TECHNICAL PAPER

The Selection of the right Air Sampling Equipment for Your Process and Quality Assurance

by Jason Kelly

LIGHTHOUSE
WORLDWIDE SOLUTIONS

The selection of the right active air sampling equipment for your process and your quality assurance

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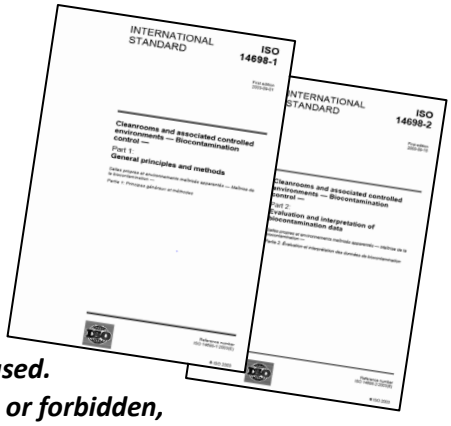
What is Bio-Contamination?

In our cleanrooms where sterile products are manufactured bio-contamination needs to be controlled and monitored frequently and in risk zones continuously during production.
The goal is to produce safe and stable products and bio-contamination monitoring becomes more critical when products cannot be terminally sterilized to kill off microbe carrying bugs.

Bio-contamination refers to biological contamination of products by fungi, bacteria or by-products of these organisms.
The control of these biological contaminates in the life science and food industries is critical for the protection of their patients and customers.

The importance of ISO 14698



ISO 14698 is a critically important international standard in terms of developing a bio-contamination 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 was released in 2003 and has two parts.
"ISO 14698 establishes the principles and basic methodology of a formal system of biocontamination control (Formal System) for assessing and controlling biocontamination".

ISO 14698-1

Part 1 highlights the importance in selection of the right air sampling equipment and methods to capture microorganisms in the Cleanroom and Clean zones. Part 1 specifies the methods required for monitoring risk zones in a consistent way and for applying control measures appropriate to the degree of risk involved. It also provides 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 evaluation of microbial data
This guidance covers; Setting alert and action limits - trend analysis, control charting. It also looks at the Significance of biocontamination corrective actions and records-sampling and sample tracking-collection of results, data recording, evaluation & validation of the results.

What should be monitored in our cleanrooms?

Tainted environments or materials can potentially contaminate the product, lead to product recalls, regulatory observations, or fines, harm the product efficacy, or even kill the patient it is intended to treat.

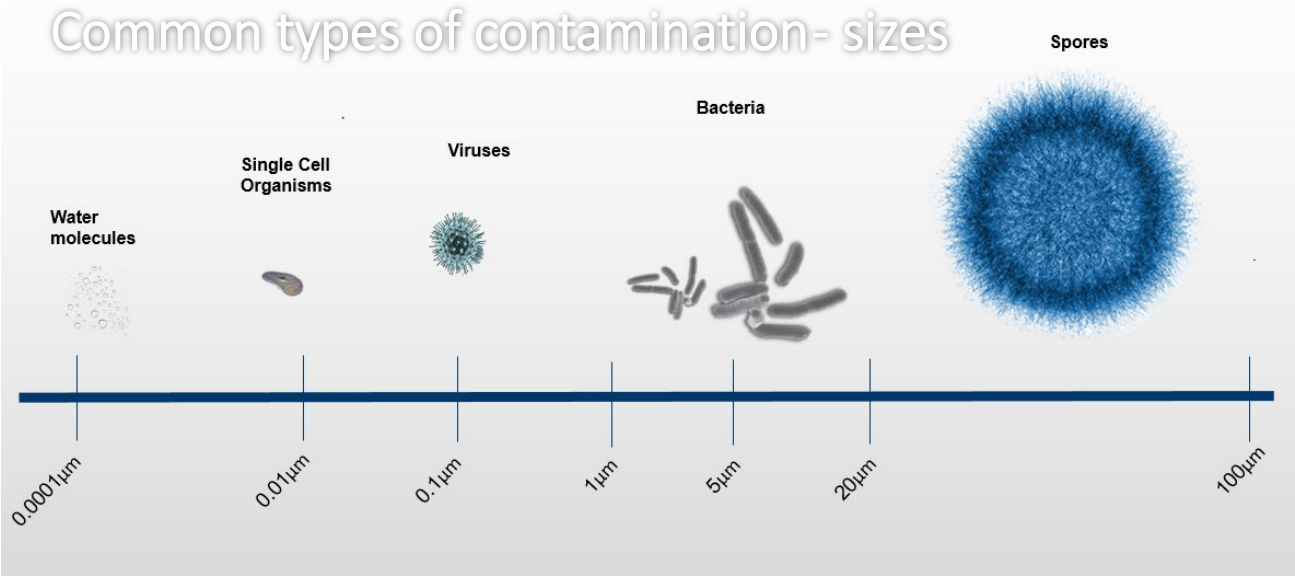
Water, moisture, high humidity all provide a vehicle for biological contamination.

Bacteria can flourish giving the right conditions and are very prominent on surfaces. Cleanroom sterile cleaning focus on surface cleaning and surface monitoring.

Cleanrooms have purposely controlled environments and rooms through HVAC systems for temperature and humidity to provide a comfortable working environment and to keep humidity and temperature at optimal settings to prevent microbial growth. Room pressures are also controlled to limit the ingress of less cleaner air into cleaner rooms which have a higher pressure for protection of this ingress.

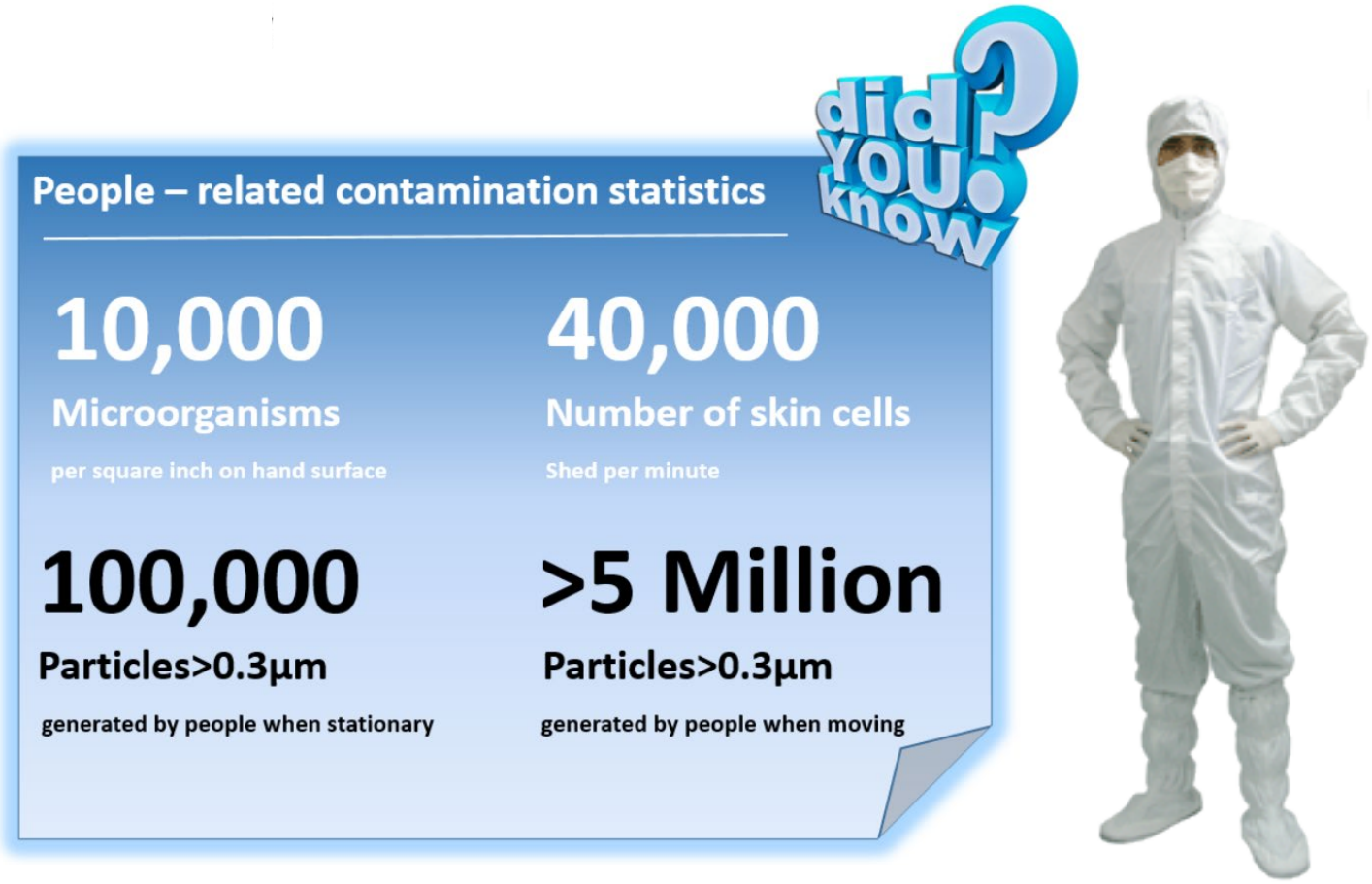
In tropical high humidity regions of the world like some parts of Asia HAVAC systems there work harder to keep the cleanroom environment temperature and humidity

Excessive sweating, coughing, sneezing etc all cause avenues for microbial contamination. Below is an example of the type and size of common cleanroom contamination.



Where does most of the cleanroom contamination come from?

One thing is clear and we are the biggest source of contamination that is brought into the cleanroom and no amount of HVAC filtration or air changes are going to make a difference. The stakes are high financially and most important in product quality and safety.



With the impact of contamination on critical products like injectable medications the ability to detect microorganisms is really a major factor in product and patient safety. Tainted products can have the lethal effect of death as seen in 2012 an outbreak of fungal meningitis reported in the United States. The outbreak was traced to a compounding company based in New England MA and sourced to contaminated injectable product which resulted in more than 64 deaths and infected over 753. The production environment was not sufficiently monitored or controlled.

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"
[ISO 14698- Part 1 Section 5 Establishing the Formal system]

What does ISO 14698 require when evaluating a suitable air sampling device?

Active Microbial Sampling Devices A.3.4

Impaction

Because there are a variety of impact and impingement samplers available for the detection of viable particles, the device selected for use should have the following characteristics:

a **Impact velocity** of the air hitting the culture medium that is a compromise between
1) being high enough to allow the entrapment of viable particles down to approximately 1µm, and
2) being low enough to ensure viability of viable particles by avoiding mechanical damage or the breakup of clumps of bacteria or micromycetes;

b **Sampling volume** that is a compromise between being large enough to detect very low levels of biocontamination and being small enough to avoid physical or chemical degradation of the collection medium.

In active air sampling the sample is taken out of the air. Passive or settle plates, sample the particles that fall onto the sample media. Active air samplers pull the sample out of the cleanroom air in real time. Not all particles will settle down on surfaces in a timely manner – they eventually will over time. Active air sampling is a snap shot of the cleanroom air based on a sample volume of 1000L which is the standard volume for regulatory monitoring.

There are two types of sampling devices, Portable Air Samplers and Continuous Air Samplers They are used in ansimilar deployment as particle counters. Portables are used for routine testing and certification based on 1000 Liters of air sampled. GMP requires Continuous sampling and remote sample heads are used at critical zones and offer continuous sampling during the process. Portable devices may also be used continuously.

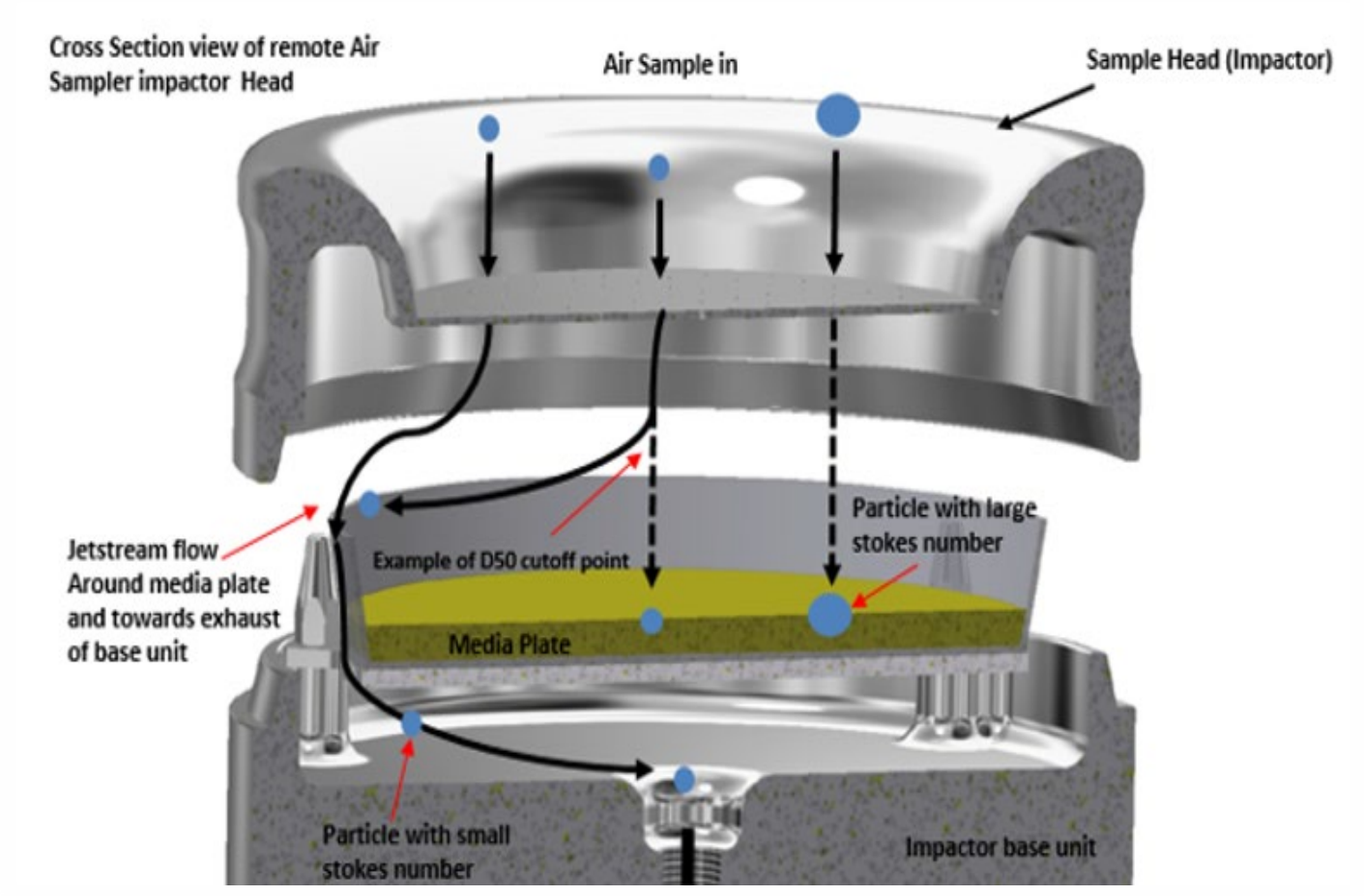
The biggest concern is to make sure the correct sample volume is taken and that the media is validated for the process and does not dehydrate before the end of sampling. A production run may use several media dishes in each location.

How do active air samplers work?

This diagram below is a cross sectional of an air sampler head. The air is pulled in through the sample head by a pump system either external or built into the air sampler. 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 as we see 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.

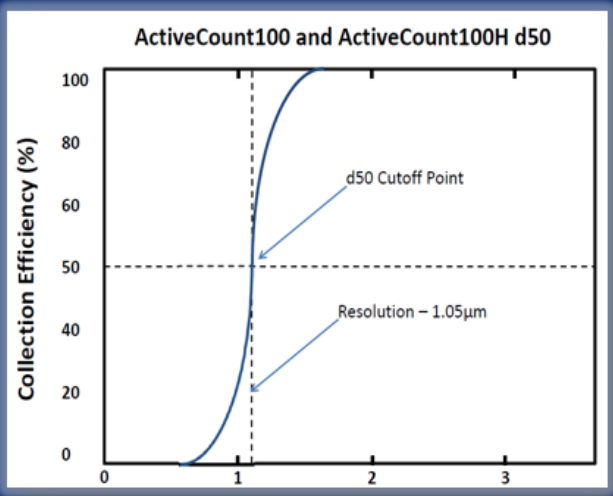
ISO 14698 also states that the sample should be HEPA filtered on exhaust. This is a critical requirement not all manufacturers abide to. The d50 is as explained critical and acts like the resolution of the air sampler. If your air sampler d50 was 10µm then you will be missing the main particles that are most concentrated in your cleanroom. This is a real critical parameter as without proper validation of the 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.



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 1.0µm.

The d50 effectively 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 taking into consideration 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 very informative international standard that will help you make in formative 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 and does it have a smooth surface void of crevices?
- Has this air sampler been validated by a recognized Industry Standard reference?
- 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?