primary engineering control ("PEC") following an action level EM result until proper remediation has been completed.
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 deem it appropriate.
C. If the pharmacy has only one ISO Class 5 PEC, 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, **only "Immediate Use CSPs"** as defined in the most current chapter of USP <797> may be compounded (if absolutely necessary) in the affected ISO Class 5 area until proper remediation has been completed.

ISO Class 7 Buffer Room(s):

Until proper remediation has been completed or unless otherwise directed by the Board, a pharmacy choosing to resume compounding during remediation in an ISO Class 7 buffer room **must limit the BUDs for all CSPs to 24 hours room temperature or 4 days refrigerated**.

ISO Class 7 Area(s) (except buffer rooms) and ISO Class 8 Area(s):

Until proper remediation has been completed or unless otherwise directed by the Board, a pharmacy choosing to resume compounding during remediation in any ISO Class 7 area (except buffer rooms) or ISO Class 8 area **must limit the BUDs to:**

A. **24 hours room temperature or 4 days refrigerated** if prepared from one or more **nonsterile** starting component(s); or
B. **4 days room temperature or 10 days refrigerated** if prepared from **sterile** starting component(s).

V. Documentation

All reports and documentation related to 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.

Authority: M.G.L. c. 112 § 39G

Please direct any questions to: **Pharmacy.Admin@mass.gov**