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IMPACT OF BS EN 17141 ON ISO 14698 VALIDATION

APPLICATION NOTE: 20200122A

In Britain and Europe, BS EN 17141 was recently released and replaces ISO 14698-1:2003, as well as ISO 14698-2.

The standard establishes new requirements, recommendations, and methodologies for microbial contamination in cleanrooms.

The purpose of this application note is to provide updated information that affects the validation of microbial air samplers in affected areas.

Regarding requirements for microbial air samplers, both ISO 14698-1 and EN 17141 are quite similar.

However, one of the key differences having most significant impact is Annex E (Informative). In particular, section E.5, ***validation of air samplers***.

Old Validation Method

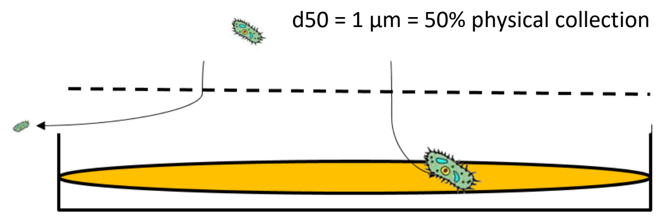
ISO 14698-1, Annex B.3, defined 'Sampling Efficiency' as a simple cfu comparison percentage.

$$Eff.of\ Sampler\ (\%) = \frac{\#\ cfu\ sampler\ under\ test}{\#\ cfu\ referrence\ sampler} \text{ x } 100$$

This method was identified almost immediately as inherently flawed (*Yao, et al.,* 2006). First, it is a *comparison efficiency*, and results will vary greatly depending on the quality of the reference sampler. In fact, several manufacturers have manipulated this criteria, which has proven to be more valuable for marketing purposes. Additionally, this method fails to account for viable particles lost (*Yao, et al*., 2006).

BS EN 17141 replaces this method of validation with a d50 value that is based on a calculated fluid dynamics equation; AND an experimental method using a particle counter (*Yao*, 2006).

The d50 is the particle size at which 50% of particles are recovered, and 50% remain in the air stream and are lost. Particles larger than the d50 size have more mass and have a higher probability of recovery. While particles smaller in size have a lower mass, generally remain entrained in the air stream and have a lower probability of recovery.



ISO 14698-1 implies a d50 of 1 µm is appropriate (Ref. §A.3.4.2(a)(2)).

EN 17141, Section E.5.2, considers a d50 value of less than 2 µm appropriate.

New Theoretical d50 Validation

BS EN 17141 uses a simplified version of the Calculated Fluid Dynamics equation (Yao, 2006):

$$d50 = \sqrt{\frac{9nW}{\rho\rho UoCc}}\ x\ \sqrt{Stk50}$$

Figure 1: Yao, et al., 2006 – d50 Equation

The new equation provided in EN 17141 is as follows:

$$d50 = \sqrt{\frac{40\ x\ Dh}{U}}$$

Where,
40 = Constant air viscosity (°C)
Dh = hydraulic diameter of inlet (mm)
U = inlet velocity (m/s)

Figure 2: EN 17141, Annex E.5.2 (Physical Collection) d50 Simplified Equation

The BS EN 17141 equation (Figure 2 above) is less susceptible to manufacturer manipulation when compared to the validation method provided in ISO 14698-1:2003, B.3, ***which is very good news!***

Based on the more complex Yao calculation, Climet has a d50 = 1.05 µm, and using the more simplified EN 17141 equation, Climet's d50 value is 1.08 µm. Both these theoretical d50 values well exceed the requirements of BS EN 17141:2020.

New Experimental d50 Validation

BS EN 17141:2003, E.6.1.2.1, further requires the manufacturer to conduct an experimental d50 validation.

It is well known that as physical collection efficiency approaches 100%, impaction velocity produces a significant decline in biological efficiency (*Stewart, et al.*, 1995).

When the experimental d50 is greater than the theoretical d50, this suggests design inefficiencies or flaws.

This method is discussed in Yao, 2006, and uses a particle counter to validate the d50 using various particle sizes:

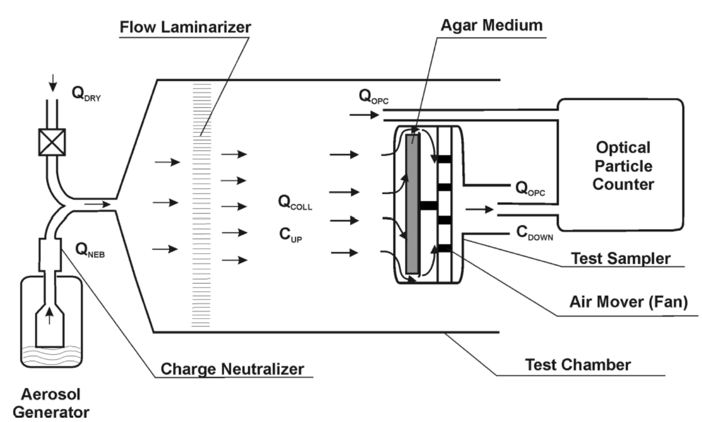


FIG. 1. A schematic representation of the experimental setup.

Figure 3: Validation of d50 with a particle counter (Yao, 2006)

As of the date of this printing, to the best of our knowledge, no other microbial air sampler manufacturer has conducted the required experimental testing as mentioned in BS EN 17141:2003, E.6.1.2.1.

Climet first conducted our testing in 2006 with a particle counter … **14 YEARS BEFORE THIS METHOD WAS RATIFIED IN A STANDARD.**

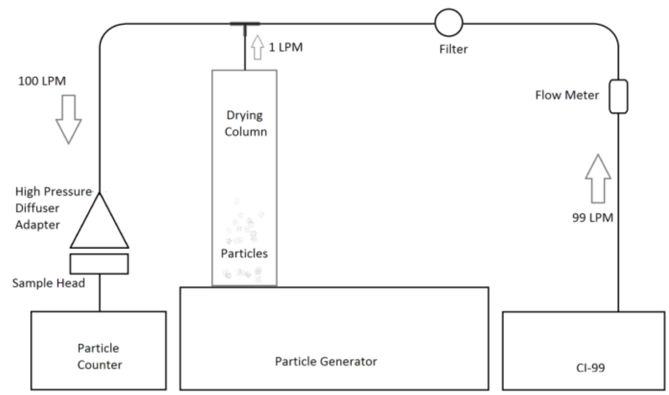


Figure 4: Climet Experimental Method/Design

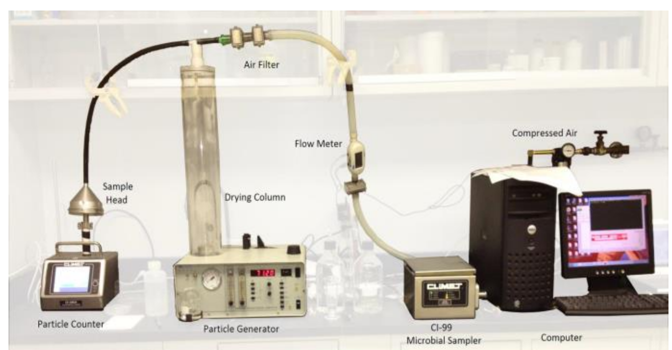


Figure 5: Climet Experimental d50 Method

Climet tested the sample head and inlet geometry in eight tests using particles of various sizes, then charted the percent recovery.

Figure 6: Charted % Recovery for various particle sizes

From the test results (Figure 6), we can confirm Climet's inlet geometry provides for an experimental d50 value less than 1 µm.

d50 Validation Summary

Climet's *experimental d50* (< 1 µm) is lower than the *theoretical d50* (= 1.08 µm). Subsequently, we can confirm that Climet's microbial air samplers do not have a design inefficiency or flaw.

Further, both theoretically and experimental d50 values satisfactorily meet the BS EN 17141 standard of less than 2 µm.

Biological Collection Efficiency

The table below provides the probability, in an occupied room, of the occurrence of a MCP equal to, and greater than a given size (*Whyte, et al*., 2007).

Equivalent particle diameter (µm)	≥1	≥4	≥12	≥20	≥50
Probability of occurrence	0.99	0.75	0.5	0.25	0.05

As shown here, 99% of the airborne microorganisms will be 1 µm or larger. Hence, good biological collection efficiency down to 1 µm is an important characteristic (d50 ~ 1 µm).

Testing of Climet's biological collection efficiency was conducted by an independent laboratory, and testing was performed against a high efficiency 12.5 LPM liquid impingement sampler (*Lin, et al*., 2000).

According to White Rose Research at the University of Leeds, the reference sampler has a d50 value of 0.3 µm (*McDonagh, et al.* 2014).

Results of the Study

The following is a graphical representation of the charts above:

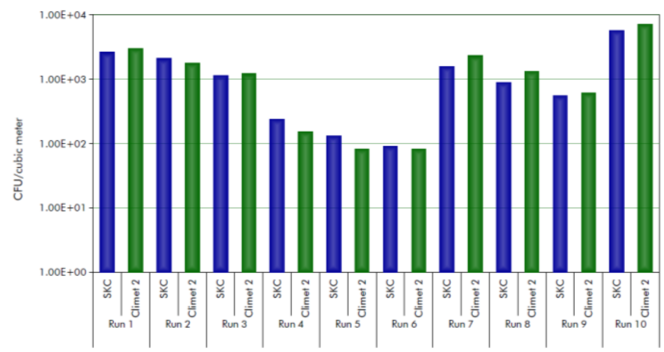


Figure 7: Chart of independent lab test - comparative results

Climet's average percent recovery was 1.4% greater when compared to the reference sampler. Per ISO 14698-1, ten tests were conducted. Statistically, the conclusion drawn is that both samplers performed comparably.

Additionally, from a metrology perspective, *stability of measurement* (or precision) is equally important as *accuracy of measurement*.

Based on the two data sets, Climet calculated the correlation coefficient and found our microbial air sampler statistically had a ***near perfect positive correlation*** (r = 0.98) when compared to the high efficiency reference sampler. This confirms Climet microbial air samplers are not only accurate, but are equally a high precision instrument.

In summary, Climet's microbial air samplers have high efficiency characteristics appropriate for pharmaceutical clean areas.

Cost of Poor Quality

Climet has designed our instruments for pharmaceutical industrial applications. We are the only manufacturer that conducts 1m drop testing, and requires our instruments to remain in calibration after the drop test.

Since 2005, when Climet first introduced microbial air samplers, as of the date of this printing (January 2021) we have yet to received a single report of an interval calibration out-of-tolerance (OOT) condition. For customers in regulated industries, this represents a substantial reduction in the number of deviation reports and investigations, which costs USD $8,000 to $12,000 on average in labor, and well exceeds the initial purchase price of the instrument.

For this reason, our competitors could quite literally give their instruments away for free, and Climet would still have a lower total cost of ownership.

References:

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ISO 14698-1:2003(E): *Cleanrooms and associated controlled environments – Biocontamination control – Part 1: General principles and methods*. International Organization for Standardization ISO, Geneva (September 2003)

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USP <1116>: *Microbial Control and Monitoring of Aseptic Processing Environments*. August 1, 2013.

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