TECHNICAL PAPER

Particle Sample Tube Lengths for Pharmaceutical Monitoring

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Particle Sample Tube Lengths for Pharmaceutical Monitoring

Lighthouse Worldwide Solutions

Airborne Particle Counters (APC) 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

The use of APCs requires the use of tubing for the sampling of the air, as the APC may be located some distance 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. Several common materials are listed below. Each type has been extensively tested at Lighthouse Worldwide Solutions.

Materials used for this testing consisted of:

Bev-A-Line XX	Co-extruded tubing consisting of PVC exterior and Hytrel® interior. This material has been the particle transport material of choice for years, due to the smoothness of the interior walls (Hytrel®).
Stainless Steel	Extremely clean, durable and conductive, stainless steel is an excellent material for particle transport. However, stainless steel tubing is inflexible and expensive to install.
Polyurethane	Smooth material is chemically resistant and is a lower cost than either Bev-A-Line XX or Stainless Steel.

Within the realm of pharmaceutical manufacturing, particle counting is performed using several types of instruments, with different particle sampling flow rates:

- 1.0 CFM (28.3 LPM) is the traditional flow rate used for testing filters and certifying cleanrooms. Some portable and remote particle counters sample air at 1.0 CFM. Nominal transport tubing for this flow rate is ¼" ID.

- 50 LPM is an alternate flow rate. One such reason for choosing a higher flow rate is because of the requirements of cleanroom certification testing at the 5.0 micron particle level. ISO 14644-1 requires a minimum sample volume of 1000 liters or 1.0 cubic meter. The one cubic meter minimum sample volume is also specified in EU Annex 1. Nominal tubing for this flow rate is ½" ID.

Pharmaceutical Cleanrooms and Particle Transport
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.

Looking at the associated data in Figures 1 and 2, an approximate 20% loss of particles 5.0 micron and greater is realized at 10 feet. For this reason, sample lengths greater than 10 feet should not be considered because of the amount of error such sample lengths could impose on the measurements.

An additional point of reference is the latest version of "EU Guidelines to Good Manufacturing Practice, Medicinal Products for Human and Veterinary Use: Annex 1 Manufacture of Sterile Medicinal Products". This document prescribes the use of short sampling tubing.

Item 6 (in Annex 1) States: "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 shall be used in unidirectional airflow systems."

This reflects upon the use of tubing for the cleanroom classification but not that of the routine or continuous monitoring during manufacturing.

The length of tubing for routing monitoring is also called out in Annex 1, Item 11, where it states: "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."

As Annex 1 states, the length of tubing as well as the radius of any bends need to be considered with particle sampling systems. Of particular importance are Grade A and Grade B cleanrooms. The maximum allowable number of 5.0 micron particles is 20 per cubic meter for Grade A, and 29 for Grade B at Rest. (2900 for Grade B in the operational state). With such low numbers for Grade A and B limits, a greater than 20% loss in 5.0 micron and larger particles represents a considerable risk and should be carefully considered when designing a particle monitoring system.

Lighthouse Worldwide Solutions recommends that continuous particle monitoring in critical locations (Grade A) be carried out only with particle sample tubing lengths of less than 10 feet or approximately 3 meters. For Grade B operations, similar practices should also be considered.

Figure 1 illustrates the effects of particle size on transport efficacy in a 1.0 CFM flow rate particle-counting test.

Figure 1

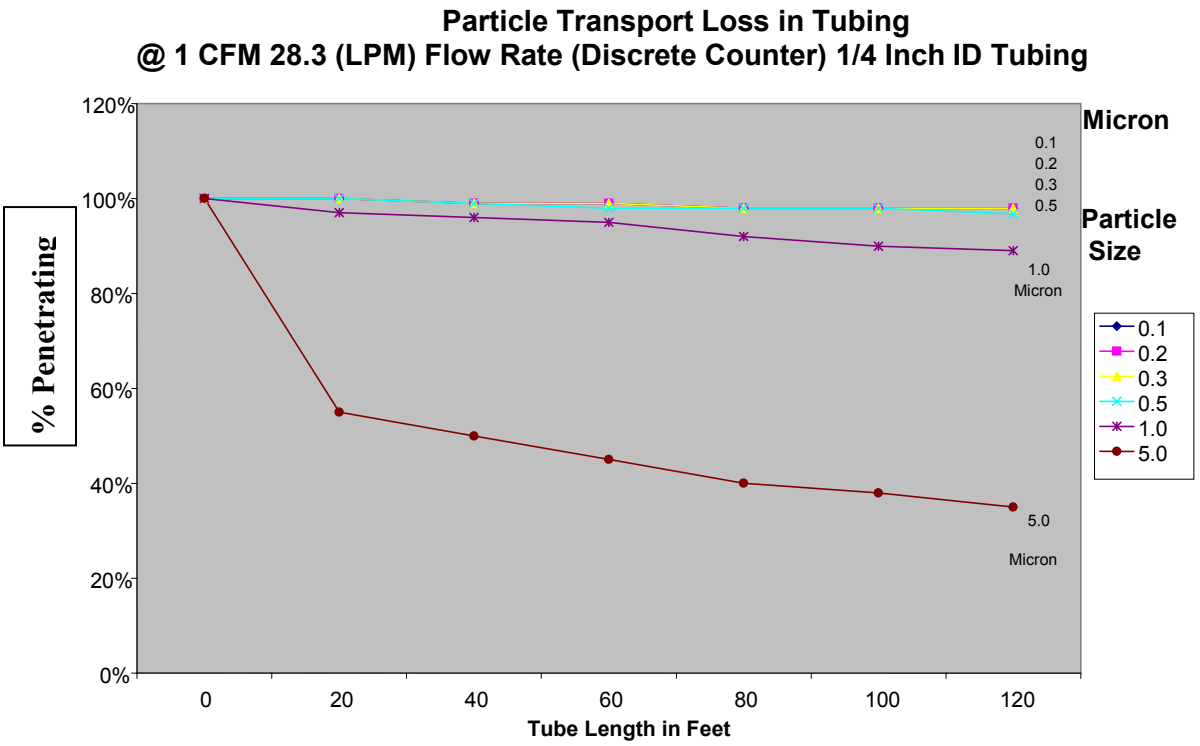
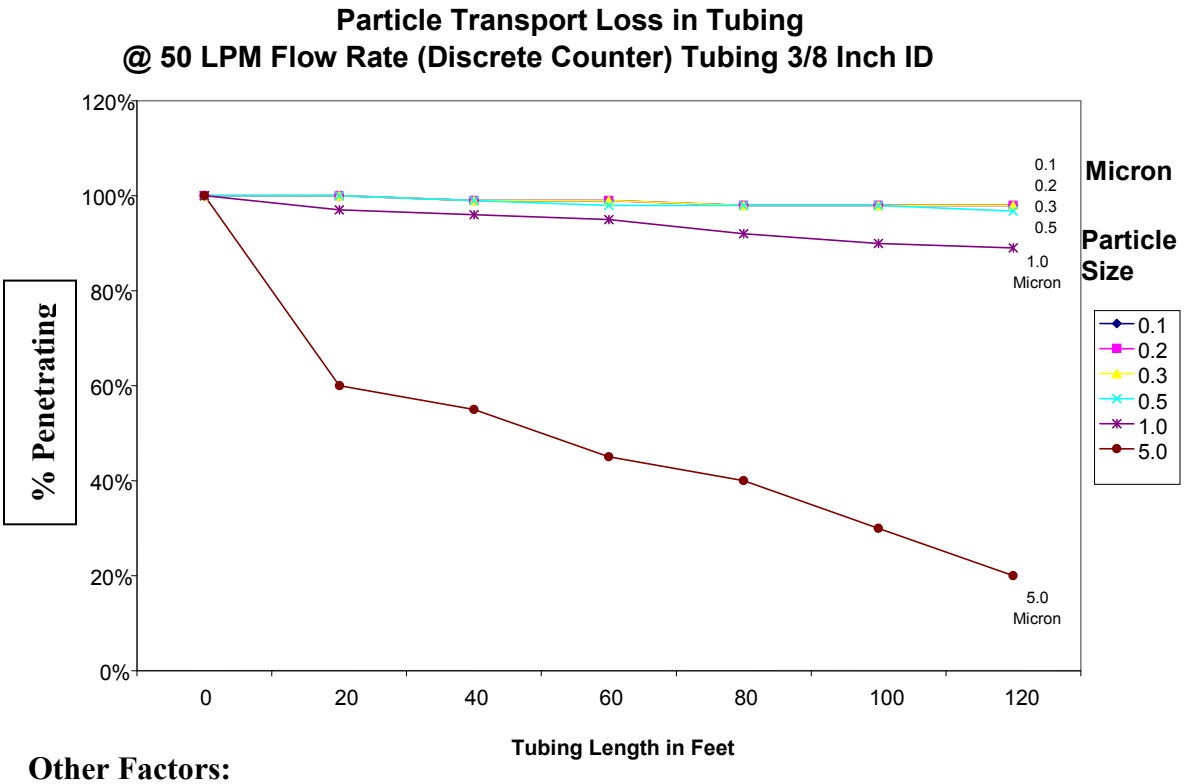


Figure 2 illustrates the effects of particle size on transport with a 50 LPM flow rate.

Figure 2



Other Factors:

As the sample tubing will retain some particles over time, this accumulation of particles can impact the results of continuous monitoring. Sudden release of particles (previously suspended on the tube walls) may result in an unusually high count outside the actual conditions inside the cleanroom or clean air device.

Sample tube cleaning or replacement may be considered to limit these sudden unexpected high particle counts.