
USP Chapter 797 (2019) Section 5 establishes the minimum requirements for the certification of ISO classified areas. Section 5 references the Controlled Environment Testing Association's (CETA) certification guide for Sterile Compounding Facilities for specific procedures. Section 5 also lists HEPA filter Integrity Testing as one of the specific tests that **MUST** be conducted at every certification (6-month intervals). Historically, this is one test that was not always completed as part of certification by every certification provider. The reason given was often "our facility was not designed to accommodate filter leak testing". While this may be true, it never was an acceptable justification to forgo this important test. Any time a HEPA filter is relied on to filter microorganisms, that filter **MUST** be proven to be leak free. It is ultimately the Designated Person/s (DP) responsibility to ensure that certification is done correctly. In this case, that means ensuring that accommodations are provided for integrity testing every HEPA filter.

HEPA Filter Leak Testing Process

CETA CAG-003 specifies that all HEPA filters must be leak tested at every certification using an aerosol photometer and an appropriate aerosol challenge medium. A challenge aerosol is introduced into the airstream upstream of the HEPA filters in a manner that ensures a good mixing of the aerosol to create a uniform challenge across the entire cross section of the filter. The upstream concentration is measured with an aerosol photometer and then the HEPA filter is scanned with a photometer comparing upstream concentration to downstream. Two methods of aerosol generation are acceptable, and both have their advantages and disadvantages. The primary method is to blow compressed air through a Laskin nozzle into a vessel containing enough oil to cover the precision holes drilled into the nozzle. The oil most commonly used is Poly Alpha Olefin (PAO) but others can be acceptable if properly tested and the output quantified. An alternative aerosol generation method used for larger systems is to heat the oil with a precisely manufactured thermal generator.

In order to ensure the HEPA filters can be leak tested using common methods (Laskin nozzle generator or thermal generator), two accommodations must be made. A method of introducing the aerosol must be provided along with a means to measure the upstream concentration.

Upstream Challenge Introduction – Laskin Nozzle Generator

When designing a new facility, it is recommended that the HEPA filter housings be equipped with a **room-side-challenge-port (RSCP)**. This will allow for the aerosol to be introduced directly into the filter housing without penetration of the ceiling. When specifying a RSCP equipped filter housing, consider:

- The fitting where the certifier connects the aerosol generator hose must provide for a leak free connection. If this connection leaks during the test, a false positive result will occur.
- The RSCP must be connected to a pipe that runs to a dispersion system located at the air inlet collar that has been tested for uniformity. The filter housing manufacture should provide assurance that the housing has been tested for spatial and temporal uniformity per IEST-RP-CC034.

- The RSCP and tubing must be large enough to ensure that the aerosol will not condense out in the tubing. Tubing smaller than 0.375" diameter has been shown to be problematic.

For applications where a RSCP is not provided, a **remote challenge system (RCS)** can be installed. An RCS is basically a tube system run from the ductwork upstream of each filter housing to a suitable place for aerosol generation and introduction. That can be a port in the cleanroom ceiling or ideally, a port located outside of the cleanroom suite. This can be a system of tubing and fittings developed by the cleanroom owner or pre-packaged systems purchased from a vendor. There are at least 3 vendors currently providing RCSs.

- CEPA Operations, Inc. Aerosol Injection Port Assembly @ www.CEPATEST.com
- The Cleanroom Parts Guys @ <http://thecleanroompartsguys.com>
- Performance Assurance Systems @ <https://www.getpassport.com>

When installing an RCS, be sure to consider:

- Ideally, the RCS introduction location is outside of the cleanroom suite. Aerosol generators often leak and when that happens in the room where the filter under test is located, the room background level increases resulting in false positive results. If the introduction port is located in a cleanroom that room is susceptible to a contamination if the RCS port cover is not sealed properly after the test.
- If the RCS is located outside of the cleanroom suite as is recommended, certification may become a two-person job. One person will most likely be stationed in the area outside the cleanroom where the introduction port is so that the smoke can be moved from filter to filter without the need to ungown and gown between filters.
- The fitting for the duct side of the tubing must be located in a manner to afford good mixing. If it is too close to the filter such as directly at the collar of the HEPA filter, adequate mixing is often not accomplished. Ideally, the aerosol is introduced into the duct at the collar where the flex duct connects to the main duct trunk line. This typically allows for the best aerosol mixing and therefore, most reliable test.
- Installation of an RCS is a one-time investment intended to make the certification process less intrusive for future testing. The cleanroom will be disturbed when the RCS is installed. Ceiling tiles will be removed. Ladders will be used. There will be disruption, so plan accordingly.

Upstream Challenge Introduction – Thermal Generator

When neither a RSCP nor an RCS is available, a thermal aerosol generator may be considered. A thermal generator creates a large volume aerosol intended to challenge multiple HEPA filters simultaneously. It is generally placed either in a return or directly at the negative pressure side of the HVAC system blower. A thermally generated aerosol should not be introduced into a positively pressurized duct without an auxiliary blower to overcome the duct static pressure.

Thermally generated aerosol will have an odor and is generated in large volume. Staff should be made aware that a thermal generator is being used. Compounding should not occur in any room served by the HVAC system being challenged by a thermal generator.

Measurement of Upstream Challenge

Leak testing HEPA filters is the process of comparing the concentration of particles upstream of the HEPA filter to the number of particles downstream. As such, it is usually necessary to measure the upstream concentration of the introduced aerosol. When testing a system where you have a direct introduction into one blower and one plenum for a HEPA filter it is possible to calculate that challenge. However, for most cleanroom applications, it is necessary to measure and record the challenge to each filter. To that end, challenge measurement accommodations must be provided. Most HEPA filter housings equipped with a RSCP are equipped with a challenge measurement port. In some cases, HEPA filters are equipped with a center runner which includes a port for measuring an upstream challenge. If no challenge ports are provided with the HEPA filter housings, a tube must be run from the upstream side of the HEPA filter to a convenient location for measurement.

Smoke Detectors

Most HVAC systems are equipped with a smoke detector system. It will need to be turned off during testing. Failure to do so has led to many false alarms and as a result, unnecessary building evacuations.

Summary

The DP is responsible to ensure that the primary and secondary engineering controls are appropriately certified, and that includes leak testing ALL HEPA filters employed in the sterile compounding operation. The DP must make sure appropriate accommodations are provided for the certification professional to do their job properly and efficiently. An RCS is only required if the HEPA filter housing is not equipped with a RSCP. Consider properly specifying HEPA filter systems to ensure an RCS is not needed.