LIGHTHOUSE
WORLDWIDE SOLUTIONS

SELECTING YOUR ACTIVE AIR SAMPLER

Lighthouse Worldwide Solutions

Overview

Biocontamination presents a serious threat to cleanrooms, as this type of contamination can grow and spread. Traditional forms of particle counting can detect contamination, but not determine the difference between viable and nonviable contamination. An active air sampler will be able to help determine the type of contamination in your cleanroom. This is a fundamental piece of your contamination control strategy and ensure your optimal process and quality assurance.

What is Biocontamination?

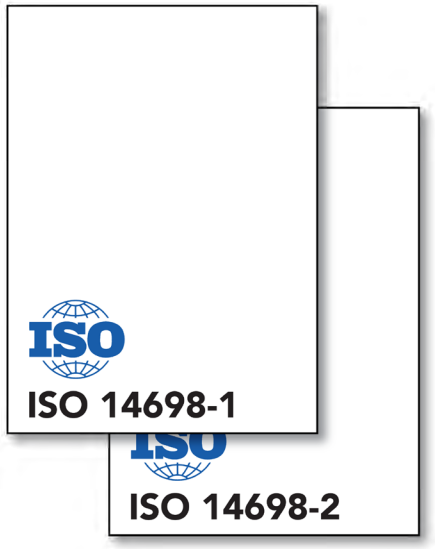
Biocontamination refers to biological contamination of products by fungi, bacteria, or byproducts of these organisms.

Cleanrooms are used for sterile product manufacturing and other sensitive applications. Contamination of these products can lead to yield loss or harm to the end-user. This is especially true in the life science and food industries. Thus, biocontamination needs to be controlled and monitored frequently. In high risk zones, contamination should be continuously monitored during production.

The goal is to produce safe and stable products. Biocontamination monitoring becomes more critical when products cannot be terminally sterilized to kill off microbe carrying bugs.

The Importance of ISO 14698

ISO 14698 is a critical international standard that outlines how to develop a biocontamination control program.



> ***"Hygiene has become increasingly important in many areas of modern society. In such areas, hygiene or biocontamination control methods are, or will be, used to create safe and stable products.***
> ***International trade in hygiene-sensitive products has greatly increased.***
> ***At the same time, the use of antimicrobial agents has been reduced or forbidden, creating a need for increased biocontamination control" [Statement from ISO 14698 – Part 1].***

> ***"ISO 14698 establishes the principles and basic methodology of a formal system of biocontamination control (Formal System) for assessing and controlling biocontamination".***

ISO 14698 was released in 2003 and has two parts: selecting the right air sampling equipment and evaluating your data. This paper provides a simplified version of information offered in ISO 14698.

ISO 14698-1

Part 1 highlights the importance of selecting the right air sampling equipment, such as an active air sampler, and methods to capture microorganisms in the cleanroom and clean zones. This part also specifies the methods required for monitoring risk zones in a consistent way. It further outlines the application of control measures appropriate for the degree of risk involved. It goes on to provide a method for sampling compressed air for microbial contamination, as well as monitoring in high-risk environments where microbial sensitive products are manufactured and processed.

ISO 14698-2

Part 2 provides guidance on methods for evaluating your microbial data. It covers setting alert and action limits, trend analysis, and control charting. It also looks at the significance of biocontamination corrective actions and records-sampling. Furthermore, it examines sample tracking-collection of results, data recording, evaluation, & validation of the results.

What Is Monitored In Cleanrooms?

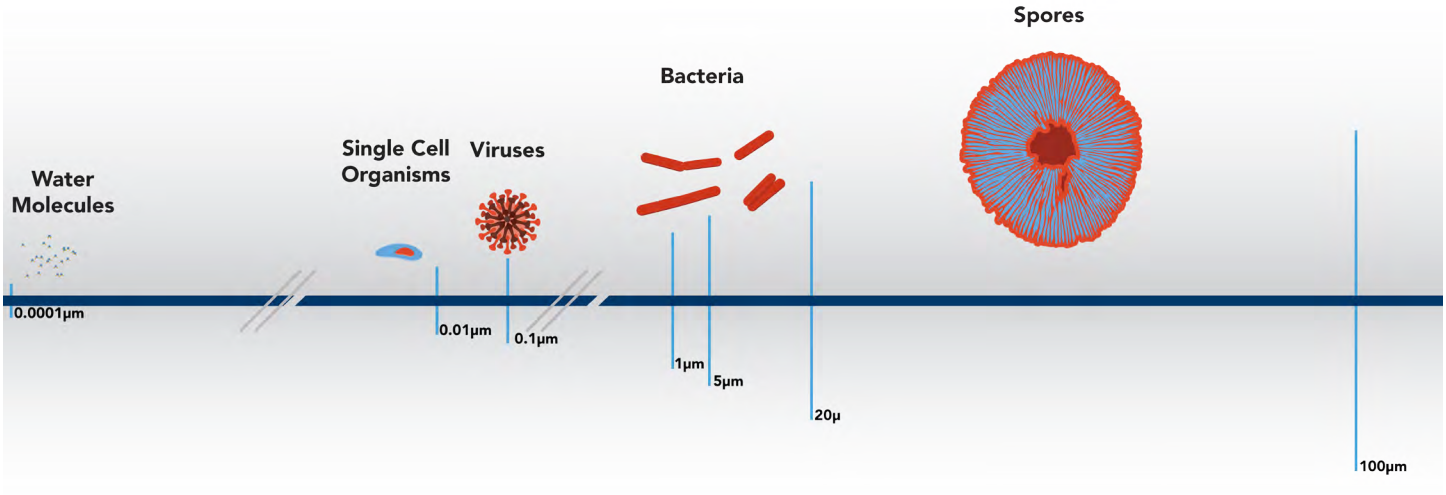
In cleanrooms, we monitor for any sort of contamination. This contamination comes in the form of particles, which can be either viable or nonviable. Viable particles are live organisms and considered biocontamination, such as fungi or bacteria. Nonviable particles are non-living organisms, like dust particles.

All contamination is dangerous in a cleanroom. Tainted environments or materials can potentially contaminate the product. This can lead to product recalls, regulatory observations, fines, faulty products, or end-user harm or death. But viable particles are particularly dangerous, because these particles can grow and spread. While particle counters just tell you the size and number of particles, active air samplers tell you the size and type of viable particles are present. This is why they are used in the process of biocontamination monitoring.

Bacteria can flourish given the right conditions and are very prominent on surfaces. Cleanroom sterile cleaning focus on surface cleaning and surface monitoring. Water, moisture, and high humidity all provide a vehicle for biological contamination.

Cleanrooms have purposely controlled environments and rooms through HVAC systems for temperature and humidity. This has multiple purposes: it provides a comfortable working environment and keeps humidity and temperature at optimal settings to prevent microbial growth. Room pressures are also controlled to prevent outside, contaminated air from entering the room. This is done through the use of positive pressure.

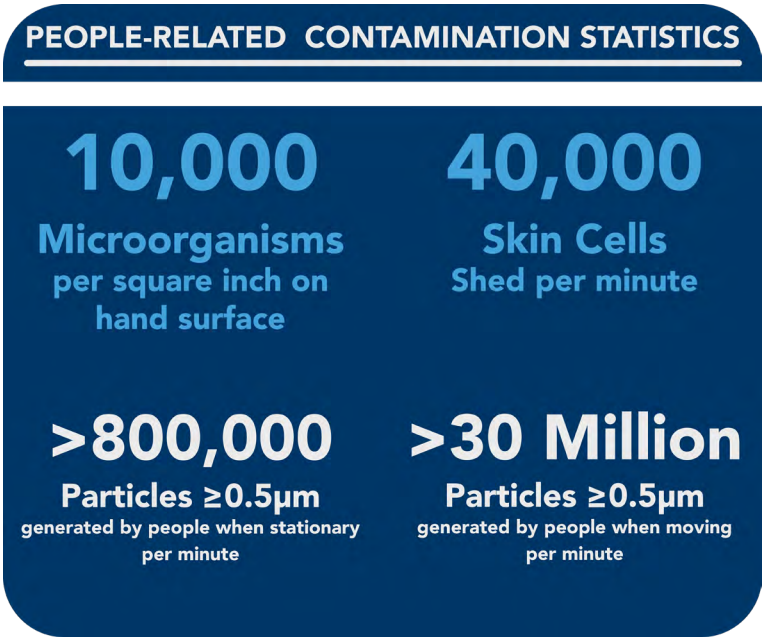
In tropical and other high humidity regions of the world, such as some parts of Asia, HVAC systems there work harder to keep the cleanroom environment temperature and humidity in the correct range.



Where Does Cleanroom Contamination Come From?

Despite our best efforts, particles do make their way into cleanrooms. From there, one thing is certain: we are the biggest source of contamination. No amount of HVAC filtration or air changes are going to make a difference because the contamination is coming from within the cleanroom. The stakes are high financially and most important in product quality and safety, so it is critical we make an effort to understand how to detect for these particles.

Contamination has a dangerous impact on critical products like injectable medications. Thus, the ability to detect microorganisms is a major factor in product and patient safety. Tainted products can be lethal, as seen in a 2012 outbreak of fungal meningitis reported in the United States. The outbreak was traced to a compounding company based in Massachusetts and sourced to contaminated injectable product.



[https://cleanroomtechnology.com/news/article_page/Study_into_human_particle_shedding/62768]

This resulted in more than 64 deaths and infected over 753 people. The ultimate cause was an insufficiently monitored and controlled production environment. To prevent this tragic event, ISO 14698 can assist in making the selection of a suitable air sampling instrument.

> ***"It is the responsibility of the user to develop, initiate, implement and document a Formal System for bio-contamination control that allows detection of adverse conditions in a timely fashion"***
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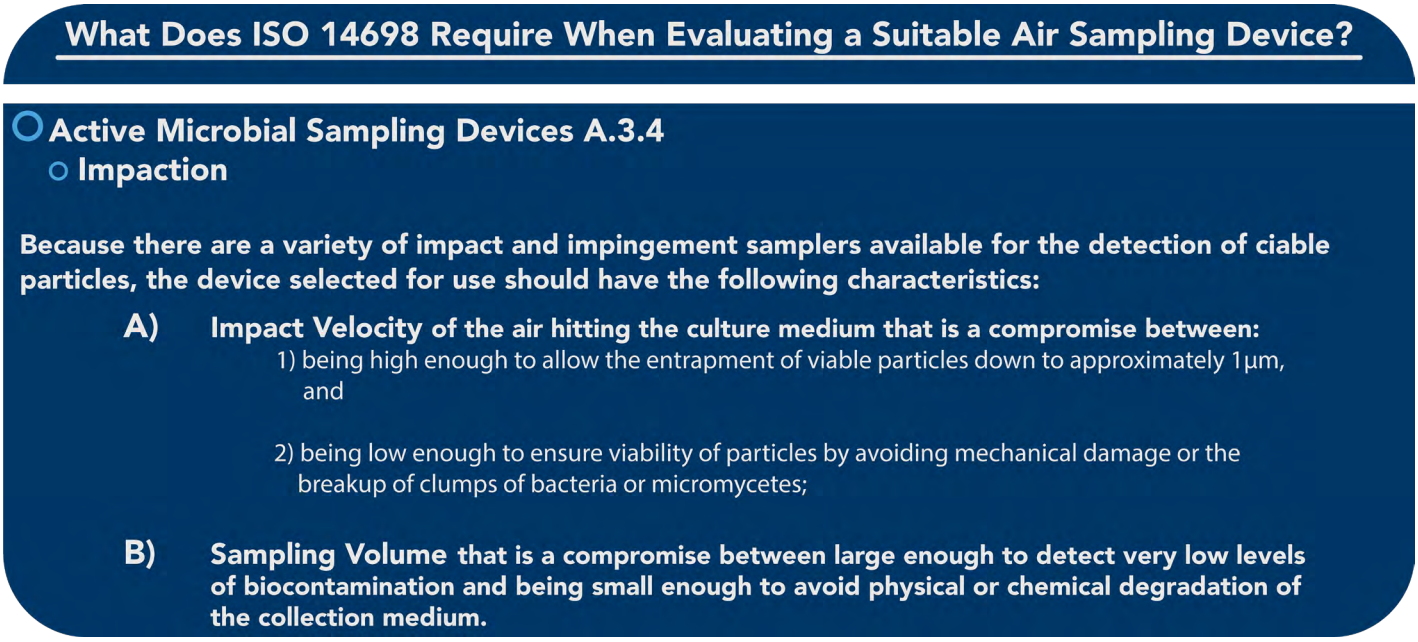
> *[ISO 14698- Part 1 Section 5 Establishing the Formal system]*

What Does ISO 14698 Require When Evaluating A Suitable Air Sampling Device?



Active air samplers pull the sample from the cleanroom air in real time. From there, the particles pass onto passive or settle plates, where particles fall onto a sample media. The reactions on this media tell us the type of contamination present. Not all particles will settle down on surfaces in a timely manner, but they will eventually over time. Thus, active air sampling is a snapshot of the cleanroom air based on a sample volume of 1000L, which is the standard volume for regulatory monitoring.

There are two types of air sampling devices: Portable Air Samplers and Continuous Air Samplers They are used similarly to particle counters. Portable Air Samplers are used for routine testing and certification based on 1000 Liters of air sampled.

GMP requires continuous sampling. In this instance, remote sample heads are used at critical zones and offer continuous sampling during the process. Portable devices may also be used continuously.

It is critical you ensure the correct sample volume is taken and that the media is validated for the process and does not dehydrate before the end of sampling. A production run may use several media dishes in each location.

How Do Active Air Samplers Work?

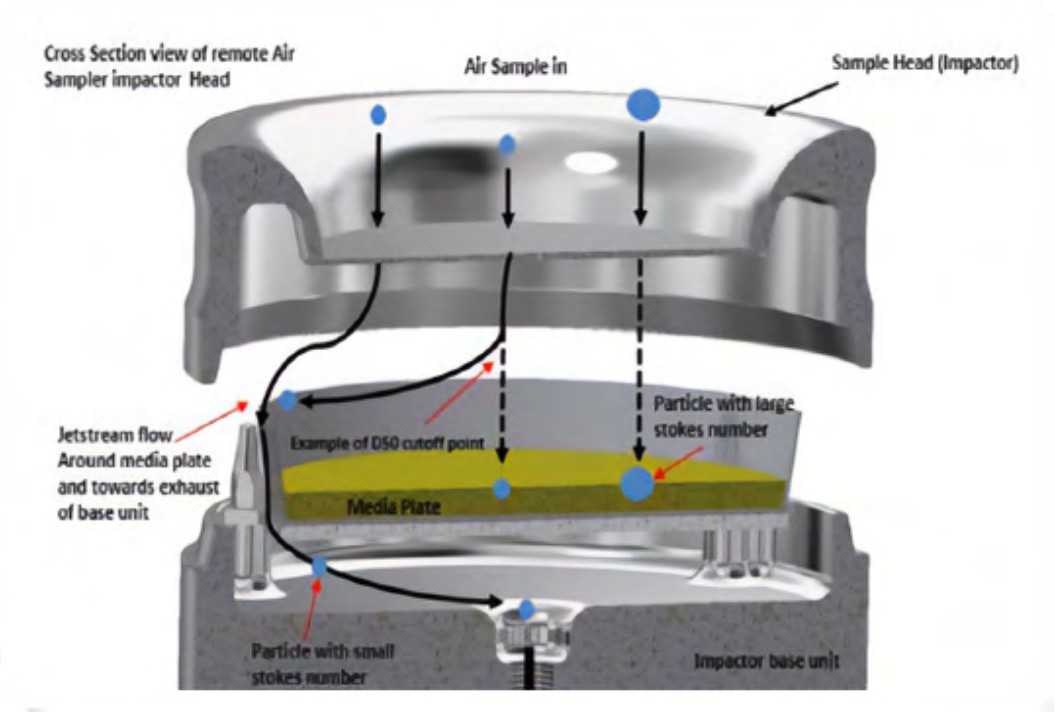
The diagram below is a cross sectional of an active air sampler head. The air is pulled in through the sample head by either an external or built-in pump system. Any particles in the air will either be impacted onto the media plate or be pulled away from the media plate due to their inertia. In effect, larger particles are less likely to be pulled away from their flight path onto the media; however, smaller particles are more likely to follow the jet stream.

The d50 is the point where 50% the particles of a specific size will be pulled away and 50% will impact on the media. To meet ISO 14698, if 100 1um particles were put through the air sampler then 50% would impact and 50% would be pulled away and exit through the pump system. The resolution of the air sampler is based on the d50.

If your active air sampler d50 is 10µm, you will miss the main particles that are most concentrated in your cleanroom. This is a really critical parameter. Without proper validation of the active air sampler, the end user may not even know that the air sampling device they are using is not physically capable of capturing contamination below 10µm.

They may have a false sense of control as CFU results would be low as most biological contamination in the cleanroom is much smaller than 10µm.

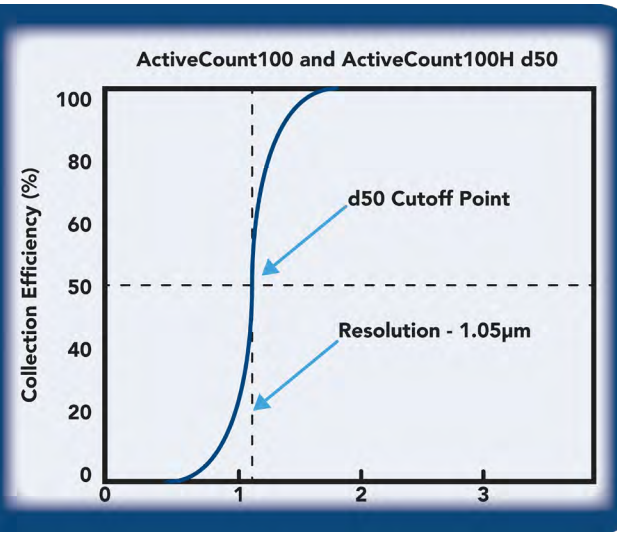
ISO 14698 also states that the sample should be HEPA filtered on exhaust. This is a critical requirement not all manufacturers adhere to.



The d50 is the diameter where a particle is 50% likely to impact on the sample media or 50% likely to be manipulated by the sample airstream and not impact on the media.

The d50 for air samplers according to ISO 14698 should be approximately 1µm.

The d50 effectivly is the resolution of the air sampler.
Poor resolution = poor collection efficiency.



According to ISO 14698, a sampling device shall be selected according to the area being monitored considering the following factors:

- **Type of viable particle to be sampled (d50 (capture resolution) of air sampler is critical).**
- **Sensitivity of the viable particle to the sampling procedure.**
- **Expected concentration of the viable particles and the indigenous microbial flora.**
- **Accessibility to the risk zones, ability to detect low levels of biocontamination.**
- **Ambient conditions, time and duration of sample, sampling method.**
- **Effect of sampling device on the process or environment to be monitored.**
- **Effective Collection accuracy and efficiency – physical and biological efficiencies.**
- **Size resolution down to 1µm.**
- **Effective HEPA filtration on the exhaust so the sample does not re-contaminate the environment that is being sampled.**

In Summary

ISO 14698 is a highly informative international standard that will help you make informed decisions about the selection of the right air sampling equipment for your process. ISO 14698 also addresses setting up a formal monitoring system with appropriate alert and action limits and evaluation of the data.

When seeking an active air sampler ask your vendor these questions;

- **What is the resolution of this air sampler? Does it meet ISO 14698 requirements?**
- **Do you know the d50 cutoff and how is it calculated and verified by your company?**
- **Is this air sampler suitable for my cleanroom, our wipe down process, and the cleaning solutions we use? Does it have a smooth surface void of crevices?**
- **Has a recognized Industry Standard reference validated this air sampler?**
- **Can you provide validation documents that prove physical and biological efficiencies?**
- **Can this air sampler be calibrated in the field locally and what are the costs?**
- **Can we sample gas lines and isolators using this same model and what are the costs?**