Viable and Non-Viable Environmental Monitoring to Meet USP <797>

Background
The USP 797 requires sterility of all Compounded Sterile Products (CSP). Environmental Monitoring is an essential component to prove that a cleanroom, or clean device, meets the defined ISO 14644-1 classifications. These classifications ensure that a designated zone is maintained in a clean state. The monitoring program is designed based upon contamination risk to finished product quality. According to USP 797, critical areas must continuously meet ISO Class 5 or better conditions for 0.5 µm particles and must exclude microbial contamination during compounding of CSPs. An effective environmental monitoring program provides meaningful information on the quality of the compounding environment and any environmental trends in surrounding areas. In addition, an effective environmental monitoring program will identify potential routes of contamination, allowing for implementation of corrections to prevent CSP contamination.

Particle Monitoring to Meet USP 797 Compliance (Non-Viable)
The Parenteral Drug Association (PDA) issued a recommendation for routine monitoring for all Aseptic Grade areas using portable particle counting devices. The recommendations are as follows:

<table>
<thead>
<tr>
<th>Air Cleanliness Classification</th>
<th>Type of Operations</th>
<th>In Operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade A - ISO 5</td>
<td>Critical aseptic preparations</td>
<td>Not less than 1 x each shift</td>
</tr>
<tr>
<td>Grade B(1) - ISO 7</td>
<td>Immediately adjacent to Grade A</td>
<td>Not less than 1 x each shift</td>
</tr>
<tr>
<td>Grade B(2) - ISO 7</td>
<td>Aseptic rooms and corridors, component storage, gowning</td>
<td>Not less than 1 x each day</td>
</tr>
<tr>
<td>Grade C - ISO 8</td>
<td>Non aseptic filling, terminally sterilized product.</td>
<td>Not less than 1 x each week</td>
</tr>
<tr>
<td>Grade D - Unclassified</td>
<td>Areas for washing and handling components.</td>
<td>Not less than 1 x each month</td>
</tr>
</tbody>
</table>

See the application note, Choosing the Most Suitable Particle Sample Point Locations in the Cleanroom.

Rooms are classified according to function.

Ante-area (Transition areas) – Must meet at least ISO Class 8 standards.

Buffer area – Must meet at least ISO Class 7 standards.

CSP preparation areas – Must meet at least ISO Class 5 standards.

ISO standards also limit the amount of particulates that can be in each class of area. See Table 2.

Viable Monitoring to Meet USP 797 Compliance
In addition to non-viable monitoring, USP 797 requires microbial or viable monitoring of CSP areas. According to the USP 797, impaction on media plates is the preferred method for viable air sampling. Settling plates that were once suggested in earlier National Formulary guidelines are not permitted in the 2008 USP 797 revision, since all sampling must now be volumetric.
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### Table 3. Viable Monitoring Frequency

<table>
<thead>
<tr>
<th>Type</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buildings and facilities certification</td>
<td>Recertification required every 6 months</td>
</tr>
<tr>
<td>Viable airborne monitoring</td>
<td>Monthly</td>
</tr>
<tr>
<td>Viable airborne monitoring for Grade A – ISO 5 ONLY</td>
<td>Daily, 1000 liters or continuous</td>
</tr>
</tbody>
</table>

-- Note --
In order to have a fully compliant ISO 5 area, monitoring must be performed each day a CSP is produced.

### Table 4. Microbial Limits Per ISO Class

<table>
<thead>
<tr>
<th>ISO Class</th>
<th>Air Sampling Action Levels (CFU/m³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>≥ 1</td>
</tr>
<tr>
<td>7</td>
<td>≥ 10</td>
</tr>
<tr>
<td>8</td>
<td>≥ 100</td>
</tr>
</tbody>
</table>


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**What Happens When Viable or Non-Viable Monitoring Is Above the Limit?**

Investigations from environmental monitoring excursions for viable and nonviable monitoring can involve more than a single product. If a sample is only taken monthly, all products made from the previous passing monitoring results can be suspect, and will require additional testing or verification of sterility.

A daily monitoring or continuous monitoring program provides a much better picture of the environment where sterile drugs are compounded.

"Prompt corrective action in response to any adverse data is essential to maintain the necessary environmental quality for CSP preparation."

USP 797 (2015 Revision)

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To help you with USP <797> compliance, **Particle Measuring Systems** recommends these products:

- **Viable**
  - MiniCapt® Mobile
  - BioCapt® Single-Use

- **Non-Viable**
  - Lasair® III

The most economical combination is:

- **Tubing**
  - Any vacuum source at 25-50 LPM
  - BioCapt Single-Use

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**References**

2. <797> Pharmaceutical Compounding - Sterile Preparations, 2015 Revision

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