CriticalPoint
a trchealthcare brand

CriticalPoint Pearls of Knowledge — April 2025

The Blueprint to Certification: What You Need to Know

Introduction

CriticalPoint is kicking off a series of Pearls focusing on device and cleanroom certification. Each month, we will dive into a particular topic or a specific test to provide pharmacies with additional insight into what certification is and what it looks like. This month, we cover airflow testing in the secondary engineering control (SEC), commonly known as the cleanroom suite or containment segregated compounding area (C-SCA), and dedicated hazardous storage rooms.

Air changes per hour (ACPH)

Proper airflow design for a cleanroom suite is the first line of defense against operational contamination. ACPH ensures a constant flow of HEPA-filtered air into the cleanroom, which reduces, dilutes, or removes contaminants through a balance of supply and exhaust airflow design parameters. The frequency of airflow changes helps maintain the required cleanliness levels for various cleanroom ISO classifications (ISO 7 and 8) by continuously cycling fresh, filtered air.

The balance of airflow is vital to the success of cleanroom functionality. The balance between air supply and return/exhaust air creates a determined amount of pressurization in each room, which can be measured at each entry/exit of every door. The intent is to create cascading airflow from the cleanest to dirtiest adjacent spaces. This relationship of airflow balance helps segregate and protect the higher ISO-classed environment. The result of cascading airflow pressures is flowing airflow from a higher pressure (cleaner ISO class) to a lower-pressure space. This constant flow of pressure aids in controlling contamination in addition to filtering ACPH that supply each respective space.

There are many cleanroom industries other than sterile compounding cleanrooms. Controlled environments and cleanrooms existed decades before the regulation of sterile compounding cleanroom. This means that cleanroom design and functionality standards existed before USP <797> required minimum ACPH. Generally speaking, an ISO Class 8 area needs to have around 10 to 25 ACPH (depending on the industry and workflow activity) according to industry standards and guidelines. For sterile compounding ISO Class 8 environments, the FDA recommends that supporting rooms have a minimum of 20 ACPH to be acceptable.[1] In other words, USP didn't arbitrarily pick the minimum requirement for ISO 8 rooms as 20 ACPH.

Science and math figure prominently in planning a successful cleanroom environment. Any general space could achieve regulatory compliance by meeting minimum-standard design requirements. But the same space could fail operational compliance as a result of workflow and staff activity challenging the capabilities of the minimum design. Unfortunately, the only way this might be revealed is by viable air and surface testing during commissioning phases post-construction. Essentially, the microbial state of control is not sufficient to support what is going on in the cleanroom despite design regulation and specification. More consideration is needed by assessing workflow, staff presence, and equipment installation. The solution is to design for higher ACPH rates and airflow balance to support high traffic and activity before cleanroom construction is completed, avoiding costly setbacks and frustration.

Room volume calculations

Determining ACPH requires obtaining dimension measurements of the room so that the cubic volume of the space can be decided. Each room must be measured by its length, width, and height. It's easy to determine the volume of a typical square or rectangle-shaped room. However, rooms aren't always perfectly constructed with four 90-degree corners.

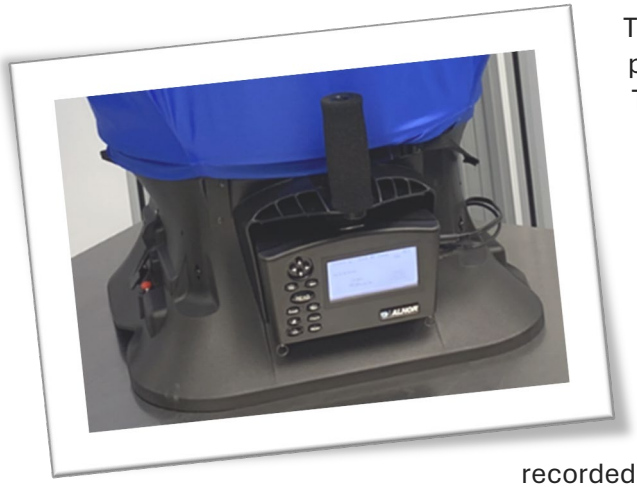
The certifier must determine the layout of the room, assess whether the ceiling height is consistent, and account for atypical cutouts or multiple corners. The best way to determine the volume of multi-cornered rooms is to break the room into smaller areas. Once this is achieved, the cubic footage of each area is added together to determine the total volume of the space. A room map or layout is typically created during this step. It is important to capture on the layout where equipment, carts, pass-through chambers, doors, etc., are located.

Taking measurements in inches is the simplest way to determine cubic volume of any given space and aids in accuracy. Most spaces measured end up being XX-feet and XX-inches. So, converting to inches is the soundest method

Most spaces aren't whole numbers (in feet) when measured, but rather feet and inches. Therefore, taking measurements in inches is the simplest way to determine the cubic volume of any given space and aids in accuracy.

Supply airflow measurements

Testing airflow in SECs involves taking measurements of the supply airflow feeding a HEPA filter housing or measuring exhaust for hazardous drug containment. The primary testing method uses a flow hood to measure airflow volume rather than velocity. The flow hood is fashioned with an air multimeter device that must be calibrated. This multimeter must also have a specific range of accuracy and ability to measure airflow with precision.



The flow hood itself must be designed to fit exactly around the perimeter of the airflow diffuser screen located in the ceiling. There are two common cleanroom screen sizes: 2 ft. x 2 ft. and 2 ft. x4 ft. A flow hood cannot go from measuring airflow from a 2' x 2' screen to a 2' x 4' screen. It must be constructed to fit the airflow screen being tested. Otherwise, the airflow volume is not represented accurately.

The certifier must measure the individual airflow of the ceiling HEPAs present in each room. The measurement value from each HEPA is recorded separately, and the values are added together to record the total airflow supply to an individual room.

Documenting the data

There are various ways to capture data, either electronically or paper based. Determining accurate dimensions of the space and recording the measurements are a must. Additionally, the individual airflow volumes are recorded either in a spreadsheet or written on the room

drawing. Once the data recording is complete, the ACPH rate can be calculated against the cubic volume of the space being tested.

$$\frac{CFM * 60}{Room Volume}$$

Calculating air changes per hour

Air volume is also known as cubic feet per minute (CFM). Since the certifier measured the space in cubic volume, it's simple to calculate the ACPH rate.

The certifier multiplies the total room air supply measured (CFM) by 60 (the number of minutes in one hour), then divides by the calculated room volume. For example, a certifier measures five HEPA filter diffusers, records the individual values, and totals them to establish the total room supply. In this example, it adds up to 1,765 CFM. Total CFM (1,765) is then multiplied by 60 (minutes per hour), which equals 105,900. The example room is 12.5 feet by 24.5 feet and has a ceiling height of 9 feet. The cubic volume of this space is determined at 2,700. The certifier divides 105,900 by the room volume of 2,700. The result is 39.22 ACPH. It's important to note that it is not appropriate to apply significant rounding to the final calculated ACPH. Although 39.22 may round off and report as 39, CriticalPoint recommends values remain as they are calculated, which may provide decimals to at least the hundredth.

USP <797> requirements

USP <797> requires reporting three separate ACPH-related values (when applicable):

1. Total HVAC facility supply
2. Supplemental air provided by the HEPA filtration of the primary engineering control (PEC)
3. Total ACPH value of both the HVAC and PEC values

As part of certification, both the PECs and SECs are tested for industry, manufacturer, and USP compliance. The certifier must retain the HEPA-filtered airflow values that were measured for each PEC that recirculates airflow into the buffer room. This enables them to add these values when reporting room airflow and ACPH. Measuring airflow in PECs is similar in process; however, the certifier must determine airflow velocity in feet per minute (FPM) that is exiting the HEPA filter and convert that value back to volume (CFM). The total CFM for a 4-foot clean bench has an average airflow rate of around 1,000 to 1,200 CFM. The total CFM for a 6-foot clean bench has an average airflow rate of around 1,700 to 1,900 CFM. These values vary due to the average airflow velocity speed and the size of the HEPA filters they have.

Let's consider our example room mentioned above. We determined that the ACPH provided from the room supply (HVAC system) was 39.22 ACPH. The certifier must calculate the supplemental HEPA-filtered airflow from each PEC and total the values. If there are three 4-foot clean benches, each having 1,050 CFM, the total value would be 3,150 CFM of HEPA-filtered air recirculating in the room as well as the HEPA filtration from the HVAC supply. The certifier must report three values. We determined the room has:

1. 39.22 HVAC supply ACPH (1765 x 60 ÷ 2700)
2. 70 supplemental PEC supply air (3150 x 60 ÷ 2700)
3. 109.22 Total ACPH (39.22 + 70)

Reporting elements

In addition to the USP <797> reporting requirements regarding airflow testing in the SEC, CETA's CAG-003 Certification of Sterile Compounding Facilities for USP Compliance provides reporting guidelines to ensure pharmacies and designated persons can easily determine and confirm compliance with comprehensive reporting data. CAG-003 lists several elements for reporting and documentation:

1. Record all airflow measurements and their corresponding filter or diffuser locations or grid identifications on a diagram
2. Calculate and report room volume
3. Calculate and report the average total room airflow volume
4. Calculate and report the total air changes per hour of the room (including LAFW and/or non-ducted BSC HEPA exhaust to room if applicable)
5. Report any correction factors used or deviations from the primary method
6. Name of test (e.g., Room Airflow Analysis)
7. Report acceptance criteria
8. Provide a pass or fail statement based on the results of the test

Summary

Require vendors to adhere to recognized industry standards and guidelines, such as USP <797> and CETA's CAG-003, to help maintain a clean and safe environment for sterile compounding. Ensure that certification vendors employ primary testing methods for airflow measurements, and follow the latest versions of these standards and guidelines. The designated person within each organization must thoroughly review the final certification report to verify facility compliance, including all reporting requirements outlined in USP <797>. Additionally, confirm that the report includes accurate room diagrams with precise dimensions and provides comprehensive, detailed data representations.

References

[1]FDA Guidance for Industry, Sterile Drug Products Produced by Aseptic Processing — Current Good Manufacturing Practice. October 2004.