Pharmaceutical Industry Whitepaper

Cleanroom Data Management Challenges

Labor and time intensive particle counting documentation can be streamlined
Cleanroom Data Management Challenges

Introduction
Pharmaceutical Cleanrooms have gone through drastic changes in recent years as mergers, acquisitions, facility closures, drug patent-cliffs, and other industry dynamics have forced manufacturing facilities to continually adapt to remain both competitive and compliant with U.S. Food and Drug Administration (FDA) regulations. The one constant element of Cleanrooms is the FDA requirement for monitoring non-viable particle counts in clean-rooms to ensure that the manufacturing of injectable drugs is performed in a safe, sterile environment. As with all regulatory environments, a substantial portion of daily work must be dedicated to managing clean room data and completing the paperwork associated with clean room particulate contamination control. In this application note, we will highlight the challenges of manual management of clean room particle count data and offer guidance on a more efficient approach to overcome change control barriers.

Current Practice Challenges
Throughout the US, Europe and Japan and many other nations, pharmaceutical manufacturing environmental monitoring (EM) manager’s, production managers, QA/QC processionals and many other team members whose primary responsibility it is to ensure their clean rooms are particle-free, generally approach particle monitoring with broadly similar methods. Portable air particle counters, typically equipped with stainless steel iso-kinetic probes, are placed on a cart and wheeled around clean rooms, sampling the air and measuring particle contamination levels. The task of measuring particles is generally routine and mundane with pre-established point of measurement being sampled at regular intervals. Location selection and sampling recipes are dependent upon each clean room’s area classification. Typically, the collection and management of particle counting data at each sampling locale can be summarized by following eight steps:

1. Measure air particle counts at the sampling location utilizing a portable air particle counter.
2. Print the data with the particle counter’s built-in thermal paper printer.
   a. Note: Thermal printers are the industry norm, as thermal printers generate the least amount of particles, but are not particle free.
3. Clean room operators review the print-out data set to ensure there are no alarm conditions (high particle counts or other sampling excursions)
4. Remove the printer paper by tearing it from the portable air particle counter.
5. Tape the print-out to an 8 ½ x 11 or A4 sheet of paper.
6. Clean room operators provide a written signature across the print-out and the sheet of paper to assure the original data is compliant to 21 CFR part 11 data security requirements.
7. Upon exiting the clean room, operators take the print-out affixed to the sheet of paper and scan the document as a secure electronic record (*.PDF) or create a physical hard copy.
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a. Note: The step of copying the print-out affixed to a sheet of paper is required, as thermal printer paper data will fade over time. The FDA requires hard copy records to be legible and stored for a minimum of 20 years. These records may be requested during FDA inspections to validate clean room operational quality.

8. The final step is performed when this print-out data is manually entered into an Excel spreadsheet or directly into LIMS for electronic storage of the data set.

Refer to Figure 1 – depicting a typical portable particle counter with on-board thermal printer

Refer to Figure 2 – current practice

The eight steps outlined above are repeated for every sampling location in every clean room in the facility. The vast majority of clean room particle counter data is managed with the eight steps above, regardless of the size or age of the facility. For a given particle count sampling location, the operator of the portable particle counter will spend an average of 3 minutes per location following the eight steps, which does not include time required to perform the sampling at each location. For larger pharmaceutical facilities with multiple injectable drugs being produced, the daily sampling locations can exceed a thousand points a day and dozens of operators. With a thousand sampling points, a pharmaceutical clean room facility generates 50 hours of wasted time per day, representing 13,000 hours annually, simply completing the eight steps outlined above at each sampling location.
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Why haven’t pharmaceutical facilities changed the way they manage their particle counter data?

Given that the vast majority of pharmaceutical facilities still manually manage clean room particle counting data following the eight steps outlined, the primary reason is that CHANGE in FDA’s Good Manufacturing Practice (GMP) processes is very difficult. The following are some typical comments given from environmental monitoring managers, when asked about change barriers:

- “Change is near impossible, when the standard operation procedures are already defined”
- “The EM department cannot make changes to procedures without quality, metrology, production and management’s approval. It’s a lengthy process with many stakeholders”
- “All it takes is one person to have a concern for risk, and the proposed change is denied”
- “Why change when the drug production process has been inspected by the FDA and no compliance gaps were raised by the FDA? Any change equals risk”
- “Change requires that we revalidate the entire process’

For readers familiar with clean room management in pharmaceutical GMP environments, risk aversion and strict change control processes are well understood. In a FDA GMP pharmaceutical manufacturing environment, change is difficult. There are no published standards that define any of these processes, so users must determine an appropriate CIP process according to their process goals.

The secondary reason the vast majority of pharmaceutical clean rooms still manually manage their particle counting data following the eight steps is that the particle counting products available in the marketplace do not meet the application needs in any other way. Most particle counting manufacturer’s offer the following three-tiered product portfolio to pharmaceutical clean rooms to conduct sampling and manage data:

- **Solution #1:**
  Portable air particle counter (see figure 1) – offering an on-board thermal printer (The most common method for particle counter sampling in the industry today)

- **Solution #2:**
  Particle counting software for use with portable air particle counters (This software is installed on a computer or laptop, requiring new standard operating procedures (SOP’s) to be created and validation qualification of a new process to manage data in the clean room. Most change control processes typically deter this solution)

- **Solution #3:**
  On-line fixed location remote particle counters, which require a continuous monitoring software suite generally installed on the network. This is also commonly referred to as facility monitoring systems (FMS)

Each of the three products offers highlighted above has advantages and disadvantages, but these solutions have been available to pharmaceutical clean rooms for over 25 years.
If a pharmaceutical facility has identified that wasting 13,000 hours a year to run clean rooms is a real problem that needs to be solved; why then has there not been mainstream adoption of particle counters that require software in the clean room? The answer is simple, but may not be obvious.

When particle counting software is considered for use in a clean room, the software becomes an additional product which injects a new set of risks and imposes substantial change to established, approved and validated clean room management processes. As any software products impose risk and require substantial change, pharmaceutical clean room operations choose to waste time following the eight steps of manual data management rather than incur the risk and change their manufacturing processes. Furthermore, given limited manufacturing capacity, production uptime is critical to profitability for pharmaceutical production and change control processes for large scale change can take weeks and months to complete and bring production back on-line.

Refer to figure 3 – depicting a portable particle counter with no on-board thermal printer.

Solution
A new particle counter solution has recently come to the global market in April 2012 that eliminates the eight wasted steps of manually managing particle counter clean room data and does not require software to be used and only requires minimal change to existing clean room procedures (SOP’s.) Hach Company, manufacturer of the MET ONE 3400 portable air particle counter, has created a unique portable air particle counter solution that requires no external software. The solution is simple; instead of manually writing the particle counting onto thermal printer paper, the MET ONE 3400 particle counter creates an electronic PDF and a separate EXCEL record written directly to a USB memory stick.
plugged into the particle counter. The secure PDF file is identical to paper printouts produced by the thermal printer, skipping the need for steps #2 through #7 outlined above. Furthermore, the data is also written to an excel file, eliminating human transcription errors that commonly occur in step #8. The particle counter operators can simply take samples throughout the clean room and return to their offices with all the data they need in the secure electronic form desired on a single USB memory stick. In most cases, the environmental monitoring manager or quality control department will only require minimal change to standard operating procedures (SOP’s), or the changes will be minimal and easy to accomplish. For further information on this specific solution, please visit the manufacturer’s website at [www.particle.com](http://www.particle.com), or refer to the MET ONE 3400 “simply paperless.”

**Author Biography**

Paul Yates is the Life Sciences Marketing Director for Hach Company. Paul has a degree in Chemical Engineering from Kansas State University and an MBA from Iowa State University. Paul spent 10 years working in the process control industry, and has spent the last 5 years working in the life science pharmaceutical manufacturing industry. During his time in life sciences industry, Paul has been focused on developing new products for liquid particle counting focused on pharmaceutical manufacturing USP<788> release test requirements and new air particle counting solutions focused on pharmaceutical clean room manufacturing environments.

Hach Company – World Headquarters
Particle Counting Business Unit
P.O. Box 608
Loveland, Colorado 80539 USA
[www.particle.com](http://www.particle.com)
Information 1-800-866-7889 ext 6508