TSI® AEROTRAK® REMOTE WITH PUMP PARTICLE COUNTERS INSTALLATION CONSIDERATIONS

APPLICATION NOTE CC-110 (A4)

Introduction

TSI Incorporated's AeroTrak Remote Particle Counters are used to monitor particulate air quality in GMP life science facilities. They are installed at critical locations throughout the manufacturing process, based on the principles of Quality Risk Management QRM ICH Q9. Detecting airborne particulate deviations and adverse trends during critical manufacturing process supports risk reduction strategies. The real-time information gathered by these sensors, when integrated into a Facility Monitoring System, leads to enhanced process understanding and increased knowledge supporting Quality by Design QbD ICH Q8(R2).

Unlike a portable particle counter used for cleanliness classification, the remote particle counter does not have a display, printer or internal vacuum source. It is designed to simply monitor and have a small foot print to enable installation into confined spaces. Remote particle counters interface with Facility Monitoring Software like TSI's FMS software. Every minute a result is collected and logged. This data is then presented as useful information via trend reports and local alarms. Process changes are immediately detected and enable an instant response to airborne particulate deviations.

Figure 1.
Left to Right: AeroTrak Remote Particle Counter, no pump, display or printer. Right image shows the remote in a stainless steel enclosure.

Inside the cleanroom, the remote particle counter is small enough to be installed in a stainless steel enclosure to protect it from cleaning solutions ingress. This allows services such as vacuum, data and power to be elegantly delivered to the particle counter, without trailing data cables and connectors being exposed, creating contamination traps.

The remote particle counter vacuum source is installed outside the cleanroom in a service void either above or in an adjacent space. Vacuum is distributed to each particle counter monitoring location via a carefully designed tubing system or manifold. This popular design approach is known to work well and meets guidance as detailed in current Good Manufacturing Practice (cGMP), keeping as much hardware as possible out of a cleanroom.

The challenge is that in some GMP cleanrooms this approach is not practical due to cleanroom design constraints. Some facilities are small, and service and support areas are not easily accessible. In these cases installing an external vacuum pump and supporting vacuum manifold is impractical and costly.

To address the issue, TSI offers a range AeroTrak Remote Particle Counters with an integrated pump and Vaporized Hydrogen Peroxide (VHP) resistance. The model numbers are listed below:

- AeroTrak Model 6510 Remote Particle Counter (0.5µm, 0.7µm, 1µm and 5µm @ 1CFM)
- AeroTrak Model 6310 Remote Particle Counter (0.3µm, 0.5µm, 0.7µm and 1µm @ 1CFM)

Figure 2.
TSI AeroTrak Models 6510 and 6310 Remote with Pump shown with mounted Isokinetic Sample Probe to facilitate room monitoring from a wall mounted location.

AeroTrak Remote Particle Counter Models 6510 and 6310 are independent monitoring systems condensed into an easy-to-clean 316L stainless steel enclosure. The integrated blower eliminates the need for an external vacuum source, and the standard 4-analog inputs means further reduced installation and integration costs. VHP resistance and sample inlet capping auto-detect makes this instrument ideal for use in any GMP controlled area where continuous particulate and environmental monitoring is required.

Monitoring applications include:

+ Isolators
+ Restricted Access Barrier Systems RABS
+ Industrial Cleanrooms
+ Hospital Pharmacies
+ Laboratories
+ Aerospace

This application note details important considerations when implementing remote particle counters with integrated pumps in critical GMP controlled cleanroom environments.

Installation Considerations

When specifying particle counters for continuous monitoring applications such as pharmaceutical aseptic manufacturing processes, there are many system design decisions to be made. These will include instrument location and how to get services such as vacuum and communication cabling to that location.

Operational considerations include protecting the unit from regular cleaning activities and considering easy access to perform ongoing calibration and maintenance.

Instrument Location

For Grade A or ISO 5 monitoring, the particle counter isokinetic sample probe should be positioned no more than 30 cm away from the critical work site. The final location should be based on the principle of quality risk management and in-operation cleanliness classification data. See US FDA Aseptic Processing Guidance 2004 and EU GMP Annex 1:2008 for detailed guidance.

Wall-mounted monitoring locations in Grade B (ISO 6 or 7) are also based on the principles of quality risk management, and in-operation classification data can be used to help support monitoring position rationale. Grade B monitoring is typically room monitoring and so the sample probe height, measured from the floor, should be based on the ISO 14644-1:1999 cleanliness classification standard. This states that a particle sample probe be mounted at the height of the work activity (section B.4.1.2).

Poor 5 µm particle recovery is minimized by ensuring all particle sample tubing is as short as possible (per EU GMP Annex 1, Clause 6) and is vertically arranged, ideally without bends. The maximum distance between the isokinetic sample probe and the particle counter for life science applications is 3 m. In the event that a bend is needed, it should have a minimum radius of 15 cm. In practice this means that the particle counter cannot be physically more that 3m away from the critical sample location. The result is that there is no option other than to install the particle counter inside the cleanroom.

To ensure suitability for cleanroom installation, the AeroTrak Models 6510 and 6310 Remote Particle Counters has a passivated 316L stainless steel enclosure. The enclosure assembly has 4 pre-drilled mounting holes. The twenty-four VDC power and data cables are routed via one or both of two cable glands at the base of the unit. See Figure 7 for dimensional drawings at the end of this application note. Once fixed in place, it is good practice to use approved sealant to ensure no crevasses or particle traps exist where the enclosure meets a wall.

There is space inside the enclosure to facilitate data and cable entry from the back panel, the side or even the top if needed. Should any power or data cables enter the enclosure from the rear panel, the entry point must be appropriately sealed to prevent contamination ingress and particle traps. We recommend consulting with TSI technical support prior to modifying the enclosure.

Environmental Sensor Integration

Integrating environmental sensors, such as temperature, relative humidity, and room differential pressure sensors, into a FMS system usually requires additional analog input modules, and associated system hardware such as instrument panels and additional cabling. To save time and reduce costs, the AeroTrak Models 6510 and 6310 are able to accept up to four loop-powered analog 4-20mA inputs. This means that local environmental parameters such as the room pressure, temperature and relative humidity are easily integrated. The data, as well as the particle counts, is transmitted back to the FMS software—see Figure 6.

Vacuum Source

In instances where installing an external vacuum source and vacuum tubing system (manifold) is impractical or undesirable, it is an advantage to have an option to install a particle counter with an integrated vacuum source, such as the AeroTrak Models 6510 and 6310 Remote With Pump, close to a critical work location.

The vacuum source utilized is a sealed reciprocating blower which runs cool and quiet. It is not a rotary carbon vane pump, and therefore generates minimal particulate contamination. The exhausted air is filtered using a HEPA filter to ensure the particle counter does not contaminate the surrounding cleanroom environment. The exhaust air exits at the bottom of the instrument (see Figure 3.)

Figure 3.
HEPA Filtered sampled air exhausts at the base of the unit, away from the critical work area. The right hand image shows the enclosure with the optics and pump chassis removed.

Cleaning

Particle counters are sensitive optical instruments and damage will result if any liquids enter via the instrument sample inlet, even when powered down. During cleaning, the inlet of the instrument requires capping or isolating. To facilitate this when centralized vacuum systems are used, end users have to power down the central vacuum system. If the end user wants to cap the sensor inlet whilst the centralized vacuum pump is running, it is necessary to install vacuum relief valves in the vacuum line to prevent damage to the pumps and the particle counter.

In the case of a remote particle counter with an integrated pump, the flow rate is controlled internally. If these units are capped when their vacuum blower is running, it may appear as though there is an inlet restriction, like a very long length of sample tubing has been attached to the inlet. Based on this, the unit could then attempt to pull 1 CFM when this is physically impossible as the inlet is blocked, resulting in instrument damage.

To solve this problem, the AeroTrak Remote with Pump has integrated *Flow Block* detection functionality. This means the unit will automatically stop the blower when it detects that the flow is restricted or blocked. The time taken for the blower to switch off (*Error Time Out*) is user configurable, as well as how long the unit will wait until it tries to restart the blower (*Pump Off Time*) see Figure 4. This feature prevents accidental damage to the particle counter and makes it easier for the end user to cap off the instrument inlet without first powering it down.

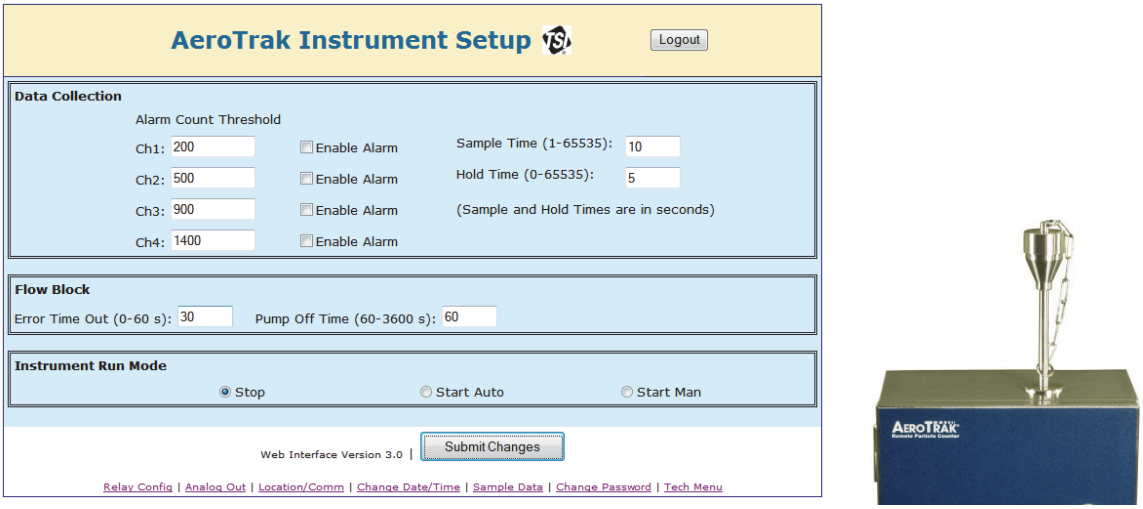

Figure 4.
Flow Block Configuration web interface screenshot and AeroTrak Remote with Pump with a capped off inlet (right).

Vaporized Hydrogen Peroxide (VHP)

It is not good practice to sample VHP through a continuous particle counter, even if it is resistant to VHP. More information on VHP surface disinfection and how optical particle counters are used in GMP controlled environments can be found in *Application Note CC-111 Implementation Best Practice TSI AeroTrak VHP Resistant Remote Particle Counters.*

Where VHP surface disinfection is used in Grade A (ISO 5) areas such as Isolators or Restricted Access Barrier Systems (RABS), the particle counter can be protected using a 3- way valve arrangement. During the VHP gassing cycle, the AeroTrak Models 6310 and 6510 will detect the inlet isolation caused by the valve and will automatically switch off the internal vacuum blower. For Grade B cleanroom monitoring, during a VHP gassing cycle, simply cap off the instrument inlet using the supplied probe cap (see Figure 4). The unit will automatically stop the vacuum source.

The internal optics and flow path for the AeroTrak Models 6510 and 6310 are designed to be resistant to inadvertent exposure to VHP. See Application Note CC-109 *TSI AeroTrak Remote with Pump Particle Counter Resistance to Vaporized Hydrogen Peroxide (VHP)*, for more detail on the testing showing that instrument's optics and flow path components are not affected, when inadvertently exposed to VHP.

Additionally the 316L passivated stainless steel enclosure provides protection for the unit's internal components from the powerful oxidizing effects of VHP.

Calibration and Maintenance

Optical particle counters must be periodically calibrated and maintained. Activities associated with calibration and maintenance generate unacceptable levels of particulate contamination, even during a shutdown. This means particle counters must be removed from the cleanroom when maintenance is needed. It is therefore best practice to install particle counters in a service or lower graded area for quick and easy access. The issue is that some units are installed in a Grade A (ISO 5) and Grade B locations due to restrictions on sample tube lengths in life science cleanrooms.

In Grade A (ISO 5) and Grade B (ISO 6 and 7) rooms, removing the whole instrument from the cleanroom for calibration is not an option as the enclosure is firmly screwed and sealed to the wall. It is a difficult and time consuming task, often requiring a handful of tools, to remove the sensor from within the enclosure. It is all the more difficult when wearing two pairs of cleanroom gloves, a pair of cleanroom goggles and forgetting to bring in the right tools!

Figure 5.
Hot swappable optical sensor and blower chassis/assembly shown outside of the enclosure assembly with the interconnect board.

With this issue in mind, TSI has designed the unit with a removable sensor assembly that comes with the blower, the main board, the optics block, the laser board and the detector board fully integrated. It can be easily removed as a single assembly (see Figure 5) without the need to bring tools into the cleanroom. Not only that, because the assembly is hot swappable, there is no need to power down the unit, reducing the risk of instrument damage. The sensor blower chassis is then calibrated as one complete assembly outside the cleanroom.

Every optical sensor and blower assembly is serialized for validated record-keeping. When re-installing the assembly into the enclosure, there is no need to take additional tools into the cleanroom. No need to adjust the flow rate as everything is checked and adjusted together during calibration. Simply slide the assembly back into place, close the door and the unit will automatically start sampling.

Calibrated optics and pump assemblies can be held as spares, facilitating a rapid hot-fix in the event of an unexpected failure.

Data Integrity

Data collection and integrity is the number one design priority for any monitoring system. It is a prerequisite that any particle counter in combination with monitoring software such as TSI's FMS must enable 21 CFR Part 11 compliance. Further consideration should also be given to system failure modes that will cause data loss, such as computer failures.

To combat a monitoring computer failure it is also beneficial to be able to maintain full system functionality. TSI's optional FMS "Buddy" automatic hot-standby monitoring software provides a robust, fault tolerant monitoring system with unrivalled levels of data redundancy. This means that it is possible to design a monitoring system to be fully compliant during an unexpected computer failure—see Figure 6

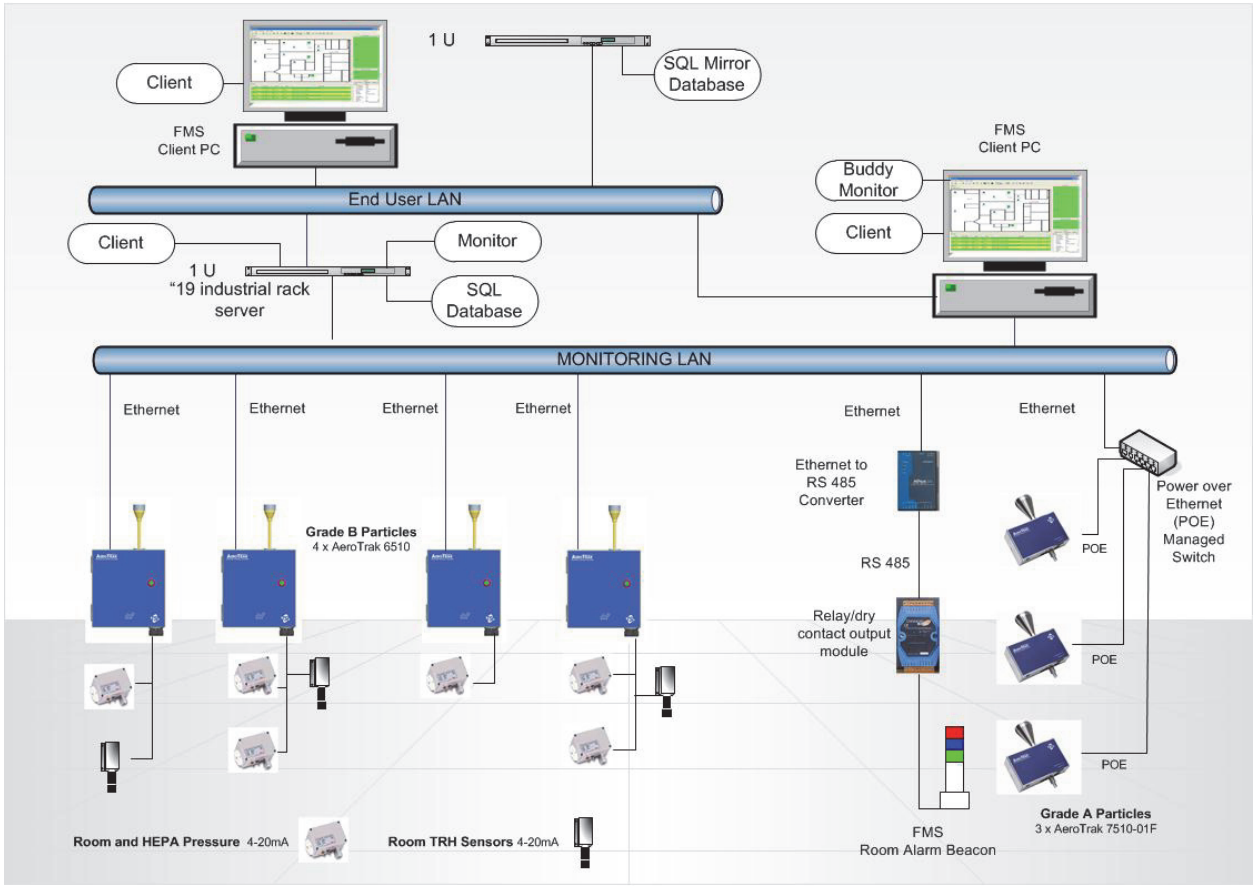

Figure 6.
4 x AeroTrak Model 6510 integrated into an FMS system. They are shown integrating local room differential pressure sensors and room temperature and relative humidity sensors. FMS Buddy Monitor automatically takes over the system should the main Monitor server computer fail.

4-20 mA Data

Meaningful data collected by the monitoring system needs to demonstrate compliance, and should give an early warning of loss of process control. Particle count data is normally presented graphically using log scaling. Large particle spikes during operation in contrast to very low particle counts at other times are impossible to interpret meaningfully on a linear scaled graph. This is particularly important consideration when planning to use 4-20 mA analog signals as a means to output particle count data. Selecting a meaningful linear scale for 0.5 µm and 5 µm 4-20 mA output signals is difficult.

The AeroTrak Remote with Pump has two 4-20 mA particle count output channels, plus a third 4-20 mA status signal. To simplify configuration and ensure that data is meaningful, both outputs can be linear or log scaled. See *TSI AeroTrak™ Remote 4-20 mA Sensors - Life Science Application Note* for a detailed explanation as to why 4-20 mA log scaling is an advantage.

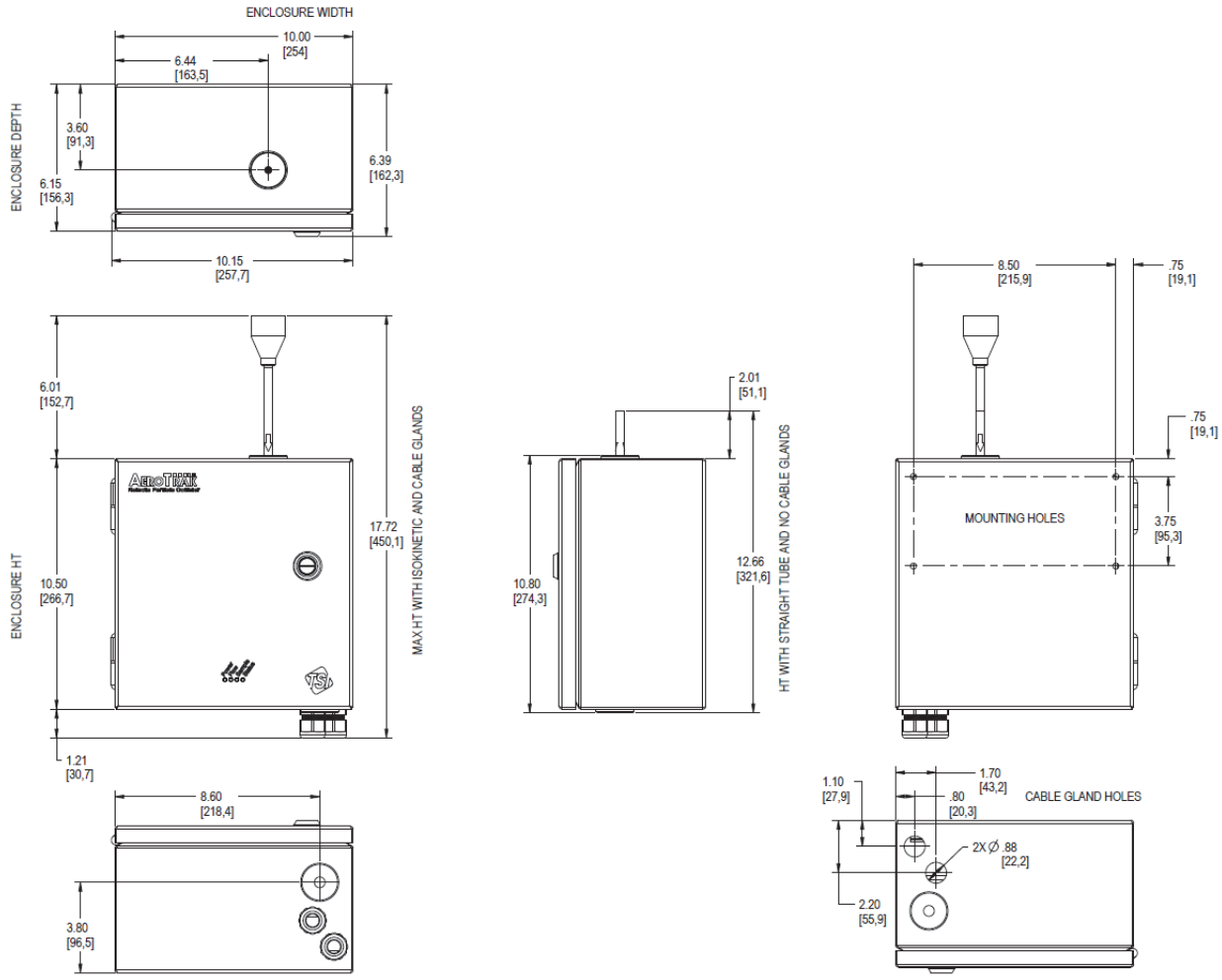

Figure 7.
AeroTrak Model 6310/6510 Dimension Drawing

Conclusion

The AeroTrak Models 6510 and 6310 Remote Particle Counters are an independent monitoring system condensed into an easy to clean 316L stainless steel enclosure. They are ideal for use in any GMP controlled area where continuous particulate and environmental monitoring is required. With integrated pumps and hot swap optics/pump chassis, they are easy to install and maintain. The units can be used in environments where VHP surface disinfection is used. Environmental sensors can be integrated directly into the enclosure without the need for additional analog input hardware, saving integration costs. Automatic flow block detect removes any possibility of human error during cleaning and maintenance.

Please contact TSI with any question regarding our AeroTrak Models 6510 and 6310 Remote Particle Counters.

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CC-110 (4/30/2014-A4) Printed in U.S.A.