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PARTICLE COUNTING SAMPLE TUBING GUIDANCE AND BEST PRACTICES

Lighthouse Worldwide Solutions

Overview

Airborne Particle Counters are used for a variety of purposes in pharmaceutical cleanrooms for such applications:

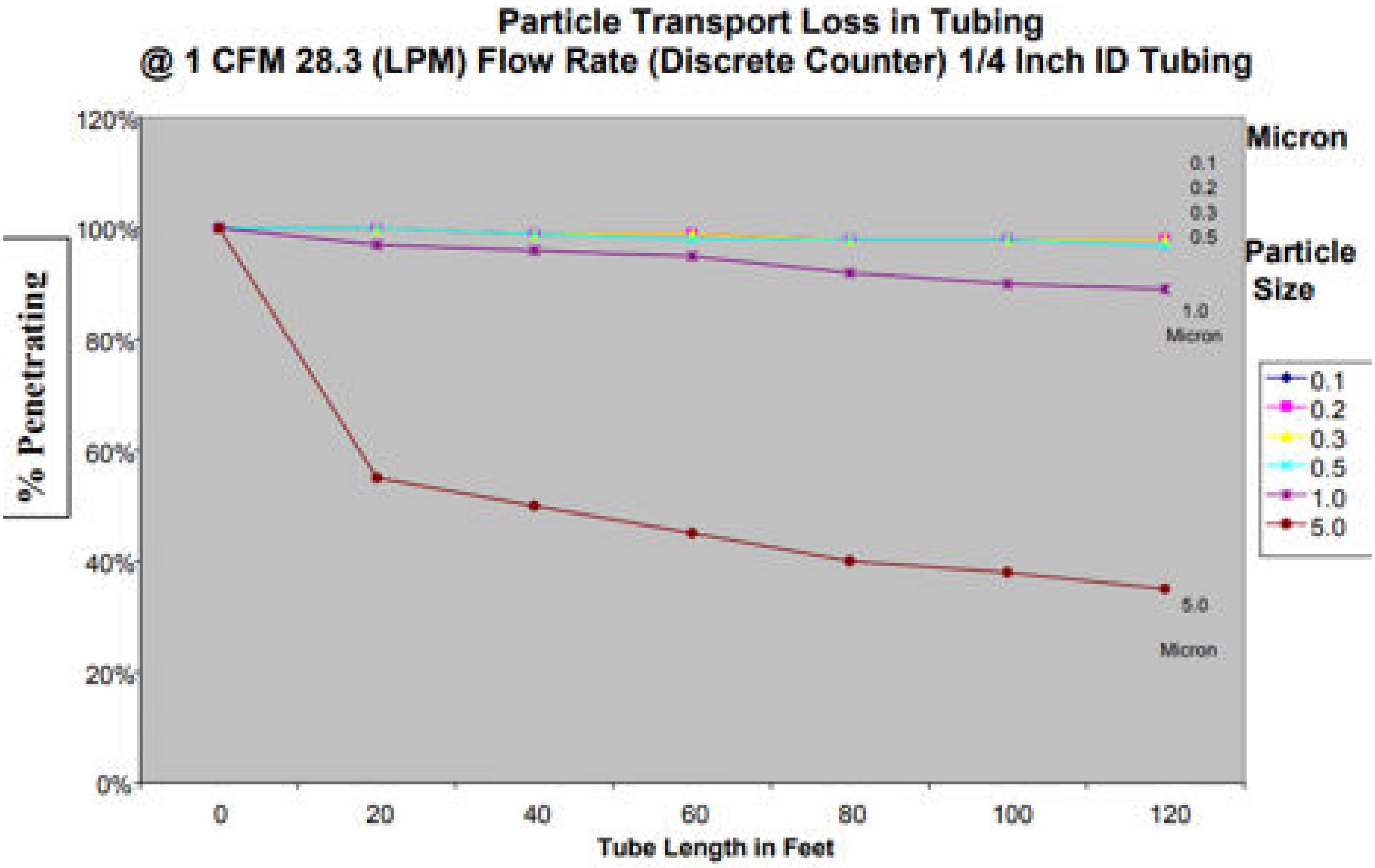
- Filter testing
- Cleanroom certification and testing
- Isolator certification and testing
- Cleanroom and clean device monitoring in Pharmaceutical Manufacturing Facilities

One area of Particle Counting technology that needs some updated attention is guidance on sampling tubing and best practices. This paper addresses issues around particle losses in sample
tubing and how to mitigate against particle losses. First of all particles do not get lost. They accumulate inside the tubing and adhere to bends and kinks that may be present in the tubing.

Sample Tubing Guidance and Best Practices

The use of Particle Counters requires the use of tubing for the sampling of the air, as the Particle Counter may be located away from the actual air being sampled. The tubing is connected to an isokinetic probe that allows for the sampling of air in both unidirectional and non-unidirectional cleanrooms or clean devices. Per various GMPs, the guidance value for this air velocity in these unidirectional environments is 0.45 meters/second ± 20%.

The tubing connects an isokinetic probe to the particle counter. Various factors impact the efficiency of particle transport in tubing. Factors such as the clean air velocity, tubing length, tubing material, the number of bends, the radius of such bends and the tubing diameter need to be considered in selecting and using such tubing. Particle size, particle velocity and tubing diameter are the key factors in determining particle transport efficacies in tubing. Tubing material is a secondary concern. Let's start at looking at studies performed many years ago by Lighthouse Worldwide Solutions on particle losses in sample tubing up to 100ft in length.



Significance of Particle Sizes in Relation to Tubing Length

Using the chart below as a reference we can derive the following table based on particle loss average percentages for different particle sizes with tubing lengths.

Particle Size	10 foot	20 foot	50 foot	100 foot
0.1μm	n/a	>1%	>2%	>3%
0.2μm	>1%	>2%	>5%	>5%
0.3μm	>1%	>2%	>5%	>5%
0.5μm	>1%	>2%	>5%	>5%
1.0μm	>2%	>5%	>8%	>10%
5.0μm	>20%	>55%	>58%	>60%

Reference of particle losses in tubing lengths for particle sizes from 0.1μm to 5μm

Looking at the particle sizes 0.1μm, 0.2μm, 0.3 and 0.5μm as the tubing is increased up to 100ft the particle losses observed are reasonably low with a maximum of less than 5%. Looking at 1μm the highest particle loss is near 10% at 100ft. However with 5.0μm we see a significant drop even at 10ft of about 20%. This drop increases up to 55% at 20ft and maxes out at 60% at 100ft.

The smaller particle sizes as we can see from the data are more influenced by the air being pulled through the sample tubing and the majority of the particles up to 95% of them make it through the sample tubing. This is due to the particles inertia and their velocity through the sample tubing for the most part is unchanged.

With the increased mass for the 1μm and 5μm particles we see that these larger particles are more prone to particle loss as the tubing length increases. This in effect is us witnessing the laws of physics in practice. Particle losses are further enhanced when tubing runs have more bends and this is the case when longer tubing runs are introduced.

In fact recent studies conducted by Lighthouse Worldwide Solutions illustrated particle losses become more significant for larger particle sizes such as 5μm when bends are introduced into the tubing. One setup had two bends were put into a length of tubing of 3 meters (10 feet) and losses up to 90% were observed. Larger particles 1 μm and above will cause issues with reliable data if long lengths of tubing is used to transport the cleanroom air sample to the particle counter. 5μm particle losses are really unacceptable and we recommend using sample tubing as short as physically possible.

What Do Current Industry Standards Say?

GMP Annex 1 Manufacture of sterile medicinal products highlights quite clearly that sample tubing should be as short as possible. Let's look at the latest publication from PICs GMP guide found on their website, www.picscheme.org, under the section Publications. Annex 1 (PE 009-14 July 1st 2018) states:

Section 6 CLEAN ROOM AND CLEAN AIR DEVICE CLASSIFICATION

"Portable particle counters with a short length of sample tubing should be used for classification purposes because of the relatively higher rate of precipitation of particles ≥5.0μm in remote sampling systems with long lengths of tubing. Isokinetic sample heads should be used in unidirectional airflow systems." Again reference to tubing length and this time particle losses and bends in the sample tubing are
highlighted below.

Section 11 CLEAN ROOM AND CLEAN AIR DEVICE MONITORING

"Airborne particle monitoring systems may consist of independent particle counters; a network of sequentially accessed sampling points connected by manifold to a single particle counter; or a combination of the two. The system selected must be appropriate for the particle size considered. Where remote sampling systems are used, the length of tubing and the radii of any bends in the tubing must be considered in the context of particle losses in the tubing."

Portable Particle Counter on a trolley with ISP connected to sample inlet

Remote Particle Counter with ISP connected to sample inlet

What is the Best Recommendation?

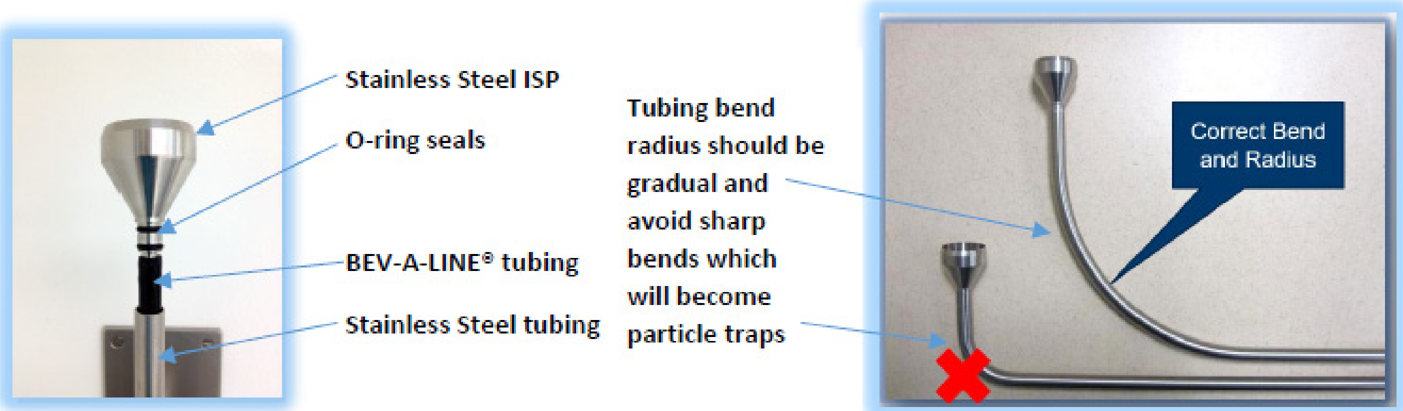
With the GMP guides clear on the sample tubing recommendations we can see that the best approach is to connect the isokinetic sample probe (ISP) to the sample inlet as standard. This can be a standard approach when performing cleanroom certification. A stainless steel trolley with your portable particle counter about 1 meter from the ground is sufficient for this purpose. The particle counter can be easily moved from location to location.

With remote particle counters they have a smaller footprint and are designed to be used in critical zones. Therefore when implementing a monitoring system the location of remote particle counters should be considered for minimizing sample tubing lengths. For example placing remote sensors under filling machines with a short sample tube length without any bends is the best possible setup. Ideally if possible placing the particle counter in the work space could be an option if that work space is not compromised and airflow over exposed vials is not impacted. Don't forget 5µm particles are going to drop out of tubing significantly as tubing length increases so it is important that tubing length are minimum.

Filling machine being monitored with remote particle counters (with internal vacuum)

In the case of a LAF or BSC remote particle counters can also be positioned under the work space with sample probes placed in the workspace. In fact remote particle counters can even be placed inside LAF and BSC cabinets to minimise the particle loss errors altogether.

In critical zones (ISO 5 and Grade A environments) the use of stainless steel for equipment, fixtures and fittings is common practice to ensure smooth surfaces are easily wiped and have a high resistance to the multitude of cleaning solutions used in cleanrooms. Although the most common tubing used for particle transportation is BEV-A-LINE® which has a low friction coefficient, this tubing is usually inserted inside stainless steel tubing. Below is an example we at Lighthouse use when installing remote particle counters in critical locations inside BSC/LAF's or filling machines.



Below is an example of a remote particle counter connected to stainless steel sample tubing. This example shows the particle counter physically as close as it can be to the critical zone. The tubing length is kept to a minimum and the bends are gradual.

Conclusion

Particle size, particle velocity and tubing diameter are the key factors in determining particle transport efficacies in tubing. In pharmaceutical applications, 0.5 and 5.0 micron particles are monitored as part of GMP Regulations. It should be noted that although 0.5 micron particles have a high transport efficacy at 1.0 CFM and 50 LPM flow rates, particles > 1.0 micron do not transport well in tubing regardless of the flow rate and tubing diameter. For applications where 5.0 micron particle monitoring is regulated, keeping tubing lengths as short as possible is recommended.

In light of the data presented and current GMP Lighthouse Worldwide Solutions recommends for cleanroom certification that ISP's be placed directly on the sample probe inlet of your portable particle counter. For continuous monitoring we recommend tubing to be as short as physically possible based on the potential particle losses at 1cfm for 5.0μm sample locations should be determined based on a risk assessment.

ISO/TR 14644-21 was released in August 2023 it represents the current thinking in terms of tubing bends, length and probe orientation. LWS recommends to consult this document when seeking further information on the physical sample setup.

ISO/TR 14644-21:2023 is a technical report that provides guidance on how to sample airborne particles in cleanrooms and associated controlled environments. It discusses the physical limitations of probe and particle counter placement, and any tubing that connects the two, particularly in providing representative samples where particles 5 micrometres and greater are of interest. It also identifies the key factors of sampling performance when classifying and monitoring, and good practice to determine and maintain an acceptable compromise between attainable accuracy in counting and feasibility of counting in real-life situations. It includes a decision tree, used to identify key considerations when sampling airborne particles, and whether the system requires further assessment. There are also examples provided to illustrate typical application challenges and show how the decision tree can be used. It is assumed that this document is read in conjunction with ISO 14644-1 and ISO 14644-2, which describe the measurement methods for determining airborne particle concentration. This document is not a manual, but an explanatory document. It is intended for users who need to understand the principles and limitations of airborne particle sampling techniques in cleanrooms and associated controlled environments.