By James T. Wagner

Choosing a Certification Professional to Evaluate Your Cleanroom and Engineering Controls

Choosing a vendor to certify your engineering controls has become even more important as choices in engineering controls have grown to include laminar airflow workstations (LAFWs), cleanrooms, biological safety cabinets (BSCs), compounding aseptic isolators (CAIs), and ventilated balance safety enclosures (VBSEs). In addition, pharmacists and facilities engineers are faced with the daunting task of revamping their compounding operations to meet the environmental requirements of USP and NIOSH. An experienced, well-trained, and knowledgeable certification professional can provide invaluable insight to assist you through this process. Most certification companies are independent firms familiar with the equipment choices employed in sterile compounding facilities. Provided your certification company does not sell those engineering controls, it can help you filter through the contradictory claims you are sure to encounter as you weigh your options for gaining compliance with today's standards.

Training and Experience

Experience alone is not an adequate gauge of a certifier's expertise. A poorly trained certifier with 20 years of unsupervised experience will likely not do as thorough a job as a well-trained and well-supervised technician with two years of experience. Consider both the experience and training of the individual who comes to your site. It is only logical that the qualifications of the company president will not mean as much to you as those of the individual working on your equipment. Make sure the company's training programs for technicians are thorough and well documented. If the company cannot provide you with training records for all of its technicians, consider it a warning sign. Most certification companies participate in industry training programs offered by the Eagleson Institute, the Controlled Environment Testing Association (CETA), and many of the equipment manufacturers. For example, NuAire, Labconco, and other engineering-control manufacturers provide comprehensive and on-going training on their equipment. Some of the larger certification companies have begun to establish in-house training capabilities, often augmented by outside training centers providing hands-on training. These programs should be run by well-documented, qualified individuals.

Training is arguably the most important aspect to consider when choosing a certification company. Insist on a detailed set of training records as part of your due diligence. Certifiers should be accustomed to this request and are generally well prepared to respond to it. When reviewing training records, evaluate both initial and ongoing training. Engineering controls change constantly; therefore, what was good basic knowledge five years ago may be out-of-date today.

Make sure that your certification provider's experience is relevant to your existing or proposed facility. The new facilities' requirements in USP <797> include equipment that may not be familiar to your contractor. For example, it is not unusual for a certifier that has spent 20 years testing only pharmacy equipment to have little or no cleanroom certification experience. If you are installing a new cleanroom, have your certifier explain their experience certifying cleanrooms before assuming they are qualified. CAIs are relatively new to the US market, so they require an explanation of what the certifier has done to become familiar with that equipment.

Accreditation

Currently, there is only one accreditation program that applies directly to certifiers of sterile compounding engineering controls. NSF International provides accreditation for individuals certifying Class II BSCs. While not every pharmacy has a BSC, the principles used to certify a BSC apply to most of the engineering controls employed in pharmacy. Individuals accredited by NSF International have proven themselves competent to certify BSCs.

Certifying cleanrooms and CAIs is also essential for pharmacy since the adoption of USP <797>. At the moment, no specific accreditation program exists for certifiers of this equipment in sterile compounding facilities. CETA is the caretaker of the applications guides referenced by USP for sterile compounding facility certification, and is currently developing an accreditation program for certifiers of sterile compounding facilities, which is expected to be available in early 2010. Participation in any industry accreditation is not considered mandatory, but is a good sign that the certifier takes their trade seriously.

Testing

Your certification provider's qualifications are best analyzed by looking at their past certification reports for completeness and accuracy. Are current certificates of calibration provided for test equipment used in the certification process? Ask about their report QA process: Are the certification reports reviewed, or is validated software employed to assure computational accuracy?

The certification report should include acceptance criteria for each test. A test that is not based on actual acceptance criteria has no regulatory value. The acceptance criteria for certifying an NSF-listed BSC is published and a professional certification provider will have access to that data.

Establishing a pass-fail criterion for cleanroom certification is more challenging, as it is often up to the end-user to assign appropriate performance criteria. This is where the value of an experienced and knowledgeable professional certifier is indispensable. Because cleanroom certification should be based on pre-established acceptance criteria, it is common for the pharmacist to look to the certifier to assist in assigning the criteria. The certification report should include unambiguous statements of pass or fail for every test, and for the cleanroom overall. **(See the Cleanroom Certification Matrix starting on page 10 for guidance.)**

A certification company should have a written QA program to ensure the quality of its work. At minimum, this should include a review of the test reports, maintenance of training programs, and calibration of the test equipment. Calibrating certification test equipment at the equipment manufacturer's recommended interval is considered minimum acceptable practice. Because of the abuse certifica-

tion equipment receives during travel from site to site, reduced intervals are recommended. This should be an influential differentiator when looking at competing firms.

Service

Certification firms are often also called on to service the equipment they certify. Therefore, you want to verify that they have adequate staff to send someone to your facility within 48 hours of notification, or that they have a network of colleagues they can call on for help in an emergency. Include expected response times and parts availability parameters in your contract.

Summary

The price difference between the least and most expensive certifiers is often marginal, but the difference in professionalism may be dramatic. Remember that quite often, "you get what you pay for." In summary, your certifier should:

- Have written training programs
- Provide a written documentation of participation in industry training and continuing education programs specific to your equipment
- Provide a written estimate and schedule of work before work begins
- Have adequate capacity to service its geographical territory
- Provide complete, accurate, and professional documentation of its testing
- Provide documentation of all stated accreditations (preferably at least NSF)
- Have access to spare parts and supplies, as needed, to keep your equipment operating
- Provide a written QA program
- Calibrate its test equipment to the manufacturer's recommended intervals at minimum, though preferably more often
- Have adequate liability insurance to protect your facility in the event of an accident

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Controlled Environment Consulting's Cleanroom Certification Matrix

The following table provides a matrix for reviewing the certification of secondary engineering controls (cleanrooms) used in sterile compounding facilities designed to comply with USP chapter <797>.

The table assumes the certification professional follows CETA's application guide CAG-003-2006 (2008). The certifier should provide specific details of each test conducted either directly in the certification report or in a standard operating procedure (SOP) referenced in the certification report.

All calculations including intermediate values should be documented. Calibration certificates should be provided for every test instrument used and the specific model number and serial number of each test instrument should be documented on the test report. Acceptance criteria that is listed in this table is customary and standard in the cleanroom industry; when no definitive criteria exists for compounding operations, criteria that has been established for cleanrooms regulated by the FDA for aseptic manufacturing have been used.

This review does not include environmental sampling; it is limited to the engineering control performance verification (certification) procedures covered in the CETA document as referenced in chapter <797>. **The complete matrix, including particle count survey, temperature, and humidity data is available at www.pppmag.com/resources.**

The control points of interest are:

1. Assuring adequate HEPA filtered air is supplied to the rooms (airflow testing)
2. Assuring separation from rooms of different cleanliness classification and purpose (differential pressure and displacement airflow)
3. Assuring the HEPA filters are leak-free (HEPA filter integrity test)
4. Providing visual verification that air flows from clean to less clean areas and that unidirectional airflow areas are free from turbulence and reverse flows (airflow smoke pattern test)
5. Assuring the design, when operating properly, yields the intended cleanliness classification under dynamic operating conditions (particle count test)
6. Assuring the temperature within the compounding facility is appropriate for sterile compounding (temperature testing)
7. Assuring the humidity within the compounding facility is appropriate for sterile compounding (humidity testing)

Item	Basis for Compliance	Minimum Reported Values	Test Equipment Requirement
Airflow (non-hazardous compounding rooms) (1)	Non hazardous sterile compounding rooms must maintain a minimum of 30 total HEPA filtered air changes per hour (ACPH). At least 15 HEPA filtered ACPH must come from outside the room. Up to half of the total HEPA filtered air can be generated by the primary engineering control.	Air volume through each supply HEPA filter __CFM. Total HEPA filtered air volume supplied to the room__CFM. Total HEPA filtered air volume added to the room total from the PEC __ CFM. Room volume __ft^3. Dimensions used to calculate the room volume__inches. If the primary engineering control is used for a portion of the minimum 30 total ACPH, specific calculations for this source should be documented. All calculations along with the total HEPA filtered room __ACPH should be documented.	The preferred test equipment is the airflow capture hood used to measure airflow volume directly in cubic feet per minute (CFM). In some rare cases, a capture hood will not fit in the given space and an air velocity measurement device will need to be used to measure airflow velocity in feet per minute (FPM), and those readings are converted to volume by multiplying the average velocity times the effective filter area. Maximum recommended calibration interval: 12 months for electronic capture hoods, 6 months for thermal anemometers.
Airflow (hazardous compounding rooms) (1)	Hazardous sterile compounding rooms must maintain a minimum of 30 total HEPA filtered ACPH. Since most primary engineering controls used for compounding hazardous drugs are vented from the building, all of the HEPA filtered air will be from outside the room. In the rare case where the low-volume exception is used and the primary engineering control is vented back into the room, a total of 15 ACPH must come from outside the room when the HEPA filtered exhaust from the BSC is used as part of the 30 total ACPH. If a CACI is used, the room must maintain a minimum of 12 ACPH.	Air volume through each supply HEPA filter __CFM. Total air volume supplied to the room__CFM. Room volume __ft^3. Dimensions used to calculate the room volume__inches. All calculations along with the total HEPA filtered room __ACPH should be documented. A statement of pass or fail should be clearly made for the room air exchange rate within each room tested.	The preferred test equipment is the airflow capture hood used to measure airflow volume directly in CFM. In some rare cases, a capture hood will not fit in the given space and a thermal anemometer will need to be used to measure velocity in FPM and those readings converted to volume by multiplying the average velocity times the effective filter area. Maximum recommended calibration interval: 12 months for electronic capture hoods, 6 months for thermal anemometers.

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Cleanroom Certification Matrix

Item	Basis for Compliance	Minimum Reported Values	Test Equipment Requirement
Room Segregation (non-hazardous compounding rooms) (2)	One of two segregation strategies must be proven: a) Differential Pressure A minimum differential pressure of 0.02" water column (w.c.) positive from the cleanroom to the ante room and all adjacent spaces and between the ante room and all adjacent spaces with the doors closed. -or- b) Displacement Airflow A minimum differential velocity of 40 FPM from the cleanroom to the ante room. Note that it is important to maintain this velocity across the entire opening.	a) Differential pressure at every door or opening from each sterile compounding room and ante room to every adjacent space __ inches w.c. displayed on a room layout diagram clearly identifying which direction the pressure is flowing. b) Differential velocity across every opening between rooms of different classification in __ FPM. A comprehensive grid should be taken across every opening to assure that the airflow is consistent across the entire opening. Every individual reading displayed on a schematic grid should be documented along with the average velocity across every opening. Statement of a visual confirmation in the form of an airflow smoke pattern test that the air is flowing out of a non-hazardous compounding room into the ante room and out of the ante room to adjacent spaces. This is performed for both pressure-controlled and flow-controlled spaces.	The preferred equipment is an electronic manometer with a resolution to at least thousandths of an inch w.c. Maximum recommended calibration interval: 12 months.
Room Segregation (hazardous compounding rooms) (2)	The only acceptable room segregation strategy for hazardous compounding rooms is differential pressure.* A minimum differential pressure of 0.01" w.c. negative from the cleanroom to the ante room and 0.02" positive from the ante room to all adjacent spaces must be proven. *Maintenance of room pressure requires the use of physical barriers such as walls and doors.	Differential pressure at every door or opening from each hazardous sterile compounding room and ante room to every adjacent space in __ inches w.c. displayed on a room layout diagram clearly identifying which direction the pressure is flowing. Statement of a visual confirmation in the form of an airflow smoke pattern test that the air is flowing into a hazardous compounding room from the ante room and out of the ante room to adjacent spaces.	The preferred equipment is an electronic manometer with a resolution to at least thousandths of an inch w.c. A magnehelic gauge can be substituted; however, it is ideally a monitoring device and not as good of a field certification device as a digital electronic manometer. Maximum recommended calibration interval: 12 months.
HEPA Filter Integrity Test (3)	All HEPA filters should be leak tested at every certification using an aerosol photometer and an appropriate aerosol challenge. A challenge aerosol is introduced into the air handling system upstream of the filters and the upstream concentration is compared to the downstream concentration to determine if there are any penetrations in excess of the maximum allowed. The maximum allowable leakage is 0.01% of the upstream aerosol concentration.	Aerosol introduction location and upstream measurement location and the measured upstream aerosol concentration in __ micrograms per liter. Note that on some rare occasions, an upstream concentration cannot be measured. In those cases, an upstream aerosol concentration can be calculated and reported as such. If a calculated challenge is used, all of the calculations should be reported along with a reason that a challenge was not measured. A diagram of the filter along with an indication of where leaks were found, if any, and the percentage penetration of leaks or a statement that no leaks in excess of the maximum allowable 0.01% were detected. A statement of pass or fail should be clearly made for every HEPA filter.	An aerosol photometer that is capable of indicating a 100% upstream concentration with an aerosol challenge of 10 micrograms per liter of polydispersed Emery 3004 particles or equivalent. Unit must have a threshold sensitivity of at least 10^{-3} per liter and be capable of measuring concentrations over a range of 10^5 times the threshold sensitivity. The sampling rate shall be 1 CFM with an inlet probe having maximum open area of 1.7 in^2 and a minimum dimension of 0.5 inches. Maximum recommended calibration interval: 12 months. An aerosol generator should be capable of supplying a polydispersed aerosol by blowing compressed air through a laskin type nozzle into oil such as poly alpha olefin (PAO) or another approved generation method.
Airflow Smoke Pattern Test (4)	Primary engineering controls, including built-in laminar airflow, LAFWs, and BSCs, must be properly integrated into the buffer area. A visual medium is used to observe airflow patterns during dynamic operating conditions. The buffer room must be segregated from the ante area and all adjacent spaces. A visual observation using smoke is used to prove the pressure/flow differential is consistent across the entire opening.	A description of the test along with the results of the airflow pattern observation should be documented for each engineering control and around every room penetration. A statement of pass or fail should be clearly made for every test.	A visual airflow observation medium such as ventilation smoke tubes. The delivery velocity of the smoke tubes should not overcome the airflow patterns being observed. Laskin nozzle generators typically generate too high of a velocity to be an appropriate medium for airflow observation.

For the complete matrix, including particle count survey, temperature, and humidity data, go to www.pppmag.com/resources