

CriticalPoint Pearls of Knowledge — May 2025 The Blueprint to Certification: Addressing HEPA Filter Testing

Introduction

CriticalPoint continues its certification series with a closer look at individual cleanroom tests—what they are, how they're performed, and why they matter. In this month's issue, we focus on a popular and essential topic: HEPA filter integrity testing. HEPA filters are critical to maintaining ISO-classified cleanroom environments—but how can you be sure they're functioning as intended? To answer this, you need to know what HEPA integrity testing involves, why it's required, and how proper execution helps ensure airborne contaminants are effectively controlled.

Regulatory expectations

In USP <797>, HEPA filter integrity testing is one of four areas of focus regarding cleanroom certification. However, the chapter does not explain the parameters of testing, only that the test must be completed before and after installation in the cleanroom and as part of routine certification, which is performed semiannually.



CETA's CAG-003 Certification Guide for Sterile Compounding Facilities for USP Compliance references minimum industry-accepted, current standards and recommended best practices when performing certification tests. This includes performing HEPA filter leak testing.

To ensure compliance with USP <797> regarding primary and secondary engineering controls (PECs and SECs), CriticalPoint recommends that pharmacies and their designated person(s) require testing be performed by their certification vendors in accordance with CAG-003.

CAG-003 details the elements of performing HEPA integrity testing. In addition to listing the test procedures, CETA's testing guidelines also provide industry-standard expectations on equipment and materials as well as repairing leaks and providing proper documentation of the data once the test has been performed.

Why integrity testing is important

Testing HEPA filters isn't a complicated process, comprised of just a few steps, But it certainly is technical. The main elements consist of how the aerosol smoke concentration is delivered above the

HEPA filter airstream and scanning the filtered air below the HEPA filter based on the smoke concentration above.

Taking the time to understand how duct systems supply the airflow delivered to the HEPA filter is key because you want to ensure this is done properly and compliantly. A leak test performed incorrectly could jeopardize cleanroom performance once the filters are damaged or no longer filtering below the 0.010% threshold. Even a pinhole leak can allow contaminants to bypass filtration, potentially compromising products, patient safety, and regulatory standing. Improper aerosol introduction can cause the photometer to miss tiny and pinhole-sized leaks.





Scanning too quickly with the photometer or skipping over critical seals and gaskets can also miss leaks. This is why industry standards written on how to properly test filters require a minimum scan rate of two inches per second. This ensures the certifier is scanning slowly enough to find the source of even the smallest leak and possibly repair it using an approved sealant.

Testing equipment and aerosol induction methods

CETA CAG-003 requires that all HEPA filters be leak tested using an aerosol photometer and an appropriate aerosol challenge during every certification. The challenge aerosol must be introduced into and mixed with the upstream airflow supplied to the HEPA filter in a manner that ensures proper mixing, producing a uniform concentration across the entire filter face. The upstream concentration is measured with an aerosol photometer, which is then used to scan the HEPA filter downstream. Before we explain the details of scanning, let's discuss the two aerosol generation methods that are considered acceptable, each with its own benefits and limitations:



- Laskin nozzle generator: Compressed air is passed through a Laskin nozzle submerged in oil, typically polyalphaolefin (PAO), which is the most commonly used challenge agent. The nozzle's precision-drilled holes atomize the oil into a fine aerosol. This method of introducing aerosol is designed for lower volumes of airflow (cubic feet per minute [CFM]) or individual HEPA filters typically producing under 1,300 CFM.
- 2. Thermal aerosol generators: These systems heat oil to produce a large amount of aerosol smoke concentration and are typically used for HVAC or facility systems that supply cleanroom HEPA filters. This method is reserved for reaching several HEPA filters at one time. Because airflow volume and aerosol concentration must remain balanced, thermal aerosol generators are better suited for systems with higher airflow rates or multiple HEPA filters tested simultaneously. These generators produce a higher output concentration of aerosol, making them more effective in maintaining an adequate challenge level across large-volume systems.

To successfully perform HEPA filter integrity testing using the Laskin nozzle method, two conditions must be met:

- 1. a reliable method for introducing the aerosol upstream of the filter
- 2. a mechanism to measure the upstream concentration accurately with a photometer

Introducing an upstream challenge

Pharmacies should understand how proper aerosol induction is achieved in their facility. As mentioned above, two conditions must be met to properly introduce aerosol smoke concentration: a way to deliver it to the upstream airflow, and a way to detect and measure the amount of smoke concentration. Common methods include selecting HEPA filter housings equipped with room-side challenge ports. This feature allows aerosol to be introduced directly into the filter housing without penetrating the ceiling. When specifying filter housings with challenge ports, consider the following:

• A leak-free connection must be provided where the certifier attaches the aerosol generator hose. Any leakage at this connection during testing can cause false positive results.



- The challenge port should connect to tubing that leads to a distribution system tested for uniform aerosol delivery designed by the manufacturer. The filter housing manufacturer should verify that the housing meets spatial and temporal uniformity standards as outlined in IEST-RP-CC034.
- The internal tubing inside the HEPA housing must be of sufficient size to prevent aerosol condensation inside the line. Tubing smaller than 0.375 inches in diameter has been shown to cause condensation issues. While tubing larger than 0.375 inches is preferred, availability can sometimes be a challenge.



Be aware that not all HEPA filter housings are designed with challenge ports. To avoid having to go above the ceiling of the cleanroom and contaminating the clean environment in order to introduce aerosol directly into the ductwork, a remote challenge system can be installed and utilized instead. Remote systems consist of tubing run from the ductwork upstream of each filter housing to a convenient aerosol introduction point. Remember, it's important to have a way to measure the concentration, as it will help facilitate the next steps of scanning the HEPA filter downstream. These remote challenge systems can be located inside or outside the cleanroom suite. There is no guidance on location of ports; it is a preference of pharmacy leadership whether to install them inside or outside of the cleanroom suite. Remote systems and tubing can also be installed as part of a new cleanroom



build or integrated carefully into an existing cleanroom design and ductwork system.

The critical takeaway: Every challenge port system must be designed to effectively deliver the aerosol, ensuring the required concentration reaches the upstream side of the HEPA filter for valid and accurate integrity testing.

What is HEPA filter integrity testing?

HEPA filter integrity testing, also known as leak testing, is a method used to verify that the filter media and its housing are free from defects, leaks, or installation errors that could compromise cleanroom classification and state of control. This is not an airflow test—it specifically checks whether any portion of the HEPA filter's paper pleats or the frame seal allows unfiltered air to bypass into the clean space. The test involves two key steps:

- 1. introducing a challenge aerosol upstream of the HEPA filter
- 2. scanning the downstream face of the filter using an aerosol photometer to detect any penetration beyond an allowable threshold of 0.010% of the upstream concentration

How is leak testing performed?

As described earlier, certifiers introduce aerosol into the airstream before the filter, known as the upstream side. The aerosol must be well-mixed and uniformly distributed across the filter face. An aerosol photometer is then used to:

- 1. measure upstream concentration (to establish a baseline challenge) with a value between 10 to 90 micrograms per liter.
- 2. scan the entire downstream surface of the filter, including the frame and seal around the filter housing. The photometer displays the percentage value of leakage by comparing the downstream reading to the upstream concentration to detect any penetration.



Any point showing a concentration greater than the allowable penetration limit (0.010%) is flagged for repair or replacement. Performing HEPA integrity testing is the "dirtiest" part of certification and is typically one of the final tests. Scanning HEPA filters also takes a considerable amount of time. Each filter must be scanned at a rate of 2 inches per second with overlapping strokes. A single, standard 2x4 HEPA filter could take nearly six minutes to scan.



Documentation for compliance

It's likely that you have witnessed HEPA filter testing being performed. However, you're probably more familiar with the documentation of the test. Documentation goes beyond a "passed" mark or a checked box. It is beneficial to have a sense of how air is tested in cleanrooms rather than relying on passing statements. Designated persons are expected to review the certification report to confirm the environment is suitable for sterile compounding. Ensure that you can identify these reporting elements specific to HEPA filter integrity testing:

- record of the upstream aerosol challenge concentration
- list of the method used to report concentration (measured or calculated)
- record of the maximum leak penetration percentage of each filter
- name of test (HEPA Filter Leak Test)
- report acceptance criteria (≤ 0.01%)
- provide a Pass or Fail statement based on the results of the test

CriticalPoint's best practice recommendation is to request documented notation of where the upstream challenge is located for each filter and how the test was conducted according to industry standards.

Critical safeguard for compounding quality

HEPA filter integrity testing is a foundational component of environmental quality control. Pharmacies must treat it not as a formality but as a critical safeguard for patients, staff, and regulatory compliance. It's important to ensure compliance is met through industry standards. Require from certifiers that CETA application guidelines (CAGs) are followed throughout every step in the certification process. This means that conversations with your certifier about how certain tests are carried out are critical to the performance of the cleanroom.

A leak that is not discovered in a HEPA filter could allow microbial or particulate contaminants into the cleanroom—directly threatening product safety and patient health. In sterile compounding, even minor contamination can lead to infections or adverse drug events.

Summary

HEPA filter integrity testing is a vital part of contamination control and cleanroom assurance. Without it, even the most advanced cleanroom design can fail to deliver the protection it promises. Regular testing, performed correctly, and supported by thoughtful facility design, ensures your cleanroom remains compliant, efficient, and most important—safe for sterile compounding activity.