LIGHTHOUSE WORLDWIDE SOLUTIONS

TECHPAPER

Air Visualization Studies

A Comprehensive Overview

Authored by:

Jason Kelly and Morgan Polen

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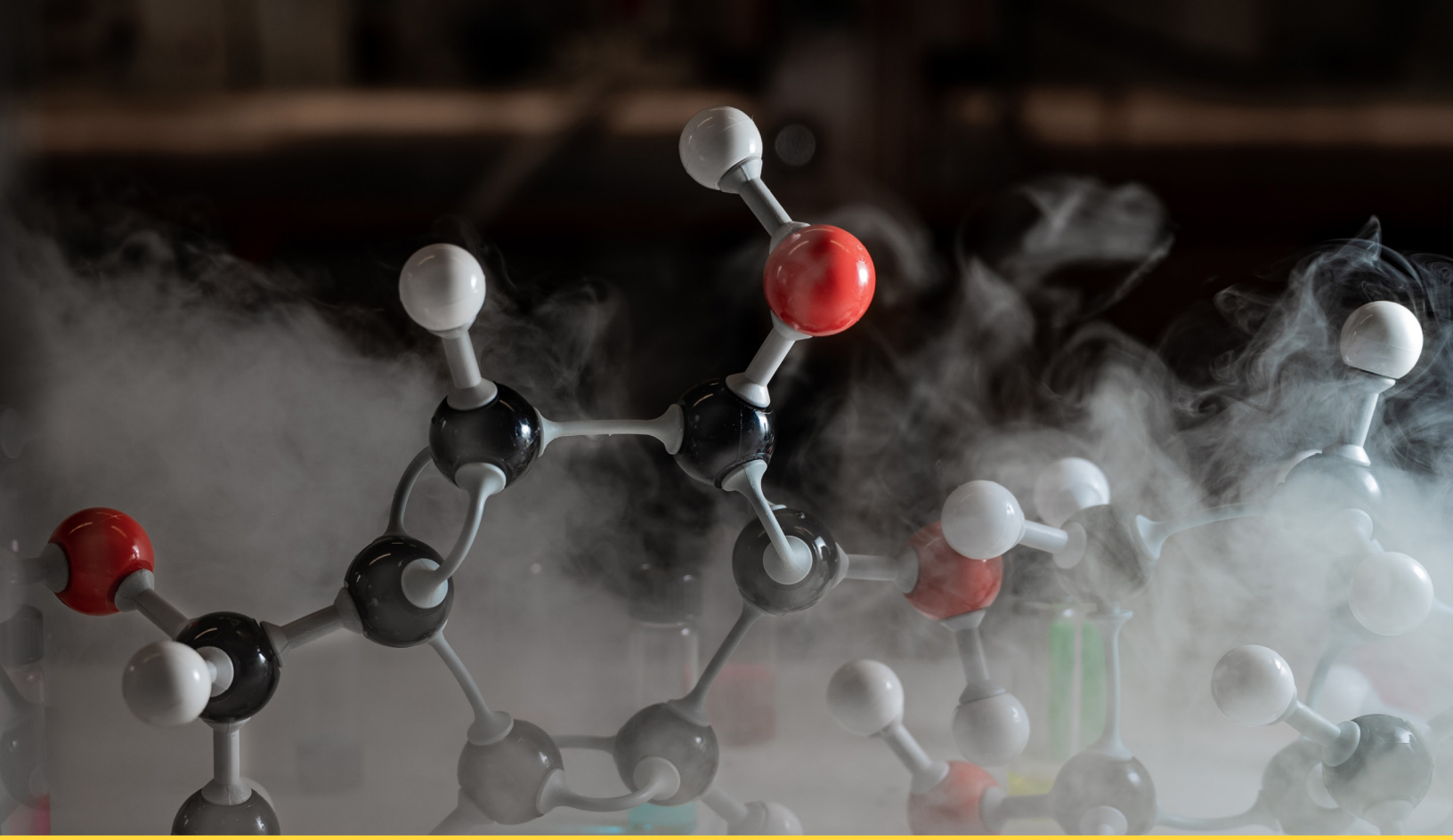


Overview

Airflow Visualization Studies, commonly referred to as *"smoke studies"*, are essential in cleanroom environments, particularly in the pharmaceutical industry, to ensure the proper design and integration of equipment and the function of air handling systems. These studies involve using visible Tracer Particles to observe and document airflow patterns, identify potential contamination pathways, validate cleanroom and barrier system designs, and integrate equipment into the cleanroom. Additionally, the movement of cleanroom personnel and automated equipment can be evaluated regarding airflow.

The Importance

of Airflow Visualization Studies

Validation of Cleanrooms, Barrier Systems Design and Integration:

By visualizing airflow, these studies confirm that the cleanroom's design and equipment integration effectively controls air movement, preventing contamination from equipment, processes, and personnel.

Regulatory Compliance:

Regulatory guidelines, such as international GMP Annex 1, emphasize the necessity of airflow visualization to demonstrate that there is no ingress from lower-grade areas and to ensure unidirectional airflow in critical zones.

Optimization of Environmental Monitoring:

Understanding airflow patterns aids in strategically placing environmental monitoring devices, such as particle counters and active air samplers, ensuring accurate assessment of cleanliness levels.

Risk Mitigation During Aseptic Operations:

Visualizing airflow during aseptic filling processes ensures that air movements do not introduce contaminants into sterile products, maintaining product integrity.

Process optimization and operator training.

The Airflow Visualization Studies can help achieve a greater understanding of airflow patterns in relation to operator movements. This information can be used to optimize SOPs and document operators' movements and actions, allowing the studies to be

Testing capper hop on sterile injectable filling machine.

Integration with Environmental Monitoring:

Environmental monitoring relies on devices like particle counters and active air samplers to validate the cleanliness classification of cleanrooms. Airflow visualization studies inform the optimal placement of these devices by:

Identifying Critical Zones:
Highlighting areas where contaminants are likely to accumulate or be transported, ensuring monitoring focuses on high-risk locations.

Validating Airflow Uniformity:
Confirming that unidirectional airflow systems provide a homogeneous airspeed in the working area, as standards recommend.

Ensuring Compliance with Cleanroom Classification:
Supporting the classification process by demonstrating that airflow patterns meet the standards for different cleanroom grades.

Airflow Visualization Studies are a critical component in the design, validation, and monitoring of cleanroom environments. They ensure that airflow patterns effectively minimize contamination risks, support regulatory compliance, and enhance the accuracy of environmental monitoring systems, thereby safeguarding the integrity of aseptic manufacturing processes.

Testing fill head on sterile injectable filling machine

How Critical

are Smoke Studies in cleanroom aseptic operations?

Regulatory compliance agencies worldwide use smoke studies as evidence to either approve a facility's manufacturing license or even to shut down pharmaceutical facilities. Sometimes, airflow visualization testing may uncover cleanroom/equipment design flaws, equipment integration errors, operator training gaps, or cleanroom furniture location selection errors. In cleanroom design, there are many expectations in the outcome of the HEPA system, the room balancing, the equipment performance, and the removal of particles and contamination from the cleanrooms. Computational Fluid dynamics (CFD) is widely used in the design of cleanrooms and indicates the room's possible performance under different conditions. CFD is recomended in the design phase of a project as it can prevent cleanroom design errors and equipment integration issues. However, there is no substitute for actual smoke studies as CFD is a computer model, and smoke studies are done in the physical world.

For example, perforated stainless steel tables are designed to let the air pass through them. There is an expectation that these tables improve airflow in cleanrooms but the reality is they are only suitable in limited unidirectional flow applications (where they are placed directly underneath a HEPA filter and the smoke studies validate the use and installation of this work surface. Perforated tables (as seen below) are completely unsuitable in non-unidirectional flow applications as air can rise up from the floor onto the work surface. Smoke studies shoud be conducted for each table in the cleanroom to prove that air flows in a favorable direction and not from the floor upwards to the work area of the table.

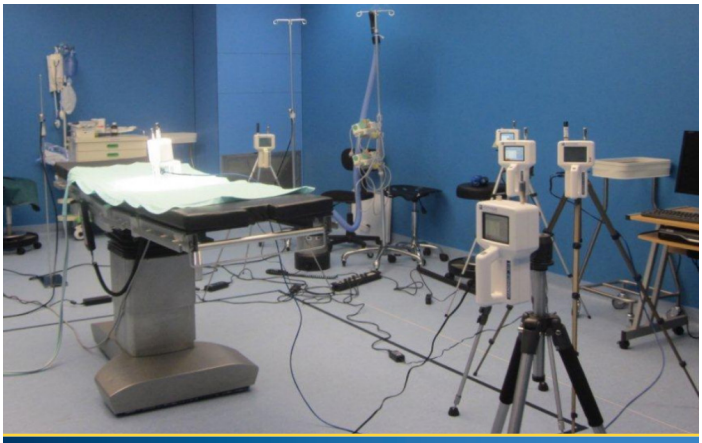
What about a possible "Bounce Back effect" where the air coming down from the HEPA filters in the ceiling at 90ft/min (0.45/sec) hits the floor and the bounce back causes air turbulence at the working height that may impact on the critical zone? Bounce back is a very common issue in cleanrooms and not only in the Pharma Industry.

"Data from a CDC's 2015 survey estimated about 687,000 HAIs in U.S. acute care hospitals, with approximately 72,000 hospital patients with HAIs dying during their hospitalizations".

To highlight this issue and how serious it can be for patients back in 2014, Lighthouse Worldwide Solutions and Dr. Jennifer Wagner Ph.D., CIC Microbiologist, Infection Preventionist conducted a study of this phenomena in a mockup of a real-life operating theatre to investigate higher rates of hospital acquired infections (HAIs) these are post operation infections that patients had that were attributed to the operation environment, (think about a patient having major surgery like an open-heart surgery).

Dr. Jennifer Wagner Ph.D., CIC Microbiologist, Infection Preventions and team simulating operating conditions

It is assumed that the Operating Room is sterile. That is a major assumption, and the study showed how badly designed the HEPA filtration airflows over the operating table were as the bounce back effect literally picked up microbes that were on the floor and plopped them on top of the patient. Air sampling and settle plate CFU data confirmed the presence of viable particles on the patient.



Further studies by Lighthouse Worldwide Solutions in the Netherlands looking at particle distributions in the operating theatre (85% of hospitals in The Netherlands use Lighthouse Monitoring Systems with increased patient satisfaction)

In both these examples, the key takeaway here is that air visualization studies unveil what we cannot see, and they also rewrite our expectations, so we don't jump to conclusions. Without proper testing using airflow visualization techniques performed by qualified experts how are you to know?

Let's take a quick look at current Regulations

"On average how often do Pharma sterile manufacturing companies conduct Airflow Visualization studies and what are the expectations from regulatory bodies?"

Regulatory requirements mandate that smoke studies be conducted during the qualification of cleanrooms and clean air devices (barrier systems), including as-built and at-rest states, typically managed by the cleanroom construction firm. However, once operational, facility owners or operators must perform airflow visualization as part of Environmental Monitoring (EM), Performance Qualification (PQ), and requalification risk assessment.

For sterile compounding under **USP 797**, dynamic smoke studies must be repeated every six months. However, this frequency does not necessarily apply to **503B outsourcing facilities**, **cGMP manufacturing**, **or Annex 1**, where guidelines leave room for interpretation based on risk assessments.

ISO 14644 provides standards for cleanroom qualification and monitoring. Initially, **Part 2 (2001)** recommended conducting smoke studies *every two years*, but in 2015, the requirement shifted to a risk-based approach. *The British Standards Institute (BSI) later set a four-year interval for airflow visualization*, which some experts argue is inadequate for pharmaceutical manufacturing due to aseptic operator turnover and ongoing facility and process changes.

In particular, experts feel that the four-year interval for airflow visualization is irresponsible for pharmaceutical and medical product manufacturing. Given the frequent changes in facilities and processes, this extended timeline does not sufficiently ensure contamination control and product safety.

A *significant issue* is that many organizations conduct smoke studies *only once at startup and fail to integrate them into routine contamination control strategies, risk assessments, and operator training.*

This lack of ongoing assessment may compromise cleanroom performance and regulatory compliance as well as product safety.

With **Annex 1**:2022 and Contamination Control Strategy (CCS) it is encouraged to have smoke studies (Airflow visualizations) as part of your CCS Risk Assessment and the frequency should be based after initial handover to a routine testing service and especially if there are any changes to the cleanroom environment, additional personal added to the cleanroom (provided the capacity is not maxed out), changes to room layout or equipment, new equipment or process introduced and they should also be used as part of operator training, showing the impact operators have so that they are conscious of their behaviors and movements and locations near to critical zones. There is a lot of staff turnover in the Pharmaceutical Industry so a good training program using airflow visualizations can significantly assist in operator understanding of their impact on the safety of aseptically products.

When it comes to cGMP, the FDA says they are minimum requirements. If we look at this in another light, would you go to the most significant person in your life, such as your husband or wife and say, *"Hey baby, what's the minimum I need to do to stay in this relationship?"*

We need to step up and not only just follow the minimum requirements but to exceed them, monitor the culture that develops in some companies and to use Risk Assessments and always have in the back of your mind patient safety. If you are part of an organization that manufactures sterile aseptic products, would you be confident if you injected them into your husband, wife or children? . We should always be thinking about patient safety and the patient needs to be in the boardrooms of Big Pharma or at least have a representation and major consideration to manufacturing operations.

Key Points

Let's take a look at some

The actual (or physical) **Contamination Control Effect** of cleanroom airflow can only be effectively understood when it is *visually represented*.

- Airflow visualization is a Science not unique to Cleanrooms
  - Accurate visual representation of air patterns is required when testing medical product cleanrooms.
  - Airflow visualization technology & techniques can impact results and influence conclusions.
- The Science of Airflow Visualization is not well understood, based upon regulators' comments and observations; reasons include:
  - Lack of well-defined standards and guidance
  - Inappropriate equipment on the market.
  - Lack of industry-accepted training.
- Airflow visualization is more than a Pass/Fail Test; it is part of a larger contamination control strategy (regardless of Industry).
- There is nothing clean about a "smoke study"
  - Airflow Visualization, like Filter Integrity Testing and Recovery Testing, is an extremely invasive test; after the "Smoke Study," comprehensive cleaning is required.
  - During the smoke study, we are Introducing test equipment, including, in some cases, ladders, cameras, tripods, suction cups, tracer particle (smoke) generators, and test personnel. All of these things contribute to the generation of billions off particles. As It is necessary to do the studies, cleanroom managers must understand this and plan accordingly, as an effective cleaning process is needed to clean the cleanroom (with environmental monitoring) before becoming operational again.
- CFD is a predictive tool, and it is a good technical aid to use in the development of cleanrooms and also for insight into RABS and Isolators.
  - However, CFD should not be a replacement for smoke studies.
  - The combination of CFD and smokes studies do make a more powerful team.
  - CFD models should be provided by equipment providers and these CFD models combined with supporting room CFD models for ISO 7 environments make a powerful visualization and can greatly aid in the development and design of cleanrooms prior to the rooms being built. HEPA filters and return air ducts can be moved around in relation to equipment and that equipment's exhausts of air to determine the optimal final locations of equipment, furniture and ceilings HEPAs.

The FDA

What are their thoughts?

"The FDA is becoming wiser, in relation to CFD models and subsequent smokes studies, and have required some companies to test their Isolators with the doors open to see the effect of the supporting rooms airflows on the impact of the isolator"

The FDA and other regulators understand the importance of smoke studies in such scenarios as air visualizations become more apparent when undertaken under dynamic conditions. Since the barrier system is opened as part of the aseptic manufacturing process, whether it is for set-up and installation of large items such as stopper bowls or filling assemblies or as part of corrective or inherent interventions, it is imperative to understand the impact of that open door on your process.

The results from smoke studies can reveal surprising outcomes, and it is important to take the "blinders" off and look at the whole cleanroom environment, how the airflows are moving in that environment, and the interaction between the critical zone and supporting room airflows. The FDA understands these factors and requires more manufacturers to undergo more dynamic smoke studies and to change their cleanrooms to protect the aseptic core.

Does Vaporized Hydrogen Peroxide (VHP) Completely Sanitize an Isolator?

Vaporized Hydrogen Peroxide (VHP) is widely used for decontaminating isolators, cleanrooms, and equipment in pharmaceutical and medical device manufacturing. However, VHP does not achieve full sterilization in all cases—it is primarily considered a decontamination method rather than a sterilization method.

Difference Between Sterilization and Decontamination

Sterilization: The complete elimination or destruction of all microbial life, including bacterial spores, viruses, and fungi, typically achieving a **sterility assurance level (SAL) of 10^{-6}** (i.e., less than one viable organism per million treated items). Common sterilization methods include autoclaving (steam sterilization), ethylene oxide (EtO), and gamma irradiation.

Decontamination: A reduction of microbial contaminants to a safe level, but not necessarily complete elimination. VHP is highly effective at reducing microbial bioburden, including bacteria, fungi, and some spores, but it may not ensure complete sterility under all conditions.

Cleanroom Flora

Which are not killed by VHP?

While VHP is highly effective against many microorganisms, certain spores and biofilm-associated bacteria show resistance:

Geobacillus stearothermophilus – Often used as a biological indicator for VHP validation due to its high resistance.

Bacillus spp. (e.g., *Bacillus cereus, Bacillus subtilis*) – Some spores may survive suboptimal VHP exposure.

Fungal spores (e.g., *Aspergillus spp.*) – Some resistant species require higher concentrations or longer exposure times.

Biofilm-associated bacteria (e.g., *Pseudomonas aeruginosa*) – Biofilms provide protection against VHP penetration, reducing efficacy.

VHP is an excellent decontamination agent but does not guarantee sterilization in all cases, particularly against highly resistant spores and biofilm-forming bacteria. If full sterilization is required, other methods such as autoclaving or ethylene oxide may be necessary, depending on the application

The Importance

of Airflow Visualizations

Airflow Visual Smoke Studies. When adequately conducted can be used to;

- Qualify a cleanroom, a Clean Air device, airlock, RABS, or an Isolator.
- Evaluate a Cleanroom's Contamination Control Effect
  - Integration of equipment into the cleanroom
  - Air patterns at the interface between clean zones
  - The effect of door openings on air patterns

Understanding airflow patterns in cleanrooms and controlled envrionments is an important aspect of contamination control.

Because cleanrooms are complex envrionments, factors such as: cleanroom design, layout, and the integration of equipment, may create areas with undesirable airflow patterns.

During operations; personnel, equipment and material flow can create undesireable airflow that can act as a channel or reservoir for contamination.

As air is transparent, the **Contamination Control Effect** of cleanroom airflow is better undersood when it is visually represented.

- Optimize cleanroom equipment integration and furniture placement
- Provide a visual tool for contamination risk assessment
- Determine risk based environmental monitoring locations
- Optimize operators' movements, standing positions for SOP development
- Assist in operator training
- Troubleshoot contamination problems that limit a cleanrooms ability to provide adequate contamination control

What other factors influence Air Patterns in the cleanroom?

As mentioned previously, CFD can significantly assist in designing and developing cleanrooms and airflow patterns. In conjunction, anything that is brought into the cleanroom, including equipment and personnel, can significantly impact the airflows. A lot of refrigerators, freezers, autoclaves, ovens etc. all can influence air flow patterns; if you ever wander into a compounding or ATMP cell and tissue cleanroom, you will notice in ISO 7 rooms BSC, Isolators, refridges and freezers located in the same room. This type of equipment has fans and exhaust air. Even BSCs have air recirculation exhausts, which (depending on the type of BSC) exhaust back into the room and will cause air airflow patterns that may not have been considered in the design of the room or the placement of the BSC.

The compressors in fridges and freezers are notorious for generating particles, and a lot of dust and other particles can accumulate in these regions, especially the older models. In some cases, compressors have been found to be the source of fungal contamination in cleanrooms. Newer models on the market have been designed better, and some recent studies indicate that they do not influence the ISO 7 environment; however, it is recommended to place these types of equipment close to (without blocking) return air ducts or add return air duct to facilitate this equipment.

If you do have equipment like this in your cleanroom, then run smoke studies to validate them and confirm that they are not interfering with air patterns or causing any unnecessary air turbulence in the cleanroom, and if you are using LAFs or BSCs (shown above) ensure that they too are tested and can be exhausted correctly out of the environment. Remember, if there is any piece of equipment in the cleanroom that moves air, it should be tested.

Contamination Control

is a multi-disciplined field of Applied Science

Contamination control in cleanrooms is a **multi-disciplined field of applied science** that integrates microbiology, engineering, physics, chemistry, and quality management. Effective contamination control ensures that controlled environments meet regulatory standards for **sterility, particulate levels, and microbial contamination**, reducing the risk of compromised products in pharmaceutical, semiconductor, and medical device manufacturing.

To achieve robust contamination control, a **facility-wide approach** must be taken, encompassing various parameters that affect **cleanroom performance, product quality, and regulatory compliance.**

These parameters include:

Cleanroom Environment & HVAC System

- **Airflow Patterns (Smoke Studies/Airflow Visualization)**
  - Verifies unidirectional or turbulent airflow behavior.
  - Ensures no stagnant zones where contamination can accumulate.
- **Air Exchange Rates & Air Changes/Hour (ACH)**
  - Higher air changes maintain particle-free environments.
  - Regulatory guidance (e.g., ISO 14644, EU GMP Annex 1) defines air change rates for different cleanroom classifications.
- **Room Pressurization**
  - Positive pressure prevents ingress of contaminants in sterile areas.
  - Negative pressure is used in containment applications (e.g., handling hazardous drugs).
  - Opening/closing doors - doors act as pistons in the cleanroom which can greatly affect airflow and can bring contamination in from lower grade, so door control is critical.
- **Temperature & Humidity**
  - Maintains optimal conditions for processes and minimizes microbial growth.
  - Controlled via HVAC and monitored continuously.
- **HEPA/ULPA Filter Integrity Testing (Leak Testing, DOP/PAO Testing)**
  - Ensures filters effectively remove airborne particles.
  - Typically conducted during initial qualification and at regular intervals.

Particulate & Microbial Contamination Monitoring

- Airborne Particle Counting
  - Conducted per ISO 14644-1 and regulatory standards.
  - Detects subvisible particles (≥0.5 µm and ≥5.0 µm).
- Surface Monitoring (Contact Plates, Swabs)
  - Assesses contamination levels on work surfaces, walls, and equipment.
  - Identifies microbial presence in critical areas.
- Personnel Monitoring (Glove & Gown Testing)
  - Evaluates contamination risk from operators through finger dab plates and garment swabs.
- Viable Air Sampling (Active & Passive Methods)
  - Active air samplers measure colony-forming units (CFU/m^3).
  - Settle plates provide a passive means of detecting microbial contamination over time.

Cleaning & Disinfection Program

- Disinfectant Selection & Rotation
  - Includes sporicidal agents, broad-spectrum disinfectants, and detergents.
  - Rotation prevents microbial resistance.
- Residue Testing
  - Ensures no harmful residues remain post-disinfection.
- Efficacy Studies & Contact Time Validation
  - Confirms that disinfectants effectively eliminate viable organisms.
- Cleaning Frequency & Protocol Compliance
  - Defined by Standard Operating Procedures (SOPs) and validated through routine audits

Equipment & Process Control

- Sterilization Validation (Autoclave, VHP, Gamma, EtO)
  - Ensures materials, tools, and garments introduced to the cleanroom are sterilized.
- Material Transfer & Gowning Procedures
  - Controls contamination introduced via raw materials, packaging, and personnel.
- Equipment Cleaning & Preventive Maintenance
  - Avoids contamination from degraded machine parts, lubricants, or biofilm buildup.

Personnel & Operator Training

- Behavioral Compliance
  - Strict adherence to gowning, hygiene, and aseptic techniques.
- Training in Contamination Control Principles
  - Includes airflow awareness, contamination risks, and corrective actions.
- Monitoring & Auditing of Human Factors
  - Regular GMP audits and media fill simulations to assess aseptic process performance.

Contamination control in cleanrooms requires an integrated, multi-disciplinary approach involving HVAC systems, process validation, microbiology, disinfection, equipment maintenance, and personnel compliance. Each parameter plays a critical role in maintaining cleanroom integrity and preventing contamination. A failure in any area—whether airflow control, improper gowning, ineffective disinfection, or poor environmental monitoring—can compromise the sterility of the final product and lead to regulatory non-compliance. A robust contamination control strategy must be proactive, data-driven, and continuously reassessed to adapt to facility changes and emerging risks.

Why do Qualified facilities have contamination problems?

The contamination control effect of the cleanroom may not be optimized:

- Locations of equipment, tables, shelves and personnel positions/movements in respect to airflow.
- Contamination Control considerations regarding the placement of HEPA Filters, air returns or doors may not have been made.
- Other issues
  - Blocked Air Returns
  - Equipment positions in respect to cleanroom airflows
  - Worktables in front of return air ducts
  - Air returns in ceilings
  - HEPA Filter short circuit into equipment inlets (RABS, BSC's ..etc)
  - HEPA Filtered airflows over personnel into critical areas

Airflow issues can be behind intermittent contamination problems, Media Fills Failures, EM Excursions

Adverse air patterns may exist:

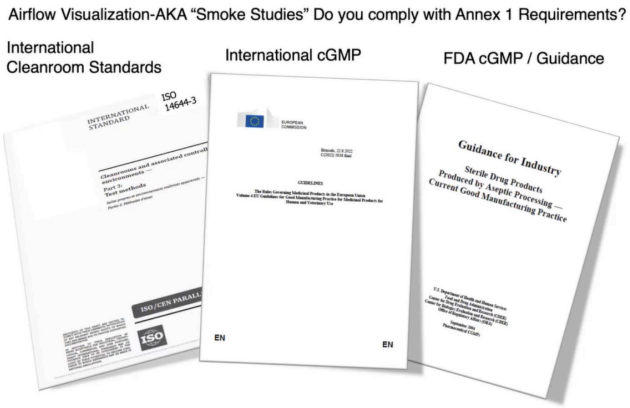
- Air that moves in such a manner that could be the source of contamination (channel or reservoir for contamination)
- Air flowing over personnel or other equipment sources such as the floor, then flowing on to products or critical surfaces
- Air coming from an uncontrolled source such as a cooling fan, heat source, refrigerator/freezer or incubator.

"Smoke studies did not suitably characterize the contamination control effect of the air patterns in the cleanroom being tested"

Standards and Regulations

Let's take a look

Airflow visualization studies, commonly called "smoke studies," are essential for assessing and validating airflow patterns in controlled environments, particularly in cleanrooms and aseptic processing areas. Various standards and guidelines outline requirements and recommendations for conducting these studies.



The table below represents a quick overview of testing required for cleanrooms looking at General Cleanroom requirements, Requirements required by USA GMP and FDA and then European Annex 1 requirements.

Cleanroom Qualification Testing

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General Cleanrooms verse Regulated Cleanrooms

Test	[1] General Cleanroom	[2] Required GMP US FDA	[3] Required GMP Annex 1
At Rest Airborne Particle Classification	Required	Required	Required
Operational Airborne Particle Classification	Required	Required	Required
Installed filter leakage and integrity testing	Optional	Required	Required
Airflow measurement - Volume and velocity	Recommended	Required	Required
Air pressure difference measurement	Recommended	Required	Required
Airflow direction and visualization	Optional	Required	Required
Microbial airborne and surface contamination	Optional	Required	Required
Temperature measurement	Recommended	Required	Required
Relative humidity measurement	Recommended	Required	Required
Recovery testing	Optional	Not Mentioned	Required
Containment leak testing	Optional	Not Mentioned	Required
Electrostatic and ion generator test	Optional	Not Mentioned	Not Mentioned
Particle Deposition test	Optional	Not Mentioned	Not Mentioned
Segregation test	Optional	Not Mentioned	Not Mentioned

[1] ISO 14644-3:2019 Cleanrooms and associated controlled environment's part 3: Test Methods

[2] FDA Guidance for Industry Sterile Drug Products Produced by Aseptic Processing Current Good Manufacturing Practice" 2004

[3] EudraLex - Volume 4 - Good Manufacturing Practice (GMP) guidelines: Annex 1 Manufacture of Sterile Medicinal Products

The following represents the requirement and recommendation of ISO, CETA, IEST, USP FDA and Annex 1 to provide a complete overview or requirements.

Standard / Guideline	Requirement / Recommendation
ISO 14644-3:2019 (International version) **ISO 14644-3:2004** **(US version)**	Specifies test methods for measuring the performance of cleanrooms and clean zones, including airflow visualization tests to ensure unidirectional airflow and to detect turbulence or stagnant areas.
Controlled Environment Testing Association (CETA) CAG-002-2006	Provides guidance on conducting smoke studies in aseptic environments, emphasizing the importance of visualizing airflow to confirm the absence of turbulence and to verify that airflow patterns protect critical areas.
USP <797> Pharmaceutical Compounding Sterile Preparations	Mandates that smoke visualization studies be performed for each Primary Engineering Control (PEC) under dynamic operating conditions to demonstrate unidirectional airflow and sweeping action over and away from the preparation areas.
USP <1160> Pharmaceutical Calculations in Prescription Compounding	While primarily focused on pharmaceutical calculations, this chapter underscores the importance of proper aseptic techniques, including the validation of airflow patterns to prevent contamination during compounding processes.
EU GMP Annex 1: Manufacture of Sterile Medicinal Products (2022)	Requires airflow patterns within cleanrooms and clean zones to be visualized to ensure that air movement does not pose a contamination risk. It emphasizes that airflow visualization studies should be documented and considered when establishing the facility's environmental monitoring program.
FDA Guidance for Industry: Sterile Drug Products Produced by Aseptic Processing—Current Good Manufacturing Practice (2004)	Recommends the use of airflow visualization studies to evaluate the adequacy of airflow patterns in critical areas, ensuring that the design and operation of cleanrooms prevent contamination.
IEST-RP-CC002: Institute of Environmental Sciences and Technology Recommended Practice	Recommends certification tests for cleanrooms, including airflow velocity measurements and HEPA/ULPA filter installation leak tests, to ensure proper airflow and contamination control.

Let's now look at an Airflow Visualization Case study and EM sensor placement in an ISO 7 room environment.

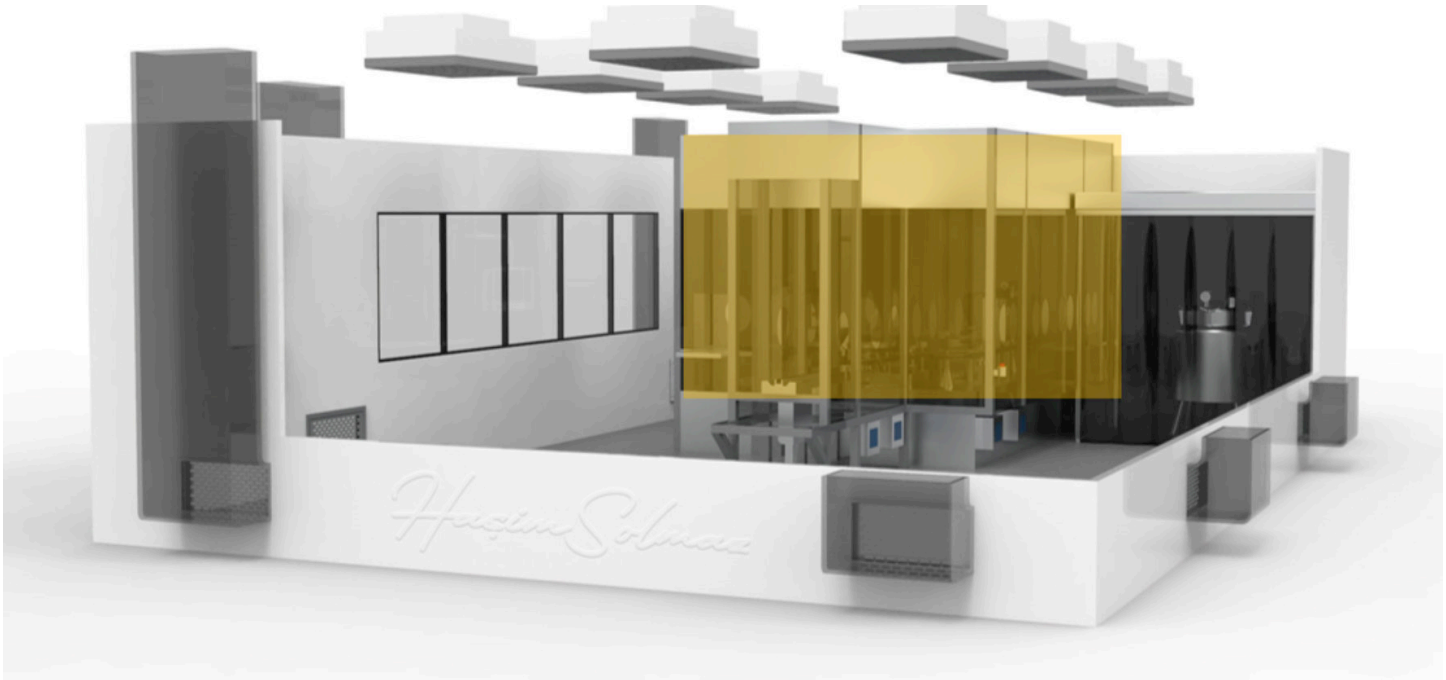
How can we determine EM sensor locations when we cannot see the full picture?

3D model of a sterile fill room

As previously discussed, we need to apply a scientific approach to understand how our cleanroom performs under as built and more importantly under dynamic conditions with the process in full swing and those random particle generators (people) in their positions at areas where they are integrated into the process. It is all relevant and so we do need to be sure that we capture the performance or possible nonperformance of airflows in and around the cleanroom and in and around critical locations.

Let's look at a RABS filling machine in an ISO 7 Cleanroom where bulk sterile product is transported to the fill heads and the product is then transferred and filled into empty sterile vials inside the RABS under ISO 5 environmental conditions. In this case study we will focus on ISO 7 particle counter sensor placement only. In the diagram below we see the HEPA Filters for the ISO 7 room, the return air ducts and the door access point.

Here we have another angle with the RABS barrier surrounding the filling machine. We can also see the LAF area with the stainless-steel bulk product tank.



What do we need to consider here?

1. We need to understand the room dynamics
2. The entry and access points the flow of components and supporting material into the room
3. The flow of product out of the room
4. The flow of operators in/out of the room
5. The location of HEPA filters in the ceiling
6. The location of return air ducts
7. Access points and door opening for the RABS barrier
8. Locations of operators during the aseptic processing
9. Most importantly we need to consider airflow visualizations

Let's ask some meaningful questions about this process

How do we know when access into the ISO 5 environment will not cause ingress of the ISO 7 environmental air into the aseptic process?

How were the positions and movements of operators accounted for? Where they considered during the smoke study?

Where RABS doors opened during the smoke study testing to see if there is ingress from ISO 7 environmental air?

Where considerations taken for any other equipment that may attribute to air turbulences, what about door openings? Access to the LAF environment to make sterile connections?

Does the HMI cause air patterns that may be detrimental to the process and influence air turbulence's?

Was EM data from particle counter room certification considered? Where any hotspots revealed?

These are the types of questions that should be asked when considering sensor placement. As it turned out the smoke studies revealed some disturbing information and showed when an operator opened the RABS door to add stoppers in the bowl there was a significant ingress of air from the ISO 7 environment into the critical zone. It was also observed that when the door opened during the process significant ISO 8 air from the adjacent corridor entered the room and air turbulences were observed.

It must be added just because a filling operation has barrier technology that the operation is safe and will be shielded from the ISO 7 environment. Assumptions can lead to product quality issues.

From the results of the smoke studies there were a few changes made to the aseptic process SOP and the balancing of the room as well as additional particle counter sensors mounted close to RABS access points and even operators were repositioned as they had been influencing air flow patterns that were causing turbulence issues and particles on the ground were scooped up and became airborne.

Summary of Air Visualization and Smoke Studies for Particle Counter Sensor Placement

Air visualization studies, commonly referred to as smoke studies, are critical in cleanroom environments for ensuring proper airflow dynamics, contamination control, and regulatory compliance. These studies provide insights into how air moves within a cleanroom, allowing for strategic placement of environmental monitoring (EM) sensors, such as particle counters.

Key Importance of Air Visualization and Smoke Studies

Cleanroom Design Validation

- Ensures that air handling systems effectively control contamination from personnel, equipment, and processes.
- Detects hidden airflow disturbances that could compromise sterile environments.

Regulatory Compliance

- Required by regulatory agencies such as the FDA, EU GMP Annex 1, and ISO 14644.
- Used as evidence for approving manufacturing facilities and detecting contamination risks.

Optimizing Particle Counter Placement

- Identifies high-risk areas where contaminants accumulate or become airborne.
- Helps validate uniform airflow to ensure accurate environmental monitoring.

Risk Mitigation in Aseptic Processing

- Prevents contamination ingress into critical zones (ISO 5 areas).
- Assesses operator influence on airflow dynamics and potential contamination risks.

Identification of Airflow Anomalies

- Detects phenomena like “bounce back” effects, where airflow from HEPA filters hits surfaces and redistributes contaminants.
- Helps assess the impact of furniture, equipment, and operator positioning on airflow patterns

Case Study: Smoke Study for Particle Counter Sensor Placement

- A Rigid Barrier System (RABS) in an ISO 7 cleanroom was evaluated.
- Smoke studies revealed unexpected air ingress when the RABs door was opened.
- Air turbulence from operator movements and adjacent ISO 8 corridor airflow was detected.
- Adjustments included:
  - Additional particle counters near RABS access points.
  - Rebalancing the cleanroom HVAC system.
  - Repositioning operators to minimize airflow disturbances..

Conclusion

Smoke studies are indispensable in contamination control, ensuring that particle counter sensors are placed optimally to detect airborne contaminants accurately. They help bridge the gap between theoretical airflow models (CFD simulations) and real-world conditions, ultimately safeguarding the integrity of aseptic manufacturing and compliance with regulatory expectations.

About the Authors

Morgan Polen
Microrite, Inc.

Morgan is an industry expert with over 40 years of experience in cleanrooms and contamination control in many industries that utilize cleanrooms. In this paper, Morgan discusses the importance of Airflow Visualizations and provides valuable insights into the air movements we do not see in our cleanrooms, the consequences of poor cleanroom designs and inadequate equipment placements, and the impact on product safety. Selection of the right test equipment is paramount. Morgan highlights this impact when discussing neutral bouncy and the effect of false positives from non-neutral buoyant air visualization products currently on the market.

Jason Kelly
Lighthouse Worldwide Solutions

Jason has also been in the cleanroom industry for over 40 years and has extensive experience in environmental monitoring as well as implementing monitoring systems based on risk assessments. In this paper, he discusses the use and importance of smoke studies to assist in EM sensor placements.