CriticalPoint Pearls of Knowledge — August 2025

The Blueprint to Certification: Primary Engineering Controls

Introduction

CriticalPoint continues its certification series with an in-depth look at individual certification tests—what they are, how they're performed, and why they matter. This month's issue focuses on primary engineering controls (PECs), outlining the specific tests required for sterile compounding in commonly used devices.

USP <797> does not detail specific testing methods of varying types of PECs. It only lists the tests that must be performed under dynamic testing: total particle count testing and airflow smoke pattern testing. USP could not provide details of certification testing of all devices because it falls outside the scope of sterile preparations, and the specific tests would be too exhaustive for the document.

This month's Pearl provides the types of testing required for sterile compounding compliance not addressed in USP <797>.

Changed but not forgotten

CETA's CAG-003 Certification of Sterile Compounding Facilities for USP Compliance was written to include testing of pharmacy ISO Class 5 devices. It outlines testing protocols for laminar airflow workbenches (LAFWs), biological safety cabinets (BSCs), and restricted access barrier systems (RABSs—formerly isolators or gloveboxes).[1] The guidance also addresses cleanroom tests for sterile compounding facilities. Like USP standards, CETA's application guides (CAGs) have been revised over time to reflect current thinking on standards compliance. Ultimately, CAG testing guidance focuses on quality, consistency, and ensuring compliance.

Since the 2008 version, USP <797> has referenced the Controlled Environment Testing Association (CETA) application guides for certification testing to ensure sterile compounding compliance for sterile compounding devices and cleanrooms. However, in the 2022 revision—official November 2023—the language changed significantly from earlier versions. Previously, USP <797> Section 5. Certification and Recertification stated that facilities "must be certified using procedures in the current CETA *Certification Guide for Sterile Compounding Facilities* or an equivalent guideline."[2]

The current official version now states that facilities "must be independently certified using the requirements in this chapter and, when applicable, manufacturer specifications."[3] While the chapter outlines cleanroom testing expectation in more detail, it provides no direction on how tests should be performed or what is needed for complete certification compliance.

USP 797 (2021, never official)[2]	USP 797 (2024)[3]
Before a compounding area is used to compound either Category 1, Category 2, or Category 3 CSPs, it must be certified using procedures in the current Controlled Environment Testing Association (CETA) *Certification Guide for Sterile Compounding Facilities* or an equivalent guideline.	Before a compounding area is used to compound either Category 1, Category 2, or Category 3 CSPs, it must be independently certified using the requirements in this chapter and, when applicable, manufacturer specifications. Certification indicates that the compounding area is meeting its design and air quality specifications.

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The changes to USP <797> certification requirements introduce a concerning gap in oversight and consistency. Without a regulatory body policing certifiers, there is no guarantee that testing is performed to the same quality standards across facilities. This change potentially removes critical quality controls from certification testing and reporting, creating room for variation, oversight gaps, and even noncompliance that may go unnoticed.

Further, the responsibility for understanding and verifying the nuances of certification testing now falls entirely on the designated person (DP)—a role already burdened with broad oversight responsibilities. This shift increases the risk that critical testing elements may be missed or inadequately evaluated. Compounding the concern, the minimum certification testing listed in the chapter does not ensure that classified environments are truly suitable for sterile compounding. Without USP including references to detailed, standardized guidance, there's a real risk that certification could meet the letter of the law while falling short of protecting product quality and patient safety.

Specific testing for PECs

Testing cleanrooms and PECs isn't that different. Under USP <797>, airflow, particle count, and HEPA filter testing follow the same methodologies for both—though certain PEC types require additional, device-specific tests to challenge their unique performance characteristics.

For example, an LAFW is open-faced to the ISO Class 7 environment; therefore, lower-quality surrounding air can compromise its ISO Class 5 unidirectional airflow. Performance tests confirm it can maintain the required conditions even under less-than-ideal circumstances.

Containment engineering controls such as BSCs and RABSs must also be tested to ensure they protect both the worker and the environment while safeguarding CSP sterility. Multiple specialized tests verify proper exhaust, containment, and overall device integrity for each design.

What's often overlooked is that these devices are also used in other industries—such as micro-electronics, research, chemical manufacturing, and even e-cigarette production—where testing standards may be less stringent. For sterile compounding, however, testing for USP compliance must go further, ensuring device design and operator practices work together to protect CSPs and, ultimately, patient safety.

Laminar airflow workbench (LAFW) tests

LAFW testing primarily verifies that the unit meets the manufacturer's parameters for HEPA-filtered airflow delivery—measuring airflow speed and ensuring HEPA filters are free from leaks beyond the allowable percentage. USP compliance adds the requirement for total particle counting to confirm the environment meets ISO Class 5 under true dynamic conditions with personnel present.

Required certification tests

- Airflow velocity (manufacturer)
- HEPA filter integrity (manufacturer)
- Total particle counts (USP <797>)
- Induction leak (CAG-003)
- Backstreaming (CAG-003)

CAG-003 outlines all LAFW testing requirements, incorporating manufacturer specifications, USP standards, and other industry guidelines. The two tests specific to CAG-003 beyond USP's minimum—

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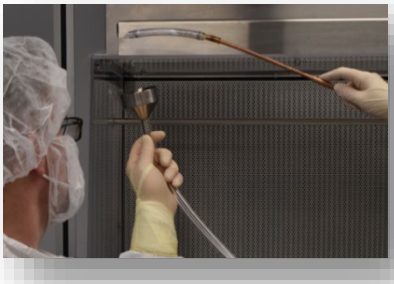
induction leak and backstreaming—are critical for ensuring the LAFW truly maintains its ISO Class 5 environment.



Induction leak testing — verifies that the LAFW work zone remains ISO Class 5 and isolates the direct compounding area (DCA) from the surrounding environment. The process uses a smoke source around the device exterior to detect potential weaknesses. The smoke must not penetrate the ISO 5 barrier, and particle counting confirms the environment remains within ISO Class 5 limits.

Backstreaming testing — ensures that the lesser-quality outside air does not enter the LAFW's interior workspace. A smoke source is moved along the front access opening, and the certifier visually confirms no smoke breaches the ISO 5 plane as it passes around the perimeter between the external environment and the work area.

Biosafety cabinet (BSC) tests

CAG-003 references NSF/ANSI 49: Biosafety Cabinetry — Design, Construction, Performance, and Field Certification for BSC testing. Annex 5 of this standard outlines the field test methods and acceptance criteria in addition to each cabinet's manufacturer-specified parameters and setpoints. While NSF/ANSI 49 serves as the primary reference for ensuring BSCs operate safely, USP compliance must also be verified when these cabinets are used for sterile compounding. Several critical certification tests for BSCs are not explicitly required by USP <797> or USP <800>, leaving potential voids that could compromise both product sterility and personnel safety.

Required certification tests

- Downflow — airflow velocity (manufacturer and NSF/Ansi 49)
- Inflow — airflow velocity (manufacturer and NSF/Ansi 49)
- Airflow pattern characteristics (NSF/ANSI 49)
- Site installation assessment (NSF/ANSI 49)
- HEPA filter integrity (manufacturer)
- Total particle counts (USP <797>)

Airflow pattern assessment

BSCs are engineered with highly specialized airflow designs to protect the environment, the workers, and the product. Despite having a front access opening, they must prevent outside, lower-quality air from entering while containing hazardous drug contaminants within the cabinet. Achieving this requires multiple airflow zones and precise directional control. This is why airflow pattern assessment is critical. Using a smoke source, the certifier evaluates airflow characteristics to confirm the BSC is delivering air properly and maintaining appropriate containment. Airflow pattern assessment involves four distinct tests, each designed to verify different aspects of the cabinet's performance.

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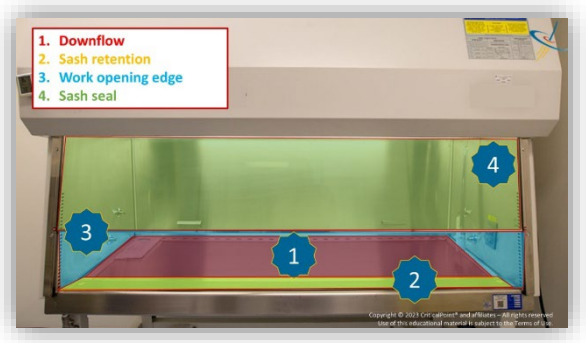
1. Downflow testing verifies a cabinet's ability to maintain unidirectional airflow across the centerline of the work surface.
2. Sash retention testing evaluates a cabinet's ability to maintain internal air quality and prevent external air from penetrating beyond the sash perimeter.
3. Work opening edge retention Testing assesses a cabinet's ability to contain interior air quality and prevent escape through the front access opening.



4. Sash seal test assesses the cabinet's ability to contain interior air quality and prevent airflow from escaping through gaps around the window sash.

Each test should be reported individually with a clear pass or fail outcome. Ideally, the report should also explain the purpose of the test and the reason for the result.

Restricted access barrier system (RABS) tests

RABS are likely less common in pharmacies today due to USP <797> changes to Category 1 compounding environments. Since RABSs no longer provide extended beyond-use dating (BUD) without cleanrooms, their use has declined. If compounding does occur in a RABS, it is usually within a segregated compounding area (SCA). Regardless of the setting, RABSs require extensive certification to demonstrate they can maintain ISO 5 conditions inside the main chamber while remaining isolated from the lesser adjacent environment.

Compounding aseptic isolators (CAIs) and compounding aseptic containment isolators (CACIs) must meet the requirements of CETA's CAG-002 Compounding Isolator Testing Guide to ensure USP compliance.[4] These devices demand specific testing focused on product transfer—from the outside environment, through the pass-through chamber, into the main chamber—without introducing contaminants above ISO 5 limits. Both certifiers and operators play a role. Certification must verify the manufacturer's operating parameters, but even a properly certified device can fail to protect CSPs if operators do not follow correct transfer procedures.

Additionally, CACIs require site installation performance testing similar to NSF/ANSI 49 BSC standards to confirm proper integration with facility exhaust systems, ensuring both external ventilation and negative containment.

Required certification tests for compounding aseptic isolators (CAIs)

- Airflow velocity (manufacturer)
- HEPA filter integrity (manufacturer)
- Total particle counts (USP <797> and CAG-002)
- Pass-through and main chamber pressure verification (manufacturer and CAG-002)
- Preparation ingress and egress – material transfer (CAG-002)
- Airflow pattern characteristics (CAG-002)

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Required Certification Tests for Compounding Aseptic Containment Isolator (CAI)

- Airflow velocity (manufacturer)
- HEPA filter integrity (manufacturer)
- Total particle counts (USP <797> and CAG-002)
- Pass-through and main chamber pressure verification (manufacturer and CAG-002)
- Preparation ingress and egress – material transfer (CAG-002)
- Airflow pattern characteristics (CAG-002)
- Site installation assessment (CAG-002)
- Particle containment integrity and enclosure leak test

The particle containment integrity test is required for negative-pressure RABSs to verify the integrity of construction joints, seams, access panels, glove ports, and entry/exit points into the main chamber—especially when elevated particle levels are detected near the work surface and other potential leak sources (e.g., damaged HEPA filters or gloves) have been ruled out. This test verifies that the chamber sustains negative pressure and proper containment without leakage through seals, gaskets, or structural joints.

CACIs that have been in service for more than 10 years often show degradation in sash seals and gaskets, making this test especially critical for confirming performance and protecting both the product and the operator.

Summary

Certification testing and reporting isn't about checking a box. Each report must include individual test results that clearly state the purpose of the test and explain the reason for the outcome. This level of detail helps the designated person (DP) evaluate whether certification truly meets USP compliance for their facility and devices.

Because no one is actively policing certifiers, testing quality can vary widely. By removing detailed guidance—such as requiring methods aligned with CAG-003—the chapter shifts the burden of verifying nuanced certification requirements onto the DP, increasing the risk of omitting steps. And the short "minimum" list of required tests? It doesn't guarantee that your cleanroom or PEC is actually fit for sterile compounding. The result may be a certification that looks compliant on paper but fails where it matters most—protecting patients.

To ensure full USP compliance, require certification vendors to follow all applicable standards and guidelines. This not only strengthens operational compliance but also reduces the risk of regulatory scrutiny and inspection findings.

References

[1]Controlled Environment Testing Association. CAG-003: Certification Guide for Sterile Compounding Facilities for USP Compliance. 2022.

[2]United States Pharmacopeia USP <797> Pharmaceutical Compounding—Sterile Preparation. (2021, never official)

[3]United States Pharmacopeia USP <797> Pharmaceutical Compounding—Sterile Preparation. 2024

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[4]Controlled Environment Testing Association: CAG-002: Compounding Isolator Testing Guide. 2006/rev. 2008.

Biosafety Cabinetry Certification: NSF/ANSI 49 | NSF

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