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Board of Registration in Pharmacy

Advisory: Smoke Studies in ISO-Classified Areas

Based on recommendations from the Advisory Committee to the Board of Registration in Pharmacy, guidance has been developed regarding smoke visualization studies in sterile compounding ISO-classified areas. “Smoke studies” include dynamic airflow smoke pattern tests for primary engineering controls (“PEC”) and visual smoke studies for secondary engineering controls (“SEC”).

I. Purpose

Properly conducted and documented smoke studies serve as an important tool for:

- evaluating the performance of engineering controls;
- assuring proper placement of PECs and other equipment (e.g., tables, etc.) within SECs;
- assuring proper placement of equipment (e.g., automated compounding devices, etc.) within PECs;
- informing compounders about the importance of proper airflow dynamics to prevent contamination;
- tracing contamination sources as part of corrective action / preventative action (“CAPA”) investigations; and
- implementing process or design modifications to optimize sterile compounding operations.

II. Recommended Frequency

A. **PECs (dynamic airflow smoke pattern tests):**

1. upon initial certification (required by USP <797>)* and recertification of each PEC; and
2. upon the permanent addition, relocation, or removal of any equipment located within the PEC.

***** Per USP <797>: “In situ air pattern analysis via smoke studies shall be conducted at the critical area to demonstrate unidirectional airflow and sweeping action over and away from the product under dynamic conditions.”

B. **ISO-Classified SECs (visual smoke studies):**

1. upon initial certification of each SEC;
2. upon the permanent addition, relocation, or removal of any PEC or equipment located within the SEC;
3. immediately following the remodeling or change in configuration or square footage of any SEC; and
4. after any major repairs or service, or any significant maintenance to an SEC that may impact airflow dynamics (e.g., HVAC, duct work, etc.).

III. Procedural Considerations

Smoke studies should be performed in accordance with the Controlled Environment Testing Association (“CETA”) application guide (“CAG”) standards or an equivalent guideline. Sterile compounding pharmacies should consult with a qualified certification vendor or HVAC professional.

To conduct a proper smoke study, a sufficient amount of neutrally buoyant smoke is used: not too much that it overcomes the airflow pattern being observed, or too little to be able to visualize air patterns. Narrated video recordings of smoke studies are strongly recommended to properly document activities and results.

In PECs, smoke studies are conducted during simulated dynamic operating conditions. However, CETA also recommends that an “at rest” (static) smoke study be conducted at every certification to confirm that the PEC is performing as designed and is properly integrated into the facility. The simulated sterile compounding should represent the most challenging conditions encountered in the operations (e.g., highest complexity of compounding, largest number of personnel, etc.).

Smoke studies in ISO-classified SECs are not required to be performed under dynamic operating conditions.

Policies and procedures should be developed to encompass the full smoke study procedure from set-up to completion, including any needed supplies for compounding simulation, typical processes, post-smoke study cleaning and disinfecting, etc.

IV. Results

A. **PECs:**

1. Observe smoke introduced at the HEPA-filter diffuser as it flows across the critical site in the direct compounding area (“DCA”) to a return or exiting from the critical area.
    a. Air exiting the critical area should not re-enter.
    b. The supply of unidirectional HEPA-filtered airflow must be adequate to sufficiently sweep over and away from product openings, points of entry, and sterile connections to protect them from contamination.
    c. Airflow should be uniform without slow moving or stagnant air at critical sites.
    d. There should not be non-uniform airflow disturbances such as turbulence, refluxing, updrafts, “eddy” currents, or backflow that may contribute to the influx of contaminants.
    e. Room air should not enter where sterile preparations may be exposed.

2. The aseptic technique of compounding personnel must not disrupt the flow of first air to critical sites or introduce contamination.
    a. Airflow should not be blocked or disrupted by the hands or movements of compounding personnel.
    b. Material transfer and handling processes of products and supplies into and within the PEC should not interfere with the flow of unidirectional air resulting in air disturbances.

3. Ensure proper placement of any equipment and supplies.
    a. Confirm proper airflow around any compounding equipment and that the equipment placement has no adverse impact on the DCA. For compounding equipment such as automated compounding devices, there should be sufficient sweeping of air across and away from sterile connections.
    b. Verify that the layout of materials and supplies is not resulting in airflow disturbances within the DCA.

B. **SECs:**

1. The smoke should illustrate a general top-down dilution of room air with HEPA-filtered make-up air and sweeping action to the low wall-mounted returns.

a. There should be no areas of excessive turbulence, other air disturbances (e.g., updrafts, vortices, etc.), or areas of stagnant airflow where particulates can accumulate.
b. Ensure airflow to returns is not impeded or blocked by any equipment (e.g., tables, carts, etc.).

2. Observe the direction of positive or negative pressure airflow (where applicable) around all openings, doorways, and pass-throughs.
    a. Into a hazardous buffer room from the anteroom;
    b. out of a non-hazardous buffer room into the anteroom;
    c. out of the anteroom to unclassified adjacent spaces, and
    d. if applicable, other ISO-classified areas (e.g., airlock, prep room, etc.) to unclassified adjacent spaces.

3. Observe the impact of airflow on PECs.
    Cross drafts caused by traffic patterns, HVAC airflow, and opening and closing of doors should not affect the unidirectional airflow of the PEC or introduce contaminants into the PEC.

C. **Using the results:**

1. **PECs**:
    a. Enhance training procedures regarding the use of proper aseptic technique to continually improve the performance of compounding personnel.
        i. Understand the principles of HEPA-filtered unidirectional airflow within the DCA and the differences between horizontal and vertical flow PECs;
        ii. determine the proper placement and movement of hands during aseptic manipulations to maximize the flow of first air over critical sites and not disrupt airflow or introduce contamination; and
        iii. understand proper placement of equipment and supplies to maintain proper airflow.
    b. If a static smoke test was conducted, review and compare the PEC manufacturer's airflow diagrams / schematics (if available) illustrating what the airflow should look like.

2. **ISO-Classified SECs:**
    a. Educate compounding personnel of the impact on airflow dynamics in SECs when opening doors, pass-throughs, or by personnel

movements that may contribute to the ingress of contamination from less controlled areas (i.e., anteroom to buffer room, buffer room to PEC).

b. Identify any areas where there is stagnation of air or irregular airflow movement (e.g., turbulent zones, updrafts, etc.) to guide cleaning and disinfecting procedures, environmental monitoring, and any actions needed to minimize abnormal airflow conditions.

V. Documentation / Follow-up

The sterile compounding pharmacy should ensure that a description and results of each smoke study are documented in a report (e.g., certification report, etc.) and not simply a "Pass" or "Fail". Maintain the report in the pharmacy's records.

According to CETA, "a written report detailing the airflow patterns with a definitive statement or acceptability for the intended purpose should be provided." The report should include:

- clear identification of the PEC(s) and SECs;
- equipment and supplies in the DCA;
- dynamic operating conditions or static;
- number of personnel present;
- all simulated activities;
- a description of the test along with the results of the airflow pattern observation using descriptive language (e.g., sweeping, smooth, undisturbed, turbulent, etc.) should be documented for each engineering control and around every room penetration; and
- a statement of pass or fail for every test.

Video recordings may be used to further support the final written report.

A qualified professional should be contacted to investigate and implement corrective actions (e.g., repair / replacement / relocation of PECs, room rebalancing, etc.) in response to any failed smoke study results. Depending on the nature of corrective actions, recertification may be required.

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

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