Interpreting Cleanroom Certification Reports
—*What Providers Should Know to Ensure Compliance*

By James T. Wagner

PHARMACISTS AND PHARMACY TECHNICIANS

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EDUCATIONAL LEARNING OBJECTIVES:

1. List the three basic types of information that should be included in every cleanroom certification report.
2. Describe the elements that are included in a thorough and useful certification report.
3. List the tests used in certification of the primary engineering controls and what they are designed to check.
4. List the tests used in certification of the secondary engineering controls and what they are designed to check.
5. List the tests used in certification of the isolator engineering controls and what they are designed to check.
6. Discuss several steps facility managers can take to ensure that they receive and understand a thorough and actionable certification report.

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AUTHOR BIO:
James Wagner is the President of Controlled Environment Consulting (CEC), and has over 34 years of experience assuring the performance of critical environments. His consulting includes design and evaluation of sterile compounding facilities, containment facilities, and other engineering controls. Wagner conducts international training on cleanroom and containment device certification. Prior to founding CEC, he was the President of Micro-Clean, a certification and validation company. Recently Wagner led the Controlled Environment Testing Association's (CETA) efforts to develop guidance documents for USP Chapter <797>. He served on the USP Sterile Compounding Expert Committee for the 2005-2010 appointment cycle and is a member of the 2010-2015 USP Hazardous Drug Compounding Expert Committee. He has presented at many USP forums on engineering controls for sterile compounding. Wagner is a steering committee member for the National Science Foundation/American National Standards Institute Standard 49 Biosafety Cabinetry: Design, Construction, Performance and Field Certification. He was one of the initial group of NSF-accredited biological safety cabinet certifiers at the program inception in 1993. Wagner served on the CETA Board of Directors and served as President in 1992-1994 and 2006.

Questions or comments regarding this article should be directed to: **jimwagner@cenvironment.com**

Certification of the primary and secondary engineering controls is a critical responsibility assumed by the director of every sterile compounding facility. USP Chapter <797> states, "Certification procedures such as those outlined in the 'Certification Guide for Sterile Compounding Facilities' (CAG-003-2006)[1] shall be performed by a qualified individual no less than every six months and whenever the device or room is relocated or altered or major service to the facility is performed." Home infusion pharmacy and sterile compounding facility managers typically hire independent certification contractors to provide these important quality control checks. Undergoing required certifications, however, does not absolve facility managers of responsibility for other essential quality control functions, such as writing and adhering to industry-based policies and procedures, executing meaningful staff training, and overseeing proper maintenance and recordkeeping. In addition, managers must play an active role in the certification process so that they are able to understand and act on the information contained in the certification report.

Ultimate responsibility for certification is borne by the facility director, not the contractor. Following each certification, the cleanroom manager must maintain adequate documentation proving that the facility performs appropriately. Importantly, the manager must also be able to explain the report findings to other entities, such as the state board of pharmacy, that inspect the facility. Yet, most directors do not know how to interpret the report provided by the certifier. This article will provide a blueprint to ensure you have adequate documentation of facility performance and how to use the certification process as an integral part of your facility set-up.

How the Report Should be Structured

The certification report should be a complete document providing all the information necessary to determine how the facility was tested and how it performed. The information contained in the report should point to:

- Which test equipment was used along with when each piece of equipment was calibrated
- Which test procedures were used along with reference standards
- Clearly stated pass or fail statements for each test

Unfortunately, there is no standardized certification report. Every certification company develops its own report and they can differ widely. The most useful reports follow the prescribed tests conducted by the certifier and offer results in accordance with the three main points listed above. Exhibits 1-3 are certification quick-reference cards that identify the critical elements that must be tested for each of the three different types of engineering controls. The reference cards detail what needs to be proven during certification and provide a basic roadmap for reading a certification report.

The Controlled Environment Testing Association (CETA) outlines cleanroom certification practices that are followed by most qualified certifiers. The organization's *Applications Guide CAG-003-2006* details the specific procedures to be used in the cleanroom certification process but it does not specify the documentation requirements. In an attempt to bridge that gap, CETA put together CAG-008-2010 (current version 2012) to provide a matrix for following the certification report for the secondary engineering controls (SEC). The association is still working on a matrix for understanding the primary engineering control (PEC) certification reports. These documents, which are available to CETA members online, are designed to identify the critical elements and data points for each test, as well as detail the instruments to be used in testing.

The sterile compounding facility manager should take control of the certification process by insisting that the certifier certify the facility in accordance with CAG-003-2006 and document the results in accordance with CAG-008-2010. This will ensure that all of the appropriate tests are conducted for both the primary and secondary engineering controls and that good documentation practices are followed. The end user should be able to clearly understand

how every test was conducted and what equipment was used for that test. Unfortunately, many of the certification reports that I have reviewed do not meet this objective.

It should be noted that cleanroom certification and environmental monitoring are not the same thing—a fact that can cause confusion among facility managers. The current USP Chapter <797> requires environmental sampling, including viable particle counts via forced air sampling, to be performed at least every six months. This happens to be the same frequency as the typical interval for primary and secondary engineering control certification, therefore, the default process often results in the certification contractor adding this to the certification process.

It is not, however, mandated that the certifier provide environmental monitoring, and not all cleanroom certifiers do. In many cases, semi-annual environmental monitoring does not provide for adequate trending data. It may be more efficient to provide those services in-house with the support of a qualified microbiologist. CETA applications guide CAG-009-00 covers environmental monitoring, including documentation, in depth. This article will discuss only the traditional certification processes.

What Makes a Good Report?

Certification reports are supposed to be tools for professional documentation of proof that the sterile compounding facility engineering controls are performing as

Exhibit 1
Certification Reference for Traditional Primary Engineering Controls

Test	Laminar Airflow Workbench (LAFW)	Biological Safety Cabinet (BSC)*
Placement of Primary Engineering Control	Placed in ISO Class 7 cleanroom, 0.02" w.c. positive or SCA	Placed in ISO Class 7 cleanroom, 0.01" w.c. negative to ante room
Airflow Velocity	Velocity 80-100 FPM 6-12" from the filter	Downflow velocity profile and face velocity tests
HEPA Filter Leak Test	HEPA filters must be certified to be free from leaks >0.01% of upstream aerosol concentration	HEPA filters must be certified to be free from leaks >0.01% of upstream aerosol concentration or aerosol penetration not >0.005% of upstream concentration for filters that cannot be scanned
Airflow Patterns Smoke Test	An observation using smoke to visualize airflow under dynamic operating conditions (with pharmacy staff compounding) to confirm laminarity of the air is undisturbed by compounding processes. Specific smoke pattern tests to ensure the device is functioning property is also performed under "at rest" conditions.	
Site Installation Assessment Tests	N/A	Verifies that the BSC is properly integrated into the facility testing airflow and sash alarms, interlocks and exhaust system performance
Non-variable Particle Counts	Particle counters capable of detecting 0.5 µm size particles are used to verify ISO Class 5 air conditions under dynamic operating conditions	

***** NSF International Criteria

KEY:

BSC Biological safety cabinet
FPM Feet per minute
HEPA High efficiency particulate arresting
ISO International Organization for Standardization
LAFW Laminar airflow workbench
SCA Segregated compounding area
w.c. Water column

Source: *Courtesy of CriticalPoint, LLC. Adapted from CETA Certification Guide for Sterile Compounding Facilities (CAG-003-2006-11) and NSF/ANSI 49-2012.*

needed to safely prepare compounded sterile preparations. A thorough and useful certification report should include the following items (see Exhibit 4 for a list).

An orientation drawing should be included with an explanation of the basis for determining the acceptance criteria. For example, a drawing showing all rooms with their purpose will be used to justify ISO classifications, air change rates, and room pressure requirements for each room.

The certification report should include either a description for each test conducted directly in the report or in a standard operating procedure (SOP) referenced in the report. Note that if a SOP is referenced, a copy of that SOP must be provided by the certifier and maintained on the end user's site. You cannot look up details in an SOP if you do not have a copy of that SOP. Additionally, many SOPs are developed as a general document meant to cover a myriad of situations with statements such as "readings shall be taken 6-12" from the diffuser." This does not adequately satisfy the end-user's responsibility to understand *exactly* how the device was tested. You need to know if it was tested at 6" or 12" from the diffuser. When negotiating with the certifier, be sure to insist on specific procedures for your operation.

Specific acceptance criteria must be developed for each facility. The primary engineering controls generally have benchmarks developed by the manufacturers in compliance with industry standards such as NSF/ANSI

Exhibit 2
Certification Reference for Secondary Engineering Controls

Test	Non-Hazardous Drug Buffer	Ante Room	Hazardous Drug Buffer
Airflow	30 ACPH (at least 15 ACPH from outside the room)	Not specified, but 20 ACPH is desirable	30 ACPH; 12 ACPH if CACI is used
Room Segregation	Minimum differential pressure of 0.02" w.c. positive from cleanroom to ante room and all adjacent spaces	Minimum differential pressure of 0.02" w.c. positive from cleanroom to all adjacent spaces	Minimum differential pressure of 0.01" w.c. negative-from the HD cleanroom to the ante room
	If displacement airflow, then velocity of 40 FPM from cleanroom to the ante room across the entire opening		Not allowed in HD compounding
HEPA Filter Test	All HEPA filters in the secondary engineering controls are tested at each certification. Maximum allowable leakage is 0.01% of the upstream aerosol concentration.		
Smoke Pattern Testing	Buffer rooms must be segregated from the ante area and all other adjacent spaces. With the doors closed, use smoke around the opening of doors to ensure air is traveling in the right direction.		
Non-Viable Particle Counts	ISO Class 7	ISO Class 8 unless it serves HD buffer then ISO Class 7	ISO Class 7
	Airborne particle counter used to sample particle levels in all locations under dynamic operating conditions.		
Temperature	No specific requirement other than comfortable, typically a temperature of 64° F		
Humidity	Not a mandatory test but relative humidity between 35% and 60% is recommended		

KEY:

ACPH	Air changes per hour	**HEPA**	High efficiency particulate arresting
CACI	Compounding Aseptic Containment Isolator	**HD**	Hazardous drug
CFM	cubic feet per minute	**ISO**	International Organization for Standardization
FPM	Feet per minute	**w.c.**	Water column

Source: *Courtesy of CriticalPoint, LLC. Adapted from CETA Certification Matrix for Sterile Compounding Facilities (CAG-008-2010).*

Exhibit 3
Certification Reference for Isolator Type Engineering Controls

Test	Compounding Aseptic Isolator (CAI)	Compounding Aseptic Containment Isolator (CACI)
Placement of PEC	Preferably room/area devoted to compounding	Room certified to have at least 12 ACPH and be 0.01" w.c. negative to adjacent room
Airflow Velocity	Measurement of actual airflow to manufacturer's design intent. The main chamber is expressed as a range of FPM with designated percent uniformity.	
Chamber Pressure Test	Determine that pass-through and main chamber pressure is adequate to provide isolator separation between main chamber and ambient spaces. Pressure range determined by manufacturer.	
Site Installation Assessment Tests	Tests to verify proper alarm function, pass-through door interlock function, and proper canopy or exhaust connection performance.	
HEPA Filter Integrity Leak Test	All HEPA filters in the secondary engineering controls are tested at each certification. Maximum allowable leakage is 0.01% of the upstream aerosol concentration.	
Airflow Smoke Pattern Test	An observation using smoke to visualize airflow under dynamic operating conditions (with pharmacy staff compounding) to confirm laminarity of the air is undisturbed	
Preparation Ingress and Egress Test	Determine if the pass-through system is capable of supporting material transfer while maintaining ISO Class 5 conditions during the transfer.	
Non-Viable Particle Counts	Particle counters capable of detecting 0.5 µm size particles are used to verify ISO Class 5 air conditions both at rest and during dynamic operating conditions.	

KEY:

ACPH Air changes per hour
CAI Compounding aseptic isolator
CAIC Compounding aseptic containment isolator
HEPA High efficiency particulate arresting
ISO International Organization for Standardization
FPM Feet per minute
PEC Primary engineering controls
w.c. Water column

Source: *Courtesy of CriticalPoint, LLC. Adapted from CETA Compounding Isolator Testing Guide (CAG-002-2006).*

standard 49 (NSF International/American National Standards Institute) for biological safety cabinets (BSC) or IEST RP CC002 (Institute of Environmental Sciences and Technology) for laminar airflow workstations (LAFW). This information will be known by the certifier and it should be clearly spelled out in the report.

Determining the specific acceptance criterion for the cleanroom is more challenging. Ideally, the cleanroom design documents will be used as a basis for secondary engineering controls acceptance criteria. USP Chapter <797> specifies minimum criteria for air change rates and room pressure, but it does not dictate the actual design airflow criteria. For example, a negative pressure hazardous drug compounding room operating at the minimum 30 ACPH will most likely result in total and viable particle count excursions, therefore failure. Hopefully, the cleanroom designer took this into account when designing the HVAC system. For these rooms, the actual design must be used to establish the acceptable airflow parameters, not the USP-mandated minimums.

In all cases, the certification report must list the acceptable range for each test along with the result of the tests. A clear pass or fail statement based on the listed acceptance criteria should also be included for each test, the overall device report, and the overall facility report.

All calculations and assumptions must be documented. The use of checkboxes alone is not acceptable. A certification report that does not provide all the details needed to support its conclusions should be rejected. Use CETA CAG-008-2010 to evaluate your certification report. After identifying what tests are required for each engineering control, use CAG-008 to determine the minimum reported values that need to be documented.

Exhibit 4
Elements of Good Cleanroom Certification Report

- Orientation drawing(s)
- Description of each test conducted
- Facility-specific acceptance criteria
- Test results with clear pass/fail indication
- All data and calculations
- Test equipment used and calibration records

Every device (LAFW, BSC, CAI, CACI, or cleanroom) will use airflow through HEPA filters to create a desired outcome, which for the purposes of sterile compounding will be an ISO classification. For hazardous drug compounding, protection for the environment and personnel must also be provided. At a minimum, every certification report must include some form of the following:

- Airflow testing
  - » Velocity for unidirectional airflow devices
  - » Air change rates for cleanrooms
- Segregation
  - » Differential pressure across a door for a traditional cleanroom
  - » Displacement airflow across an opening for open architecture rooms
  - » Airflow smoke pattern testing for LAFWs and BSCs
- HEPA filter integrity testing
  - » All PECs and SECs have HEPA filters that must be leak tested
- Non-viable particle counts (total counts)
  - » USP Chapter <797> requires counts to be taken under dynamic operating conditions.
  - » For PECs it is recommended that counts also be taken under at-rest conditions. This is with the device loaded as it will be used but with no compounding activities being performed. This is not an alternative to dynamic testing, but it will provide a baseline of how that device is performing.
- Viable particle counts
  - » Environmental monitoring must be done under dynamic operating conditions. Details for performing and documenting this can be found in CAG-009. It is not part of this discussion.
- A dynamic smoke pattern test must be performed on all unidirectional airflow spaces.

The test equipment used for certification must be calibrated at no greater than a 12-month interval. Calibration certificates should be provided for every test instrument used and the specific model and serial number of each test instrument should be documented on the certification report.

How Do I Prepare for Certification?

Ensuring a compliant cleanroom requires both the certifier and the sterile compounding facility manager to work together to properly address all issues. The first key step in working together is having a clear understanding of your role as the end user as well as the role of the certifier.

For his/her part, the certifier is responsible for determining the appropriate tests for all primary and secondary engineering controls and following industry guidance in establishing test protocols. The certifier works with the end user in advance of the testing to determine the acceptance criteria for the facility and should provide immediate notification of any and all findings that fall outside those ranges. The certifier must also ensure that all of the people and equipment he/she is employing are up to snuff. Technicians should be accredited by both the CETA National Board of Testing and NSF International. As mentioned earlier, testing equipment should be properly calibrated and accompanied by all appropriate records.

The certifier should also ensure that the certification report complies with CETA CAG-003 guidance and provide a final report in a timely manner (typically within two weeks). While the end user is ultimately responsible for understanding and being able to communicate the report's findings to inspectors, the certifier plays a role in reviewing the report, answering questions, and assisting the facility manager in this regard.

The certifier can and should also advise the facility manager about the most efficient scheduling plan for the certification. Pharmacy staff must be able to participate in the dynamic testing, including particle counts and smoke pattern testing. In addition, the certification process requires generation of a significant amount of particulate contamination, visual "smoke" medium, and a particulate HEPA filter challenge aerosol. Therefore, all primary engineering controls must be disinfected following the certification and prior to use in sterile compounding.

The facility manager is responsible for selecting and working with a certifier both in advance of the testing and after. Getting off on the right foot is of the utmost importance. Begin by making use of accredited technicians and use the CETA applications guides as a requirement of your purchase agreement with the certification contractor. Remember that the end user plays a significant role in determining the acceptance criteria for testing, which if possible should include providing the original HVAC mechanical plans so the certifier has an understanding of how the cleanroom was engineered. For this reason, it is important to be prepared with the proper documents.

Review the certification reports using CAG-008 as a review tool. If you selected a qualified certifier, the report should mirror this document, but note that there is no standardized format for certification reports and documentation. If you do not understand any part of the report, ask the certifier to review it with you. Certification reports must be understood so they can be used to determine if the critical facility is in a state of control. In addition, you must also be able to explain the report and any subsequent actions taken to an inspector. Be prepared.

Most importantly, work with your certifier and facility engineers to address all problems noted in the certification report. Most certifiers can troubleshoot and repair the primary engineering controls. You may have to coordinate secondary engineering control repairs with the facility engineers. To learn more about working with cleanroom certifiers, read "It's Not Just About the Stickers—Building a Positive Relationship with a Certifier is Key to Maintaining a State of Aseptic Control in Your Cleanroom" on page 25.

[1] Controlled Environment Testing Association, 1500 Sunday Drive, Ste. 102, Raleigh, NC 27607; www.CETAinternational.org