Issue 124
July 2022
Division of Technical Resources
Office of Research Facilities
National Institutes of Health
Technical News BULLETIN

HEPA Air Filtration in Cleanrooms – Design, Construction and Testing Requirements

Introduction

NIH maintains a portfolio of cleanrooms that are designed, built, and operated as Aseptic Processing Facilities (APFs). Supply Air (SA), delivered via terminal High Efficiency Particulate Air (HEPA) filters, is the primary method of reducing airstream contaminant levels in these facilities to maintain the specified ISO classifications. HEPA filters and their housings have specific design, construction and testing requirements that must be followed to ensure that the integrity of these filters is maintained throughout the life cycle of the facility. Maintaining certified HEPA filters in APF spaces ensures the safety of patients, workers, and the environment, as well as the integrity of research at NIH.

Design and Construction Requirements

HEPA filters are rated by their minimum particle removal efficiency of 99.97% of 0.3-micron (µm) diameter sized particles. Velocity and filter thickness and/or density impact filter performance (higher filter velocity means more particles will pass, and a thicker or more dense filter media will impact pressure drop). Terminal HEPA filters are generally designed with a face velocity not to exceed 0.5 m/s (100 fpm). Within the cleanroom, HEPA filter selection and placement should minimize areas of stagnation and turbulent airflow, avoid short cycling to exhaust and return grilles, and not disrupt the air curtain at the sash of any primary engineering controls (PEC) in the room, such as a biosafety cabinet (BSC).

A HEPA filter has a gel seal that forms a positive seal when the filter is properly installed in its housing, eliminating air bypass around the filter edge. Filter housings are fully welded stainless steel or aluminum with an exposed stainless-steel trim. They should be equipped with room-side accessible aerosol challenge and pressure test ports as well as a damper adjustment. HEPA filters designed to be replaced room-side are preferable, except where there is sufficient service space above the ceiling, which is atypical. Filter housings must be cleaned prior to filter installation using IPA, Vesphene, or other pre-approved cleaning chemical(s).

HEPA filters must be handled with care during shipping and inspected for damage both upon arrival and immediately prior to installation. Damage can occur due to rough handling, touching the face with hands or tools, or even storage in the wrong orientation. Filters must be stored per the manufacturer's requirements: indoors, protected from damage (including water intrusion), and between 4.4°C and 37.8°C (40°F and 100°F) and 25% to 75% relative humidity. Despite best efforts to protect the filters from damage, some filters will fail the test during the initial installation, so keeping at least 20% additional spare filters on hand will help avoid project delays.

Testing Requirements

The FDA Guidance for Industry: Sterile Drug Products Produced by Aseptic Processing – cGMP (also known as Filter Integrity Testing) mandates HEPA filter leak tests. This test applies to all HEPA filters in the cleanroom suite, including filters located in the pass-through chambers and PECs. ISO standard 14644-3 and the Institute of Environmental Science and Technology's (IEST) standard IEST-RP-CC034.5 provide additional guidance on this testing. Leak testing is performed initially at the factory and then in situ to verify the integrity of the filter and its installation. Individual leaks should not exceed 0.01% of the upstream challenge. It is important that the airflow rate through the filters is verified prior to testing to ensure that airflow velocity and volume are within specified limits.

HEPA filters are tested with a challenge media, typically Poly Alpha Olefin (PAO), aerosolized through the injection port of the filter housing upstream of the HEPA filter at a concentration between 20-80 ug/l. Per ISO 14644, scanning is performed by using a series of overlapping strokes with the probe, holding it approximately 1 inch from the filter face and moving it at a maximum velocity of 10 linear feet per minute. An appropriate scanning velocity of the probe used across the face of filter is important to provide sufficient time to detect any leak.

Unless approved otherwise, HEPA filters are tested at minimum once every 12 months, except those installed in ISO Class 5 facilities, which are tested every 6 months. If testing detects a leak in the HEPA filter, repairs must follow an approved patching procedure based on the IEST RP-CC034.5 standard, which states, "Fill repair should not block or restrict more than an additional 3% of the filter face area, and no single repair should have a dimension exceeding 3.8 cm (1.5 in)." After the repair is complete and suitable cure time of the approved silicone patching material has passed, the repair area is rechecked for leaks. Patching along the edges of the HEPA filter is not acceptable. If a leak exceeds the allowable limit (> 0.01%), then filter replacement is required. Field repair is not allowed for HEPA filters in ISO 5 environments (typically found inside PECs).

References

Institute of Environmental Sciences and Technology. (2022). *HEPA and ULPA Filter Leak Tests* (IEST-RP-CC034.5). IEST. https://www.iest.org/