Massachusetts Board of Registration in Pharmacy

Recommended Pharmacy Response to Above Action Level Environmental Monitoring Results

I. Purpose
Based on recommendations from the Advisory Sub-Committee on Abnormal Results to the Board of Registration in Pharmacy (Board), guidance has been developed regarding proper response and successful remediation of above action level environmental monitoring (EM) results.

II. Definition: Above Action Level Environmental Monitoring Results

Above Action Level Environmental Monitoring Results:
Environmental monitoring results for non-viable air and viable air and surface meeting or exceeding the criteria as outlined in USP <797>.

III. Required Board Notification: Above Action Level Environmental Monitoring Results

Initial Notification:
In accordance with 247 CMR 6.15, the pharmacist Manager of Record or his/her pharmacist designee is required to notify the Board via email at abnormalresults@MassMail.State.MA.US within 7 business days of receiving notification* of above action level environmental monitoring results. Disclosure of Above Action Level Environmental Monitoring (EM) Results Form 1 should be utilized for this reporting requirement:

*The Board recommends that licensees submit the initial notification [Disclosure of Above Action Level Environmental Monitoring (EM) Results Form 1] to the Board immediately upon receipt of the final EM report.

Final Report:
The Board also requires a follow up report outlining the completed remediation plan, including the microbiology report from repeat EM within 21 days of the pharmacy’s submission of Form 1. The Disclosure of Above Action Level Environmental Monitoring (EM) Results Form 2 should be used for this purpose:
IV. Action Levels

Environmental Monitoring Action Levels (per USP <797>):

Non-Viable Air Sample Action Levels:

<table>
<thead>
<tr>
<th>ISO Class 5</th>
<th>&gt; 3520 particles 0.5 µm or larger per cubic meter of air</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISO Class 7</td>
<td>&gt; 352,000 particles 0.5 µm or larger per cubic meter of air</td>
</tr>
<tr>
<td>ISO Class 8</td>
<td>&gt; 3,520,000 particles 0.5 µm or larger per cubic meter of air</td>
</tr>
</tbody>
</table>

Viable Air Sample Action Levels:

<table>
<thead>
<tr>
<th>ISO Class 5</th>
<th>&gt; 1 CFU</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISO Class 7</td>
<td>&gt; 10 CFU</td>
</tr>
<tr>
<td>ISO Class 8</td>
<td>&gt; 100 CFU</td>
</tr>
<tr>
<td>Highly pathogenic microorganisms, including gram-negative rods, coagulase positive staphylococcus, and fungi</td>
<td>≥ 1 CFU</td>
</tr>
</tbody>
</table>

Surface Sample Action Levels:

<table>
<thead>
<tr>
<th>ISO Class 5</th>
<th>&gt; 3 CFU</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISO Class 7</td>
<td>&gt; 5 CFU</td>
</tr>
<tr>
<td>ISO Class 8</td>
<td>&gt; 100 CFU</td>
</tr>
<tr>
<td>Highly pathogenic microorganisms, including gram-negative rods, coagulase positive staphylococcus, and fungi</td>
<td>≥ 1 CFU</td>
</tr>
</tbody>
</table>
V. Response to Above Action Level Environmental Monitoring Results

A pharmacy should immediately assess and investigate above action level environmental monitoring results and should not prepare any compounded sterile products (CSP’s) until a remediation plan is developed and initiated. Repeat EM should confirm remediation efforts and state of control in the affected classified space.

A pharmacy should engage the assistance of qualified personnel, such as a microbiologist, infection control professional, or an industrial hygienist to develop a remediation plan.

A pharmacy should properly remediate above action level environmental monitoring results by conducting a thorough investigation and developing a Root Cause Analysis (RCA) and Corrective Action Preventative Action (CAPA) plan based on the results.

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.

VI. Recommended Conditions for Resuming Sterile Compounding Following an Above Action Level Environmental Monitoring Result

After initiation of remediation efforts, a pharmacy may consider resuming sterile compounding with limited BUDs1 depending on the location of the above action level result and after performing a risk assessment. The pharmacy’s risk assessment should include, but not be limited to, a thorough review of the EM excursion and trending history, personnel monitoring (i.e. operator failure of glove fingertip or media fill test), and product defect2 reports (i.e. failed sterility test).

**ISO 5 Classified Area:**

A pharmacy should not resume compounding in an ISO Class 5 primary engineering control (PEC) following an above action level environmental monitoring result until remediation is completed and proven by microbiology reports of repeat environmental monitoring demonstrating results within acceptable levels (i.e. within action levels). If the pharmacy’s design is an ISO Class 7 buffer room with multiple ISO Class 5 PECs consisting of CAI, BSC or LAFW, 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.

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1 See “Sterile Compounding During Remediation” on p.5 for limited BUD dating.

2 MGL Chapter 112 Section 39D (e) If a pharmacy knows or should have reason to know that a drug preparation compounded, dispensed or distributed by the pharmacy is or may be defective in any way, the pharmacy shall immediately recall the drug preparation. Any of the same drug preparation remaining in the possession of the pharmacy shall be located and segregated and shall not be distributed or dispensed. A defective drug preparation log documenting the recalled drug preparation shall be kept by the pharmacy.
Pharmacies with clean room designs consisting of custom built (non-commercially manufactured) “open” ISO Class 5 designs, including integrated vertical flow ISO Class 5 workbenches (vertical clean benches) should not resume compounding until proper remediation is proven by repeat environmental monitoring-microbiology reports demonstrating results within acceptable levels.

For pharmacies that suspend compounding activities, the pharmacist Manager of Record or their pharmacist designee should implement the pharmacy’s continuity of care plan to ensure patients’ needs are met during the remediation process.

**All Other ISO Classified Areas (ISO Class 7, ISO Class 8):**

**Low and Medium Risk Level:**
Upon receipt of an above action level environmental monitoring result, a pharmacy may resume compounding for **low and medium risk** level CSP’s if:

A. The current above action result does not represent the third consecutive sampling report\(^3\) with above action level results for the specific classified space; and

B. The pharmacy has immediately assessed the above action level environmental monitoring results, developed and implemented a remediation plan, and scheduled repeat monitoring; and

C. The pharmacy has evaluated product risk and implemented an appropriate risk mitigation plan (see “Sterile Compounding During Remediation” below).

**Note:** A pharmacy **should not resume compounding of low and medium risk level CSP’s** if the environmental monitoring data indicates 3 consecutive sampling reports with above action level results until remediation is completed and proven by microbiology reports of repeat environmental monitoring demonstrating results within acceptable levels.

**High Risk Level:**
Upon receipt of an above action level environmental monitoring result, a pharmacy may resume compounding for **high risk level** CSP’s if:

A. The current above action result a does not represent the second consecutive sampling report\(^4\) with above action level results for the specific classified space; and

B. The pharmacy has immediately assessed above action level environmental monitoring results, developed and implemented a remediation plan, and scheduled repeat monitoring; and

C. The pharmacy has evaluated product risk and implemented an appropriate risk mitigation plan (i.e. reduced BUDs – see below).

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\(^3\) Third consecutive sampling report is defined as two consecutive above action level results immediately preceding the current above action level result for the specific classified space.

\(^4\) Second consecutive sampling report is defined as an above action level result immediately preceding the current above action level result for the specific classified space. **Triple cleaning means the act of cleaning twice with a germicidal agent and once with a sporicidal agent in succession.**
Note: A pharmacy should not resume compounding of high risk level CSP’s if the environmental monitoring data indicates 2 consecutive sampling reports with above action level results until remediation is completed and proven by microbiology reports of repeat environmental monitoring demonstrating results within acceptable levels.

**Sterile Compounding During Remediation:**

A pharmacy choosing to resume compounding of CSP’s during remediation of above action level results should limit the BUDs for CSP’s to 24 hours room temperature or 3 days refrigerated until the repeat environmental monitoring reports demonstrate results within acceptable levels. In addition, the Board recommends that licensees conduct adverse event surveillance for all dispensed CSP’s until the affected ISO classified area(s) are properly remediated.

A pharmacy should not freeze any CSP upon receipt of an above action level environmental monitoring result until repeat monitoring reports demonstrate results within acceptable levels.

**VII. Proper Remediation**

Proper remediation is demonstrated by repeat environmental monitoring results being restored to within USP <797> action levels, and includes at a minimum the following elements:

**Root Cause Analysis (RCA):**
A pharmacy should conduct a root cause analysis in response to any above action level environmental monitoring result or adverse trend in environmental monitoring.

Note: An example RCA form may be found in the appendix.

**Repeat Environmental Monitoring:**
A pharmacy should demonstrate successful remediation by performing repeat environmental monitoring of viable air and surface (bacterial and fungal) as part of remediation to above action level environmental monitoring results. The pharmacy may limit the repeat environmental monitoring to the affected ISO classified space based on the pharmacy’s environmental monitoring sampling plan unless otherwise directed by the Board.
If the repeat EM falls within acceptable limits of USP <797>, the pharmacy may resume standard BUDs or resume compounding, as applicable.

**Corrective Action and Preventative Action (CAPA) Plan:**
The CAPA plan should, at a minimum, include:
1. Document actions taken as result of RCA
2. Triple clean with appropriate agent(s) all affected PECs and SECs (secondary engineering controls)
3. Repeat EM (resampling) and review microbiology report

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5 Triple cleaning means the act of cleaning twice with a germicidal agent and once with a sporicidal agent in succession.
4. Retraining

**Note:** An example CAPA form may be found in the appendix.

**Appendix:**
RCA Template
CAPA Template

**Adopted date:** 1/5/17
# Root Cause Analysis (RCA) Form

## 1

<table>
<thead>
<tr>
<th>Name</th>
<th>Job Title</th>
<th>Department or Group</th>
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**Who was included in the root cause analysis?** At a minimum, the following people should be involved in the process [Manager of Record, individual with the most knowledge pertaining to the specific issue, frontline staff member, specialists in the specific area (Infection Control, Microbiologist, etc.)]

## 2

**When did the event occur?** (i.e. Time period – date(s), day of the week, time of day)

**What are the details of the event?** (i.e. full event description)

## 3

**Describe the process step by step as it occurred.** The process can be written in numerical sequence or provided as a typical flow chart diagram.
Identify Root Causes
As an aid to avoiding “loose ends,” the last three columns on the right are provided to be checked off for later reference:

“Root Cause?” should be answered “Yes” or “No” for each finding. Each finding that is identified as a root cause should have an assigned action plan. Number each finding that is identified as a root cause so that it can be correlated to specific strategies.

“Contributing Factor?” should be answered “Yes” or “No” for each finding. Consider how it relates to the event and create action plans as appropriate.

“Take Action?” should be answered “Yes” for each finding of a root cause or contributing factor that can reasonably be assigned a risk reduction strategy.

<table>
<thead>
<tr>
<th>Questions</th>
<th>Factors Identified</th>
<th>Is this a root cause? (If yes, assign #)</th>
<th>Is this a contributing factor?</th>
<th>Take action?</th>
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</thead>
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Write root cause statements for each root cause.
Create a causation statement for each root cause. Write concise descriptions of the cause-and-effect relationship between the findings and the error. Ensure that the team has focused on the system-based causes and not on the actions of individuals or in any way placed blame on the individuals.

<table>
<thead>
<tr>
<th>Root Cause #</th>
<th>Statement</th>
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Create an Action Plan
For each of the root causes identified above, assign at least one strategy. To be most effective, choose strategies based on the rank order of error reduction strategies. Once strategies are identified, develop measures that will provide strategy effectiveness over time. Some measures will be straightforward (something is completed or not completed by a particular date), while others may require several steps. Interim dates for sub step completion should be established. If a decision is made not to implement an action for a particular root cause, indicate the rationale for not taking action at this time.

<table>
<thead>
<tr>
<th>Root Cause #</th>
<th>Risk-reduction strategy</th>
<th>Measure of effectiveness</th>
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</table>

<table>
<thead>
<tr>
<th>Contributing factors</th>
<th>Risk-reduction strategy</th>
<th>Measure of effectiveness</th>
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</thead>
<tbody>
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</table>
**Corrective Action and Preventative Action (CAPA) Form**

<table>
<thead>
<tr>
<th>CAPA #</th>
<th>Click here to enter text.</th>
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</thead>
<tbody>
<tr>
<td>Facility Cleanroom</td>
<td>Click here to enter text.</td>
</tr>
<tr>
<td>Issue at hand</td>
<td>Click here to enter text.</td>
</tr>
<tr>
<td>Incident date</td>
<td>Click here to enter text.</td>
</tr>
<tr>
<td>Team lead for RCA completion</td>
<td>Click here to enter text.</td>
</tr>
</tbody>
</table>

**Synopsis of events**

Click here to enter text.

**Root cause(s)**

Click here to enter text.

**Corrective action(s)**

Click here to enter text.

**Preventative action(s)**

Click here to enter text.

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**Submitted by:**

Click here to enter text.  
Date:

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**Reviewed by:**

Click here to enter text.  
Date:

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**Approved by:**

Click here to enter text.  
Date: