CONTAMINATION CONTROL IN CLEANROOMS

HEPA Filter Validation Testing via Port Devices

Abstract

Protecting the integrity of the sterile environment, product, and safety of personnel has never been more important, nor more in the forefront of practice than since the failures of the New England Compounding Center. The current science and methodology of HEPA filter testing is outdated. It relies on methods that at best yield results which are subject to interpretation, are seldom repeatable by similarly trained technicians using similar technology at different times. The introduction of access ports into HEPA filter integrity validation testing offers many advantages. There are multiple access ports on the market each with its unique characteristics, pitfalls, and advantages.

Peter Day R.Ph., C.Ph.

Peter@getPASport.com

Contamination Control in Cleanrooms, HEPA Filter Validation Testing via Port Devices

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Why it is important to perform HEPA filter integrity testing and what does it have to do with safety?

Nothing we do in pharmacy is more important than getting the right drug, to the right patient, at the right time to have its intended effect in ameliorating disease. By all accounts this is true. However, when providing sterile drug products other considerations are equally important. Being able to ensure that the drugs we provide not only meet the requirements for strength, but we must also ensure that they meet the requirements for purity and are free of contaminants, harmful excipients, are free of pyrogens, bacteria, mold, and fungus. If there is any doubt of this, one only need look back to the New England Compounding Center debacle of 2012. In which an unfortunate 76 people lost their lives and hundreds more were made ill due to a meningitis outbreak related to tainted steroids. The pharmacist and cofounder were both charged with second degree murder as a result.

Nothing puts a halt to a thriving business quicker than patients dying. Nothing can be more costly to a business than a lawsuit that arises due to patient harm especially when it is as the result of substandard product. Regardless of the compounding risk level, ensuring the sterility of the final product is of paramount importance. The life blood of every sterile suite is it's HEPA filters. Failure of the filters whether in the hoods or in the ceilings most certainly increases the opportunity for failure of your duties even if you are lucky enough not to have caused direct patient harm. In contrast to the New England Compounding Center is KRS Global Biotechnology. A company that spared no expense in obtaining equipment of the highest quality. Although they spent multi millions of dollars perhaps tens of millions on equipment. The top of the line sterile suites fully electronically monitored environmental controls. They employed very high-quality extremely qualified people in all positions. Unfortunately, on any given day even in the best of circumstances things can go wrong. They made some mistakes which resulted in a voluntary drug recalls of sterile product. A recent Sun Sentinel article by Marcia Heroux Pounds states…

"The company's bankruptcy reorganization, which means the company is restructuring in order to continue operation, follows a voluntary recall by KRS Global of unexpired human and animal drugs "due to lack of sterility assurance," according to an FDA statement. Drugs taken that are not sterile could cause infection and be life-threatening, the FDA said".

Experience shows that on any given day if you look hard enough you can find something wrong even at the best of facilities. Some of which may not even be under your control. Therefore, it is incumbent upon everyone who practices in, or is responsible for operating and maintaining a sterile processing operation to take every precaution to ensure that we employ the most effective technology to ensure every single dose we dispense is one which we would not hesitate to give to our loved ones if the need arose.

According to current USP standards, the HEPA filters used in sterile drug processing are required to undergo integrity testing twice a year. The selection of the certification company employed to validate your HEPA filter integrity is as important to the environmental safety plan as the practices you employ daily to execute that plan. You must know that your certification company utilizes best practices and has provided their technicians with extensive training to ensure that the service they provide to your facility truly confirms that you're meeting or exceeding standards set by such organization such as USP, and IEST.

From a risk management perspective, you must do everything in your power to protect both your patients welling being and your organizations ability to execute its vision and mission by safeguarding it and your patients from harm. You must ensure that it uses the most up to date and certified equipment to perform the job as the standards demand. Failure is not an option! There is always a lawyer around the corner just waiting for an opportunity to hold someone accountable. Put yourself for a moment on a witness stand and the prosecution attorney says to you Mr./Ms. Jones were you aware of product XYZ and you answer; "Yes, I am". Mr./Ms.Jones were you aware of the benefits provided by product XYZ? You answer "Yes". Mr./Ms. Jones if you were aware of product XYZ, and the benefits and safety that it provided, why didn't you employ it in your practice?"Well we looked at it, but we just weren't prepared to add the extra expense at that time". "The jury finds forthe plaintiff your honor".

Environmental monitoring is a critical component of a company's overall quality activities. It must be performed in cleanrooms or any other associated controlled environment. It is in fact integral to the quality of the product produced at these facilities.

The Institute of Environmental Sciences and Technology (IEST) is a nonprofit non-governmental membership industry association of and for professionals whose work centers around controlled environments. They write standards and provide Technical Guidance International Standards, Recommended Practices, and educational programs developed by experts in the fields of contamination control, environmental test and reliability, and nanotechnology facilities.[1] The IEST standard for HEPA filter testing is known as **IEST RP-CC034.4** or commonly referred to as RP 34. It covers definitions, equipment, and procedures for leak testing HEPA filters and ultralow penetration (ULPA) filters in the factory as they are manufactured, at the job site before they are installed, and after they are installed in cleanrooms and unidirectional airflow devices (hoods, BSC, isolators, etc). Other RP's which may be used in conjunction with RP34 are IEST-RP-CC001, IEST-RP-CC002, IEST-RP-CC006, IEST-RP-CC007, IEST-RP-CC021, IEST-RP-CC028, and IEST-RP-CC036. RP34 also includes procedures for measuring the special and temporal uniformity of the aerosol challenge introduced upstream of the filter being tested. The importance of aerosol uniformity will be discussed later in this paper. In this revision of the RP, the recommended procedures for factory and insitu testing are separated for ease of use. In factory and insitu testing, if a leak is detected while scanning a filter, it is recommended that the magnitude of the leak be quantified with the scanning probe stationary over the detected leak.[2]

The International Organization for Standardization (ISO) is a standard-setting body composed of representatives from various national standards organizations. The organization promotes worldwide proprietary, industrial, and commercial standards. The ISO standard for HEPA filter testing is known as **ISO 14644.3** which covers test methods and **ISO 14644.4** which covers design, construction and start up.

[1] Institute of Environmental Sciences and Technology home page.

[2] Institute of Environmental Sciences and Technology Contamination Control Division Recommended Practice 034.4

In order to ensure accurate and relevant test results, a test method should be "explicit, unambiguous, and experimentally feasible.",[3] as well as effective[4] and reproducible.[5] These are four key concepts that you MUST be thinking about when you are having your HEPA filters integrity tested. Is the company that I choose to perform my testing using and providing explicit instructions to their technicians? Are those instructions unambiguous? In other words, if you and I each read those instructions can and will we carry out the test in the exact same way? This is frequently the reason company-A may come in to test your facility and you may pass while when company-B who comes in immediately behind them or at your next certification fails you when all other factors have remain unchanged. Is the method of testing they are using not only experimentally feasible, but is it practically feasible? Are they carrying out the test in a way that accomplishes the goals, are their methods minimally destructive to my facility, to my processes, and to my bottom line? Will their methods obtain the intended results? That being to identify with certainty the status or integrity of the HEPA filters in my facility and provide me with the confidence to know that portion of my environment monitoring plan is or isn't in compliance with the standards to which I will be held. Finally, can similarly trained technicians using similar equipment obtain similar results employing these methods? These concepts are apparently much more difficult to achieve than one would think, yet at the same time a whole lot less difficult than ever before.

Methods employed to test the integrity of HEPA filters

HEPA filter integrity testing is commonly performed using an aerosol generator and photometer. With the proper generator and photometer combination, filter deficiencies such as pinholes, thin spots, gasket leaks, frame leaks or seal problems can be quickly and quantifiably pinpointed and corrected thus protecting product and personnel[6]

The most common method of integrity testing HEPA filters is known as DOP or dispersed oil testing and originally used Dioctyl Phthalate (DOP) as the medium. DOP produces mono or poly dispersed aerosol of sub-micron particles, generated to challenge the integrity of HEPA filters. DOP is no longer widely used in the pharma industry because it has been identified as a carcinogenic agent. These days the term DOP testing no longer stands for Dioctyl Phthalate but rather the process of "dispersed oil testing".

Today, DOP testing more commonly uses PAO polyalphaolefin. Polyalphaolefin is a non-organic product. It does not contain any ring structures, double bonds, sulphur, nitrogen, or waxy hydrocarbons. It is a non-polar base oil with a high viscosity index (VI) of approximately 130-140. Very importantly it has excellent low temperature flow characteristics. This is important because this property makes it an ideal oil for use in a standard aerosol generator which uses a sheering force to create the aerosol mist up to about 2,000 CFM's. It can also be used in a thermal generator which is capable of producing an aerosol mist up to 20,000 CFM's. HEPA filter testing is generally carried out with a concentration of aerosol medium of between 10 and 90 micrograms per liter of air. In order to introduce the aerosol into the system the certifier must introduce it upstream of the filter media. Typically, this involves opening the ceiling to access the ductwork in the interstitial space. They must then choose a location to create an opening in the duct work from which to introduce the aerosol. Once they introduce the aerosol, they then use a calculation to determine the amount of aerosol that reaches the filter. The resultant number obtained using the calculation represents the basis or

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[3] Committee E-11 on Quality Control of Materials (1963). *ASTM Manual for Conducting an Interlaboratory Study of a Test Method*. American Society for Testing and Materials. p. 3. Retrieved 8 February 2018.

[4] Nigh, P.; Gattiker, A. (2000). *Test method evaluation experiments and data*. *Proceedings from the International Test Conference, 2000*. **2000**. pp. 454–463. doi:10.1109/TEST.2000.894237. ISBN 978-0-7803-6546-9.

[5] Bridwell, H.; Dhingra, V.; Peckman, D.; et al. (2010). "Perspectives on Method Validation: Importance of Adequate Method Validation". *The Quality Assurance Journal*. **13** (3–4): 72–77. doi:10.1002/qaj.473.

[6] ATI Air Techniques International, Laskin Nozzle Generators TDA-4B and TDA-4B Lite Operation and Maintenance Manual; Revision M April 29th, 2016

100% of the challenge. Using a photometer, they then scan the face of the HEPA filter looking for 0.01% or more of the basis which represents a leak. A leak can occur either in the filter media itself, or in the filter housing. Depending upon the physical plant and conditions therein, this process may require two technicians to complete. It is also heavily time consuming.

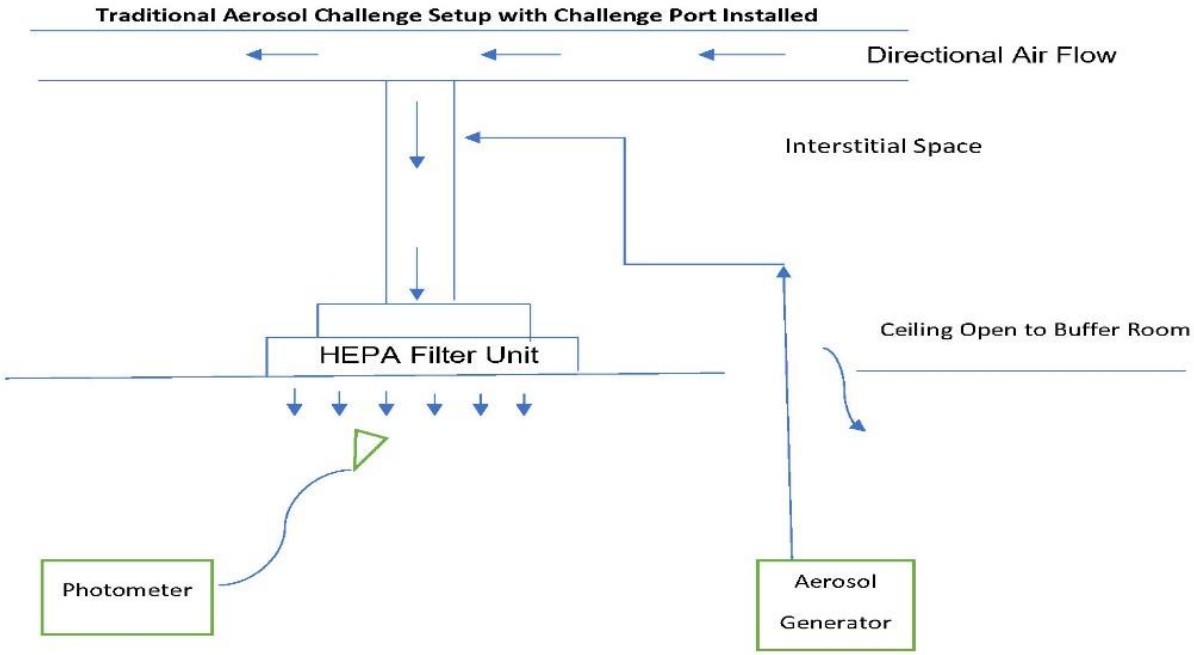
Field Calculation Used by Certifiers Today : "Laskin Nozzle Output Calculation":

$$13{,}500 \times \frac{\text{\# of Laskin Nozzels beign used}}{\text{CFM's the filter is generating}} = \text{ug/liter of aerosol that reaches the filter}$$

13,500 Represents the micrograms (ug) of aerosol produced by one Laskin nozzle

# of Laskin Nozzles: The standard Laskin III-A Nozzle has four jets located beneath four entraining holes. The volume of compressed air required to produce a given amount of aerosol is dependent upon the pressure of compressed air applied to the nozzle. When 20 psig is applied to the nozzle and diluted with 135 cfm of air, the output of one Laskin Nozzle provides a concentration of 100 micrograms per liter of DOP. The data also indicates that each nozzle requires 2.67 cfm of compressed air to maintain the 20 psig pressure drop.[7]

Ultralow penetration filters (ULPA) are tested in much the same manner however they use polystyrene Latex liquid spheres (PSL) as the aerosol media and they scan the filters using particle counters. PSL is available in particle sizes ranging from 0.12um to 0.3um which is normally associated with testing mean particle



[7] ATI Air Techniques International; Laskin Nozzle Aerosol Concentration, ATI Marketing 2019, Author unknown

penetration size (MPPS) and come in 25ml bottles marketed under the name HEPA CHECK which are diluted in one gallon of water which is then aerosolized using a ultrasonic PSL generator. According to IEST and European Norm Standards (EN) they are optimized for performance, aerosolization, safety and economy for both HEPA and ULPA filter testing. [8] The PSL aerosol is introduced into the upstream airflow in much the same manner as in DOP testing. The face of the filter is then scanned with a particle counter to determine the integrity of the filter and filter housing.

Types of HVAC/HEPA filtration systems typically encountered in cleanrooms

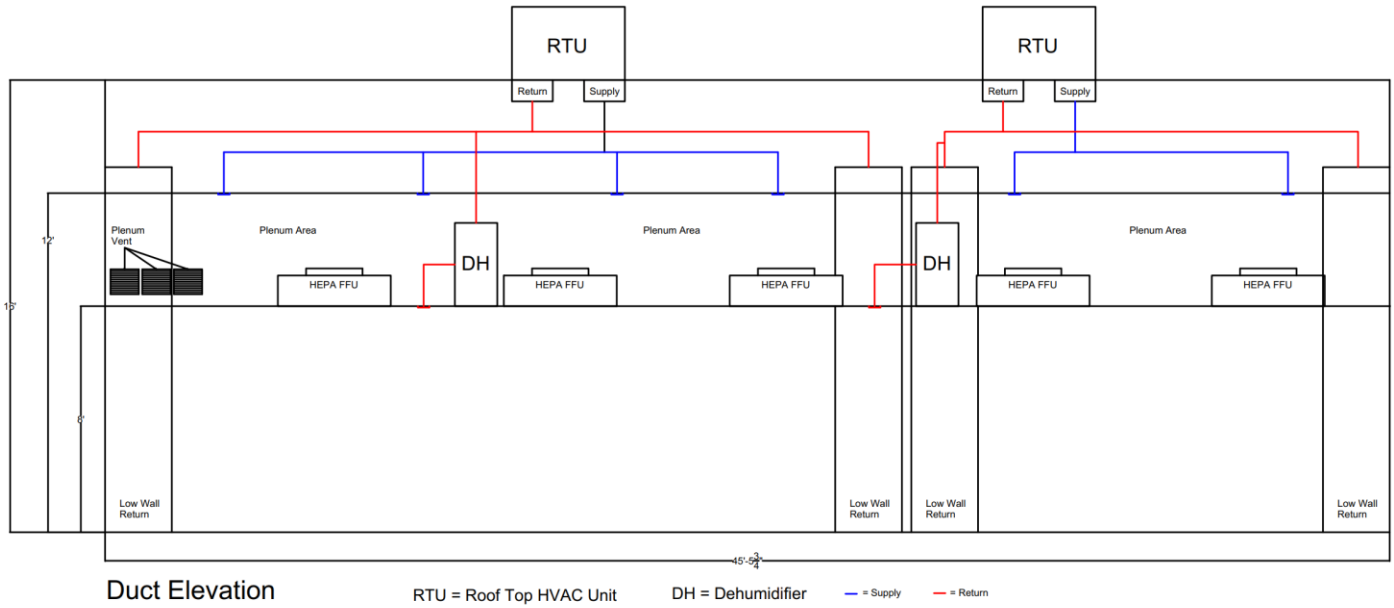
Current standards demand that those practicing USP <797> or USP <800> sterile compounding employ terminal HEPA filtration in their compounding suites. Whereas original USP <797> allowed for in line HEPA filtration. The reason that the change to the standard was made is due to the fact that in in-line HEPA filtration systems, the duct work between the HEPA filter and the cleanroom suite is all considered sterile space and is required to be cleaned on a regular schedule just like the rest of the cleanroom suite. In large hospital or institutional settings, the HVAC unit is typically located on the roof of the building and the cleanrooms are located several floors below. In smaller pharmacies the HEPA filters were typically located somewhere in the interstitial space of the ceiling or on the roof. In both cases cleaning of the duct work between the ceiling of the cleanroom and the HEPA filter rarely if ever occurred. Since HEPA filters have a life span of several years you can imagine what may be potentially growing in those spaces. Today, HEPA filtration must, and rightly so, occur immediately as the air enters the cleanroom space. Unfortunately, this concept has not yet been adopted for operating room suites or outpatient surgical suites.

Have you ever been up in the ceiling of your facility? Except for certain large institutional facilities this space is not climate controlled. There is often an assortment of workers who may be performing work in the ceiling at any given time. They could be alarm people, sprinkler system people, IT people running data lines, the Fire Marshal performing a routine inspection, an electrician running a feed to a new workstation, or HVAC people performing routine maintenance. Whatever the reason people running around in your ceiling is never a good thing. They may disturb or even dislodge or puncture critical duct work that supply your cleanroom suites. I am sure that it happens because I've seen it happen time and again. I am sure that well intentioned workers don'tever go into the ceiling intending to cause damage, but it happens, and they may not even be aware of it. Especially when the systems they disturb are not their area of expertise, they might not even realize they just created a problem. Every crack, leak, or tear in your duct work represents an opportunity for infiltration of dust, dirt, bacteria, mold, or fungus to be introduced into your classified space. Now, if coupled with a faulty HEPA filter whether it be a leak in the media or a leaking filter housing, you are now introducing those contaminants into your environment. You may think that you work in a quality organization with top notch personnel and equipment. You are probably correct in your assessment. However, how many buildings have you walked into and looked up at the ceiling and saw brown spots on the ceiling tiles? I bet it has happened far more often than you have noticed or acknowledged. It is a fact that if you have a roof on your building it will at some point in its life cycle leak. If you have a flat roof which is what most commercial buildings have that probability becomes a certainty. If you have an A/C unit in your ceiling or on your roof, at some point in time it will back up and leak water to whatever is below. Hopefully your designers were smart enough not to place an A/C unit above your cleanrooms. That is just asking for disaster to strike. Water and hot humid air trapped between floors of a hospital or in the interstitial space of a ceiling are perfect breeding grounds. Now if you have an imperfect HVAC system you may be pulling in whatever is growing up there. Even if your system has no leaks, but there is even a tiny area that is not completely sealed with insulation there will

[8] Applied Physics inc. https://www.appliedphysicsusa.com/pslspheres-hepacheck/ retrieved Jan, 2019

be condensation occurring which can breed living organisms. Which may very well unintentionally end up in your product especially if you're working in a negative pressure room environment.

Beyond terminal vs in line HEPA filtration there are ducted systems and plenum systems both which are commonly employed in providing sterile air to cleanrooms. In a ducted system the air supply comes from a main trunk before it is split off and runs via either hard or flex duct to each individual HEPA filter. The trunks may also be a combination of hard and soft duct work. Ultimately, each terminal filter is feed by its own individual supply of fresh air which may also be comprised of some portion of recirculated air from the return.



A plenum system uses a large closed space in the ceiling above the cleanroom with individual filters placed throughout the space. The fresh air supply is supplied to the plenum rather than directly to each filter. The filters then pull in air from the plenum before dumping it into the room. A leak in the plenum or an open plenum which we have seen represent a potential source of contamination.

Concepts of aerosol distribution

Two factors that come into play when considering how an aerosol particle (PAO) is distributed through a liquid in this case the incoming air stream from the HVAC system are Brownian diffusion, and Stokes Law which has to do with the drag force exerted on a particle as it moves through a fluid (in this case the air stream). In simple terms individual particles of PAO will stick together as they move through the air stream to form larger heavier particles which in turn will collide with the internal surfaces of the ductwork through which they travel and condense in the ductwork due to their heavier weight, coefficient of drag, velocity, and distance traveled. This process is known as coalescence. Additionally, the air stream moving within the duct moves faster along the outside of the duct than it does in the center of the duct. This creates a barrier to even distribution of the challenge within the airstream. This all combines to inhibit uniform distribution of the challenge within the upstream air flow. The result is that there is inevitably a loss of the challenge aerosol (PAO) in the system due to the aforementioned factors which result in less aerosol reaching the filter being tested than the simple calculation employed accounts for. This coupled with any potential losses from the system due to imperfections in the duct work could potentially mean that a leaking filter or filter housing may go undetected

with traditional test methods. When looking for 0.01% (0.0001) of a given number even a slight deviation in the basis can result in a significant margin of error.

IEST RP-CC034.4 sets out procedures for testing the uniform distribution of the aerosol challenge delivered upstream for the filter. These procedures must be followed to ensure adequate mixing of the aerosol before it reaches the filter. In the past standard operating procedure carried out by many certifiers has been to open the ceiling and access the ductwork wherever possible create an opening and place the aerosol generator tube into the opening and introduce the aerosol. Direct observations of this procedure have been observed on many occasions being employed by certifier after certifier. Eugene Bryan of Milholland and Associates has proven that this technique is ineffective in creating adequate mixing of the aerosol. A demonstration of just how difficult to adequately diffuse the PAO challenge throughout the air stream can be found at; https://www.youtube.com/watch?v=K1YAv74Xz44

It is not sufficient simply to place a hose into a duct or even the throat of a fan filter unit and expect that there will be adequate diffusion of the aerosol throughout the airstream. It is simply not possible. A specialized device designed to fully disperse the aerosol must be employed to meet the requirements of RP34.4. In fact testing shows that there are significant differences in concentrations measured when a properly designed dispersal pipe isn't used. [9]

Another factor to consider is that the PAO used in the aerosol generators is an oil. Oils can thicken over time, oils can attract foreign debris which may clog the jets in a Laskin Nozzle. The Laskin Nozzle Output Calculation equation is intended for calculating the aerosol concentration when required and assumes a nozzle pressure of either 20 psi for DOP (DEHP) or 23 psi for PAO-4. The results may be expressed as either micrograms per liter (µg/l) or milligrams per meter3 (mg/m3). [10]

"As far as the calculation goes there is a main driving formula for a Laskin nozzle generator, but the output varies depending on the oil used."[11] "One thing to note is that often when multiple nozzles are used, the output formula does not hold."[12] The formula references the number of Jets. A Laskin nozzle has four jets or holes in the nozzle. If two of the holes are plugged, this becomes a ½ Laskin nozzle generator. Six jets would equal a 1.5 Laskin nozzle generator etc. There is a more basic formula if specifying nozzles vs jets. When looking at most standards the Laskin nozzle formula found above is typically used, but manufacturers are moving to generators with ½ (2 jets) and 1.5 (6 jets) Laskin Nozzles so the trend may be to move towards the jet formula.

Types of failures that occur during tests

- As eluded to earlier the validation test of HEPA filters can be affected by imperfections in the design and integrity of the HVAC system itself. Most commonly duct work can have leaks which allow PAO to escape from the system during the test rendering the calculation method imperfect.
- The internal surfaces in the duct work itself can be smooth or corrugated and have multiple bends all of which can result in impaction and condensation of the PAO in the system. Smooth straight runs of

[9] Bryan, E; Aerosol Challenge Spatial Uniformity Test IEST RP – CC034.4 – Performance Assurance Systems PASport Dispersal Installation Kits (Plenum and Ducted) November 4, 2019

[10] ATI Air Techniques International, Laskin Nozzle Generators TDA-4B and TDA-4B Lite Operation and Maintenance Manual; Revision M April 29th, 2016

[11] Bryan, E; quote taken from direct correspondence January 2020

[12] Bryan, E; Quote taken from direct correspondence January 2020

duct work are less helpful to adequate mixing of the aerosol challenge while corrugated duct with multiple bends tend to increase aerosol mixing but increase coalescence. Condensation and impaction are two factors that the calculation fails to account for meaning less PAO reaches the filter media than the calculation predicts resulting in a basis that may be lower than calculated.

- Length of travel of the challenge from point of insertion to the filter media can play a role because of the time it takes for the aerosol to adequately mix with the upstream air. If it is introduced too close to the filter there is insufficient time & distance to mix and therefore may not fully distribute across the media.
- Duct work may in fact be dislodged from the HEPA filter altogether which means when using the calculation to determine how much PAO reaches the filter this very important fact would go unnoticed because when scanning the face of the filter with the photometer the technician would not detect PAO coming through the filter.
- If the system being tested is of a plenum design the challenge is introduced to the plenum. The problem with this is that plenums can also have leaks. In fact, I have seen plenums that are not fully closed meaning PAO will escape the system into the interstitial space rather than reaching the filters. Additionally, there is no guarantee that the aerosol challenge in a plenum will reach all filters evenly. One filter may receive a high load of PAO while others may receive a much smaller load. An additional factor that should be considered is that the entire plenum is charged during the test procedure meaning that you are unnecessarily loading all filters while each individual filter is being tested. This contributes to filter overload which can shorten the filter life.
- Quality and maintenance of equipment play a role. If for example two of the jets in a Laskin Nozzle were clogged, then one Laskin Nozzle becomes ½ Laskin Nozzle meaning that the calculated output of the generator would be in error thus effecting the test result.
- The quality and type of aerosol generator used to test the filters may play a role in generating background PAO which may be picked up by the photometer and therefore a non-leaking filter may be identified as leaking and be unnecessarily replaced resulting in unnecessary expense and down time.
- Uneven distribution of the challenge within the airstream may mean that the aerosol challenge does not evenly distribute across the filter media meaning that a leak present in an area of the filter that is not sufficiently bathed in the aerosol challenge may go unnoticed.
- Method of testing. Currently increasing emphasis is being place on validation of process by the FDA. It is a little talked about, but nevertheless a well-known fact that company-A can come in and certify a facility and company-B can come in immediately behind them and get varying test results. This is mainly due differences in equipment, differences in carrying out the test procedures, and differences in how and where they introduce the aerosol challenge. The simple fact is that unlike a simple mathematical equation that can be proven, the real-world variables that are not accounted for by the Laskin Nozzle Output Calculation render it unverifiable.

The figure to the left shows an antiquated aerosol generator still in use today. Despite leaking produced sufficient aerosol to test 6 of 9 filters but stopped producing aerosol on the last 3 filters. The problem was only identified because there was no up-stream concentration reading. Three potentially bad filters could have passed certification if it had not been identified by Up-Stream verification.

Above a technician scans the HEPA filters at a well-known teaching hospital using the PASport System

Why would I spend money on ports?

Because employing ports can have advantages for both the pharmacy as well as the certification company saving time and money for both organizations.

Advantages offered by ports

- They can reduce workers compensation claims because there is no need to climb a ladder to open the ceiling to access the duct work to introduce the aerosol challenge thus providing a safer test. This can have a direct effect on your workers comp insurance rates.
- Not having to access the interstitial space means that traditional garbing and disinfection of equipment introduced to the rooms can be followed. Post-test cleaning time is reduced because the ceiling has not been breached introducing particulates and contaminates to the space.
- Introduction of the aerosol challenge via a properly placed and constructed challenge port ensures adequate mixing of the challenge within the airstream.
- The use of ports can get your organization back to work faster which lessens the impact that the certification process has to your productivity and therefore your bottom line.
- Use of port technology can reduce risk to process, people, and product.
- Use of certain port technology can identify flaws in the existing HVAC system which would otherwise go unnoted and therefore may result in the certification of bad filters.

Types of ports on the market and advantages and disadvantages of each

Challenge ports

Challenge ports offer a solution to half the equation required by IEST RP-CC0034.4

Currently there are two companies known to this writer that have aerosol challenge ports on the market;

- **The Cleanroom Parts Guys** the first player to market with a challenge port going back to 2009
  The Cleanroom Parts Guys Aerosol Challenge Port www.thecleanroompartsguys.com




- **CEPA Test** this company offers a challenge port remarkably similar in type and construction to the above manufacturer. Photos not available

Both port systems offer the ability to deliver an aerosol challenge to the upstream airflow and both systems can be retrofitted to introduce the aerosol challenge from outside the buffer room. The thinking is that if the aerosol challenge is introduced from outside the buffer room, then there is no need to drag the aerosol generator into the room. This thought process considers that some aerosol generators may leak PAO into the atmosphere creating background readings which may affect the test result. What it fails to account for is loss due to coalescence due to extended distance and leaking duct work. It also doesn't consider that when it comes to validating the HEPA filters in your laminar flow hoods, biological safety cabinets, or isolators that you must inevitably bring the aerosol generator into the room anyway.

Both ports listed above are thru hull fittings that are sealed with a nut or cap that seals the unit when fully seated. When the cap is removed the system allows unfiltered air to enter the classified space. Potentially, whatever is in the interstitial space may make its way into the cleanroom.

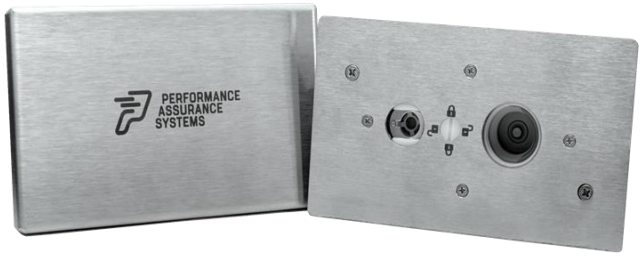
Upstream verification ports

The deployment of an upstream verification port allows the certifier to pull a sample of air immediately upstream of the HEPA filter media.

- Knowing with certainty the concentration of PAO that actually reaches the filter negates the uncertainty of the Laskin Nozzle Output calculation.
- The ability to know the Up-stream concentration allows the certifier to dial back the aerosol generator output to between 10-15mcg/liter. This reduces filter loading and extends filter life accordingly.
- Being able to read the concentration of aerosol that reaches the filter allows the certifier to know with certainty that the photometer reading when scanning the filter face is in fact plus or minus 0.01% of the basis.
- Having certainty in the photometer reading when scanning the face of the HEPA filter prevents intact filters being identified as bad, and bad filters being passed.
- Knowing with certainty the concentration of PAO that reaches the filter allows the certifier to identify whether or not there may be upstream problems in the system.
- Knowing with certainty the concentration of PAO that reaches the filter negates the effect that imperfections in the upstream system would have on the test result.
- Having a more accurate and repeatable test provides the end user with high level of confidence in the certification process and the quality of their sterile environment.

One manufacturer on the market incorporates both an upstream verification port and a challenge port into a system designed to handle both sides of the standards demanded by IEST RP-CC0034.4.

- **Performance Assurance Systems, llc** markets their system under the trade name **PASport**. It is a closed loop plug and play system with valves that remain shut until actuated by the certifier connecting their equipment to both sides of the system and close immediately upon disconnection. The systems uniquely designed aerosol distribution pipes are tested and demonstrated to provide uniform aerosol distribution in either a ducted or plenum application. The plenum pipe may also be used in limited access installations when it may not be possible to install the challenge the recommended distance from the filter. The male inserts which the certifier uses to connect their aerosol generator and photometer to the system are also fitted with closed valves that remain closed until connected to the ports and immediately close when disconnected. This prevents PAO from inadvertently being released into the room. PAO is thought to be linked to pneumocystis. This provides an added level of safety to both the certifier and the pharmacy staff. The plug and play feature reduces the time needed to test each filter to 6 minutes start to finish and allows each filter to be individually tested even in a plenum environment. The system is suitable for ULPA filter testing with polystyrene latex (PSL). The design and operation of the system ensures that test results are repeatable by similarly trained technicians using similar equipment.



Single Filter Stainless Steel Passport System

Two Filter Stainless Steel Passport System

Four Filter Stainless Steel Passport System

Standard Ducted Aerosol Distribution System

Plenum Aerosol Distribution System

Performance Assurance Systems patented System available in 316 medical grade stainless steel or bright white acrylic to fit any cleanroom décor. www.getPASport.com

BOP/FDA emphasis on validation of processes and why it matters to you

As stated at the beginning of this paper the life blood of any sterile processing operation is its HEPA filters. They are required to be certified at least semi-annually. Proposed standards are getting stricter. Boards of Pharmacy inspections are getting more detailed and State Boards and the FDA are looking deeper into systems and processes employed. There is an ever-growing emphasis being placed on validation not only of the processes being employed but also on the equipment used in your practice. As healthcare professionals we should be striving to employ the most effective technology and processes to deliver the safest most effective products to our patients that we can. Going along to get along should not be the mindset. Whether a high-level C-level executive, Director of Pharmacy, Staff Pharmacist, Technician, Risk Manager, or Quality Control expert those of us on the provider side as well as those on the certification side must continually seek to push the boundaries of the status quo in the direction of ever-increasing certainty and safety. You never want to be the person on the witness stand that answers the question in the affirmative that you were aware of a technology that could have potentially prevented a bad batch or improved your process but didn't elect to employ it in your practice because of price. Use of any of the aforementioned systems offers improvements to the old ways, but only one stands out above the others as a complete solution for superior results.