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CriticalPoint Pearls of Knowledge — July 2025

The Blueprint to Certification: Room-to-Room Pressure Testing

Introduction

CriticalPoint continues its certification series with an in-depth look at individual cleanroom tests—what they are, how they're performed, and why they matter. This month, we focus on room-to-room pressure testing, also known as pressure segregation.

As referenced in USP <797>, pressure testing is part of the listed primary cleanroom tests for airflow testing and is described as the measurement of "pressure differential in doorways between adjacent rooms to ensure consistent airflow and that the appropriate quality of air is maintained under dynamic operating conditions." [1] While USP chapters specify required pressure gradients between hazardous and nonhazardous spaces, they do not detail how the testing should be performed.

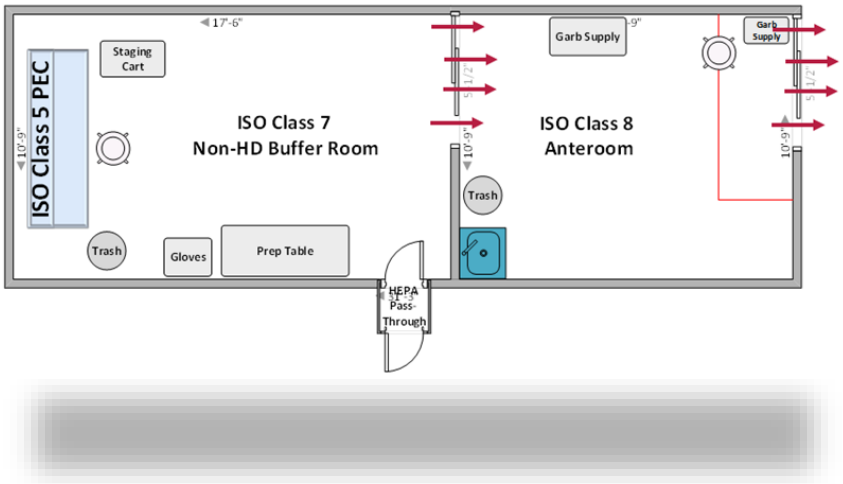
This month's Pearl explores the role of airflow pressure segregation in cleanroom design and how it serves as a primary defense against contamination in sterile compounding environments.

What is room pressure segregation?

Room pressure segregation helps control airflow between cleanroom spaces by maintaining pressure differences. In nonhazardous designs, this is achieved by supplying more clean air into a room than is removed, creating positive pressure. This design helps prevent contaminated air from entering when doors are closed.

As mentioned in our airflow testing series, balanced airflow is critical to cleanroom performance. By managing supply and exhaust air, rooms are pressurized to create cascading airflow—air moves from cleaner (higher ISO class) spaces to less clean ones. This pressure gradient supports contamination control and ensures each space meets its required air changes per hour (ACPH).

In hazardous drug (HD) compounding environments, containment is critical—not only for protecting staff within the cleanroom suite, but also those in adjacent areas. Unlike nonhazardous cleanrooms, HD containment relies on negative pressure, created by exhausting more air than is supplied. This helps prevent hazardous contaminants from escaping into adjacent areas.



However, negative-pressure systems constantly remove conditioned, filtered air, making them more energy-intensive. They also increase the risk of drawing in microbial contamination from adjacent "dirtier" areas, such as anterooms where staff are ungowned and water sources are present. Because of this, cleanroom behavior and awareness are essential. Staff must follow proper procedures and maintain good conduct to support the facility's airflow design and assist with preserving a proper microbial state of control.

USP Requirements for Airflow Pressure

- USP 797 requires a minimum pressure differential of at least 0.020 inches of water column (w.c.) between each positive-pressure ISO-classified environment and between ISO-classified and unclassified environments.
- USP 800 requires a negative-pressure range of 0.010 to 0.030 inches w.c. relative to all adjacent areas regardless if the space is part of a cleanroom suite or a containment segregated compounding area (C-SCA).
- Pressure monitoring devices are required for all classified areas.
- Data from the pressure monitoring device must be reviewed and documented at least daily when compounding is occurring.
- Pressure monitoring devices must be calibrated, or performance verified at least annually.

Remember, if you perform hazardous sterile compounding, you must follow USP 797 in addition to USP 800.

USP Certification Elements for Airflow Pressure

Room pressure segregation testing is a required component of the semiannual cleanroom certification process and one of several tests used to assess USP <797> compliance. In addition to measuring pressure differentials, a smoke source should be used at each doorway to visually confirm airflow direction,[2] following guidance in CETA's CAG-003: Certification of Sterile Compounding Facilities for USP Compliance.

Per CAG-003, test reports should include measured pressure values for each room, along with a clear PASS/FAIL designation. A room diagram is also strongly recommended to provide visual context for testing locations and airflow direction.

Airflow Direction and Pressure Segregation Testing

Although only briefly mentioned in USP <797> as part of airflow testing, door pressure testing is a simple yet important assessment. The test itself is not performed under dynamic conditions but still requires careful attention to ensure pressurization is properly maintained throughout the cleanroom suite.

All doors and ingress/egress points must be fully closed during testing. While staff may continue to work in the space, the key is to maintain stable pressure at the moment readings are taken. Even a single open door can disrupt the airflow design and skew test results.

Door pressure design only functions correctly in a "static" state, when doors are fully closed. Yes, staff can enter and exit as needed, but every temporarily opened door disrupts the cleanroom's controlled state. That's why it's critical to understand how cleanrooms "breathe" and operate.

Leaving doors open unnecessarily, such as for casual conversation, or failing to maintain automatic door closures leaves the cleanroom vulnerable to contamination from less clean adjacent spaces. Proper door function and training on entry/exit behavior are essential to maintaining control.

Of course, it's impossible to prevent all contamination—people are the dirtiest thing in the room after all. But the goal, both in design and operation, is to minimize unnecessary contamination risk. This is why consistent pressure, proper door mechanics, and trained staff behavior are so important.

Finally, if a room struggles to return to proper pressure quickly after a door is opened, it could signal a larger problem. Older rooms may develop gaps, cracks, or deteriorating seals that allow air to escape. If you notice "lazy" or delayed pressure recovery, it's worth inspecting the space to improve its ability to maintain proper containment during routine use.

General testing procedure:

1. Confirm that all certification test equipment and facility-installed room pressure monitors are functioning properly and display accurate readings before beginning the test.
2. Identify doorways between the anteroom, buffer rooms, or other adjacent spaces that require airflow-direction testing.
3. If the door is tightly sealed, open it slightly to allow for visible airflow testing.
4. Using an approved visible smoke source, pass the smoke around the entire perimeter of the doorway opening.
5. Observe the direction of the smoke to ensure airflow is moving in the intended direction (from higher to lower ISO-classified space in positive pressure areas, or into the room in negative pressure environments). Clearly report the direction of the pressure cascade between rooms.
6. Visually confirm that the airflow is uniform around the entire perimeter of the door opening and flows in the correct direction as per the room pressure design. Note in the certification report that airflow direction was visually confirmed.
7. Record all measured pressure values using a calibrated certification instrument.
8. Report results to at least the nearest 0.001" w.g. and recording at least to the thousands decimal.
9. Ensure all readings, airflow observations, and pressure relationships are thoroughly documented in the certification report, along with PASS/FAIL criteria based on established acceptance thresholds. The criteria are typically based on the facility airflow pressure design or USP minimum requirements.

Reporting Room Pressure Testing

Airflow pressure testing is one of several cleanroom certification tests required to verify compliance and environmental control. Like all other certification components, this test must be clearly and thoroughly documented in the final report.

The report should answer the fundamental questions of who, what, when, where, and why, allowing the reader to understand the purpose of the test, the data collected, and how it meets or fails to meet acceptance criteria. In other words, the report should "tell the story" of the test from setup to outcome.

Key reporting elements for pressure segregation testing include the following:

- the measured pressure differential between adjacent rooms or spaces
- a comparison of room pressure monitor performance (if applicable)

- whether smoke visualization at entry doors confirms correct airflow direction
- the name of the test (e.g., Room Pressure Differential Test)
- the acceptance criteria used to determine compliance
- a clear PASS or FAIL statement based on the test results

Summary

Room-to-room pressure testing plays a crucial role in maintaining cleanroom integrity and ensuring compliance with USP <797> and <800>. By verifying pressure differentials and confirming airflow direction with visual smoke tests, certification professionals can assess whether cleanroom environments are functioning as intended to control contamination risks.

When documented thoroughly and tested with precision, pressure segregation results not only support regulatory compliance but also promote a culture of safety and accountability in sterile compounding operations. As with all elements of certification, understanding both the purpose and process behind each test empowers pharmacy teams and certifiers alike to uphold the highest standards of cleanroom performance.

References

[1]United States Pharmacopeia USP <797> Pharmaceutical Compounding—Sterile preparation. 2024

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