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AIR VELOCITY MEASUREMENTS AND CORRELATION TO SMOKE STUDIES FOR ASEPTIC OPERATIONS

KEYWORDS

Air Velocity, Air Flows, Smoke Study, Air Pattern Analysis, Working Height, Unidirectional Flow, Air Flow Visualization.

ABSTRACT

Air velocity measurements in conjunction with smoke studies are an important part of the qualification and monitoring of cleanrooms used for the processing of aseptic, sterile and low bioburden medical products. Done in tandem, air velocity measurement and smoke studies allow for the characterization of air flow patterns in critical environments. A baseline air velocity profile supported by static and dynamic smoke studies should be evaluated, as part of the initial qualification of the cleanroom. As part of a Risk Assessment this evaluation should also consider the selection of locations for critical control points for monitoring air velocity, as well as viable and non-viable particles.

As indicated by numerous inspector's observations and warning letters, there is confusion regarding the methodology, sample location selections and acceptance criteria regarding air velocity measurement. Often overlooked is the correlation between air velocity measurements and smoke studies.

It is important to understand that in the evaluation of air movement within a cleanroom, studying airflow visually by smoke studies is more useful than using air velocity measurements. For critical areas too much emphasis is placed achieving air velocities within the [1]range of 0.36 - 0.54 meter/second rather than achieving air patterns that provide a robust sweeping action that protects products and components. [2]"First Air" should contact critical components or products before contacting anything else. It should be free of eddy currents or deviant air that can act as a channel or reservoir for contaminants.

INSPECTOR'S OBSERVATIONS AND WARNING LETTER

Inspector's comments related to air velocity indicate areas of confusion or misunderstanding related to air velocity measurements.

"Your firm did not evaluate work height air velocities in the ISO class 5 Filling Room."

"Your outside vendor's airflow velocity measurements only evaluate the velocities at the filter face, no more than 12 inches from the source of the laminar flow air supply."

"Your firm lacks uniformity assessment specifications for airflow velocities within the same filter and between adjacent filters in the ISO Class 5 Filling Room.

"HEPA filter airflow velocity measurements from filters were found to be lower than your specification of greater than or equal to 0.36 meters/second."

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UNIDIRECTIONAL AIR FLOW

Unidirectional Air Flow as it applies to cleanrooms is HEPA filtered particle free "First Air" moving in a single direction and in a robust and uniform manner. First air should move at sufficient speed to reproducibly sweep particles away from the critical processing or testing area. Because of the complexity of equipment used in processing medical products, cleanroom air flow is seldom laminar air flow.

Critical areas for aseptic, sterile and low bioburden medical products may be provided with localized air flow protection in the form of barrier technologies such as; Biological Safety Cabinets (BSC), Laminar Air Flow (LAF) work stations, Restricted Access Barrier Systems (RABS) or isolators. These systems often utilize unidirectional air flow in conjunction with walls or curtains to act as barriers that direct air flow and act as a barrier for contamination.

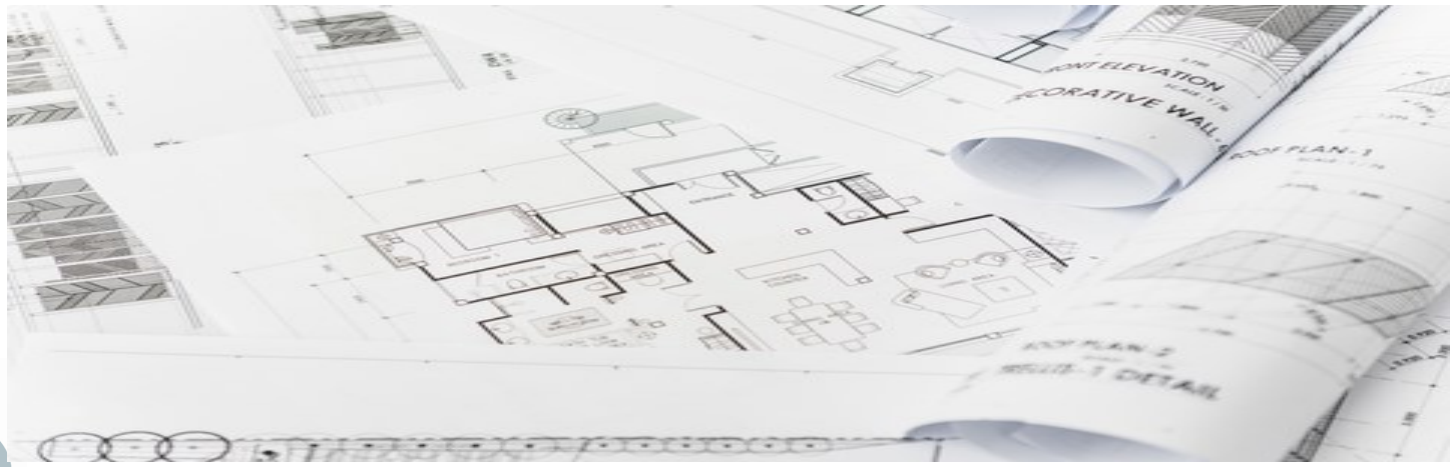
FDA recommends velocities of unidirectional air should be [3]measured 6 inches from the filter face and at a defined distance proximal to the work surface (working height) for the critical area. The position of the working height measurement as well as the acceptance criteria for air velocities at the working height is a common source for inspector's comments.

ACCEPTANCE CRITERIA

Because every cleanroom installation with equipment is unique, air pattern analysis is a subjective process. The evaluation of cleanroom air patterns requires experienced personnel familiar with interpreting smoke studies for the purpose of contamination control.

Because of the complexity and uniqueness of each cleanroom installation, the guidance air velocity range of 0.36 – 0.54 m/sec (71 -106 ft/min) can only be reliably established ≤15 cm (6 inches) from the filter face. Because of this the FDA recommends taking filter face velocity measurements at locations proximal (close to) the work surface. Locations selected as well as acceptance criteria with data must be justified as part of the contamination control policy.

Obstacles such as filling needles, syringe pump towers, stopper bowls or feeding rails, significantly alter air velocities and patterns. Achieving an air velocity at the working height ≥0.36 m/sec may not be practical or suitable for each unique installation. Increasing the air velocity at the working height also increases turbulence in the overall critical area. This is why it is important to establish a suitable airflow for each particular critical area.



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Considerations in Air Velocity Measurement and Correlation with Air Pattern Analysis

1. Characterize air velocity uniformity for each HEPA Filter (multiple locations/ filter) and calculate the average air velocity of each filter.
2. Characterize the uniformity of the Critical Area airflow via comparisons between HEPA filters across the entire critical area.
3. Perform Investigative Static Smoke Studies (Cleanroom is in the At-Rest Occupancy State).
4. Evaluate the Investigative Static Smoke Studies to identify any areas of concern. (eddy currents, deviant air or dead spaces). If any corrective actions are required, upon completion repeat the air velocity measurements and Investigative Smoke Study.
5. Perform Dynamic Smoke Studies, simulating operations.
6. Evaluate the Dynamic Smoke Studies to identify any areas of concern. (eddy currents, deviant air or operator techniques).

AIR VELOCITY MEASUREMENTS FOR HEPA FILTERS IN CRITICAL AREAS

Several air velocity measurements are required for each filter in critical areas. The number of measuring points depend on:

- The size of the filter, the larger the filter the more measuring points that are required
- The closer the filter is to the critical operations, open or exposed containers, the more measuring points required.

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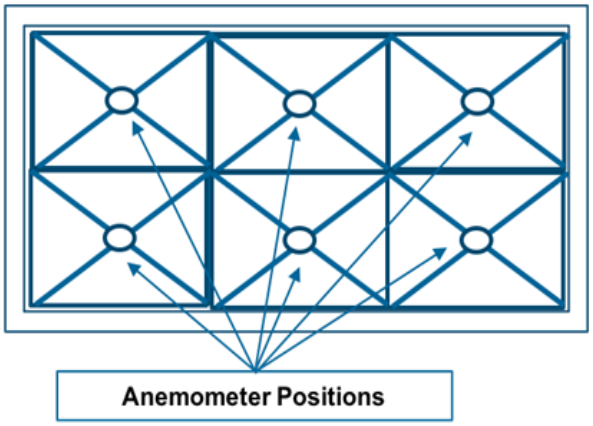
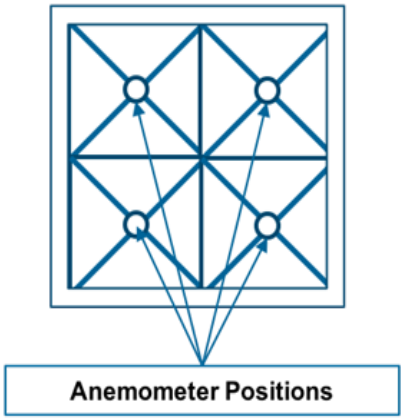
EXAMPLE OR MULTIPLE AIR VELOCITY MEASUREMENTS PER HEPA FILTER FOR COMMON FILTER SIZES

600 mm x 1200 mm (2 ft x 4 ft)
HEPA Filter:
6 Point Air Velocity Measurements



600 mm x 600 mm (2 ft x 2 ft)
HEPA Filter:
4 Point Air Velocity Measurements



It is important to retain air velocity measurements for each grid location of each HEPA filter. Comparisons to the initial test data should be made for every successive test. HEPA filters are the last line of defense in critical high risk operations. Filters can be damaged or compromised by regular operations, decontamination practices or other testing methods such as filter integrity testing.

DIFFUSERS (COVERING MULTIPLE HEPA FILTERS)

In some barrier systems (e.g., RABS or isolators) the grid space between HEPA filters creates a low pressure area above critical operations. This low pressure area forms eddy currents (swirling air) that is unsuitable in a unidirectional flow environment. To compensate for these eddy currents a diffuser membrane is used. These membranes create a more unidirectional air flow, but reduce air velocities. It is important that air velocities and smoke studies correlate air flow conditions, with and without the membrane.

FREQUENCY OF TESTS

After the initial qualification the frequency of air velocity testing and smoke studies should be clearly justified and defined in your Contamination Monitoring Plan or Strategy. Common frequencies for air velocity testing is every six months as part of the cleanroom classification testing for aseptic operations and the surrounding support areas. Once per year for all other cleanrooms. However more frequent air velocity measurement could be considered. As air velocity measurement is less disruptive and less contaminating than smoke studies, these measurements can be carried out on a more frequent basis.

Smoke Studies should be performed initially as part of the qualification and repeated whenever changes in operations, personnel or equipment are made. As indicated in the first edition of ISO 14644-2:2000, the maximum time interval between smoke studies is [4]two years.

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CONCLUSION

Done in tandem, air velocity measurement and smoke studies allow for the characterization of the critical air flow. Once a baseline air velocity and smoke study profile is established for each filter and the overall critical area, routine monitoring of air velocity at critical control points should be considered as part of the overall contamination monitoring plan.

ABOUT THE AUTHOR

Morgan Polen has been involved with cleanrooms and contamination control since 1984. He has Worked in over 40 countries involved with projects ranging from cleanroom design, construction, validation, monitoring program development, particle counter design and product management for cleanroom related products and systems. He has addressed monitoring and control solutions in a wide variety of clean industries such as pharmaceutical, medical device, semiconductor, data storage, aerospace, defense, automotive, optical and others.

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REFERENCES

1. FDA Guidance for Industry, Sterile Drug Products Produced by Aseptic Processing – Current Good Manufacturing Practice: 2004 “A velocity of 0.45 meters/second (90 feet per minute) has generally been established, with a range of plus or minus 20 percent around the set point *(a range of 0.36-0.54 meters/ second)*. Higher velocities may be appropriate in operations generating high levels of particulates.”
2. USP 797 “The “first air” at the face of the filter is, for the purposes of aseptic compounding, free from airborne particulate contamination.”
3. FDA Guidance for Industry, Sterile Drug Products Produced by Aseptic Processing – Current Good Manufacturing Practice: 2004 “Velocities of unidirectional air should be measured 6 inches from the filter face and at a defined distance proximal to the work surface for HEPA filters in the critical area.”
4. ISO 14644-2:2000 Annex A, Table A.1 Schedule of Optional Tests